NOTE. At a few places in the MOOP, a small number of words appears to be missing, e.g., Sections 15.7.2.c and 24.3.

MANUAL OF OPERATIONS

{Full-Scale Clinical Trial -- Phase III}

for the

Diabetes Control and Complications Trial

Prepared by

Diabetes Control and Complications Trial Research Group

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The Manual of Operations for the study, Diabetes Control and Complications Trial (DCCT) to compare the effects of two treatment regimens designed to produce different levels of metabolic control on the clinical course of early vascular complications in persons with insulin-dependent diabetes mellitus (IDDM). The protocol describes a randomized controlled clinical trial. Blood glucose and hemoglobin Alc will be primary indicators of metabolic control. Diabetic retinopathy will be the principal outcome assessed as will nephropathy, neuropathy and cardiovascular events or other known or putative risk factors.

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PREFACE

1. INTRODUCTION

This Manual of Operations has been prepared by the DCCT Study Group. Protocols and procedures specified herein thus represent as thorough a review as possible of all major issues. This is the Manual of Operations for the Phase III Protocol. Future revisions in this Manual of Operations will introduce some heterogeneity in the data collection process; therefore, it is hoped that no changes will be necessary. However, there may be a need for revisions of varying degrees. The only changes to be permitted in this Manual of Operations are those which will improve efficiency, enhance scientific validity and/or further ensure patient safety in this study.

2. PROCEDURE FOR REVISIONS

During Phase III, proposed revisions should be discussed with the Principal Investigator at the clinical center and submitted to the Executive Committee. The Executive Committee will make judgment on all proposed changes as to the need for consideration by the Planning Committee and the Steering Committee.

3. DISSEMINATION OF REVISIONS

After any revisions have been approved, the Coordinating Center will be responsible for initial drafts and final retyping of the appropriate sections of the Manual of Operations. A cover letter along with the updated chapter of the Manual of Operations will be sent to each clinical center. The cover letter will describe the reason for the change and explain the change itself as well as the effective date. Any subsequent questions are to be directed to the Coordinating Center. Additionally, any revisions in this Manual of Operations will be discussed at the next DCCT meeting.

4. FINAL DISPOSITION OF THE DCCT MANUAL OF OPERATIONS

In May 1993, at the conclusion of data collection, the Manual of Operations and forms for the trial were put together in publishable form and registered with NTIS. Copies may be obtained from United States Department of Commerce, National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161, Telephone (703)487-4650. The registration number is PB93-183382. Other protocols developed by the study, such as the Protocol for Close-Out, are also available.

INTRODUCTION

1. SCOPE AND IMPACT OF DIABETES

Diabetes is a major public health problem.[1] Approximately 5.8 million persons, about 2.6% of the United States population, have been diagnosed by a physician as diabetic. The insulin-dependent form of diabetes mellitus (IDDM) is estimated to be approximately 10% of all known cases, but virtually all diabetes diagnosed before age 20 is of this type.

Diabetes is not a benign disease. The complications of diabetes may involve every tissue of the body, but the blood vessels, nerves, kidneys, and eyes are particularly susceptible. Diabetes causes:

. 12% of all new cases of blindness;

. 25% of all kidney failure;

. 40% of all non-traumatic amputations of the foot and leg among adults.

Additionally, diabetes is one of the four major risk factors for cardiovascular disease. Heart disease, hypertension, and stroke are two to six times more likely to occur in persons with diabetes.

While complications occur in all types of diabetes, persons with IDDM may account for a disproportionate share of blindness, kidney failure, problems associated with child bearing, and premature deaths. In those with IDDM:

. 3% are legally blind after 15 years of diabetes;

. 12% are blind after 30 or more years of diabetes;

. 30% have diabetic nephropathy after 15 years of diabetes;

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[1] Extracted from statistics provided in "Diabetes in America, Diabetes Data Compiled 1984" by the National Diabetes Data Group, NIADDK, NIH.

. 2 to 7 times more prenatal and perinatal complications and 2 to 3 times more congenital malformations occur in infants of diabetic mothers; and

. 12% are dead within 20 years after diagnosis of diabetes.

The United States ranks among the five nations in the world with the greatest mortality due to diabetes. It is the seventh leading cause of death in the United States and accounts for 150,000 deaths annually. In persons with IDDM, the majority of early deaths are due to kidney and cardiovascular diseases. Above age 20, over half of the deaths occurring in people with IDDM are due to kidney disease; this is about 500 times more frequent than in similarly aged nondiabetic persons. Deaths attributable to cardiovascular disease are about 13 times higher in persons with IDDM than in nondiabetics of similar ages. The overall mortality rate for persons with IDDM is five to 11 times greater than the rates for nondiabetics of the same age; however, the risk of death markedly accelerates after age 25 to approximately 20 times that of nondiabetic persons.

Diabetes places a major drain on our health resources. Persons with diabetes have two to three times as much disability as nondiabetics and spend over twice as many days in the hospital as persons without this disease. Over 25% of all diabetics require hospitalization each year, accounting for three million hospitalizations annually and about 30 million hospital days. Additionally, about 16 million visits to physicians are made each year by persons with diabetes. It is the fourth leading cause of visits to general and family practice physicians.

Finally, the economic toll of diabetes has almost tripled in the ten years since the report of the National Commission on Diabetes. Excluding its complications, the cost in hours of work lost due to disability and premature mortality and in medical and hospital costs is at least $14 billion.

While there is no known cure for diabetes, the future, nonetheless, looks promising for people with diabetes. Improved treatment approaches have been developed and others are under active investigation. These new approaches may lead to even better methods of treatment that will reduce the occurrence of both the acute and long-term complications. Major research advances in biomedical research have greatly expanded our understanding of the pathogenesis of diabetes and its complications. This enhanced knowledge may lead to the ability to prevent diabetes or its complications. Reducing the severity of diabetes will result in enormous savings in the human toll exacted on persons with diabetes and their families as well as the costs to society due to medical care, hospitalization, rehabilitation and economic losses due to shortened life-spans and lost days of work.

2. RATIONALE FOR THE DCCT STUDY QUESTION

One of the critical issues in diabetes mellitus has concerned the relationship between metabolic control[2] and the chronic complications of the disease. Controversy and debate regarding this relationship has been ongoing for 50 years.

Those who advocate the general use of rigid control (i.e., attempts to maintain blood glucose as close to normal as possible) believe that there is sufficient evidence to support the claim that such control lessens or delays the appearance of most chronic complications. Those who do not advocate the general use of rigid control contend that the evidence is inconclusive, that rigid control increases the frequency and severity of potentially dangerous side effects (e.g., hypoglycemia), and that there is some indication of potential harm (e.g., acute worsening of mild retinopathy).

Debate on the issue has centered largely on three questions:

. whether, or to what extent, the chronic complications of diabetes are related to the metabolic derangements which characterize insulin dependent diabetes mellitus;

. whether improvement of the abnormal metabolic state will lead to prevention or amelioration of the complications; and if so,

. what level of metabolic control is necessary to prevent the development or ameliorate the progression of such complications.

Conduct of the controlled clinical trial needed to resolve this issue was impeded by lack of a treatment which could achieve consistently lower blood glucose levels than those attainable with conventional therapy. In the late 1970's, technological advances in treatment approaches were made which offered significant promise for enhanced metabolic control. Experience in the application of these technologies demonstrated that it was feasible to alter the level of control achieved compared to more conventional treatment approaches. Given the capabilities available in 1985, the DCCT will test whether therapies that enable alterations of metabolic control can change the natural history of early vascular complications in persons with IDDM compared to conventional treatment approaches.

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[2] As used in the Protocol, "metabolic control" should be understood to mean the entire spectrum of metabolic and hormonal derangements that comprise the syndrome known as insulin-dependent diabetes mellitus. Although blood glucose control is generally used as an indicator of overall metabolic control, this is for simplicity and should not be interpreted as meaning that the DCCT investigators have equated the two.

3. BACKGROUND

In its report to the Congress in 1975, the National Commission on Diabetes recommended that the National Institute of Arthritis, Metabolism and Digestive Diseases (NIAMDD)[3] and the National Heart, Lung, and Blood Institute (NHLBI) initiate and support a five-year clinical study to assess the effect of treatment of IDDM on the development of microvascular complications.

In 1977, the NIDDK and NHLBI convened an ad hoc committee to consider whether, how, and when such a clinical trial should be initiated. In 1978, that committee issued its report recommending that such an undertaking was both ethical and feasible and that the Institutes should proceed with a phased clinical trial to compare the effects of "strict" versus "conventional" treatment regimens. In attempting to effect this recommendation, it became clear that a conjoint study of both macrovascular and microvascular complications would not be feasible due to major differences in the natural history of the two types of complications. Accordingly, it was agreed that the NIDDK would proceed alone with the study and that the study would focus on early vascular complications.

As the planning for the study proceeded, it became increasingly clear that significant and ongoing progress in the development of new treatment approaches related to the metabolic aspects of diabetes had been made since the committee's report, notably the open loop devices for the delivery of insulin and methods for self monitoring of blood glucose concentration, and that these new technologies might offer considerable potential for achieving improved metabolic regulation. Furthermore, if they could be used in a controlled clinical trial, it might be possible to make a more clear-cut distinction between treatment groups and, thus, provide a better basis for comparison of the two treatment regimens. The NIDDK determined that initiation and implementation of such a study should be delayed so that the trial could incorporate the most current and effective methods of treatment.

In September 1980, the NIDDK convened a second group of advisors to reassess the timeliness of initiating the study. This committee issued a report reaffirming the recommendations of the first ad hoc advisory group to proceed with the study. It was further recommended that diabetic retinopathy be the principal outcome assessed in two separate groups of subjects: those with no evidence of background retinopathy at entry (a primary prevention group) and those with evidence of minimal background retinopathy at entry (a secondary intervention group). The rationale for studying both groups concurrently was that the secondary intervention trial would have the potential of showing a beneficial effect of one of the treatments sooner than a primary prevention trial; however, a negative result from a secondary intervention trial would not address the question posed in a primary prevention trial. Accordingly, it was

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[3] In 1986, the name of the Institute was changed to National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

recommended that both trials be undertaken simultaneously. The committee stipulated that the trial progress through sequential phases which would include a feasibility study preliminary to a full-scale trial. It was directed that the feasibility study address the utility, subject acceptability, safety and efficacy of intensive treatment regimens compared to conventional treatment regimens which might be suitable for application in a full-scale trial. The juncture between the feasibility study and the full-scale trial was to serve as a major decision point at which time a detailed assessment of the results of the feasibility study would be conducted by an independent group of expert advisors. The decision regarding initiation of a full-scale, long-term clinical trial would be based on this advice. The committee urged that the NIDDK proceed as quickly as possible to initiate the feasibility study.

Acting upon this recommendation, in 1981 the NIDDK issued a Request for Research Cooperative Agreement Applications for clinical centers and a Request for Proposals for a Data Coordinating Center willing to participate in a study consisting of the following four phases:

Phase I -- Planning (6-12 months)
Phase II -- Feasibility Study (2 years)
Phase III -- Full-Scale Clinical Trial (7-10 years)
Phase IV -- Data Analysis/Reporting (1 year)

Twenty-one clinical centers in the United States and Canada and a Data Coordinating Center were subsequently selected to participate in the study on the basis of scientific peer review.

Phase I (Planning) was initiated in March 1982 for the purposes of designing the Phase II Protocol (DCCT Research Group, 1986), assembling the Manual of Operations and establishing certification requirements for the clinical centers, central laboratories and reading and coding units preparatory to recruitment of subjects. The nomenclature specified for the two treatment groups in the DCCT was: experimental to denote the intensive treatment regimen and standard to denote the conventional treatment regimen.

Phase II (Feasibility) commenced in August 1983 and was completed in March 1985. The specific objectives of Phase II were the following:

1. To determine whether a well-informed cohort of subjects, comprising both adolescents and adults who fulfilled all the stringent eligibility criteria, could be recruited in a reasonable period of time.

2. To determine whether both a clinically meaningful and statistically significant difference in the level of blood glucose control could be achieved between the randomly assigned standard (conventional) and experimental (intensive) therapy groups, as assessed by hemoglobin A_{1c} (HbA_{1c}) and blood glucose measurements, while maintaining both treatment groups within acceptable ranges of glycemic control.

3. To determine the safety of the two therapies with major emphasis on assessment of: symptoms attributable to hyperglycemia, episodes of ketoacidosis, and episodes of hypoglycemia.

4. To determine whether the randomly assigned therapies would be equally acceptable to subjects as assessed by measures of adherence to the randomly assigned therapies over time and completeness of followup.

5. To determine whether biochemical and pathological characteristics of IDDM could be measured and documented with acceptable precision and accuracy.

Two hundred seventy-eight subjects were enrolled in the feasibility study. By March 1985, the data from 12 months of followup on all subjects had been collected (DCCT Research Group, 1986). These data were independently reviewed by two separate expert advisory groups. Both groups found that by all essential criteria, the feasibility objectives had been met and recommended that the NIDDK proceed with Phase III of the DCCT utilizing the protocol developed for the feasibility study with appropriate modifications.

In October 1985, the NIDDK notified the DCCT Study Group that a decision had been reached to proceed with Phase III, the full-scale clinical trial. In November 1985, a Request for Research Cooperative Agreement Applications was issued for additional clinical centers to participate in Phase III. Six additional centers were selected on the basis of peer review bringing the total number of participating clinical centers to 27 for Phase III of the DCCT.

4. FUTURE DIRECTIONS

The outcome of the DCCT will influence the course and direction of clinical management of persons with insulin-dependent diabetes. Recruitment of subjects will continue until the full cohort of 1400 is reached. It is planned that followup of all subjects will continue until the fifth anniversary of the last subject randomized.

An independent external group of scientific peers will review all emerging study data at regular intervals for subject safety and data quality and report to a second body of independent scientific peers. The latter group is charged with recommending to the Director of NIDDK the continuation or termination of this study, a decision to be based on careful consideration of the information resulting from the emerging data.

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CHAPTER 1

OBJECTIVES AND DESIGN

1.1 OBJECTIVES

The major objective of the DCCT will be to compare the effect of an experimental and a standard approach to the control of blood glucose on early vascular complications in persons with IDDM.

Principal Objectives:

1. To compare the following separately for the

   a) Primary Prevention Trial: Rate of onset and progression of diabetic retinopathy; and for the

   b) Secondary Intervention Trial: Rate of progression of pre-existing mild non-proliferative diabetic retinopathy.

2. To compare the rate of major adverse events associated with the treatment of diabetes or participation in the trial.

Other Objectives in Both Trials:

1. To compare the rate of onset and progression of nephropathy.

2. To compare the rate of onset and progression of neuropathy.

3. To compare the rate of onset and concomitant progression of retinopathy, neuropathy, and nephropathy.

4. To compare the incidence of cardiovascular events and their known or putative risk factors.

Operational Objectives in Both Trials:

1. To recruit and randomize the numbers of subjects required to provide adequate statistical power for both trials.

2. To maintain both a clinically and statistically significant difference in the level of blood glucose control between the randomly assigned standard and experimental therapy groups as assessed by hemoglobin A_{1c} (HbA_{1c}) and blood glucose measurements.

3. In treatment of individual subjects in both groups to maintain clinical well-being, to maintain glycemia below predefined limits, and to minimize the occurrence of severe hypoglycemia.

4. To maintain acceptable levels of adherence to the randomly assigned standard and experimental therapies as assessed by measures of adherence over time, including completeness of followup.

5. To monitor and maintain the precision and accuracy of the assessments of the biochemical and pathological characteristics of IDDM.

Natural History Objectives:

To describe the natural history of IDDM among subjects who receive the experimental therapy and among subjects who receive the standard therapy. This includes the evaluation of the above objectives within subgroups of subjects defined on the basis of age, gender, duration of IDDM, entry C-peptide, level of blood glucose and HbA_{1c}, blood pressure, renal status, serum lipids, and other factors suspected to be associated with the risks for the development of complications of IDDM.

1.2 DESIGN

In accordance with these objectives, the DCCT has the following design features:

1. All 278 subjects recruited for the feasibility study will continue to be followed until completion of the study in either the primary or secondary trial as indicated by post-randomization stratification on the subject's baseline retinopathy status.

2. Additional subjects will be recruited over a period of three years and their eligibility determined (see Chapter 8). Subjects without evidence of diabetic retinopathy suitable for a primary prevention trial and subjects with evidence of minimal retinopathy (see Chapter 8) suitable for a secondary intervention trial will be recruited.

3. Eligible and consenting subjects in each of the clinical centers will be assigned randomly to receive either standard or experimental therapy.

4. A total of 1400 subjects will be randomized within two retinopathy strata with approximately equal numbers in each stratum.

5. This sample size provides power >0.91 to detect a 32.5 to 37.5% reduction in the annual hazard for the onset or progression of diabetic retinopathy allowing for 10% loss of followup and 20% nonadherence to assigned treatment.

6. For the primary prevention trial, the preferred outcome measure is a compelling clinically defined event such as proliferative diabetic retinopathy (PDR). However, the incidence of such an outcome in this population is low, even with the planned ten-year followup. Therefore, the sample size required to achieve a statistically significant result would be excessive. Thus, a different outcome measure is needed. This measure needs to accurately reflect the underlying physiological process of worsening of retinopathy and have an event rate higher than that for PDR. Thus, the DCCT has selected the appearance of any retinopathy, defined as the onset of persistent microaneurysms, as the outcome measure upon which the sample size is based. Therefore, the study has less power to detect treatment group differences at the more clinically meaningful levels of retinopathy. Nevertheless, a treatment group difference with respect to the appearance of any retinopathy will be evaluated in consideration of its consistency with a treatment effect at more clinically meaningful levels.

7. Standard therapy will consist of not more than two injections of insulin daily. The dose and insulin mixture will be determined on an individual basis by the physician. Clinical well-being is the first priority. Special efforts will be made to insure that the subject's hemoglobin A_{1c} does not exceed two standard deviations above the mean of a sample of IDDM subjects (13.11%) and that all criteria for good clinical health are met.

8. Experimental therapy will permit the subject and his/her physician to choose either multiple daily injections of insulin (MDI) or a continuous subcutaneous infusion of insulin (CSII) or a combination. Both will employ frequent self blood glucose monitoring and will strive to maintain hemoglobin A_{1c} levels within two standard deviations of the mean for a sample of persons without diabetes (6.05%, mean $\pm$ 2 S.D.).

9. All subjects will be analyzed according to their original treatment assignment and all efforts will be made to treat subjects according to their assignment until the end of the study. Changes in treatment are discussed in Chapter 11.

10. All subjects will be followed at least until the fifth year after enrollment in the study or until the study is terminated. Thus, some subjects will be followed for up to ten years while others will be followed for less and varying lengths of time.

11. All study personnel are masked to study outcomes, therefore, two independent advisory groups will review periodically the study results and are authorized to recommend to the NIDDK that the trial be terminated if the study objectives have been met. However, clinical thresholds for safety have been created and approriate personnel will be alerted when a patient passes a threshold.

12. Clinical, physical, and biochemical evaluations will be conducted prior to randomization and periodically during followup according to the schedule depicted in Table 1.1.

13. The two treatment regimens will, of necessity, be conducted in an unmasked manner. With the exception of HbA_{1c}, all centrally determined outcome measurements will ordinarily be masked from the investigator responsible for the treatment regimens and from the subjects. The results of these centrally determined outcome measurements relating to complications will be reported as "within acceptable limits" when no therapeutic intervention is indicated. In the event that an outcome measurement would dictate a change in subject management, the results will be promptly communicated to the responsible investigator who will inform the subject and institute appropriate therapy.

    Hemoglobin A_{1c} values will be unmasked in the experimental group because the treatment regimen is directed toward achieving specific values. Hemoglobin A_{1c} values will ordinarily remain masked in the standard group because the treatment regimen is not directed toward achieving specific values. However, in this group, subjects with HbA_{1c} values that exceed the upper action limit of two standard deviations above the mean of samples of IDDM subjects (13.11%) will be reported monthly to the investigator until the situation is corrected.

REFERENCES

1. The Diabetes Control and Complications Trial Research Group: The Diabetes Control and Complications Trial (DCCT). Design and Methodological Considerations for the Feasibility Phase. Diabetes 35:530-545, May 1986.

2. The Diabetes Control and Complications Trial Research Group: The Diabetes Control and Complications Trial (DCCT): Results of the Feasibility Study. Diabetes Care, 10:1-19, February, 1987.

CHAPTER 2

ADMINISTRATIVE STRUCTURE

2.1 INTRODUCTION

The organizational structure of the DCCT has been developed to coordinate the activities of the necessary committees, laboratories, units and review groups, and to assist in the conduct of this trial by ensuring careful and uniform adherence to the Protocol and Manual of Operations.

2.2 STRUCTURE

The organizational structure for the DCCT trial is presented in Figure 2.1.

The Director of the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) is responsible for the use of Institute funds and the management of Institute programs. He bears ultimate responsibility for the conduct of the DCCT and serves as the final decision-maker for all major issues affecting the DCCT. The Institute Director appoints the Chairmen and members of the Policy Advisory Group (PAG), the Data, Safety and Quality Review Group (DSQ), and the Chairman of the Steering Committee.

The Director, Division of Diabetes, Endocrinology and Metabolic Diseases (DEMD), is the principal representative of the Director of NIDDK and is responsible for ensuring that the scientific and technical goals of the study are consistent with the mission and responsibilities of the NIDDK.

Within the Diabetes Program Branch of the DEMD Division, the Diabetes Clinical Trials Program Office provides liaison between the DCCT Research Group and the NIDDK. This office represents the Institute in all matters which concern the administrative, scientific and technical direction of the trial. A program representative is a member of the study's Executive and Steering Committees and an ex-officio member of each of the working committees. All DCCT communications with the commercial sector (i.e., companies which are vendors of diabetes-related supplies and services) and with the general public are coordinated by the Diabetes Clinical Trials Program Office.

The Policy Advisory Group (PAG), is comprised of individuals who are professional and lay representatives of the diabetes community and not otherwise connected with the trial. The PAG Chairman will serve as an ex-officio member of the DSQ. The PAG will meet every two years and at other times deemed necessary by its Chairman or by the NIDDK Director. They will receive annual reports on the progress of the trial and advise the NIDDK regarding overall trial policy including decisions to make major changes in the Protocol or to conclude the study.

The Data, Safety and Quality Review Group (DSQ) is comprised of individuals not otherwise involved in the trial who are expert in the methodological, operational, medical, psychological, ethical and biostatistical aspects of clinical trials. The DSQ will monitor all study data at regular intervals and has primary responsibility for ensuring patient safety and welfare as well as data quality and analysis. They will review all Protocol changes and ancillary studies and will advise NIDDK regarding substantive Protocol changes, termination of the trial and other major issues that may arise.

The Steering Committee is the representative body of all trial participants. It is comprised of a Chairman, the Principal Investigator from each of the clinical centers, one representative from the NIDDK Clinical Trials Program Office, and one representative from the Coordinating Center. The Chairman is appointed by the Director of NIDDK and the Vice-Chairman is elected by the Steering Committee from among its own members. It provides overall scientific direction for the trial through consideration of recommendations from the working committees. The business of the Steering Committee is conducted in accordance with customary parlimentary procedures. Members unable to attend a meeting may designate an alternate to act on their behalf. Steering Committee recommendations for changes in the Protocol require prior consideration by the appropriate DCCT committee(s) and an affirmative vote by three-fourths of the Steering Committee members (or alternates) present and voting.

The Executive Committee acts in behalf of the Steering Committee during the intervals between Steering Committee meetings to make the day-to-day management decisions needed for the trial to proceed in a smooth, efficient and orderly way. The Executive Committee is comprised of the Chairman of the Steering Committee, the Co-Director of the Coordinating Center, and the Director of the Diabetes Clinical Trials Program Office. Actions taken by the Executive Committee will be reported at the next meeting of the Steering Committee and major decisions (e.g., those that in the opinion of any member of the Executive Committee may affect the integrity of the trial or require a Protocol change) will be made only after consideration by the Steering Committee.

The Planning Committee integrates the activities of the working committees to ensure that material is presented to the Steering Committee in an orderly manner. The makeup of this group includes the Vice-Chairman of the Steering Committee who serves as Planning Committee Chairman, the Chairpersons of the seven working committees, the Director of the Coordinating Center and the three members of the Executive Committee.

The working committees which support the Steering Committee are: Treatment, Standards/Methods, Complications, Eligibility/Adherence, Publications/Presentations, Ancillary Studies and Trial Coordinators. These committees are appointed by the Steering Committee Chairman from among the professional personnel from each of the clinical centers, the Coordinating Center staff, the NIDDK staff, and necessary consultants. The three members of the Executive Committee are ex-officio members of each of the working committees.

More description is provided below regarding the nature of the activities of the clinical centers, the working committees, the Clinic Monitoring Group, the Coordinating Center, and the central study units.

1. Clinical Centers. The clinical centers are staffed by a Trial Coordinator and other necessary personnel under the supervision of a Principal Investigator. The Principal Investigator will work with the Coordinating Center, Chairman of the Steering Committee, and NIDDK staff assigned to this project to conduct the study in accordance with the Protocol and Manual of Operations. The clinical centers are expected to meet the patient recruitment goals as specified by the Coordinating Center and will work with the Central Ophthalmologic Reading Unit, the Central Biochemistry Laboratory, the Coordinating Center, and other central units to maintain the quality of the data.

2. Working Committees. All working committees have specific responsibilities as outlined below and will assume such other responsibilities as requested by the Steering or Executive Committee(s).

   a) Treatment. The Treatment Committee will consider any and all proposals to update and revise the treatment strategies described in the Protocol and Manual of Operations and make recommendations to the Steering Committee via the Planning Committee. The Treatment Committee will review modification of the treatment regimen. Periodically, they will review deviation from treatment and transfer to inactive status. All products and/or devices used by the clinical centers to implement the treatment strategies must have the prior approval of the Treatment Committee. They will also revise, update and develop additional guidelines for the management of intercurrent events. The Treatment Committee will provide consultation to the clinical centers regarding implementation of the treatment protocol.

   b) Standards/Methods. The Standards/Methods Committee will assist the Coordinating Center in monitoring the performance of the Central Biochemistry Laboratory and the Central Nutrition Coding Unit. They will consider any and all proposals for changes in the procedures used for making the measurements performed by these laboratories/units as specified in the Protocol and Manual of Operations. They will consider the need for additional laboratory procedures and/or the deletion of

ongoing laboratory procedures and make recommendations to the Steering Committee via the Planning Committee.

c) Complications. The Complications Committee is responsible for review and consideration for presentation to the Planning and Steering Committees of all matters pertaining to primary prevention and secondary intervention study endpoints. They will assist the Coordinating Center in monitoring the performance of the Central Ophthalmologic Reading Unit, the Central EKG Reading Unit, the Central Neurobehavioral Coding Unit and the Central Autonomic Coding Unit. They will consider any and all proposals for changes in the procedures used for making the measurements performed by these laboratories/units as specified in the Protocol and Manual of Operations. They will consider the need for additional reading or coding unit procedures and/or the deletion of ongoing reading or coding unit procedures and make recommendations to the Steering Committee via the Planning Committee.

d) Eligibility/Adherence. The Eligibility/Adherence Committee will assist the Coordinating Center in interpreting the eligibility/exclusion criteria specified in the Protocol and Manual of Operations. They will consider any and all proposals for changes in these criteria and make recommendations to the Steering Committee via the Planning Committee. They will assist the Coordinating Center in monitoring patient adherence, in promoting the implementation of ongoing adherence programs, and in developing additional strategies intended to optimize patient adherence.

e) Publications/Presentations. The Publications/Presentations Committee will implement the policies and procedures pertaining to all DCCT publications, presentations, media releases, interviews, and other communications.

f) Ancillary Studies. The Ancillary Studies Committee will implement the policies and procedures pertaining to all DCCT ancillary studies.

g) Trial Coordinators. The Trial Coordinators Committee will review and consider the impact of proposed ancillary studies and changes in the Protocol and Manual of Operations on the day-to-day activities of the clinical centers and on patient adherence. They will make recommendations to the Steering Committee via the Planning Committee. They will assist the Coordinating Center in evaluating proposed changes in the data forms and in updating the Trial Coordinators Handbook. They will also assist the Coordinating Center in ensuring that DCCT personnel are adequately trained and certified so that study data are collected and reported in a standardized way and that the Protocol and Manual of Operations are implemented in a uniform manner.

3. Clinic Monitoring Group. The Clinic Monitoring Group (CMG) is appointed by the Steering Committee Chairman to assist the Steering Committee and especially its Executive Committee in monitoring the performance of the clinical centers. The CMG is comprised of four physician investigators, one of whom is appointed as Chairman, and one Trial Coordinator. The three members of the Executive Committee serve as ex-officio members. The Coordinating Center provides the CMG with the operational study data (as opposed to masked, outcome study data) that will enable them to monitor clinic adherence to the Protocol and Manual of Operations in a timely fashion.

4. Coordinating Center. The Coordinating Center will participate in all aspects of the design and implementation of the DCCT. The Director of the Coordinating Center or his designee is a member of the Planning Committee and the Steering Committee and the Co-Director is a member of the three-person Executive Committee. Coordinating Center personnel will provide scientific, technical and staff services to the Steering Committee and each of its working committees/groups. The Coordinating Center has the responsibility for implementing the systems necessary for data collection, editing, management and statistical analysis and for the maintenance of permanent study records and files. They have the responsibility of providing appropriate and timely data reports to the Executive Committee, the CMG, the DSQ and its subcommittees, the PAG, and to the NIDDK Director. They are responsible for all aspects of intrastudy communication and will work with the Publications/Presentations Committee in providing appropriate statistical analyses of study data in a timely fashion for use in approved publications and presentations. The Coordinating Center will implement its responsibilities as specified in its internal procedures manual, ensuring that study data are safely maintained and not released in an unauthorized manner. The following seven central units are the responsibility of the Coordinating Center. In general, these units provide scientific and technical guidance to the Study Group, specific working committes and the Coordinating Center.

   a) Central Ophthalmologic Reading Unit. The Central Ophthalmologic Reading Unit will receive and evaluate the quality of all photographs of the eye; utilize the modified ETDRS classification system for evaluating the grading of fundus photographs and maintain study records of all photographic data.

   b) Central Biochemistry Laboratory. The laboratory will provide eligibility baseline and repeated measurements of HbA_{1c}, blood glucose, lipids, and other serum and urine constituents.

   c) Central EKG Reading Unit. The Central EKG Reading Unit will provide baseline and follow-up coding of all EKG tracings from eligible patients.

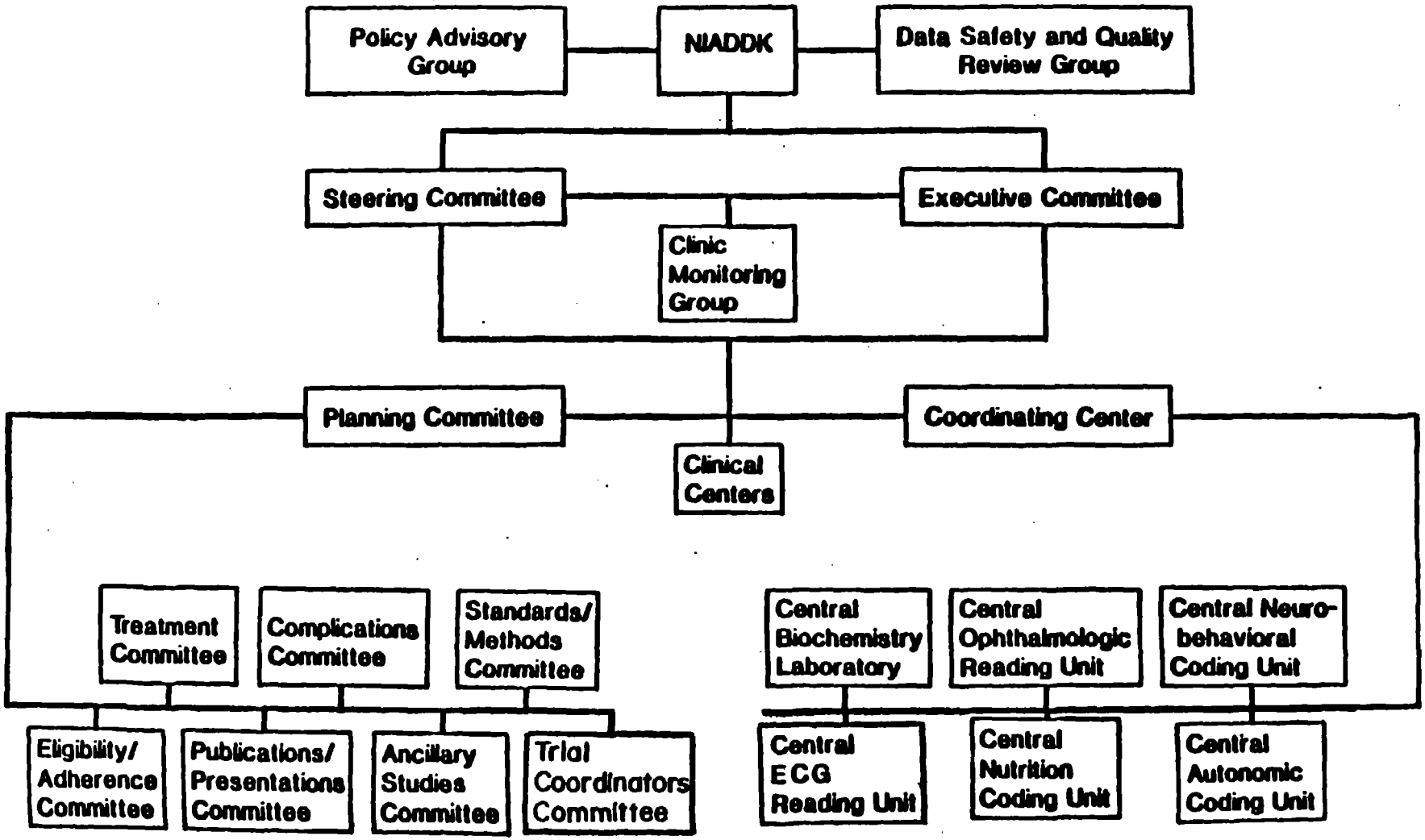
d) Central Nutrition Coding Unit. The Central Nutrition Coding Unit will provide baseline and follow-up analysis and coding of diet history data.

e) Central Neurobehavioral Coding Unit. The Central Neurobehavioral Coding Unit will provide scoring and coding of baseline and follow-up analysis of performance results of the neurobehavioral test battery.

f) Central Autonomic Coding Unit. The Central Autonomic Coding Unit will provide baseline and repeated coding of the results of tests of autonomic nervous system function.

2.3 MORBIDITY/MORTALITY CLASSIFICATION COMMITTEE

The Morbidity/Mortality Classification Committee is a wholly independent committee established by NIDDK to review and classify all deaths and major intercurrent events that occur among patients randomized into the DCCT. The events reviewed and classified will include: death, major accident, myocardial infarction, cerebrovascular accident with persistent neurological deficit, non-traumatic amputation, loss of vision, renal insufficiency, and neuropathy, as defined in the Manual of Operations. The purpose served by these reviews will be to: determine the primary and contributing causes of death, validate the basis for diagnosis of morbid events, and determine the likelihood that the event is attributable to diabetes. The classifications by this committee will be the basis of statistical analyses for the DCCT.


Policy Advisory Group
NIADDK
Data Safety and Quality Review Group
Steering Committee
Executive Committee
Clinic Monitoring Group
Planning Committee
Coordinating Center
Clinical Centers
Treatment Committee
Complications Committee
Standards/ Methods Committee
Central Biochemistry Laboratory
Central Ophthalmologic Reading Unit
Central Neuro-behavioral Coding Unit
Eligibility/ Adherence Committee
Publications/ Presentations Committee
Ancillary Studies Committee
Trial Coordinators Committee
Central ECG Reading Unit
Central Nutrition Coding Unit
Central Autonomic Coding Unit

CHAPTER 3

POLICY

In this chapter, study policy regarding informed consent, protocol changes, publications and presentations, ancillary studies, internal monitoring procedures, and statistical issues are described.

3.1 GENERAL PRINCIPLES OF INFORMED CONSENT

In order to be eligible for the trial, each participant must be willing to sign a statement of informed consent prior to randomization. This will document the agreement of the subject to participate in the study activities. For subjects less than 18 years old, a parent or guardian must also sign the informed consent statement.

The basic elements of the informed consent are:

1. A straightforward statement that the study involves research and a clear explanation of the purpose of the trial, including a description of the procedures to be followed in the screening, eligibility determination, baseline and follow-up examinations as well as those procedures to be followed in the two treatment regimens, and the identification of experimental procedures, the method of treatment assignment, and the expected duration of the subject's participation.

2. A description of the outcome(s) of primary interest, the length and schedules of treatment and followup, and methods of locating and following up subject participants who transfer to inactive status.

3. A description of the attendant and reasonably foreseeable discomforts and risks, as well as a description of any reasonably expected benefits.

4. A disclosure of alternative procedures that might be advantageous for the subject.

5. A statement that participation is voluntary and the subject is free to refuse to participate or withdraw consent and to discontinue participation in the project or activity at any time without jeopardizing his/her medical care.

6. No exculpatory or exonerating language through which the subject is made to waive, or appear to waive, any of his legal rights, or to release the institution or its agents from liability for negligence.

7. A description of the measures taken to ensure confidentiality of subject information.

8. A description of the measures taken to ensure subject safety.

9. An explanation of a subject's rights to compensation for research-related injuries and identification of specific individuals to contact regarding injury and/or questions related to rights as a research subject.

10. A description of subject responsibilities, including an explanation of the information that will be available during and at the conclusion of the trial.

11. An offer to answer all inquiries concerning participation in the research including identification of specific individuals to contact for answers to pertinent questions about the research.

12. A statement that participation in the study may involve risks which are currently unforeseeable.

13. An explanation of circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.

14. An explanation of the health consequences of a subject's decision to withdraw from the research and the need for orderly termination of participation.

15. A statement that significant new findings developed during the course of the study which may influence the subject's willingness to continue participation will be provided to the subject.

In accordance with DHHS policy on informed consent, it is necessary "to recognize that each subject's mental and emotional condition is important .... and that in discussing the element of risk a certain amount of discretion must be employed consistent with full disclosure of facts necessary to any informed consent."[1]

The Steering Committee recognizes that individual collaborating clinical centers may require that the recommended Informed Consent Form be amended to include additional statements or be reworded to clarify existing statements. All such modifications to the Informed Consent Form will be reviewed, and those which retain and do not detract from the

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[1] Salgo vs. Leland Stanford Jr. University Board of Trustees (154 C.A. 2nd 560; 317 p. 2-1701).

content of the suggested DCCT Informed Consent Form will be approved.

3.1.1 Sequence of Procedures

A two-stage informed consent procedure is part of a multi-level screening process. It is desirable that the Principal Investigator or the DCCT physician who will care for the subject be involved in the early stages of the sequence. The first Informed Consent Form obtains the subject's permission, and in the case of adolescents, the parent's permission, for the eligibility tests to be performed.

The second Informed Consent Form obtains the subject's permission, and in the case of adolescents, the parent's permission, to participate in the clinical trial.

These signed informed consent forms are secured at the Coordinating Center in separate files from the patient data files.

The tools utilized for securing informed consent are the DCCT Recruitment Flyer, Volunteer Information Handbook, Manual of Diabetes Tests, Terms and Special Procedures, DCCT Slide Presentation, Volunteer Understanding Questionnaire, and Informed Consent Forms Numbers 1 and 2.

3.2 PROTOCOL CHANGES

The objectives of Phase III of the DCCT are most likely to be achieved if the Protocol does not require alteration during that phase of the study. Any changes in the Protocol will result in some degree of heterogeneity of the data, which complicates the analyses and may compromise the scientific integrity of the study. However, occasions may arise in which Protocol changes are necessary.

3.2.1 Steering Committee Policy

Changes in the Protocol will be recommended by the Steering Committee only if they are required to insure subject safety or will significantly enhance the scientific validity of the study. To recommend Protocol change, three-fourths of the Steering Committee must approve the change.

3.2.2 Procedures

The Planning Committee will consider proposals for Protocol changes that may originate from the DSQ, the NIDDK, the Coordinating Center or one of the working committees. The DSQ will recommend changes on the basis of recruitment information and post-randomization follow-up data. Other groups could propose changes based on procedural or operational factors. The Planning Committee will make a recommendation to the Steering Committee as to whether or not a change of Protocol is warranted and, if so, what form it should take. The recommendations of the Steering Committee will be considered by the DSQ who will advise the NIDDK concerning the proposed change. If the change of Protocol is of sufficient magnitude to represent "a key decision point in the trial" (e.g., a change in fundamental design), the NIDDK will seek the advice of the Policy Advisory Group. NIDDK will make any final decision regarding Protocol change.

3.3 PUBLICATIONS AND PRESENTATIONS

3.3.1 Introduction

During the conduct of the DCCT, there will be no effort to publicize study plans or results which have not been reviewed and approved by the participants. The Publications and Presentations Committee will coordinate, monitor, review and assume responsibility for arranging the preparation of all study-wide press releases, interviews, presentations, and publications relating to the DCCT. Recommendations will be presented to the Executive or Steering Committee of the DCCT for approval. Copies of approved material will be provided promptly to the NIDDK.

3.3.2 Duties of the Publications and Presentations Committee

Specifically, the Committee shall:

1. Recommend policy and procedures for review and approval of all communications regarding the DCCT to outside groups.

2. Identify publications to be written during the course of the study, with target dates for each.

3. Propose policy guidelines for authorship of DCCT publications, and/or recommend to the Steering Committee senior authors and co-authors for each paper.

4. Monitor the writing of each paper to ensure publication in a timely fashion.

5. Establish standards of excellence for DCCT publications.

6. Inform the Steering Committee, NIDDK, and advisory groups of all public dissemination of DCCT information.

7. Approve any publications and presentations including those that arise from ancillary studies prior to their submission.

8. Suggest appropriate journals for DCCT publications and monitor the process of publication.

9. Perform other writing, reviewing, or editing tasks assigned by the Steering Committee or its Executive Committee.

10. Establish an Editorial Board that will review and edit all DCCT publications and presentations prior to submission, enlisting the special assistance of the DCCT committees whenever appropriate. The Publications/Presentations Committee will recommend members of the Publications/Presentations Committee and other members of the DCCT Research Group for the Editorial Board. Its activities will be conducted pursuant to the following editorial policy:

    a) Ensure that all publications preserve the scientific integrity of the DCCT.

    b) Correct factual and conceptual inaccuracies if necessary.

    c) Maintain the highest standards for scientific publications and presentations.

    d) Safeguard the rights of volunteer participants.

    e) Prepare comments to assist collaborating scientists in publishing papers of the highest quality and clarity.

    f) Avoid conflict with and/or duplication of other DCCT publications.

11. The Editorial Board will also review and suggest necessary revisions for any publications arising from approved ancillary studies prior to their submission for publication. In addition to the issues cited in the editorial policy above, proposed publications of ancillary studies will be scrutinized to ensure that their presentation will not threaten the viability of the DCCT, if still ongoing.

3.3.3 Specific Definitions and Policies

3.3.3.1 Press Releases and Interviews

A press release is defined as a document given to radio, television, newspapers, popular periodicals, or scientific journals not indexed in the Index Medicus. An interview is any discussion with a member of the

press, a science writer, or a radio or television commentator, which in turn provides information for public dissemination.

Except for the purposes of local recruitment, press releases and interviews will not be initiated by clinical centers. Centrally prepared press releases will be reviewed by the Publications/Presentations Committee and distributed to the centers. It is suggested that these prepared releases be given to the media when interviews are requested. This procedure will help ensure uniformity and accuracy in the information disseminated through the media. In this instance, use of such press releases and interviews need not have received prior appproval from the Publications/Presentations Committee. If a center is solicited for a press release or interview, then such may be given without prior review and approval by the Publications/Presentations Committee provided that the substantive content is limited to information available either in the final Protocol, the Manual of Operations, or in papers already published as peer reviewed articles, with no added interpretations or inferences.

Should a clinical center be solicited for information other than that detailed above, then the clinical center should refer the soliciting party to the Chairman of the Publications/Presentations Committee.

3.3.3.2 Presentations

A presentation is the delivery of information to scientific, professional or public groups, such that public dissemination might ensue through publications, press releases, etc.

A presentation may be given without prior review and approval by the Editorial Board provided that the content is limited to substantive information available either in the final Protocol, the Manual of Operations, or other published data, with no added interpretations or inferences.

All DCCT presentations involving any "new" data (not published as peer reviewed article) must be reviewed by the Editorial Board as described below:

1. Forum identification: The Publications/Presentations Committee will identify scientific and professional forums where presentations about DCCT should be made on behalf of the group. Suggestions for such forums and topics for presentations will be sought from the Publications/Presentations Committee itself and individual investigators and brought to the Steering Committee for approval. The Publications/Presentations Committee will identify one or more persons from a list of volunteer investigators to prepare and present the material.

2. Invited presentations: If members of the DCCT Research Group are personally invited to present DCCT data or represent the DCCT

Study Group, the invitation must be forwarded to the Publications/Presentations Committee as soon as possible. The Publications/Presentations Committee reserve the right to accept or not accept the invitation and suggest a presenter other than the DCCT Research Group member who received the original invitation.

3. Preparation and review schedule:

a) Requests for additional data from the Coordinating Center must be made sufficiently early to allow for delivery of the data requested (at least 60 days).

b) An abstract for a proposed presentation must be received by the Editorial Board Chairman at least 14 days prior to the scientific society's deadline for receipt of abstract to provide time for review, possible revision and rewrite.

c) A copy of the abstract is to be distributed by the Editorial Board Chairman to each DCCT center and the NIDDK at least 60 days before presentation.

d) A presentation script (talk copy) with tables (bibliography not required) must be sent to the Editorial Board Chairman at least four weeks prior to the scheduled presentation.

For an invited presentation for which there is no scientific society abstract review, an abstract should be prepared and submitted to the Editorial Board at least 60 days plus two weeks prior to the presentation to allow Editorial Board review and distribution of the abstract to the DCCT centers 60 days prior to presentation. Data requests and presentation scripts for invited presentations have the same deadlines as indicated in a) and d) from above.

3.3.3.3 Publications

A publication is any document submitted to a professional journal listed in the Index Medicus or any popular periodical with national circulation. All publications of results of the DCCT will be prepared under the overall review of the Publications/Presentations Committee. Publication of results of ancillary studies by individual investigators will be allowed with approval by the Publications/Presentations Committee. It must be recognized that approval of publications or presentation of ancillary studies that may jeopardize the outcome of the DCCT may be withheld until such time as is deemed appropriate by the Publications/Presentations Committee.

1. Journal identification: The Publications/Presentations Committee will suggest (or endorse) the choice of an appropriate journal for the publication of each proposed manuscript so that the manuscript can be prepared according to the guidelines of a specific journal and be direct towards its known readership.

2. Preparation and review schedule: The Publications/Presentations Committee will select a writing group of three to seven individuals for each proposed manuscript. One individual will be designated as Chairman and will be responsible for ensuring that the first draft of the publication is written. The first draft should be produced within six months following approval by the Steering Committee.

   The Chairman of the Editorial Board will usually, but not necessarily be, the Chairman of the Publications/Presentations Committee. The Editorial Board Chairman will coordinate the efforts of the writing teams, help establish priorities for data analysis by the Coordinating Center, help edit the manuscripts produced by the writing teams, and may participate in the writing chores. In order to facilitate this activity, an Editorial Office will be established at the office of the Editorial Board Chairman.

   A reasonable number of data tabulations will be prepared by the Coordinating Center to assist the writing group for each manuscript. The Co-Directors of the Coordinating Center will designate one of their staff to work with each writing group in order to provide liaison and resource material for their particular manuscript.

   The Editorial Board Chairman will designate at least two DCCT reviewers (including one from the Coordinating Center) who must submit their review to the Editorial Board within 30 days. The Editorial Board Chairman will distribute the paper and reviews to the Editorial Board for its consideration and then will inform the writing groups of its action, as well as any suggestions for revision.

   If revisions are requested, the writing group must obtain approval of the revised manuscript from the Editorial Board Chairman who will consult with the original reviewers. Upon receipt of such approval, the final manuscript will be reviewed by the Publications/Presentations Committee and distributed to each DCCT center (each sub-specialty paper will be sent to the designated specialists in the clinic) and the NIDDK. Those manuscripts not requiring revision may be distributed as soon as Editorial Board approval is received.

   Fourteen days after distribution to the DCCT centers and the NIDDK, a paper approved by the Editorial Board may be submitted for publication. Any member of the DCCT Study Group who wishes to comment on the paper must communicate his/her concerns directly to the writing group and/or the Editorial Board Chairman within the

fourteen days. The writing group Chairman and/or the Editorial Board Chairman will delay the submission until resolution is reached.

3.3.4 Standards of Excellence

In addition to the review system established for the critique of publications and presentations as described in the previous section, the following guidelines are suggested for maintaining the highest standards of excellence for DCCT publications and presentations.

If, in the opinion of the members of the Editorial Board, there is no member of the DCCT who has sufficient scientific background to review the pertinent material, then outside (of DCCT) expert consultants will be selected by the Editorial Board and asked to critique the material. However, it is expected that sufficient expertise will be available from the members of the Steering Committee and Research Group to provide a review of all publications and presentations.

For the major publications and presentations, the completeness or adequacy of the reports may be assessed by the following twelve criteria:

1. Purpose of the report should be clearly stated.

2. Selection of the population exclusion criteria should be explicitly delineated.

3. Documentation of eligibility screening process to preclude the suggestion of bias in the selection of eligible subjects.

4. Specific information about the randomization including the method so that the reviewer or audience can determine the appropriateness of the method. Data should be presented to show the effectiveness of the randomization in producing groups which are comparable.

5. Information regarding the efforts made to achieve masking to defend against the introduction of additional bias.

6. Information on the loss of subjects during the study including reasons for loss to followup. Data should be presented to demonstrate comparability of the subjects who participated and who exited from each treatment group throughout the whole clinical trial.

7. Information on the administration of and adherence to the treatments should be presented.

8. Information on the exact statistical tests should be presented as well as a presentation of the actual data.

9. Information on the estimated range of treatment effects, i.e., use of confidence intervals in reporting results.

10. Information on the power to assure the reader of the strength of the conclusion, if a negative conclusion is reached.

11. Significance testing should be used in conjunction with an empirical review of the data.

12. Conclusions should not be derived from restratification on measures obtained after randomization.

3.3.5 Topics for Publications

Following is a list of topics for publications from the DCCT during or at the end of Phase II:

1. Design rationale and considerations.

2. Ethical issues including a description of the unique procedure for obtaining informed consent in the DCCT.

3. Feasibility issues, e.g., problems with recruitment.

4. Compliance/adherence.

5. Metabolic results.

6. Methodological considerations, e.g., fluorescein angiography versus stereo fundus photographs.

7. Safety issues.

Topics for publication during Phase III include:

1. Modification of design for Phase III evolving out of Phase II.

2. Cross-sectional and prospective results that are not masked during Phase III and that are of general interest and value to the diabetes community. Examples of these topics include the glycemic results of the two intervention strategies over time. Long-term adherence, safety and non-endpoint sequelae of these therapies will be of great interest.

3. At the conclusion of Phase III, results of major and minor study questions.

3.3.6 Authorship

Four categories of manuscripts are anticipated:

I. Official DCCT Manuscripts: These are papers which address themselves to the principal goals and objectives of the trial. Examples are: Baseline, Protocol Design, and Primary Endpoint papers.

II. Other DCCT Manuscripts: These are papers that utilize the data base from all participating centers, but address issues that are peripheral to the major objectives of the trial. Thus, the major features of these papers are that they include study-wide data generated by the DCCT. Examples are: recruitment, assessment of compliance, informed consent procedures, methodological analyses (e.g., fluorescein versus stereo fundus photographs), etc. Impetus for these papers will often come from the Publications/Presentations Committee.

III. Manuscripts that utilize only limited subgroups of DCCT subjects and/or a significant amount of non-DCCT data: These papers would either utilize data from certain subgroups of clinics or from one clinic and/or would utilize significant amounts of non-DCCT data. Examples would be: complete neurological profile in the DCCT in selected DCCT clinics, apolipoprotein measurements in selected DCCT clinics, etc. These protocols would receive approval by the Ancillary Studies Committee before activation.

IV. Miscellaneous Category: Some papers, mostly concerned with methodologic issues, may arise which do not deal with the DCCT population or the DCCT study directly but which were prompted by discussions during the development of the DCCT study design. For example, a survey of hemoglobin A_{1c} methods and results in the participating clinics might be undertaken to provide a sense of the methodologies currently used and the levels of glycemia achieved in academic centers. A manuscript such as this, prepared by a member of the DCCT Research Group, should include an acknowledgement of their NIH/DCCT support.

Responsibility for the category assignment for all manuscripts rests with the Publications/Publications Committee. Studies that are approved by the Ancillary Studies Committee may be assigned to Category II, III, or IV.

Authorship in each of these categories will be as follows:

I. Official DCCT Manuscripts - The DCCT Research Group[1]

[1]The list of investigators appears as part of the manuscript, usually at the end of the manuscript.

II. Other DCCT Manuscripts - The DCCT Research Group[a]

Footnote at bottom of the title page:

[a]Prepared for the DCCT Research Group by Dr. Smith (Chairperson), A, B, C. A complete list of investigators and members of the DCCT Research Group appears in Diabetes, 35:530-45, 1986.

III. Manuscripts that utilize only limited subgroups of DCCT subjects and/or non-DCCT resources: - Drs. Q, C, A, B[+]

[+]Acknowledge DCCT Research Group (complete list of the Research Group can be found in Diabetes, 35:530-45, 1986).

IV. Miscellaneous Manuscripts: - Dr. Q. Dr. B*

*This study was partially supported by the Diabetes Control and Complications Trial, NIH. RO. . .

For Category II and III papers, the Editorial Board Chairman may be included as an acknowledged author with the writing team consistent with his/her level of involvement in the writing process. Authorship for Category II papers will be determined by the Chairman of the Writing Committee with the support and advice of the Publications/Presentations Committtee. Category II papers will contain an acknowledgement of the Chairman of the Editorial Board unless the Chairman is a member of the writing team. This acknowledgement will appear on the last page of the manuscript.

All professional participants of the DCCT who have the approval of the Principal Investigators and have served at least two years in a significant capacity with the study will be listed at the end of each Category I paper and will be considered as authors. In addition, a Principal Investigator may provide justification in writing to the Publications/Presentations Committee to include individuals who have been with the DCCT for less than two years for inclusion.

A list of all participating centers will appear in the Category I manuscript. Under each center, a roster of names, as described above, will appear, each followed by the academic degree(s). For the purposes of this listing, the Coordinating Center, the central laboratories, and the NIDDK will be considered as special units and be listed as participating centers. If such a roster of credits for the manuscript is deemed to be too lengthy by a journal considered desirable for publication of that particular manuscript, the Publications/Presentations Committee may request the NIDDK to pay a reasonable amount towards page costs to permit such a roster to be printed intact.

3.4 ANCILLARY STUDIES

Ancillary studies will be evaluated with careful consideration of their potential impact on the objectives and performance of the DCCT. Ancillary studies which complement the objectives and thereby enhance the value of the DCCT are to be encouraged. Such studies should augment and promote the continued interest of both subjects and investigators. To protect the integrity of the major study, a proposal to conduct an ancillary study must be reviewed and approved by the Ancillary Studies Committee before its initiation. In some cases, ancillary studies must also be approved by the Steering Committee. All approved ancillary studies will be reviewed yearly by the Ancillary Studies Committee for progress and impact on the DCCT as a whole.

3.4.1 Definition of an Ancillary Study

An ancillary study is defined as research or data collection involving DCCT subjects using any technique, medication, procedure, questionnaire or observation other than those set forth in the DCCT Protocol.

The investigator responsible for the conduct of an ancillary study must be a member of the DCCT Study Group.

3.4.2 Reason for Requirement of Approval

Investigators and subjects are entitled to prior assurance that all ancillary studies are of high scientific merit and that no ancillary study will:

1. Cause a deviation from the Protocol;
2. Complicate interpretation of the study results;
3. Potentially adversely affect subject cooperation;
4. Jeopardize the public image of the study;
5. Create a significant diversion of the study resources locally or at the Coordinating Center or any other DCCT unit;
6. In any way negatively influence the cooperative spirit of the collaborating investigators;
7. Otherwise compromise the scientific integrity of the study.

3.4.3 Levels of Approval Required for Ancillary Studies

There are two levels of approval for ancillary studies:

Level I: Approval by the Ancillary Studies Committee.

Level II: Further approval by the Steering Committee.

In general, Level I approval will suffice if the ancillary study involves analyzing available data from the DCCT for questions not addressed in the major study, and no additional tests or observations will be made on the subjects. Other types of ancillary research will customarily require both Level I and Level II approval. The decision regarding the necessary level of approval will be made on a case by case basis by the Chairman of the Ancillary Studies Committee in consultation with the Executive and/or Steering Committees.

After approval by the Ancillary Studies Committee and the Steering Committee, final approval is contingent upon the Ancillary Studies Committee receiving a letter signed by the principal and all collaborating investigators in which they agree to abide by the policies for ancillary studies herein described including that regarding publication or presentation of results (Figure 3.1).

3.4.4 Funding of Ancillary Studies

The DCCT will not provide funds for ancillary studies. In particular, no funds are provided for Coordinating Center activities or services in support of ancillary studies. If funds are needed, the investigator must explore other avenues such as: (1) submission of a new research grant application; or (2) use of other sources of funds (i.e., a foundation, drug company, etc.). The anticipated source of funds must always be identified.

3.4.5 Publication of Ancillary Study Results

All manuscripts, abstracts or presentations for scientific meetings based on ancillary study data must be reviewed and approved by the DCCT Publications/Presentations Committee before publication or presentation.

3.4.6 Preparation of Request for Approval of Ancillary Studies

The request for approval of an ancillary study should be in narrative form. It should contain a brief description of the objectives, methods, significance of the study, plans for analysis and publications, and information regarding funding level and source. If a proposal is being submitted elsewhere for funding (e.g., a grant application), the source

of funding should be identified and the application may be used as the basis for the request. Full details should be given concerning any procedures or tests to be carried out on a study patient including: any ophthalmologic, renal, cardiovascular, neurologic, psychological or other evaluation to be performed; any substances to be injected or otherwise administered to the patients; any observations to be made or procedures to be conducted on patients outside of the clinic; any extra clinic visits required of the patient or any prolongation of the patient's usual clinic visits; any additional specimens (blood, urine, etc.) to be obtained or additional procedures to be done on specimens collected according to the DCCT Protocol. The proposal should discuss the measures to be taken to ensure patient safety and confidentiality and an assessment by the investigator(s) of the potential impact of the ancillary study on the DCCT. Prior approval by the appropriate Human Subjects Review Committee should be demonstrated. The proposal should also specify whether Level I or both Levels I and II approval is requested.

3.4.7 Procedures for Obtaining Ancillary Study Approval

The investigator should send his ancillary study proposal to the Coordinating Center, which will distribute it to all members of the Ancillary Studies Committee. The proposal should be written in sufficient detail so that the Ancillary Studies Committee can assess the study's scientific merit and potential impact on the DCCT. To ensure thorough scientific review, the Chairman of the Ancillary Studies Committee may elect to seek outside expert opinion in advance of the Committee meeting. Within 30 days of receiving the proposal, the Chairman of the Ancillary Studies Committee will summarize the questions and objections (if any) raised by members of the Committee and refer this summary to the applicant so that he may amplify, clarify, and/or withdraw his request. The members of the Ancillary Studies Committee will have another opportunity to review the request and the Chairman will then prepare a statement of the Committee consensus, including any remaining reservations or objections. This statement will be sent to the investigator requesting approval for the ancillary study. If only Level I approval is required and the study has been approved by this Committee, the investigator may proceed with the study when it has been approved by the DSQ and authorized by NIDDK. Approval or disapproval is based on majority opinion.

If Level II approval is also needed, the approval statement of the Ancillary Studies Committee will be forwarded to the Steering Committee. Each member should respond to the Chairman of the Ancillary Studies Committee within one month. No response will be considered approval. Recommendations of the Ancillary Studies Committee and Steering Committee will be forwarded to the DSQ for assessment of impact on the DCCT. Approved ancillary studies will then be forwarded to NIDDK for final authorization. The investigator may proceed with the ancillary study once it has been authorized by the NIDDK.

In the event that the Ancillary Studies Committee disapproves of a proposed ancillary project, the investigator can apply directly to the Steering Committee, whose decision may override that of the Ancillary Studies Committee. If the Steering Committee also disapproves of the ancillary study, the proposed study will not be undertaken.

3.4.8 Funding of Ancillary Studies

The DCCT will not provide funds for ancillary studies. In particular, no funds are provided for Coordinating Center activities or services in support of ancillary studies. If funds are needed, the investigator must explore other avenues such as: (1) submission of a new research grant application; or (2) use of other sources of funds (i.e., a foundation, drug company, etc.). The anticipated source of funds must always be identified.

3.4.9 Publication of Ancillary Study Results

All manuscripts, abstracts or presentations for scientific meetings based on ancillary study data must be reviewed and approved by the DCCT Publications/Presentations Committee before publication or presentation, as described in the Chapter on Publications and Presentations.

3.5 INTERNAL MONITORING

Mechanisms have been instituted for continuous performance monitoring of all DCCT study units by the Study Group. External quality control surveillance has been instituted by the DCCT to assess the precision of all measurements made by the Central Biochemistry Laboratory (CBL), Central Ophthalmologic Reading Unit (CORU), and other central units. In addition, the performance of these units, the clinical centers and the Coordinating Center has been monitored through site visits and appropriate tabulations of indices of performance. These tabulations have been reported periodically to the appropriate study committee, and to the individual study unit, and to the Data, Safety, and Quality Review Group (DSQ).

3.6 RESPONSIBILITY FOR MONITORING

1. Performance monitoring of each study unit will be conducted by working committees of the Study Group. The Coordinating Center will participate in monitoring all study units by preparing tabulations of performance indices, by participating in site visits, and by maintaining permanent records of the performance of each study unit. Responsibilities of the working committees are as follows:

   a) Standards/Methods Committee

      i) Central Biochemistry Laboratory

      ii) Central Nutrition Coding Unit

   b) Complications Committee

      i) Central Ophthalmologic Reading Unit

      ii) Central EKG Reading Unit

      iii) Central Autonomic Coding Unit

      iv) Central Neurobehavioral Coding Unit

   c) Clinic Monitoring Group

      i) Clinical Centers

2. The NIDDK has appointed an independent group to review the performance of all study components to ensure the continued timeliness, quality of study data, and safety of subjects entered into the trial.

3.7 PERFORMANCE MONITORING

3.7.1 Clinical Centers

All aspects of clinical center performance will be monitored regularly by the Clinic Monitoring Group (CMG). In particular, the CMG will monitor success of recruitment, adherence to treatment and follow-up schedules, standardization of study procedures, success in meeting treatment goals, and the occurrence of adverse effects of treatment, as allowed by required masking of outcome data. Review of performance data shall be conducted with sufficient frequency to allow timely detection of deviations from expected performance. Such deviations shall be investigated by the CMG and corrective actions recommended to the clinical center. Monitoring shall also include site visits conducted at appropriate intervals. If discussions between the CMG and the clinical center do not lead to improved performance, the CMG may recommend other actions to the DCCT Steering Committee.

Each central unit has established mechanisms by which the standardization of procedures performed by the individual clinical centers can be assessed and monitored. These will be reviewed periodically by the CMG.

3.7.2 Central Units

Central Biochemistry Laboratory

External quality control surveillance programs have been established to monitor the performance of the CBL. This will entail the masked submission of duplicate specimens from the clinics for analysis by the laboratory. The resulting data will allow an assessment of the on-going precision of the laboratory test results. Bench quality control assessment by each laboratory alone, though useful, will be inadequate because laboratory performance alone is but one step in a chain of activities which could influence the test results. A program of external duplicate surveillance will allow assessment of the total system starting with the collection of a specimen in the clinic and ending with the entry of the data into the Coordinating Center computer. The duplicate quality control data are analyzed periodically by the Coordinating Center and presented to the Standards/Methods Committee for review. Any deficiencies detected will be investigated and corrected.

Because of the critical nature of hemoglobin A_{1c} data and the lack of an adequate external standard for this assay, special measures are needed to ensure precision over time under all circumstances. Therefore, a backup hemoglobin A_{1c} laboratory has been established. Aliquots of a single pool of blood will be analyzed regularly by both laboratories for the duration of the DCCT and the assays maintained to achieve comparable results. In addition, split duplicate aliquots of subject specimens are analyzed in both laboratories and the comparability of results assessed.

Central Ophthalmologic Reading Unit

Likewise, an external quality control surveillance program has been established for the CORU which entails the duplicate masked evaluation of fundus photographs. These data are analyzed periodically by the Coordinating Center and presented to the Complications Committee for review. Any deficiencies detected will be investigated and corrected.

Other Central Units

To the extent that other evaluations are standardized or are conducted in part by a central facility, comparable mechanisms for quality control surveillance will be initiated.

3.7.3 Coordinating Center

A specially constituted subcommittee of the DSQ will site visit the Coordinating Center periodically to review procedures.

3.8 CORRECTION OF DEFICIENCIES

If monitoring procedures detect deficiency in the performance of any study unit, the matter will be investigated by the appropriate working committee and then considered by the Executive Committee and/or Steering Committee. Expert consultants will be used as necessary. Steps will then be instituted to correct the deficiency. If, after a reasonable period, deficient performance persists, the matter will be referred to the NIDDK.

3.9 STATISTICAL ANALYSES

3.9.1 General Principles

The objectives of the DCCT described in Chapter 1 will be assessed through statistical analyses of those measurements and events described below. For the primary prevention study, these are the incidence of new cases of retinopathy, neuropathy or nephropathy. For the secondary intervention study, these are the incidence of progression of retinopathy, and development or progression of neuropathy or nephropathy. Also, these include measurements of level and variability of blood glucose control, the frequency of clinically significant events, measures of overall subject adherence to followup, and the precision and accuracy of study measurements.

3.9.2 Baseline Results and Analyses

The DCCT patient group is not a random sample from the general population of individuals with IDDM. It is a selected group of diabetics who are sufficiently motivated to be involved in a long-term study and who have satisfied a comprehensive set of admissibility criteria. The distributions of the baseline variables among the combined treatment groups will serve as a detailed description of these characteristics for the group of subjects enrolled into the study.

The baseline variables included in these analyses will be grouped into the following categories:

1. Demographic characteristics,

2. IDDM historical and clinical characteristics,

3. Biochemical and other laboratory measurements,

4. Ophthalmologic evaluations,

5. Renal evaluations,

6. Cardiovascular evaluations,

7. Neurological evaluations, and

8. Psychological evaluations.

In addition, the means, standard errors, and frequency distributions of the variables will be presented by treatment group and statistical tests of differences between the groups will be conducted. Such a manner of displaying and analyzing baseline data is useful in assessing the comparability of the two treatment groups at baseline.

The principal method to be used for comparison of groups for quantitative measures will be the t-test, or if not normally distributed, the Wilcoxon test (1). For the comparison of data presented as proportions, treatment-specific frequency distributions will be compared by goodness of fit tests, e.g., chi-square tests for contingency tables.

3.9.3 Outcome Variables

To address the DCCT objectives, the following outcome measures will be employed in various statistical analyses to determine whether statistically significant and clinically meaningful differences exist between the treatment regimens.

Principal DCCT Objectives

1. Onset or progression of retinopathy

   a) Primary Prevention Trial. The outcome variable which is the basis for the design of the primary prevention trial is the development of persistent diabetic retinopathy in individuals with no evidence of retinopathy on the detailed grading of the entry fundus photographs. Diabetic retinopathy is defined as the presence of at least one microaneurysm in either eye. The clinical significance of a treatment group difference for this outcome variable will be evaluated in consideration of trends at higher levels of retinopathy as defined by the DCCT index of retinopathy.

   b) Secondary Intervention Trial. The outcome variable which is the basis for the design of the secondary prevention trial is the definite worsening of retinopathy in individuals who had mild to moderate nonproliferative diabetic retinopathy on the detailed grading of entry fundus photographs. A reliably

detectable worsening in retinopathy is defined as a progression of three or more steps on the DCCT index of retinopathy. The clinical significance of a treatment group difference for this outcome variable will be evaluated in consideration of the proportions in each treatment group with proliferative diabetic retinopathy in either eye, DRS high risk characteristics in either eye, clinically significant macular edema in either eye, and any retinopathy in either eye for which the patient received photocoagulation treatment.

2. Adverse Events

   a) Death

   b) Episodes of severe hypoglycemia.

   c) Episodes of diabetic ketoacidosis.

   d) Inability to maintain normal growth and development.

   e) Inability to maintain acceptable body weight.

   f) Inability to maintain psychological well-being.

   g) Neuropsychological evidence of cerebral dysfunction.

Other Objectives

1. Onset of nephropathy

   a) The development of persistent albuminuria.

   b) The development of persistent renal insufficiency.

2. Onset or progession of neuropathy

   a) Among subjects free of any neuropathy on entry, the development of definite clinically evident peripheral neuropathy based upon the standardized examination.

   b) Among subjects with minimal neuropathy on entry, the definite worsening of clinically evident peripheral neuropathy based upon the standardized examination.

3. Incidence of cardiovascular events as defined in the Manual of Operations: The occurrence of at least one of the following:

   a) Major events:

      i) Myocardial infarction.

      ii) Significant ventricular arrhythmia documented by EKG.

iii) Diagnosis of congestive heart failure.

iv) Definite cerebrovascular accident.

v) Transient ischemic attack.

b) Minor events:

i) Hypertension.

ii) Development of severe lipid abnormality associated with increased cardiovascular risk.

Operational Outcomes

1. Recruitment: Ability to recruit the full cohort of subjects within the specified time.

2. Glucose control: Maintenance of a difference between experimental and standard treatment groups.

a) HbA_{1c}

b) Capillary blood glucose profile.

3. Individual subject management.

a) Occurrence of severe hypoglycemia.

b) Incidence of HbA_{1c} greater than 13.11.

4. Adherence

a) Transfer to inactive status.

b) Deviation from the treatment protocol.

c) Missed visits

5. Precision and accuracy

a) HbA_{1c}

i) Coefficient of reliability from external quality control.

ii) Laboratory variability measured by between-run coefficient of variation.

iii) Agreement with backup Hemoglobin Alc laboratory.

b) Capillary blood glucose profile.

i) Coefficient of reliability from external quality control.

c) Stereo fundus photographs.

i) >80% agreement between repeated gradings of randomly selected photographs.

3.9.4 Statistical Methods

Statistical analyses will be conducted using statistical methodologies appropriate to the data and the question being asked.

Thus:

1. For simple outcome events which are not time-dependent, such as the comparison of proportions of patients experiencing adverse events between the two treatment groups, simple methods for contingency tables will be employed (chi-square test of association). The Mantel-Haenszel procedure or others will be employed in those cases when it is necessary to take into account the influence of a third variable (e.g., age) on the association between treatment group and an outcome variable (2).

2. For dichotomous outcome events which are time-dependent, such as the time to the first episode of hypoglycemia, life-table methods (3,4,5) will be employed. In these procedures, each patient is counted in the analyses during the time he or she actually is followed to an exit or the outcome event, and all patients contribute to the overall estimate of the event rates at each endpoint visit. The life-table proportions for an event are slightly higher than the simple proportions because the life-table method adjusts for exists from the study.

   Since all patients will be followed from the date of randomization (between August, 1983 to September, 1988) through September, 1993, patients will be followed for differential lengths of time varying between five and ten years. By the life-table method, analyses can be conducted of event rates over the full ten year period using the data available for each patient including data on patients followed for less than ten years. Of course, event rate comparisons in the latter part of the period are less precise because few patients would be followed that long.

3. For quantitative continuous measures obtained periodically during the follow-up period, such as the HbA_{1c} and blood glucose profile at three-month intervals, the mean values will be compared between the two groups at each successive point in time using analysis of covariance, adjusting for the baseline measurement of that variable and possibly other baseline variables (6). In addition, non-parametric methods which allow for missing data, as will result from staggered patient entry, will be used to compare the profile of the mean values over time between the groups (7).

For the data and questions outlined above, various multiple regression models will also be employed to assess the combined influence of treatment group and baseline characteristics on outcome variables. These include the logistic regression model for simple proportions (8), the Cox model for life-tables (5), and the least-squares general linear model for quantitative outcomes (9). In these models, the effects of treatment group on the outcome variable will be assessed after accounting for the influence of other variables in the model according to the reduction-in-sums-of-squares principle (1).

3.9.5 Analysis Plan

All statistical analyses will be based upon the total cohort of subjects randomized into the trial. Although data on some subjects may be missing at points in time, all relevant data available from each subject will be employed in all analyses.

In all analyses, all subjects will be included in the group to which they were initially randomly assigned and group assignment will not be altered based on the subject's adherence to the assigned treatment program. Thus, subjects who deviate or transfer to the alternate treatment will be included in the initial randomly assigned group for statistical analysis.

Analyses of each outcome will include preliminary tests for interaction between clinic strata and treatment group in their effects upon the outcome variable. If an interaction is detected, additional analyses of that variable will be conducted with stratification by clinic. The analysis will be performed separately for the primary prevention and secondary intervention studies.

Differences between the groups in their baseline characteristics could bias the comparison of the treatment groups. Likewise, differences between the groups in the baseline characteristics of the subjects who later exit from the study could bias the comparison of the treatment groups on outcomes measured only in the subjects remaining in the study. If such differences in baseline characteristics are observed, analyses will also be conducted of the effects of the treatments on outcomes adjusting for the potential confounding effects of these baseline characteristics. If only a few such baseline characteristics are identified, analyses will be conducted stratifying for those characteristics. If, however, any more than a few baseline characteristics are identified, because of paucity of data, it will be necessary that regression models be employed to adjust the treatment comparison for the confounding effects of those characteristics.

Likewise, stratified analyses will be conducted adjusting for the effects of age, duration of IDDM and other known prognostic variables, and such variables will also be used in regression models to adjust the treatment comparison.

Intercurrent events such as death, major accident, myocardial infarction, cerebrovascular accident with persistent neurological deficit, non-traumatic amputation, loss of vision, renal insufficiency and neuropathy, as defined in the Manual of Operations will be reviewed and classified by an independent committee -- Morbidity/Mortality Classification Committee. The results of this classification will be the bases for the statistical analyses of intercurrent events.

3.9.6 Interim Analyses

The interim analyses are intended to assess patient safety, Protocol integrity and data quality, and to determine whether the study objectives (Chapter 1) have been met. The Data, Safety and Quality Review Group (DSQ) will meet regularly during the conduct of the study to monitor the emerging results and to assess the risks and benefits of each mode of therapy, thus insuring the safety of the subjects enrolled in the study. Statistical analyses will be conducted of all outcome variables for review by the DSQ prior to each meeting of the committee. These analyses will be conducted recognizing the effects of repeated statistical tests whereby the nominal Type I Error level increases after each such examination of the data. Plans for these interim statistical analyses and the statistical methods to be employed will be specified by the DSQ and will be documented in a separate document entitled "Operating Procedures for the DSQ."

The interim analyses will include all outcome variables defined in Section 3.9.3. The DSQ will recommend modification of the Protocol or early termination of the study if differences are found between the treatment groups which are statistically significant and are deemed clinically important.

3.10 REFERENCES

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8. Cox, D.R. The Analysis of Binary Data, Methuen, London, 1970.

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Figure 3.1

May 5, 1987

John Doe, M.D.
University of America
111 Main Street
Somewhere, AM 00000

Dear Dr. Doe:

Your proposed ancillary study entitled "_____" was approved by the Steering Committee at its _____ meeting. Final approval for this ancillary study is contingent upon you (and your co-investigators) signing and returning a copy of this letter indicating that you agree to abide by the policy and procedures for ancillary studies and the publication and presentation of results from ancillary studies as described in the DCCT Protocol.

Annually, the Ancillary Studies Committee requests that you submit a very brief status report on your project. We will send you a reminder at the appropriate time.

Sincerely,

Jerry P. Palmer, M.D.
Chairman, DCCT Ancillary
Studies Committee

Agree as above:

_____ _____
SIGNATURE DATE

CHAPTER 4

RECRUITMENT

4.1 OVERVIEW

All 278 subjects recruited for the feasibility study will continue to be followed until completion of the study in either the primary prevention or secondary intervention trial as indicated by post-randomization stratification on the subject's baseline retinopathy status.

Additional subjects will be recruited over a period of three years. Subjects without evidence of diabetic retinopathy suitable for a primary prevention trial and subjects with evidence of minimal retinopathy suitable for a secondary intervention trial will be recruited.

Eligible and consenting subjects in each of the clinical centers will be assigned randomly to receive either standard or experimental therapy.

A total of 1400 subjects will be randomized within two retinopathy strata with approximately equal numbers in each stratum.

Clinics that participated in the Feasibility Study (clinics 01-21) will be expected to enter 55 subjects. Fifty percent of the subjects should be subjects for the primary prevention stratum. Those additional clinics that were certified later are expected to enter between 30 and 43 subjects with equal numbers in each retinopathy stratum.

Each clinic is required to randomize subjects into the two retinopathy strata. No clinic will be allowed to recruit and randomize much more than 50% of one type of subject than other. This policy may prevent the slower to randomize clinics from being responsible for recruiting the more elusive type of subject. It is not possible to predict the actual rate of randomization; therefore, when the randomization quota is met studywide for either retinopathy stratum, recruitment for that component will cease and full efforts will be concentrated on the other. Recruitment will continue for three years or until the full cohort for each stratum has been met.

The Study Group has adopted interim randomization goals in order to facilitate the monitoring of recruitment on a clinic-by-clinic basis. The Clinic Monitoring Group monthly reviews the clinics' performance relative to these goals.

4.2 RECRUITMENT POLICIES -- CENTRAL VERSUS LOCAL

In order to enhance and effectively manage recruitment strategies, it is recommended that the activity be delegated to a full-time employee of the local clinic. The sources yielding subjects will vary from clinic to clinic. Referral for participation can originate from a variety of sources in addition to physicians and self-referrals.

Everything works for some centers, but nothing works for everyone. Additionally, some clinics are not as efficient as others. Local recruitment activities cannot be replaced by central or national effort. The national effort will be directed at coordinating the publicity regarding the trial and transmitting successful recruitment strategies.

Recommendations based on practices at the most successful centers should be passed on to all centers. (For example, do screening at the convenience of the volunteer, always have the Trial Coordinator show the slide show, be highly enthusiastic, have coffee available for the volunteer and his family, start being personally helpful to the volunteer even before he/she is enrolled, etc.)

When one center comes up with a good technique or tool, such as an ad prepared by one center, it should immediately be shared with all others.

Assessment of Clinic Potential. Estimate the pool of patients and community sources of referral by obtaining the following information:

1. Number of insulin dependent diabetes patients, age, percent of adolescents and adults in Principal Investigator's clinic.

2. List of diabetes clinics in area with number of patients, age, percent of adolescents and adult patients, type and duration of diabetes.

3. List of physicians in the area who treat diabetic patients (adolescents and adults); include number of potential candidates for the DCCT trial.

4. Numbers, type and duration of diabetes, age of patients who are seen by local community health nurses.

5. List of dietitians who work with diabetic patients and a list of their potential candidates for the study.

6. List of groups working with diabetic patients in area (i.e., Diabetes Association, self-help groups, Lions Club, etc.).

7. List of other local community organizations which could be instrumental as source of referrals.

8. List of pharmacies in the area.

Recruitment Materials. The DCCT Coordinating Center will provide the following materials and resources to each clinic:

1. A flyer to be mailed to physicians, nurses and dietiticans.

2. The Research Volunteer's Information Handbook.

3. Written information about DCCT for a direct mail letter to physicians, groups serving diabetic patients, clinics, health departments and other local sources of referral. (A copy of the official DCCT Fact Sheet is shown in Figure 4.1.)

4. The study exhibit which is available on request.

5. Services of a media consultant (Ms. Benzaia -- (212) 866-0661).

6. A toll-free 800 telephone number to screen potential volunteers. (The written response sent to the interested and eligible volunteers is shown in Figure 4.2.)

4.3 RECRUITMENT PLAN

The following procedures are recommended as a minimum:

1. Set the stage with physicians and other potential patient sources of referral by arranging a presentation at the local medical society, relevant grand rounds, diabetes associations, and at various other relevant local organizations.

2. Place an article about the DCCT recruitment efforts in the various state and local journals, newsletters and community newspapers.

3. Solicit physician referrals by mailing available materials (i.e., articles, brochures, posters, etc.) for dissemination of information and waiting room display.

4. Solicit referrals also from all other relevant groups (Diabetes Association, other health professionals and community groups) by using procedures described in above item.

5. Prepare a bi-monthly newsletter to all of the aforementioned sources to maintain awareness of the DCCT goals and to inform them about the progress of the trial.

Diabetes Control and Complications Trial

FACT SHEET

The Diabetes Control and Complications Trial is a 10-year study, sponsored by the National Institutes of Health, comparing the effects of two forms of insulin treatment on preventing or slowing the development of diabetic complications of the eyes, kidneys, and nervous system. It is now underway at 27 medical centers in the U.S. and Canada.

Why is it needed?

People who have insulin-dependent diabetes do not produce insulin needed for metabolism. As a result, digested sugars (glucose) can build up to high levels in the blood. In order to control the disease, patients must take daily insulin shots. Medical scientists have long debated whether the long-term complications of diabetes—such as nephropathy that can cause kidney failure, retinopathy that can threaten vision, and neuropathy, an often painful nerve disorder—are a result of the diabetes itself or of excess glucose in the blood. The DCCT seeks to resolve this controversy and show whether more intensive treatment can prevent or delay complications.

What treatments are provided?

Traditional treatment (called "standard" in the DCCT) involves one to two insulin injections a day. In the trial, the goal is to maintain clinical well-being and long-term blood glucose levels within the usual range for conventionally treated Type I people.

A newer form of treatment (called "experimental" in the DCCT) that has entered widespread use in recent years is more intensive. It involves three or more insulin injections a day or the use of a device, called an insulin pump, which continuously delivers small amounts of insulin day and night, more closely mimicking the body's normal function. The goal for this group is to maintain long-term blood glucose control as close to normal—non-diabetic—levels as possible.

DCCT volunteers are assigned to either traditional or intensive treatment and visit their center for regularly scheduled medical evaluations. During the five to seven years they participate, they receive expert medical care for their diabetes, including the most sophisticated monitoring for complications, as well as insulin and other supplies needed, all *at no cost.*

What will the results show?

The DCCT already has shown that a significant difference in blood glucose levels can be achieved between the two treatment groups. At the end of the study, doctors will be able to assess whether or not intensive treatment can help prevent or slow the development of diabetic complications.

Are volunteers still needed?

Yes! Volunteers must have had insulin dependent diabetes for 15 years or less, be taking one or two insulin shots a day, and be between the ages of 13 and 39. For pre-screening and information on nearby clinical centers, volunteers are urged to call our toll-free numbers.

In the U.S. 800-522-DCCT In Canada 800-533-DCCT

Press Spokesperson: David Nathan, M.D., *Chairman,* DCCT Publications/Presentations Committee, Massachusetts General Hospital, (617) 726-2875.
Press Liaison: Diana Benzaia, Wordcrafters Unlimited, (212) 866-0661.

Steering Committee Chairman

DIABETES CONTROL AND COMPLICATIONS TRIAL

May 5, 1987

Jane Smith
11111 Main Street
Rockville, MD 20852

Dear Ms. Smith:

We are delighted that you have expressed an interest in acquiring further information about the Diabetes Control and Complications Trial (DCCT). This trial is one of the most important studies in the history of diabetes research. If you decide to become a volunteer in this study, you may be able to help change the way diabetes is treated. Furthermore, during the five to seven years you participate, you will receive expert medical care for your diabetes at no cost, including insulin and all other treatment supplies that you need to care for your diabetes.

The minimum qualifying criteria are that you must:

- o have had insulin-dependent diabetes for more than one year and less than 15 years;
- o be between the ages of 13 and 39;
- o have no major complications of diabetes;
- o (for women) not be planning to become pregnant for at least two years.

If you meet these criteria, we strongly encourage you to contact the Trial Coordinator of the clinical center that we have indicated on the attached list. She will be able to answer your questions in greater detail. She will make an immediate appointment, at your convenience and at no obligation, to show you a slide presentation about the study.

Also enclosed is a pamphlet which provides further details about the study.

Again, we deeply appreciate your interest in the DCCT.

Sincerely,

Oscar B. Crofford

Oscar B. Crofford, M.D.
Chairman,
DCCT Steering Committee

CHAPTER 5

CLINICAL CENTER PROCEDURES

5.1 MEDICAL STAFF AND RESPONSIBILITIES

Each clinical center should have at least two, but not more than four, permanent physicians responsible for the medical care of the subjects participating in this trial. This does not include consulting staff necessary for the collection of baseline and follow-up data, such as the ophthalmologist, neurologist and psychiatrist/psychologist. The group of physicians responsible for patient care under this Protocol should have a system enabling availability 24 hours a day, seven days a week.

5.1.1 Patient's Personal Physician

Each subject in the trial should be assigned to a single physician member of the trial team. This physician will have overall responsibility for the medical care of that patient including history and physical examinations required by the Protocol, guidance and reinforcement necessary to achieve and maintain the aims of the patient's study group, reinforcement necessary for adherence to the Protocol, and management of intercurrent events. Many of these functions may be carried out by the nurse clinician under the supervision of the responsible physician. The patient's personal physician should discuss with the Principal Investigator any occurrence which might mandate deviation from the Protocol, or any patient requests for deviation from the Protocol. The physician will also be responsible for discussing with each patient his/her progress and results, as per the guidelines of the Manual of Operations.

5.1.2 Principal Investigator

The Principal Investigator is responsible for the overall operation of the Protocol within each center. He/she will oversee the operation of each individual team member and periodically monitor each member's performance. The Principal Investigator will be responsible for failure to adhere to the Protocol by either subjects or staff. He/she is responsible for any local decisions related to deviation from the Protocol, and should personally communicate these to the Coordinating Center. He/she is responsible for the hiring and training of new staff, informing the Coordinating Center and the NIDDK of any changes in staff,

and the appropriate distribution and accounting of funds allocated for this trial. In his/her absence, the Co-Principal Investigator will function as the Principal Investigator, including attending national DCCT meetings.

5.1.3 Other Physicians

The ophthalmologist is responsible for performance of ophthalmalogic examinations necessary for eligibility and endpoint analysis, as outlined in appropriate sections of the Manual of Operations and for the completion of the necessary forms related to these procedures.

Similarly, the neurologist is responsible for the performance of the necessary examinations outlined in the Manual of Operations, and the completion of the necessary forms.

The psychiatrist/psychologist is responsible for the performance of the necessary psychological assessments, as outlined in the Manual of Operations and should communicate to the responsible physician any change in psychological status which might require deviation from the Protocol, or impair compliance to the treatment regimen or adherence to the Protocol.

5.2 TRIAL COORDINATOR

Each clinical center should have one individual designated as the Trial Coordinator. The Trial Coordinator will be responsible for the day-to-day operation of the Protocol, as outlined in the following sections, and should devote full time to the DCCT. The Trial Coordinators Handbook was created by the Trial Coordinators to contain only information regarding the duties of the Trial Coordinator or Nurse.

5.2.1 Scheduling Visits

The Trial Coordinator should schedule each follow-up or interim visit for subjects in both standard and experimental groups. Visits should be scheduled within the allowable window for the designated date and visit type, and at least two weeks prior to the date of the visit. See Chapter 6 for the description of visits and their windows. The coordinator should find a time suitable for the patient and all necessary personnel from the center, and arrange a specific time and location for the visit to take place.

Scheduled visits should be confirmed with the patient by mail at least two weeks in advance, and by phone two to three days before the visit.

5.2.2 Preparing for a Patient's Visit

In preparing for a patient's visit, the Trial Coordinator should be certain that all center personnel necessary for that visit are aware of the specific time and place for the visit. The Trial Coordinator should review with each team member the procedures necessary during the visit and be certain that all the necessary forms and equipment are available. An orderly schedule for each visit should be prepared so that the visit can be completed as efficiently as possible and without confusion. Long periods of waiting during the visit should be avoided.

5.2.3 General Visit Procedure

At each visit, the subject will be met by the Trial Coordinator to review the procedures and schedule for that visit. Any questions or concerns about the procedures to be performed should be addressed before the visit. The Trial Coordinator should do everything possible to keep the visit on schedule. Each team member should perform the necessary tasks for that visit, as outlined in the appropriate chapter of the Manual of Operations, and complete the necessary forms. Forms and other information should be returned to the Trial Coordinator. Prior to the termination of the visit, the patient should again meet with the Trial Coordinator and review the progress of the visit. This will assure that all necessary aspects of the visit have been completed prior to the patient leaving, thus avoiding the need for a return visit. The coordinator will be responsible for sending necessary laboratory work and data to the central laboratory, local laboratory or Coordinating Center.

5.2.4 Checking Forms

All forms from a given patient visit should be returned to the Trial Coordinator as soon as possible. The coordinator will check all forms for the following:

1. Completeness: All items should be appropriately answered. If the information is not available, this should be noted in the margin by writing NA next to the item.

2. Internal Consistency: Some items will involve branching in which case one or more items should or should not be completed based on the response to a preceding item. Each form should be checked to insure that there is consistency within the branch. For example, a question that includes the phrase "If yes" (to the preceding item) should only be filled out when the preceding item was answered "yes."

3. Numerical Fields: Numerical responses will be edited to identify extreme values which might be due to misplaced decimal points, transposition of digits or other recording errors. In certain

cases, extreme or unusual values may be legitimate in which case a note should be entered into the margin to indicate that the value has been verified as correct.

4. Legibility: All write-in responses must be clearly legible.

After reviewing all of the forms, the coordinator will send them to the Coordinating Center in the weekly mailing.

5.2.5 DCCT Medical File

Each subject in the trial should have a medical file containing DCCT medical records kept for purposes of the trial. This medical record should include notes from each patient contact, results of locally run laboratory tests, summaries of the management of any intercurrent event, and a checklist indicating completion of the various laboratory work, and forms required by this trial. This medical record should be kept up-to-date by the Trial Coordinator, should be kept in files, and separate from the general hospital or clinic records and should be readily available to necessary team members. The patient's personal physician, Principal Investigator, Trial Coordinator, and study nurse should have access to this medical record. However, the record is otherwise confidential except with permission of the Principal Investigator and the subject. In genuine medical emergencies, permission to access the medical records may be waived.

5.2.6 Data Corrections

The need for corrections of data should be kept to a minimum by carefully recording data at the time of collection and review of the forms prior to completion. After the forms have been received at the Coordinating Center, they will be entered into a computer and inspected in detail for completeness and errors. The Trial Coordinator will be contacted by the Coordinating Center if it is determined that a data error has occurred and that the error is attributable to the clinic. Any necessary corrections should be discussed directly with the responsible team member. The appropriate form should be completed again and note should be made that this represents a correction of previously submitted data. The Coordinating Center should be contacted by mail about any correction of data.

5.2.7 Other Responsibilities

In addition to the above, the Trial Coordinator should perform the following duties:

1. Notify the Coordinating Center of all personnel changes within the clinic, including positions of responsibility in affiliated units.

2. Maintain an inventory of all DCCT supplies (including those required by affiliated units) and reorder supplies as necessary.

3. Maintain a file of all general DCCT correspondence from the Coordinating Center, central laboratories and units.

4. Maintain a calendar of forthcoming study related events such as meetings.

5. Obtain death certificates, autopsy reports, and other pertinent information on deceased patients, and perform other aspects of patient followup as directed by the Principal Investigator.

6. Insure proper mailing of specimens, photographs, and assessments to the Central Biochemistry Laboratory, the Central Ophthalmologic Reading Unit, Central Neurobehavioral Coding Unit, Central ECG Reading Unit, Central Nutrition Coding Unit, and Central Autonomic Coding Unit.

7. Contact the participant and the Principal Investigator about any missed visits, and complete the form for a missed clinic visit.

8. Take steps whenever possible to encourage patient adherence. (See Chapter 20, Compliance/Adherence Procedures.)

5.3 DIETITIAN

The dietitian is responsible for conducting an in-depth nutritional history on all DCCT patients at baseline, at follow-up annual visits, at two, five year and the last annual visit which will meet specific criteria as stated in the Manual of Operations, Chapter 16, Dietary Procedures.

Further responsibilities include contact with patients for the purpose of maintaining an individualized meal plan which provides for the total nutritional needs of the patient and facilitating the goals of the treatment group intervention strategies.

CHAPTER 6

VISIT PROCEDURES

6.1 INTRODUCTION

6.1.1 Overview

Patients who are candidates for participation in the DCCT are examined for eligibility and their entry status is documented during a series of evaluation examinations. The evaluation examinations may be scheduled and completed in any order. However, evaluation forms and materials must be received and processed at the Coordinating Center to document that no more than four months have elapsed from the date of the first examination or procedure to the date of completion of the randomization visit. In addition, certain baseline laboratory specimens must be collected within the two weeks prior to randomization (see below).

At the randomization visit, the Coordinating Center is telephoned to obtain the patient's treatment assignment and the patient officially enters the study. Thereafter, the patient is expected to return to the clinical center for regularly scheduled endpoint (follow-up) examinations for five to eight years.

The DCCT Protocol calls for masking the results of outcome determinations from both patients and investigators. This includes the results of eligibility screening. The only exception is hemoglobin A_{1c} results in experimental group patients. Masking serves: to prevent drawing premature conclusions about study questions on the basis of individual patient or single DCCT center experiences; to avoid unwarranted crossovers from one treatment regimen to the other or dropouts from the Trial; to avoid introduction of patient or staff bias in management of blood glucose control. For these reasons, all samples for measurements of outcome data are transmitted to central units in masked fashion. These units include the Central Ophthalmologic Reading Unit, the Central Biochemistry Laboratory, the Central Autonomic Coding Unit, the Central Neurobehavioral Coding Unit, and the Nutrition Coding Center.

The schedule of patient visits and a summary of the important features of each examination are outlined in this chapter. Resolution of problems that may be encountered during completion of examinations is also discussed. Table 6.1 presents the Schedule of Patient Evaluations for Endpoint Analysis. Table 6.2 is an outline of Visit Organization and Time Windows for Scheduling Visits. Table 6.3 is the list of Screening, Eligibility and Baseline Tests and Procedures. Table 6.4 is a summary of

the Evaluation Schedules. Table 6.5 summarizes the allowable actions for repeating eligibility tests. The DCCT Examination and Forms Schedule is Table 6.6.

Guidelines for staff and patient interactions are given in Section 6.1.2. Terms used in this chapter are defined in Section 6.1.3. The features of each examination are discussed in subsequent sections.

6.1.2 Guidelines for DCCT Staff and Patient Interactions in the Course of Outcome Determinations

Although official recording and interpretation of outcome measurements is carried out in the central units, in some instances the process of data collection makes it unavoidable that certain DCCT staff will see outcome data before it is transmitted centrally. Examples include visual acuity testing, inspection of fundus photographs for quality prior to submission to the Central Ophthalmologic Reading Unit, measurement of nerve conduction times, neurobehavioral testing, neurologic exam, SMAC-20, urinalysis, etc. In these circumstances, patients (and possibly other DCCT staff members) will naturally be curious as to the results. It is therefore important that neither by manner or speech, information should not be provided unnecessarily or inappropriately. If in the process of data collection a staff member is asked for information by a patient, he/she should respond by reminding the patient that all data collected is sent to a central source for analysis and interpretation and that no information is available locally. The patient should be reassured that outcome data will be examined promptly at central units and that any adverse results which would require a change in treatment will be immediately transmitted to the DCCT center for appropriate action (see Chapter 6).

It is equally important that other DCCT staff members, including the Principal Investigator, should not be informed spontaneously of any perceived change in results from inspection of data by a technician or by the M.D./Ph.D. in charge. Incomplete data or imcomplete assessments transmitted casually to some or all other staff members can only generate rumors and speculation that may impact adversely on carrying out the DCCT protocol. All of us can be influenced by such fragmentary information which could lead us to alter a patient's treatment when no change is called for by the protocol.

On the other hand, if a patient complains of visual symptoms, of neurological symptoms, or of mental symptoms to the corresponding technician, that technician should promptly report such symptoms to the ophthalmologist, neurologist, psychiatrist, or psychologist, as the case may be. In addition, the Trial Coordinator and/or diabetologist caring for that patient should be info med of the patient's complains.

A decrease in visual acuity (the ophthamologist will decide if the visual acuity change is real) not perceived by the patient should be immedidately communicated to the opthalmologist. If the latter decides

that the loss of vision is not due to diabetic retinopathy, he/she will inform the patient and appropriate DCCT staff, and will recommend treatment. If loss of visual acuity is thought to be due to diabetic retinopathy, the ophthalmologist will follow treatment recommendations outlined in the Manual of Operations. Neither the patient nor the appropriate DCCT staff should be informed until an ophthalmological course of action has been agreed upon.

Elevation of blood pressure above 140/90 on two consecutive readings within one month constitutes an outcome for hypertension. Of necessity, the patient and all pertinent staff must be informed of this, since specific treatment is required.

Sporadic measurements of serum creatinine or urine protein may become available locally in the course of attending to other medical problems. These should be recorded in the patient's chart. If such results are abnormal, reversible causes other than diabetic nephropathy must be sought. Hence, the patient and appropriate staff need to be informed to the extent necessary to account for the additional diagnostic procedures or for therapy, should these be indicated.

6.1.3 Definitions

6.1.3.1 Patient Identification Number

A permanent DCCT identification number (ID No.) is assigned to each patient who appears at a clinical center for one or more of the evaluation examinations. The patient identification numbers are assigned in order on DCCT Form 001, Initial Clinic Visit. The five-digit patient identification number consists of two digits which designate the clinical center in which the patient is first screened for eligibility and a three-digit code to identify the patient. At the start of screening, a patient is assigned the next available five-digit code for that clinic. Once a number has been assigned to a particular patient it remains associated with this patient even if he/she does not enter the study or if he/she later transfers to another clinical center. If a patient is ineligible or excluded on the basis of the results of the screening exams, refer to Table 6.5 for a list of screening exams that may be retested during the four-month evaluation period (retakes). Some patients who are excluded may be restarted six months later. If a patient is restarted, a new identification number is assigned.

Issuance of a patient identification number does not imply that the patient is enrolled in the DCCT. Entry into the study takes place when the patient is randomized.

6.1.3.2 Patient's Initials

The patient's initials, comprising the patient's first, middle and last initials, constitutes a second patient identifier. If the patient has no middle name or initial, an "X" is used as the middle initial. With one exception, the initials identifier, once determined, is never changed, although the patient may change his/her name during the course of the study. If a patient is ineligible and then restarted with a new identification number and his/her initials have changed, use the new initials.

6.1.3.3 Examination Date

Some examination procedures may require more than one day to complete. The date an examination is begun is regarded as the examination date. A number of procedures may be associated with each examination. An examination is not regarded as complete until all procedures have been completed.

6.1.3.4 Follow-up Visit Number

The follow-up visit number is the number of quarters (three month time period) post randomization. This number is sequentially numbered from 0 for baseline, 1 for first three month visit, 4 for first annual visit, 8 for second annual visit, through 40 for tenth annual visit.

0 = Baseline	4 = 12 months	9 = 27 months
1 = 3 months	.	.
2 = 6 months	.	.
	8 = 24 months	40 = 120 months

6.1.3.5 Treatment Allocation

Each patient who enters the DCCT is randomly assigned to one of the treatment groups. A treatment allocation is issued only after all criteria for entry into the study have been satisfied and are documented at the Coordinating Center.

6.1.3.6 Informed Consent

The potential participant begins the informed consent process by viewing the DCCT audiovisual presentation. Each patient who is to be

further evaluated for eligibility for the DCCT is presented with the patient information documents and the first Informed Consent Form (DCCT Form 031). See Chapter 7 for more details concerning the procedures for orientation of the patient and for obtaining the patient's consent to be screened, randomized, managed and followed in the study.

6.1.3.7 Date of Randomization

The patient's official date of randomization into the DCCT is defined as the date the treatment assignment is given by the Coordinating Center. This date is considered the patient's baseline. This date must be within four months of the first eligibility test. If any exceptions are necessary, the clinic should clarify the situation with the Coordinating Center.

Most importantly, this date is the marker used to characterize a subject's duration of IDDM; for example, a subject with no retinopathy and who is a candidate for the primary prevention trial should be at or have not yet reached his/her five year anniversary of IDDM at the time of randomization.

6.1.3.8 HOLD Conditions

On certain evaluation visit forms, there are boxes marked "HOLD" which may be checked during form completion. These boxes indicate a condition which makes the patient temporarily ineligible for the study. There should be an explanation made to the patient of the cause for temporary ineligibility and information on the patient should be filed so that he/she can be contacted at a later date.

6.1.3.9 STOP Conditions

On the Baseline Medical History and Physical Examination Form (DCCT Form 002) and the Baseline Ophthalmic Examination and Ocular History (DCCT Form 008), for example, there are a number of responses which are marked "STOP" to indicate that an exclusion criterion was encountered for the patient being evaluated. The term "STOP condition" refers to these exclusion criteria. STOP conditions are summarized on the DCCT Eligibility and Exclusion Checklist, (DCCT Form 038).

6.1.3.10 Patient Accession Number Schedule

The Coordinating Center provides patient schedules to the clinics to identify visit windows and to assist in proper use of accession labels for laboratory samples. A listing of regularly scheduled visits

indicates which forms are to be completed and what the allowable window is for that visit. A second sheet highlights laboratory information including visit numbers, visit target dates, samples to be collected, samples to be quality controlled, and the accession numbers to use for each sample. Pre-printed self-adhesive labels are provided by the Coordinating Center and accompany these schedules.

6.2 ROUTINE PROTOCOL VISITS

6.2.1 Evaluation

After preliminary screening, at the start of the first evaluation examination, the prospective participant will be asked for written consent to undergo the baseline history and physical examination and other eligibility evaluations. All examinations will be scheduled to coordinate with other pre-randomization requirements to optimize convenience for prospective study participants and to minimize cost by performing first those tests which are least expensive and most likely to yield abnormal results (e.g., dipstick screen for urinary protein before urinary albumin by radioimmunoassay).

All assessments required for eligibility are outlined in the Evaluation Schedule, Table 6.4. The criteria to be met by each patient for entrance into the DCCT are described in Chapter 8. Assessments to document baseline status are also included in this schedule; it is the outline of all examinations and assessments which must be completed for each patient before he/she is randomized. No more than four months should elapse between the date of the first examination or procedure to the date of completion of the randomization visit; baseline assessments for the HbA_{1c}, blood glucose profiles, and lipids must be performed within two weeks of randomization. All baseline laboratory specimens have to be reviewed by the appropriate central unit and notification of their suitability relayed to the Coordinating Center before a patient can be randomized. All other baseline assessments (such as ANS tapes, diet histories, neurobehavioral batteries) must be present at the appropriate central unit before the patient can be randomized.

6.2.1.1 Initial Visit

During the patient's initial visit to the clinic, he/she is introduced to the DCCT and the local clinical center and the informed consent process is begun (see Chapter 7, Informed Consent Process).

The Initial Clinic Visit Form (DCCT Form 001) is filled out, whether or not any STOP or HOLD conditions are encountered. If any HOLD conditions are encountered, the patient's name is filed for future contact and he/she is referred to a physician if necessary.

The potential participant views the DCCT audiovisual presentation and receives the first Informed Consent Form, the Volunteer Information Handbook and the Manual of Diabetes Tests, Terms and Special Procedures. This visit should be an informational and exciting introduction to the DCCT for each potential participant.

6.2.1.2 Medical History and Physical Examination

The Baseline Medical History and Physical Examination Form 002 should be completed during the following visit to the clinical center after the patient signs the first Informed Consent (DCCT Form 031).

Certain questions on the Baseline Medical History and Physical Examination Form specifically refer to eligibility criteria and have answers which are marked "STOP." If a box with STOP is checked, the patient is ineligible for the DCCT. Note that some of the exclusion criteria will only temporarily exclude the patient. If the patient is only temporarily excluded, he/she should be encouraged to return to the center for another evaluation once the excluding condition has been removed.

Some of the questions on this form call for written specification of medications, conditions, etc. For these questions, type or neatly print the answers. Do not use abbreviations.

Some questions ask you to specify the average number of times an event has occurred (e.g., episodes of hypoglycemia) or the amount of a substance that was used (e.g., amount of alcohol consumed). For these items, you should round the value to the nearest whole number. For example: Two and one-half glasses of wine is reported as three glasses. Put zeros before the number if necessary to fill in extra boxes.

Clarifications of several of the questions on the Baseline Medical History and Physical Examination Form are given in the text that follows:

1. Predominant race/ethnicity. Use the following definitions:

   a) American Indian or Alaskan Native -- A person having origins in any of the original peoples of North America, who maintains cultural identification through tribal affiliation or community recognition.

   b) Asian or Pacific Islander -- A person having origins in any of the original peoples of the Far East, Southeast Asia, the Indian subcontinent, or the Pacific Islands. This area includes, for example, China, India, Japan, Korea, the Phillipine Islands, and Samoa.

   c) Black -- A person having origins in any of the black racial groups of Africa.

d) Hispanic -- A person of Mexican, Puerto Rican, Cuban, Central or South American or other Spanish culture of origin, regardless of race.

e) White -- A person having origins in any of the original peoples of Europe or the Middle East.

2. Occupation.

a) Professional, technical, and similar workers -- Includes aeronautical, agricultural, chemical, civil, electrical, industrial, mechanical, metallurgical, mining and sales engineers, and agronomists and metallurigists, chiropractors, dentists, dietitians, healers, medical and dental technicians, nutritionists, optometrists, osteopaths, pharmacists, physicians and surgeons, professional nurses, psychologists, therapists, veterinarians, school principals, supervisors, and teachers, accountants and auditors, actors, airplane pilots and navigators, architects, artists and art teachers, athletes, authors, clergymen, college presidents, professors, and instructors, dancers, dancing teachers, designers, draftsmen, editors, technicians, entertainers, farm and home management advisors, foresters and conservationists, funeral directors and embalmers, judges, lawyers, librarians, musicians and music teachers, natural scientists, reporters, sports instructors, and officials and surveyors.

b) Managers, officials, and proprietors -- Includes buyers, building managers and superintendents, credit men, lodge, society and union officials, postmasters, public administration inspectors and officials, purchasing agents and buyers, railroad conductors, ship officers, pilots, pursers, and engineers.

c) Craftsmen, foremen, and similar workers -- Includes brickmasons, carpenters, cement and concrete finishers, electricians, excavating, grading, and road machinery operators, painters (construction and maintenance), paperhangers, pipefitters, plasterers, plumbers, roofers and slaters, stone masons, structural metal workers, tile setters, repairers of air conditioning, heating, and refrigeration equipment, airplanes, automobiles, office machines, radios and television, railroad cars, blacksmiths, boilermakers, coppersmiths, die makers and setters, forgemen and hammermen, heat treaters, machinists, metal jobsetters and molders, metal rollers and roll hands, millwrights, pattern and model makers, (except paper), sheet metal workers, tinsmiths, toolmakers, bakers, bookbinders, cabinetmakers, compositors, cranemen, derrickmen, electrotypers, engravers, furriers, glaziers, goldsmiths, inspectors, jewelers, lens grinders and polishers, lithographers, locomotive engineers, locomotive firemen, log and lumber scalers and graders, loom fixers, millers, motion picture projectionists, opticians, piano and organ tuners and

repairmen, plate printers, printing pressmen, shoemakers (except in factories), silversmiths, stereotypers, stationary engineers, stone carvers, stone cutters, tailors, telegraph and telephone linemen and servicemen, typesetters, upholsterers, watchmakers, window dressers.

d) Clerical and similar workers -- Includes clerk-typists, public stenographers, typing pool supervisors, secretaries, baggagemen, bank tellers, bill and account collectors, bookkeepers, cashiers, dispatchers and starters of vehicles, express messengers, file clerks, insurance adjusters, insurance examiners and investigators, library attendants and assistants, mail carriers, messengers and office boys, office machine operators, payroll and timekeeping clerks, postal clerks, physician's and dentists's office attendants, railway mail clerks, receptionists, shipping and receiving clerks, stock clerks, storekeepers, telegraph messengers, telegraph operators, telephone operators, ticket, express, and station agents.

e) Sales workers -- Includes advertising agents and salesmen, actioneers, demonstraters, hucksters, insurance agents and brokers, insurance underwriters, lottery ticket agents, lottery ticket sellers, newsboys, peddlers, real estate agents and brokers, stock and bond salesmen, salesmen and sales clerks in retail trade.

f) Operative and similar workers -- Includes bus drivers, chauffeurs, deliverymen, routemen, taxicab drivers, truck and tractor drivers, apprentices, asbestos and insulation workers, assemblers, auto service and parking attendants, blasters, boatmen, bus and street railway conductors, canalmen, furnacemen, graders and sorters in manufacturing, laundry and dry cleaning operatives, lockkeepers, meat cutters, metal heaters, milliners, mine operatives and laborers, motormen, oilers and greasers, packers, painters (except construction and maintenance), photographic process workers, powdermen, power station operators, railroad brakemen and switchmen, sailors, sawyers, sewers and stitchers in manufacturing, smeltermen, stationary firemen, surveying chainmen, rodmen and axmen, textile knitters, textile spinners, textile weavers, welders and flame cutters, wrappers.

g) Service workers -- Includes bailiffs, bridge tenders, constables, detectives, firemen (fire protection), guards, marshals, policemen, sheriffs, watchmen, cooks, counter and fountain workers, waiters, attendants and ushers in amusement places, barbers, bartenders, bootblacks, boarding and lodginghouse keepers, elevator operators, hairdressers, housekeepers and stewards, janitors, kitchen workers, porters, sextons.

h) Laborers -- Includes carpenters' helpers, car washers, fishermen, garage laborers, gardeners, longshoremen, lumbermen, oystermen, raftsmen, stevedores, teamsters, truck drivers' helpers, warehousemen, woodchoppers.

i) Farmers -- Includes owners, operators, tenant farmers, and sharecroppers.

3. Diabetes History

Interpretations of questions C7, C8, C9 and C10 on DCCT Form 002:

a) Question C7 -- "Hospitalizations" implies overnight admission to the hospital; an emergency ward visit that did not result in hospitalization does not apply.

b) Question C8 -- The number of episodes during which the patient "lost consciousness or experienced seizures" may be only approximate if the patient was not observed during all episodes. Should an event involving impaired consciousness not be remembered by the patient but the observations of another person indicate that neither full loss of consciousness nor seizures occurred, then it would not be included in this category.

c) Question C9 -- The need for "professional medical assistance" should be interpreted as signifying that the person assisting the patient felt that oral glucose administration was either impossible to perform or inadequate to treat the episode effectively. The administration of intravenous glucose or parenteral glucagon should be considered "professional medical assistance" whether or not the person providing the treatments had formal medical training.

d) Question C10 -- This category implies that the patient required assistance to obtain oral treatment for hypoglycemia either because he was too symptomatic to help himself or because he failed to recognize the need for treatment.

4. Psychiatric Review of Systems

The psychiatric review of systems section is designed to highlight important psychiatric problems which might interfere with performance during the trial. These topics are not exhaustive and supplement earlier questions on drug and alcohol abuse and medication history. Thus, answers to earlier questions may already have identified possible psychiatric problems not sufficient to exclude the patient.

The diagnostic topics are not designed as exclusion criteria. Rather they serve as landmarks, to heighten awareness of the medical team and depending on the level of concern raised, could

lead to further interviewing by the nurse, diabetologist and/or health care professional.

Please note these questions are widely used in medical histories and survey interviews. If treated matter-of-factly as part of the interview, the patient will perceive them as a standard part of our concern and interest in them and their lives.

The questions which follow are keyed to the topic areas. They are suggestive or useful lines of inquiry but are designed to be adapted to your own interview style. They are not exhaustive.

a) This question is used to identify a history of psychiatric treatment and may be followed by inquiries about the nature of the problem, specific symptoms, their persistence, and the timing of the treatment. Subsequent items identify diagnostic and symptomatic categories for specific inquiry.

b) Does the patient have a history of the following:

i) Have you ever considered yourself a nervous person? How disruptive do you consider these feelings?

ii) Some people have phobias or unreasonable fears. Do you have any? Do they limit your activities?

iii) This section is designed to explore problems related to anorexia nervosa and bulimia. These eating problems are more common in young women and are especially important for this group.

I would like to ask a few questions about eating problems you might have had with weight. Have you ever thought you were too fat or in danger of getting too fat? Have your friends or family thought you had become too thin? Have you ever binged and then tried to lose weight by vomiting?

iv) In your lifetime, have you ever had two weeks or more when you felt very sad or depressed or lost all interest in things you usually care about? Were these periods (this period) accompanied by symptoms like weight loss, troubled sleeping, extreme fatigue, trouble concentrating or feeling worthless?

v) A history of suicidal thought or action can be asked in a straightforward manner by asking the following questions which may flow directly out of preceding questions about depression:

Has there ever been a period of two weeks when you have felt like you wanted to die?

Have you ever felt so bad that you thought of committing suicide?

Have you ever attempted suicide?

vi) Have you ever had any legal problems? If yes, have these involved criminal charges? If yes, please describe.

c) Since this section does not include automatic exclusions, this question may only be answered "yes" after further data is gathered.

5. Measurement of Height and Weight.

These measurements must be obtained in an accurate and reproducible manner at the evaluation visit, quarterly clinic visits and annual visits.

a) Devices:

i) Measurement of weight -- a standard weight scale that has been calibrated regularly is acceptable. Calibration will be performed at least once per year. It is recommended that the patient be weighed on the same scale throughout the study, if possible. The 0 adjustment should be checked before each measurement.

ii) Measurement of height -- The widely available measurement rod attached to a weight scale found in many offices is not accurate for height measurement. Two types of measurement devices are recommended. One consists of a metal tape measure or a wooden ruler that is attached permanently in a vertical position on the wall or that is attached to a wooden board that is, in turn, mounted permanently on the wall. For this type of device, a horizontal board is necessary; the board is placed on the patient's head in a perfectly horizontal position and the height is read directly at the intersection of the board and the vertically mounted measuring tape or ruler (a carpenter's square or a wooden box with a handle work well for this purpose). The second type of measuring device is called a stadiometer. This uses a sliding horizontal board which runs up and down on a vertical column using a rack and pinion mechanism with a counter weight attached to give direct readout of height.

b) Procedure for measurement of height -- For the actual measurement, the patient will stand erect with heels, buttocks, thoracic spine and head against the vertical surface with the feet slightly apart and eyes looking straight ahead. He/she will be asked to take a deep breath and stretch as tall as possible, keeping the shoulders relaxed. Slight upward pressure can be applied gently on the mastoid processes to

assure the position is attained. It is important to be certain that the patient's heels are flat and that the knees are straight. If a vertically mounted metal tape or ruler is used, a horizontal board will be placed on the top of the head as the patient looks straight ahead; the height is read directly at the intersection between the horizontal board and the certically mounted tape measure or ruler. If a stadoimeter is used, the horizontal device will be lowered to the top of the head and the measurement will be read directly from the digital counter. With both methods, it is important that the height be measured several times until successive measurements are no further apart than 0.2 cm. It is recommended that, if possible, the same individual measure study patients throughout the study, although with strict attention to the measurement procedure, reproducible results should be attainable by any skilled measurer.

c) Procedures for measurement of weight -- It is recommended that the patient's weight be measured with the patient in a hospital gown and in stocking feet. It is recommended that he/she be weighed on the same scale for the entire study. The 0 adjustment should be checked before each use.

d) Procedures for determination of eligibility -- In order to determine if the potential adult participant meets the eligibility criteria for weight (Section 8.2.1.15), a determination should be made of his/her body frame by elbow breadth. The patient's weight should be compared to the appropriate category of Tables 8.2a and 8.2b.

To make an approximation of frame size, have the patient extend his/her arm and bend his/her forearm upwards at a 90 degree angle. Fingers should be kept straight and the inside of the wrist turned away from the body. Measure the elbow breadth at the two prominent bones on either side of the elbow with a caliper.

These tables list the elbow measurements for medium-framed men and women of various heights. Measurements lower than those listed indicate a small frame and higher measurements indicate a large frame.

Definition of Medium Frame

MEN

Height	Elbow Breadth
5'1" - 5'2"	2 1/2" - 2 7/8"
5'3" - 5'6"	2 5/8" - 2 7/8"
5'7" - 5'10"	2 3/4" - 3"
5'11" - 6'2"	2 3/4" - 3 1/8"
6'3"	2 7/8" - 3 1/4"

WOMEN

Height	Elbow Breadth
4'9" - 5'2"	2 1/4" - 2 1/2"
5'3" - 5'10"	2 3/8" - 2 5/8"
5'11"	2 1/2" - 2 3/4"

6.2.1.3 Other Evaluation Assessments

See the Evaluation Schedule (Table 6.4) and the appropriate Chapter in the Manual of Operations for details concerning procedures and forms to be filled out during each evaluation module.

1. Laboratory

The evaluation examinations include local clinical laboratory procedures which are given in Table 6.3. In addition, some specimens will be sent to the Central Biochemistry Laboratory (CBL) for determination of eligibility and to serve as baseline data.

2. Ophthalmologic

The evaluation ophthalmologic examination consists of the following standardized procedures:

a) Visual acuity;

b) Intraocular pressure measurement;

c) Slit-lamp and ophthalmoscopic examinations;

d) Stereo fundus photography consisting of seven standard fields;

e) Stereo fluorescein angiography only in consenting patients who are being screened for the primary prevention trial.

Original fundus photographs and angiograms will be sent to the CORU for determination of photographic quality and patient eligibility. Copies of the photographs and angiograms will be maintained at the clinical centers (Chapter 13).

3. Renal

The evaluation renal examination consists of the following standardized procedures:

a) Preliminary urine dipstick screen, urinalysis (UA) and urine culture (UC). If UC reveals 10^5 colonies per ml, a repeat culture is obtained. UC is mandatory in females and will be done for males when indicated by UA (2-4 WBC/hpf).

b) Microalbuminuria (four-hour timed collection) (Chapter 12).

c) Serum albumin.

d) Creatinine clearance (Chapter 12).

e) Serum creatinine.

Urine and serum will be sent to the CBL for analysis.

f) The baseline renal examination consists of the following standardized procedures:

i) 24-hour timed urine collection (Chapter 12).

ii) 125-I iothalamate glomercular filtration rate.

4. Neurologic

The baseline neurologic examination consists of the following standardized procedures:

a) Neurological history and physical examination (Chapter 17).

b) Standing and supine blood pressures and pulse (Chapter 17).

c) Sample of autonomic nervous system function tests (RR-variation on EKG) (Chapter 17).

d) Noninvasive nerve conduction studies (Chapter 17).

Autonomic Nervous System Function Tests (RR-variation on EKG) will be centrally read at the Central Autonomic Coding Unit (CACU).

5. Cardiovascular

The evaluation cardiovascular examination consists of the following standardized procedures:

a) History and physical examination (Chapter 18).

b) Peripheral vascular history and physical examination (performed as part of the medical history and physical examination) (Chapter 18).

c) Resting ECG.

Results will be documented on the Resting Electrocardiogram Mailing List, DCCT Form 053, and the Eligibility and Exclusion Checklist (DCCT Form 038). All ECG's are mailed to the Coordinating Center. ECG's determined to be abnormal on the basis of local reading may be sent to the Central ECG Reading Unit for confirmation. All EKG's on eligible patients will be mailed to the Central ECG Reading Unit for coding. These data will be sent to the Coordinating Center (see Chapter 18).

6. Psychological

The evaluation psychological assessment includes:

a) Neurobehavioral Assessment: A battery of neurobehavioral measures will be performed. The scope of the assessment includes: learning, memory, problem solving, and visuoperceptual and visuomotor functions. Performance results will be sent to the Central Neurobehavioral Coding Unit (CNCU) for scoring and coding (Chapter 19).

b) Psychological Symptoms: The Symptom Checklist-90-R (DCCT Form 035) will be completed (Chapter 19).

c) Quality of Life: A questionnaire will be completed for evaluation of several areas including social functioning, work and school performance, attitudes toward diabetes and toward the specific demands of the DCCT Protocol. It will include age-specific and developmentally relevant inquiries (Chapter 19).

7. Compliance/Adherence

The pre-randomization compliance/adherence assessment of the DCCT will consist of the following components:

a) Prospective subjects will be screened during a structured session in an effort to evaluate areas that are known to relate to adherence to Protocol requirements and compliance with prescribed regimens. A counseling-educational session with the patient and the family will be required to improve participation through a good understanding of trial procedures. Making use of written and audiovisual aids, a study

representative will also discuss the following areas in detail with the subject and family:

i) expectations regarding the study

ii) mobility

iii) personal availability

iv) family and social supports

v) past history of adherence of treatment regimen

vi) attitude about the DCCT

b) Potential subjects will be given behavioral tasks prior to randomization to evaluate compliance regimens. These tasks will include skills training and assessment of behaviors which are relevant to the protocol of this trial, i.e., insulin injections, urine testing. All subjects will be placed on a regimen similar to standard treatment and will be asked to record, in a diary during a two-week period, a number of tasks to include eating habits, urine testing, time of injections, a 3:00 a.m. blood capillary collection (Chapter 20).

8. Dietary

The dietary evaluation assessment consists of two parts:

a) Interview by the dietitian to assess each candidate's present level of education and potential ability to learn and implement the dietary recommendations necessary for the experimental group. The three-day food record obtained from the behavioral tasks, the research diet history and other techniques may be used to assist this screening process.

b) Collection of data on the dietary habits of each participant by the dietitian using the diet history methodology. The data should be collected in the standardized method described in Chapter 16, then sent to the Central Nutrition Coding Unit for analysis.

6.2.1.4 Forms to be Completed

During evaluation for eligibility, the following forms are to be completed:

Form	Name
001	Initial Clinic Visit
002	Baseline Medical History and Physical Examination
004	Locally-Performed Blood Count and Chemistry
005	Neurologic History and Physical Examination
006	Locally-Performed Urinalysis and Urine Culture
008	Baseline Ophthalmic Examination and Ocular History
011	Randomization Report
012	Personal Information on Study Volunteer (not mailed to CoC)
018	Diet History (completed by dietitian) (send to Coding Unit if patient is to be randomized)
021	Quarterly Clinic Visit (completed at randomization visit)
025	Fundus Photography (completed by photographers)
026	Fluorescein Angiography (completed by photographers)
029	Food Pattern Questionnaire (local use)
030	Food Preparation Questionnaire (local use)
031	First Informed Consent
032	Second Informed Consent
035	Symptom Checklist-90-R (SCL-90-R)
036	Quality of Life Questionnaire
037	Nerve Conduction Studies
038	Eligibility and Exclusion Checklist
045	Volunteer Understanding Questionnaire (Version A)
046	Volunteer Understanding Questionnaire (Version B) (if necessary)
047	Availability, Adherence and Expectation Interview
048	Family Understanding and Expectation Interview
049	Request Behaviors Confidence Questionnaire (completed before and after the two-week behavioral tasks)
056	Clinic Evaluation of Volunteer's Performance on Behavioral Tasks I (Clinic)
057	Clinic Evaluation of Volunteer's Performance on Behavioral Tasks II (Home)
061	Daily Behavioral Tasks Log
062	Three-Day Food Record
070	ANS Documentation Sheet

Neurobehavioral Test Battery

In addition, multiple mailing lists have to be completed to ship photographs, neurobehavioral test results, specimens and data forms to the appropriate central unit. The Eligibility and Exclusion Checklist (DCCT Form 038) must be completed and on file at the Coordinating Center before any patient can be randomized.

6.2.1.5 Missed Visits

A patient missing a scheduled evaluation visit should be contacted as soon as possible (preferably the day of the missed appointment) by the clinic staff and the visit should be rescheduled as soon as possible. Missed visits should be brought to the attention of the Principal Investigator who should take this into account when determining patient eligibility.

6.2.1.6 Eligibility Evaluation Rules

Explicit eligibility definitions, definite procedures for verifying suspect results, and time frames for these procedures were agreed upon by the Study Group. This is important so that exceptions to eligibility rules are not made on a case-by-case basis and the treatment group's actual baseline condition, as opposed to some transition state, can be characterized.

The evaluation period for each patient should not exceed four months from the date of the first examination or procedure to the date of randomization. During that time period, retakes of visual acuity are allowed. The following are allowed under specific conditions: rereads or retakes (but not both) of photographs, and retakes of HbA_{1c}, albuminuria, and cholesterol. During that four-month time period, the following should apply:

HbA_{1c} may be retaken within two weeks if the Principal Investigator thinks the reported value does not reflect the patient's clinical status.

For retinopathy, considering patient and clinic convenience as well as morale and scientific integrity, one reread OR retake is allowed during the initial four month time window exclusively in the situation where a patient has more than five years duration of diabetes and where the investigator feels retinopathy is present, but the CORU has failed to detect it. In the situation where the investigator feels reasonably sure that the photographs show the retinopathy in question, a reread would be requested. In the alternative situation, where the investigator feels that retinopathy was unequivocally present on clinical exam but is not well represented on the photographs, then a repeat set of photographs would be submitted. No rereads or retakes are allowed in patients who are graded as having P_2 retinopathy or worse.

For cholesterol and albumin, apparent mishandling (to be determined by the Director of the CBL) by clinic staff or the CBL are sufficient conditions for retakes. Also, if the local laboratory determination of TSH indicates an elevation, the cholesterol can be retaken to determine eligibility after the TSH has returned to normal. If the reported value for cholesterol is still above the threshold, the patient may be restarted in six months. If the reported value for a retake of albumin is still over the threshold, the patient will be permanently excluded.

If a patient has been declared ineligible, the patient may be restarted six months from the date of the collection of the test that caused ineligibility. However, any patient who has more than minimal retinopathy ($\geq P_2$), elevated albumin, or elevated creatinine may NOT be restarted. This patient is permanently excluded.

In Table 6.5, the definitions of reanalysis or reread, retake and restart are presented. These are actions which are allowable and investigator initiated.

6.2.1.7 Procedures to Restart a Patient

In some situations, a patient who was excluded may be restarted in the eligibility screening process after a six month waiting period.

Another Eligibility and Exclusion Checklist (DCCT Form 038) must be used to document the patient's screening progress.

A baseline examination, test, or procedure which is a measure of a study endpoint (see Table 6.1) and is to be repeated at follow-up visits, must be conducted within four months prior to the day of randomization. Therefore, these examinations, tests, and procedures must be redone. Since the C-peptide test is not a measure of a study endpoint, this test will not need to be repeated for patients with C-peptide less than 0.2 pmol. For patients with duration of IDDM less than five years and with stimulated C-peptide greater than 0.2 pmol but less than 0.5 pmol, however, the C-peptide may be repeated at the annual visit. Therefore, the baseline test must be within the four month window for these patients.

6.2.2 Randomization

Before a patient is randomized, all screening, eligibility, and baseline tests and procedures must be completed (see Table 6.3) and the Eligibility and Exclusion Checklist must be on file at the Coordinating Center. The baseline laboratory specimens must have been received at the appropriate central laboratory and assessed as being in good condition.

DCCT Form 021, Quarterly Clinic Visit, and DCCT Form 011, Randomization Report must be completed during the randomization visit and sent to the Coordinating Center.

The patient must be present at the time of the randomization phone call to the Coordinating Center. There are two reasons for this requirement: First, as noted above, DCCT Form 021 must be completed. Secondly, the patient may be disappointed with the treatment group assignment. If the patient is present, the staff will be better able to detect this disappointment and work to encourage him/her to accept and adhere to the assigned treatment regimen.

6.2.3 Routine Management Visits for Experimental Group

6.2.3.1 Time of Visits

Visits in the experimental group will be weekly until the investigator feels the goals defined for metabolic control have been achieved. Following this, the visits will be monthly, or more frequent if necessary to maintain the goals. The date of the monthly visit should be scheduled within the visit window from the date of randomization, not the date of initiation of treatment. See the patient accession number schedule for visit target dates.

6.2.3.2 Preparation

The clinic staff will notify the patient one to two days prior to the scheduled visit by phone, reminding the patient to bring glucose monitoring records. The Trial Coordinator will also inform the research nurse and, if necessary, the physician or dietitian of the scheduled visit.

6.2.3.3 Features of Visit

These routine management visits will center mainly around discussion of metabolic control including blood glucose determinations at home. Suggestions or changes will be made, and continued education and support given, to aid in achieving the goals of the experimental group.

6.2.3.4 Forms to be Completed

An HbA_{1c} sample will be collected at the monthly visit and sent to the CHL. Routine management accession number labels should be used and the Hemoglobin A_{1c} Mailing List (DCCT Form 055) should be completed.

6.2.3.5 Missed Visits

Missed routine management visits are not as damaging to the overall implementation of the Protocol as missed quarterly endpoint visits (see Section 6.2.4), but may result in inability to maintain the goals of the experimental group or may indicate impending poor compliance with the regimen or adherence to the Protocol. Therefore, missed routine management visits should be handled similarly to other missed visits. The patient should be contacted as soon as possible, and another visit scheduled. The Missed Visit Form (DCCT Form 014) should be completed if the visit does not occur within the specified time window.

6.2.4 Endpoint Visits (Follow-up Visits)

During the course of the study, participants will be asked to undergo a set of regularly scheduled standardized procedures for patient followup and analysis of study endpoints. All visits will be scheduled to coordinate these procedures and examinations with other endpoint requirements in order to optimize convenience for the study participants and to minimize costs. Additional visits may be scheduled as necessary for the clinical care of the patient.

Endpoint visits for the standard and experimental groups will take place every three months. Three-month, six-month, and nine-month visits are termed quarterly visits. Twelve-month visits are termed annual visits. With the exception of annual visits, these visits should take place on an outpatient basis and should be coordinated so that all necessary features of the visit can be performed on the same day, thereby minimizing trips to the center by the patient. Because of the time required for performance of the studies scheduled annually, these visit procedures may require more than one day. These annual visits may be performed either on an inpatient or outpatient basis, depending on the clinical center, but all necessary studies should be performed within the window of the scheduled date for that visit (see Table 6.2). The term "endpoint" refers to the type of data being collected and not to any action with respect to the patient. All patients will be followed for at least five years after randomization.

6.2.4.1 Preparation

In preparation for each endpoint visit, the clinic staff will arrange a date and time appropriate for the patient and assure the availability of any staff or laboratory personnel required for that visit. Any necessary appointments will be arranged with the ophthalmologist, neurologist, psychologist, or dietitian at least two weeks in advance. After the necessary arrangements have been made, the visit will be confirmed by mail with the patient. This written confirmation should be sent two weeks before the visit, and should include the date and time of the visit, the estimated time needed to complete the visit, and a

specific schedule for the visit including times and locations for seeing various trial team members. This written confirmation should be followed by phone contact with the patient two to three days prior to the scheduled visit. The patient should be reminded to bring urine or self blood glucose monitoring records as well as the Profilset.

At the same time, the staff person responsible for visit scheduling should make certain that the various clinic team members are aware of the date and time of the visit, and have the necessary forms to complete during that visit.

6.2.4.2 General Features of Visit

Each endpoint visit should include the following:

1. Discussion with the physician or nurse responsible for care of the patient regarding the state of metabolic control and the attainment of goals. In the standard group, discussion should center around symptoms of glycosuria and hyperglycemia, and urine test results as the main indicator of metabolic control. The patient should be questioned with respect to frequency of nocturnal urination and thirst, and the frequency with which work or classroom activities are interrupted by the need to urinate or drink fluids. Exercise tolerance should be assessed particularly with regard to declining performance. The frequency and causes of episodes of hypoglycemia should be determined. If first or second priorities of the intervention strategy for the standard group are not being met, discussion should include means to meet these goals within the guidelines outlined in Chapter 9. In the experimental group, discussion should include detailed analysis of results from blood glucose monitoring obtained by the patient and episodes of hypoglycemia since the last visit. Methods should be discussed to best achieve the aims of the intervention strategy for the experimental group within the guidelines of the Manual of Operations.

2. A brief physical examination with particular attention to diabetes management, symptoms of hypo- and hyperglycemia, ketonuria, complications of diabetes, blood pressure, growth parameters, maintenance of body weight, condition of feet, and other assessments felt to be clinically indicated.

3. In the experimental treatment group, a ten- to thirty-minute session with the dietitian, which may include a diet recall when indicated, for discussion of any problem areas or questions related to diet. Standard group patients meet with the dietitian every six months, unless more frequent meetings are required in order for the patient to meet the goals of the treatment group (see Chapter 9).

6.2.4.3 Blood Glucose Control

1. HbA_{1c} to be run in the CHL. (Use the follow-up visit accession number labels.)

2. Collection of blood samples from the quarterly home blood glucose profiles to be analyzed at the CBL. In addition, in the experimental group, recorded results of self blood glucose monitoring corresponding to samples collected for the blood glucose profile.

3. Recorded average number of self blood glucose determinations per week in experimental group.

4. Recorded 3:00 a.m. blood glucose results.

5. Recorded daily insulin dosage: total, basal, and sum of preprandial boluses for experimental group; total, sum of rapid acting, and sum of intermediate or long acting for standard group.

6.2.4.4 Ophthalmologic

Examination schedules for routine ophthalmologic followup and procedures are the same for all patients: baseline, six months, and every six months thereafter.

Original fundus photographs and angiograms will be sent to the Central Ophthalmologic Reading Unit for analysis. Copies of the photographs and angiograms will be maintained at the clinical centers.

There will be two different examination routines. Stereo fundus photography will be performed at baseline, six months, and every six months thereafter. The yearly examination includes fundus photography as well as the following additional procedures:

1. Visual acuity;

2. Intraocular pressure measurement;

3. Slit-lamp and ophthalmoscopic examinations.

Fluorescein angiography, performed at baseline in patients who are in the primary prevention trial, will be repeated at five years and study termination.

6.2.4.5 Renal

Renal examination will be performed at each annual visit. Urinalysis (UA) will be done in conjunction with the annual history and physical

examination. Urine culture (UC) will be done on all females and on any male if an abnormal urinalysis is indicated. The UA and UC will be analyzed locally. Urine and serum will be sent to the CBL for the following:

1. Microalbuminuria (four-hour timed collection);

2. Serum albumin;

3. Creatinine clearance;

4. Serum creatinine.

At three years and/or study termination, a 125-I iothalamate clearance will be done simultaneously with the four-hour timed collection for microalbumin. At two years and again at five years and/or study termination, urine will be sent to the CBL for the determination of urine creatinine, sodium and urea nitrogen (24-hour home urine collection).

6.2.4.6 Neurologic

The following procedures will be performed every two years:

1. Standing and supine blood pressures and pulse;

2. An autonomic nervous system function tests (RR-variation on ECG);

Update of the neurological history and physical examination and noninvasive nerve conduction studies will be performed at five years and/or study termination.

The autonomic nervous system function tests (RR-variation on ECG) will be centrally read at the Central Autonomic Coding Unit.

6.2.4.7 Cardiovascular

Cardiovascular endpoint examinations will be scheduled every two years. These examinations will include a standardized follow-up history and physical examination for peripheral vascular disease. Resting ECG's will be sent to the Central ECG Reading Unit and the results forwarded to the Coordinating Center.

In addition, triglycerides, total cholesterol, and high density lipoprotein cholesterol will be measured annually on serum collected after an eight-hour overnight fast and analyzed by the CBL. Low density lipoprotein cholesterol will be calculated from the above measurement.

6.2.4.8 Psychological

The following psychological assessments will be made during the course of the trial:

1. Neurobehavioral Assessment: A partial neurobehavioral battery assessing visuoperceptual and visuomotor functioning will be performed yearly. The full battery, performed initially at baseline, will be repeated at years two, five and study termination. Performance results will be sent to the Central Neurobehavioral Coding Unit for scoring and coding.

2. Quality of Life: The quality of life questionnaire will be completed yearly (see Chapter 19). Quality of Life should be completed before the patient completes the SCL-90-R.

3. Psychological Symptoms: The SCL-90-R will be completed yearly (see Chapter 19).

6.2.4.9 Compliance/Adherence

The post-randomization compliance/adherence program will be accomplished through the implementation of such strategies as participant counseling, encouragement of peer and social supports, periodic educational programs, regular meetings, and newsletters. Guidelines for these strategies are presented in the Manual of Operations (see Chapter 20).

6.2.4.10 Dietary

The dietary history should be completed at the second and fifth annual visits and at study termination.

6.2.4.11 Forms to be Completed

The forms to be completed at the various types of visits (evaluation, quarterly, annual, interim) are presented in Table 6.5. In addition, various mailing lists have to be completed to ship photographs, specimens and data forms to the appropriate central unit.

6.2.4.12 Missed Visits

A patient missing a scheduled visit should be contacted as soon as possible (preferably the day of the missed appointment) by the Trial Coordinator. The Trial Coordinator should reschedule the visit as soon

as possible. If the visit is not held within the specified time window, the Missed Visit Form should be completed. Missed visits should be brought to the attention of the Principal Investigator, and two consecutive missed visits should be followed up by the Principal Investigator personally.

6.3 MAKE-UP VISITS

Make-up visits are visits scheduled for quarterly or annual endpoint assessments outside the allowable (16 or 21 day) time windows for those visits. When an endpoint visit cannot be scheduled within the proper time window, a make-up visit must be scheduled as soon as possible within the allowable time window for make-up visits (see Table 6.2).

If an illness or other condition that is defined as an intercurrent event occurs close to or at the time of an endpoint visit to assess complications, the visit may be rescheduled. For example, if a patient has a renal intercurrent event near the time of the annual renal studies assessment, that portion of the annual visit may be rescheduled to a time when the assessment may be more valid. A Missed Visit Form should be filed for that assessment to document the reason for the rescheduled visit. However, the assessments for other complications could be scheduled within the time window if the patient is willing and able to undergo them.

6.4 INTERIM VISITS

Interim visits are of two types, those unrelated to diabetes management and those related to diabetes management. In both standard and experimental groups, visits initiated by the patient or his/her private physician for problems unrelated to diabetes or to this clinical trial should be handled using good medical judgment following the guidelines for Management of Intercurrent Illness (Chapter 10). In certain cases, the Notification of Intercurrent Event (DCCT Form 020) must be completed.

In the standard treatment group, interim visits for treatment of diabetes (between scheduled quarterly endpoint visits) should be scheduled only as necessary to meet first or second priorities of this group (see Chapter 9) including patient safety, to manage intercurrent events, and at the patient's request. These visits should be documented on the next Quarterly Visit Form (DCCT Form 021) or Annual Medical History and Physical Examination Form (DCCT Form 003).

In the experimental treatment group, interim visits (between scheduled monthly routine management visits) may be scheduled to maintain compliance to the prescribed regimen, for patient safety, for special management of metabolic deviation, to manage intercurrent events, and at patient request. No procedures other than those clinically indicated

should be performed. These visits should be documented on the next Quarterly Visit Form (DCCT Form 021) or Annual Medical History and Physical Examination Form (DCCT Form 003).

6.4.1 Time of Visits

Regular visits in the experimental group will be weekly until, in the judgment of the investigator, the goals have been achieved; then monthly, or as necessary to maintain goals. Visits outside of this schedule will be termed interim visits.

6.4.2 Preparation

If the physician has requested an interim visit for metabolic control, the Trial Coordinator will notify the patient one to two days prior to the scheduled visit by phone, reminding the patient to bring urine or self blood glucose monitoring records. The Trial Coordinator will also inform the research nurse and, if necessary, the physician or dietitian of the scheduled visit.

6.4.3 Features of Visit

These interim visits will center mainly around discussion of metabolic control including blood glucose determinations at home. Suggestions or changes will be made regarding insulin type or dose, diet, or activity, and continued education and support given, to aid in achieving the goals of the experimental group or to meet priorities in the standard group.

6.4.4 Missed Visits

Missed interim visits are not as damaging to the overall operation of the Protocol as missed follow-up visits, but may result in inability to maintain the goals of the experimental group or may indicate impending poor compliance with the regimen or adherence to the Protocol. Therefore, missed interim visits should be handled similarly to missed follow-up visits and documented with a DCCT Form 014, Notification of Missed Clinic Visit. The patient should be contacted as soon as possible and another visit scheduled. There is no window for interim visits.

6.5 VISIT PROCEDURES FOR PATIENTS WHO HAVE PASSED CLINICAL SAFETY THRESHOLDS

Safety thresholds have been incorporated into the monitoring of all endpoint measures that are determined or graded at a central laboratory or central reading unit. In the following sections, the threshold is given and the allowable local responses are described.

HbAlc -- In standard group patients, any baseline or followup HbA_{1c} greater than 13.11 is reported to the clinic by the Coordinating Center. The clinic is to repeat the HbA_{1c} on the patient monthly until the value falls below 13.11. Use the monthly visit accession numbers. At that time, the patient reverts to his quarterly visit follow-up schedule. (Of course, all HbA_{1c} values from experimental group patients are reported to the clinic.)

Retinopathy -- The Central Ophthalmologic Reading Unit (CORU) will notify the Principal Investigator and ophthalmologist when high risk characteristics (HRC) or pre-proliferative diabetic retinopathy (PDR) is detected (DCCT Form 071). Visual acuity should be performed and documented on the DCCT Form 027 when HRC is detected. The DCCT Form 020 should be used to record the diagnosis and treatment.

The CORU will notify the Principal Investigator and ophthalmologist when the results of gradings of the fundus photographs indicate that an eye has progressed to severe non-proliferative diabetic retinopathy or has progressed three or more steps to moderately severe NPDR within the past year. The patient is to be seen every three months until the ophthalmologist is comfortable with the patient returning to the six month visit schedule. The photographs for study endpoint should be taken as scheduled, that is, every six months. If the ophthalmologist wishes to photocoagulate for retinopathy less severe than HRC, he must consult with the Ophthalmologic Sub-committee (DCCT Form 076). No study forms need to be used at these monitoring ophthalmic visits. When the subject returns to the study ophthalmic visit schedule, the Return to Routine Ophthalmic Followup Form (being created) is completed.

Clinically significant macular edema (CSME) -- The CORU alerts the Principal Investigator and ophthalmologist when CSME is detected (DCCT Form 094). The patient is to be seen every three months by the ophthalmologist. No extra forms or photographs are necessary. Treatment by photocoagulation is a clinical option. The diagnosis of CSME should be recorded on DCCT Form 020, and if and when laser treatment is used another DCCT Form 020 should be used to record that.

Any time unscheduled photographs are required (such as before photocoagulation), labels should be requested from the Coordinating Center. These labels will assign a new accession number.

Nephropathy -- The Coordinating Center will notify the Principal Investigator when a serum creatinine is greater than 2 mg/dl. The Principal Investigator is to treat the subject by any means necessary. The DCCT Form 020 should be completed to document that the patient has

had an intercurrent event (renal insufficiency) and also to record the unmasking of the patient's nephropathy status. The Coordinating Center will notify the Principal Investigator whenever a subject has a 25% or greater change in creatinine clearance. Additional specimens are not processed centrally until the following annual visit.

Albuminuria -- No threshold exists for albuminuria.

Neuropathy -- No thresholds exist for data from the Central Autonomic Coding Unit with respect to the RR-variation and the valsava ratio.

Cardiovascular -- ECG thresholds have yet to be defined.

Lipids -- The Coordinating Center alerts the Principal Investigator when the total cholesterol is greater than the mean + 2 SD (LRC adjusted for age and sex norms), or greater than 265 mg/dl. The patient should have another lipid specimen drawn within one month of the original notification and analyzed centrally to document persistent hypercholesterolemia. If the second cholesterol value is also elevated to the degree described above, then a DCCT Form 020 should be completed. The Principal Investigator and dietitian are to treat the volunteer by reinforcement of dietary fat and cholesterol restrictions. These reinforcements should take place at a regularly scheduled visit.

If total cholesterol is greater than 3 standard deviations above the mean (LRC adjusted for age and sex norms) or calculated LDL-cholesterol is greater than 190 mg/dl, the Coordinating Center alerts the Principal Investigator. The patient should have an additional specimen drawn within one month of notification and analyzed centrally. If the second value is also elevated, the Principal Investigator is to consider the use of drug therapy to lower the cholesterol and/or LDL-cholesterol. A DCCT Form 020 should be completed when the cholesterol or LDL cholesterol value is unmasked to the clinic.

Extra lipid accession numbers are provided for each patient with each yearly set of labels to be used for these purposes.

If triglycerides are greater than 500 mg/dl, then the Coordinating Center will notify the Principal Investigator. A DCCT Form 020 should be completed. Presently, no guidelines exist for the clinic procedures.

Neurobehavioral -- The Coordinating Center will notify the Principal Investigator when a change in the clinical rating indicates the patient is substantially worse since the previous examination. No guidelines exist for how the clinic should handle this situation.

Safety Thresholds

CENTRAL ASSESSMENT OF	THRESHOLD	LOCAL ACTION
Glucose Control		
HbAlc	>13.11	Monthly visit (HbAlc centrally measured) until HbAlc falls below 13.11
Retinopathy		
Fundus photographs	1) HRC 2) PDR 3) Severe NPDR 4) Moderately severe NPDR and progression in past year of 3 or more steps on the retinopathy index scale	Photocoagulation CORU alerts PI and ophthalmologist for more frequent patient contact
Clinically significant macular edema		
Fundus photographs	1) Retinal thickening or associated HE at or within 500 microns of the center of the macula (center may or may not be involved); 2) Retinal thickening >1 DA, part within 1 DD of center of macula	CORU alerts PI and ophthalmologist for more frequent patient followup and consideration of treatment
Nephropathy		
Serum creatinine	>2 mg/dl	CoC alerts PI
Creatine clearance	25% change from baseline	CoC alerts PI to look for reasons for decompensation of renal function such as illicit drugs, asympomatic UTI
Albumin excretion	Currently no alert is in place	Not applicable
Neuropathy		
ANS	None	Not applicable
Cardiovascular		
ECG	To be defined; changes in Q-waves, ST segment and T-wave	To be determined
Lipids		
Total cholesterol	>X + 2SD for age and sex or >265 mg/dl	CoC alerts PI; reinforcement of dietary fat and cholesterol restriction
	>X + 3 SD for age and sex	drug therapy considered
Calculated LDL-cholesterol	>190 mg/dl	Drug therapy considered
Triglycerides	>500 mg/dl	
Neurobehavioral		
Clinical rating	Patient's functioning substantially worse (rating 5) since the last examination	CoC alerts PI

Table 6.1

Diabetes Control and Complications Trial
Schedule of Patient Evaluation for Endpoint Analyses

EXAMINATIONS	BASELINE	1 YR	2 YR	3 YR	4 YR	5 YR	6 YR	7 YR	8 YR	9 YR or LAST
GENERAL										
History and Physical Exam	X	X	X	X	X	X	X	X	X	X
BLOOD GLUCOSE CONTROL										
Home Blood Glucose Profile (Baseline, quarterly, annually)	X	X	X	X	X	X	X	X	X	X
HbA1c (Baseline, quarterly, annually)	X	X	X	X	X	X	X	X	X	X
OPHTHALMOLOGIC										
Visual Acuity	X	X	X	X	X	X	X	X	X	X
Intraocular Pressure	X	X	X	X	X	X	X	X	X	X
Slit Lamp	X	X	X	X	X	X	X	X	X	X
Ophthalmoscopic Exam	X	X	X	X	X	X	X	X	X	X
Stereo Fundus Photography (Baseline, semiannually, annually)	X	X	X	X	X	X	X	X	X	X
Stereo Fluorescein Angiography*	X					X				X
RENAL										
Microalbuminuria	X	X	X	X	X	X	X	X	X	X
Creatinine Clearance	X	X	X	X	X	X	X	X	X	X
I 125 Iothalamate Clearance	X			X						X
Serum Creatinine, Albumin	X	X	X	X	X	X	X	X	X	X
Urine Creatinine, Albumin	X	X	X	X	X	X	X	X	X	X
Sodium urea and nitrogen and urine creatinine (24 hour urine collection)	X		X			X				X
NEUROLOGIC										
Standardized Symptom History & Physical Exam	X					X				X
Autonomic Nervous System Function Tests (RR-Variation on EKG)	X		X		X		X		X	
Noninvasive Nerve Conduction	X					X				X
CARDIOVASCULAR										
History & Physical (Including Peripheral Vascular History & Physical Exam)	X	X	X	X	X	X	X	X	X	X
Blood Pressure, Pulse (Baseline, quarterly, annually)	X	X	X	X	X	X	X	X	X	X
Resting EKG	X		X		X		X		X	
Serum Triglycerides	X	X	X	X	X	X	X	X	X	X
Serum Total Cholesterol, HDL, Calculated LDL	X	X	X	X	X	X	X	X	X	X
PSYCHOLOGICAL										
Neurobehavioral Assessment										
Full	X		X			X				X
Partial		X		X	X		X	X	X	
Psychologic Symptoms (SCL-90-R)	X	X	X	X	X	X	X	X	X	X
Quality of Life Questionnaire	X	X	X	X	X	X	X	X	X	X
COMPLIANCE/ADHERENCE										
Assessment of Adherence (Baseline, quarterly, annually)	X	X	X	X	X	X	X	X	X	X
Diet History	X		X			X				X

*Stereo fluorescein angiography will be performed only in those patients in the primary prevention trial.
Note Bene: Assessment of blood glucose control is performed quarterly. Stereo fundus photography is performed at baseline, six months post randomization, and every six months thereafter. Assessment of blood pressure, pulse and adherence are performed quarterly.

Table 6.2

Visit Organization and Windows for Scheduling Visits

Type of Visit	Visit Name	Window
I. ROUTINE PROTOCOL VISITS	A. Evaluation	
	B. Randomization	
	C. Routine management visits for the experimental group only:	
	Weekly	Within the week, but not within 4 days of another weekly visit
	Monthly	Plus or minus 16 days
	D. Endpoint visits for both groups:	
	Quarterly	Plus or minus 16 days
	Annual	Plus or minus 21 days
II. MAKE-UP VISITS	A. Quarterly	Up to the opening of the next quarterly or annual window
	B. Annual	Up to the opening of the next annual window
III. INTERIM VISITS (Non-Protocol)	A. Intercurrent events	
	B. Special management visits (metabolic modification)	
	C. Patient initiated visits	

Table 6.3

Screening, Eligibility, and
Baseline Tests and Procedures

LOCAL SCREENING	ELIGIBILITY	BASELINE***
1) Initial contact 2) Presentation of Informed Consent information on DCCT 3) Consent #1 to undergo Eligibility Exams 4) History and Physical Examination 5) Local laboratory procedures* Hb electrophoresis CBC Multichannel analysis of serum (including NA+ K+ CL- uric acid CA++ PO4-- SGOT Alkaline Phosphatase total protein albumin cholesterol) Dipstick screen for urinary protein Serum creatinine Urinalysis Urine Culture (mandatory in females; in males only if indicated by specified abnormalities in urinalysis) T4 TSH Pregnancy test	1) Laboratory** a) Blood Glucose Control HbA1c b) C-peptide (basal & stimulated) c) Fasting Cholesterol 2) Ophthalmic a) Visual acuity b) Intraocular pressure c) Slit-lamp and ophthalmoscopic exam d) Stereo fundus photographs** 3) Renal a) Microalbuminuria by radioimmunoassay** b) Serum creatinine** (at investigator's discretion a creatinine clearance may be done at this stage of the eligibility screen) 4) Cardiovascular a) History and Physical (including blood pressure) b) Resting EKG 5) Adherence assessment 6) Pregnancy test 7) Volunteer's Understanding Questionnaire 8) Consent #2 to participate in DCCT	1) Laboratory** a) Blood Glucose Control HbA1c Capillary blood glucose profile (CBG) b) Lipids Cholesterol Triglycerides HDL Calculated LDL 2) For subjects with less than or equal to 5 years duration of IDDM, ophthalmic fluorescein angiography** (if necessary another pregnancy test prior to angiography) 3) Renal a) Creatinine Clearance** b) 24-hour urine collection c) I-125 iothalamate clearance 4) Neurologic a) Standardized Symptom History & Physical Exam b) Autonomic Nervous System Function** (RR variation on ECG) c) Non-invasive nerve conduction study 5) Psychological a) Full neurobehavioral assessment** b) Symptom Checklist-90-R (SCL-9-R) c) Quality of Life Questionnaire 6) Dietary -- Diet history of past year** 7) Additional and sufficient blood will be drawn and stored in the CBL freezer for purpose of performing in the future assays which are not currently specified.

* Local lab procedures are employed to document the general health of patient.
** Central lab or Central Reading Unit.
*** Baseline occurs before randomization. It is performed to obtain a reference point for each patient and not to exclude participants.

Table 6.4

EVALUATION SCHEDULE

SCREENING

Content:
- Telephone or other contact with staff of clinical center (DCCT Form 060)
- Initial Clinic Visit (DCCT Form 001 if in-clinic contact
- Flyer mailed or given to potential participant

Staff: Any one member of clinical center staff

Time: 10 minutes

MODULE 1 INTRODUCTION

Content:
- DCCT Information Presentation (slide show)
- Initial Clinic Visit Form completed (DCCT Form 001)
- Medical History Form (DCCT Form 002), pages 1-11
- Patient takes home first Informed Consent Form (DCCT Form 031), Handbook and Manual
- Meet the Investigator
- Appointment made for Module 2.

Staff: Trial Coordinator/Nurse
(possibly Behavioral Scientist)
Investigator

Time: 2-3 hours

MODULE 2 PHYSICAL EXAMINATION/ADHERENCE

Content:
- Question and answer concerning first Informed Consent (DCCT Form 031)
- Signing of first Informed Consent Form
- Completion of Personal Information on Study Volunteer (DCCT Form 012)
- Medical History Form, pages 12-19; Systems Review and Physical Examination (DCCT Form 002)
- Explanation and Commencement of two-week behavioral tasks to assess compliance (DCCT Forms 061 and 062)
- Interview to assess availability and adherence (DCCT Forms 047 and 049)
- Appointments made for Module 3

Option:
- Blood drawn for local eligibility tests and urine specimen obtained for local urinalysis (DCCT Forms 004, 006, 043)

Staff:
Physician
Behavioral Scientist
Trial Coordinator/Nurse/Secretary
Technician

Time: 4 hours

MODULE 3 — LABORATORY/PSYCHOLOGICAL
(a.m. fasting - hold a.m. insulin)

Content:
- C-peptide testing, including blood drawn for cholesterol, creatinine and Glucose (DCCT Form 043)
- Blood drawn for local eligibility tests and urine specimen obtained for local urinalysis (if not done in Module 2) (DCCT Forms 004 and 006)
- Reinforcement of Behavioral Task (Phone call is acceptable)
- Quality of Life Questionnaire (DCCT Form 036)
- SCL-90-R (DCCT Form 035)
- After the results come back from the central laboratory and the patient still appears eligible, appointments should be made for the next evaluation modules:

  a) Renal Studies (Module 4)
  b) Ophthalmic Evaluation (Module 5)
  c) Neurologic Evaluation (Module 6)

Staff: Trial Coordinator/Nurse

Time: 2 hours

MODULE 4 — RENAL STUDIES
(a.m. - post breakfast and morning insulin)

Content:
- 125-I iothalamate clearances (DCCT Forms 097 and 100)
- 24-hour urine collection (DCCT Forms 044 and 101)
- Creatinine and albumin clearances (DCCT Form 044)
- Blood drawn for serum albumin and creatinine (DCCT Form 044)
- Patient to remain quiet

Staff: Trial Coordinator/Nurse

Time: 4 hours

MODULE 5 — OPHTHALMOLOGIC
(Patient will have his/her eyes dilated and will need a driver or public transportation)

Content:
- Visual acuity (DCCT Form 008)
- Measurement of intraocular pressure (DCCT Form 008)
- Slit-lamp and ophthalmoscopic examination (DCCT Form 008)
- Stereo fundus photography consisting of 7 or more standard fields (DCCT Form 025)
- Stereo fluorescein angiography (DCCT Form 026)

Staff:
Ophthalmic technician
Ophthalmologist
Nurse

Time: 2 hours

MODULE 6 — NEUROLOGIC
(a.m. fasting)

Content:
- Resting electrocardiogram (DCCT Form 053)
- Neurologic symptom history and physical examination (DCCT Form 005)
- RR-variation on EKG (DCCT Form 054)
- Postural testing/vasalva maneuver
- Breakfast
- Nerve Conduction Study (DCCT Form 037)
- Patient takes second Informed Consent Form home (DCCT Form 032)

Staff:
Neurologist
Neurologic technician
Trial Coordinator/Nurse

Time: 4 hours

MODULE 7 — COMPLIANCE/ADHERENCE
BASELINE DIET AND LABORATORY
(a.m. fasting)

Patient should have received in the mail 10 days earlier the Food Pattern and Food Preparation Questionnaires (DCCT Forms 029 and 030) and should bring completed questionnaires.

Content:

- Blood drawn for baseline determinations at central laboratory (DCCT Forms 055 and 058)
- Breakfast
- Patient takes Volunteer Understanding Questionnaire, Version A or B (DCCT Form 045 or 046)
- Slide show repeated if necessary
- For females, final pregnancy test
- Interview with dietitian to assess patient's potential dietary abilities
- Diet history (DCCT Form 018)
- Second interview to assess patient estimate of adherence (DCCT Form 049)
- Family understanding and expectancy of DCCT (DCCT Form 048)
- Patient signs second Informed Consent Form (DCCT Form 032)
- Assessment of behavioral tasks (DCCT Forms 056 and 057)

Staff: Trial Coordinator/Nurse
Dietitian
Behavioral scientist

Time: 3-4 hours

MODULE 8 NEUROBEHAVIORAL

Content:
- Neurobehavioral Assessment (DCCT Form 010) (Blood glucose monitoring before and after)

Staff: Psychometric Technician or Clinical Psychologist

Time: 4 hours

MODULE 9

Content:
- Review Eligibility Checklist (DCCT Form 038)
- Randomization of patient (DCCT Form 011)
- Completion of Quarterly Clinic Visit Form (DCCT Form 021) including delivery of home blood glucose profile by patient
- Treatment initiated
- Coordinating Center generates schedule for follow-up visits and sends it to the clinic

Staff: Physician
Trial Coordinator/Nurse

Time: To be estimated

Table 6.5
Allowable Investigator Initiated Actions
with Respect to Screening of DCCT Candidates

Measurement or Procedure	Reanalysis[1] or Reread by Central Unit	Retake[2] (# Within Four-Month Window)	Restart[3]
C-peptide	No	No	6 months
Fundus photographs			
No microaneurysms	Yes or	Yes(1)	6 months
Retinopathy >P2	No	No	No
HbAlc	No	Yes within two weeks of report(1) **	6 months
Visual Acuity	NA	Yes(1)	6 months
Albuminuria*	No	Yes if evidence of infection, trauma or contamination is present*(1)	No
Cholesterol	No	Yes if due to elevated TSH(1)	6 months
Obesity	NA	No	6 months
Blood Pressure	NA	No	6 months
Creatinine	No	No	No

[1] Reanalysis is defined as a reread or redetermination of the same photograph, specimen, etc., within the four-month window.

[2] Retake is defined as a recollection of the specimen, a retake of the fundus photograph, etc., at a different point in time but within the four-month window.

[3] Restart is defined as the complete re-evaluation of a previously screened candidate who was declared ineligible.

* The burden of proof is on the Principal Investigator. Since a locally performed urinalysis is performed, the four-hour collection should not be scheduled until there is no further evidence of infection (WBC) or trauma or contamination (RBC). The Planning Committee recommended that two negative dipsticks (one before and one after the four-hour collection) should be sufficient evidence for a retake.

** if the Principal Investigator has reason to believe the reported value does not reflect the patient's clinical status

TABLE 6.6

DCCT Examination and Forms Schedule
(Continued)

Type of Visit	Visit Number	Examination, Test or Procedure (Form Number)	Minimum/Maximum Time
Annual	04,12,28,36	Annual Medical History & Physical Exam (003) Local blood count & chemistry (004) Local urinalysis & urine culture (006) HbA1c (055) Capillary blood glucose profile (050) Ophthalmic examination & ocular history (027) Fundus photography (025) Four-hour urine collection (044) Cardiovascular Lipids (058) Blood pressure, pulse (003) Adherence assessment (003) Neurobehavioral battery (partial) (051) Quality of Life Questionnaire (036) SCL-90-R (035)	±12 days about target date for visit
Bi-annual	08,16,24,32	Same as annual visit except full neurobehavioral battery (008) only, partial autonomic nervous system function tests, and diet history (008 only) are done	±21 days about target date for visit
Fifth annual	20	Same as annual except full neurobehavioral battery fluorescein angiographs (in primary prevention trial subject only) neurological history and examination, nerve conduction studies, and diet history	±21 days about target date for visit
Tenth annual or termination	40 or termination	Same as fifth annual	±21 days about target date for visit

CHAPTER 7

INFORMED CONSENT PROCESS

The Diabetes Control and Complications Trial (DCCT) is a multi-center, randomized clinical trial studying the effect of two different treatment regimens on the development or progression of early vascular complications in insulin-dependent diabetes mellitus. Because of the complexity, length, and significant patient demands of the trial and the need for randomization, an intensive educational program that utilized audiovisual and written material was developed to provide prospective volunteers with enough information so that they could make an enlightened decision whether to participate. An evaluation of the efficacy of the education process and of anticipated adherence were included as part of the informed consent process.

During the feasibility phase of the DCCT, evaluation of the subject's knowledge of the trial revealed that the educational process was very efficacious in teaching subjects. Retention of the information one year after informed consent was obtained was excellent. Moreover, the high degree of adherence during the first year of the trial mirrored the subjects predictions and suggests that the informed consent process provided the subjects with a realistic notion of the trial demands. The informed consent process developed for the DCCT may serve as a model for other complex and demanding clinical trials where prospective subjects must be highly educated about the trial in order to participate effectively and highly motivated to participate completely for the duration of the trial. The DCCT uses several innovative approaches to obtain informed consent and establish eligibility. These include new tools for patient orientation, evaluation of knowledge, assessment of adherence to assigned tasks, and attitudes of potential volunteers.

7.1 SEQUENCE OF PROCEDURES

The sequence of procedures for obtaining the patient's consent are given in Table 7.1. A two-stage informed consent procedure is part of a multi-level screening process. It is recommended that the Principal Investigator or the DCCT physician who will care for the patient be involved in the early stages of the sequence. The first Informed Consent Form obtains the patient's permission and in the case of adolescent patients, the parent's permission for the eligibility tests to be performed.

The second Informed Consent Form obtains the patient's permission and in the case of adolescent patients, the parent's permission for the

patient to participate in the clinical trial for at least two years and for possibly ten years.

Both consent forms must be signed by the DCCT Principal Investigator. Copies of the signed Informed Consent Forms must be forwarded to the Coordinating Center. It is the responsibility of the Trial Coordinator to maintain a supply of the two forms. Prototypes for these forms are DCCT Forms 031 and 032).

In the following sections, the tools utilized for securing informed consent are described.

7.2 RECRUITMENT FLYER

The DCCT Recruitment Flyer is a brochure designed for wide-scale distribution. The Coordinating Center will supply each clinic with a sufficient number of these brochures during the recruitment stage of Phase III. The Trial Coordinator must keep an inventory of these as well as the other DCCT materials.

7.3 DCCT SLIDE PRESENTATION

Each clinic will be supplied with two types of audio cassettes, one carousel of numbered slides and a written script. In one of the cassettes, an audible sound will indicate when the slides have to be changed manually by the person managing the presentation. The basic units needed for this are a slide projector and a regular play-back cassette player. In the other, the audio cassette will be automatically synchronized by an inaudible signal to work with Kodak or Bell and Howell equipment.

The slide presentation is designed to be made during the initial clinic visit and then again before randomization. The second viewing can be shortened so as to omit the screening for eligibility segment.

Various stopping points along the presentation are designed to enable the clinic staff to answer specific questions or to make special remarks or clarifications. Suggested answers to likely questions are given below. Some of these, for example demonstration of blood glucose monitoring equipment and insulin infusion pumps, should be available for inspection during these intermissions.

7.3.1 Guidelines for Presentation of the DCCT Slide-Tape Show

The DCCT slide-tape show is designed to be shown to prospective participants for the DCCT on two occasions. The first occasion is during the first clinic visit. At this showing, the slide-tape offers the first presentation of the DCCT to the volunteer. As such, it provides a standard introduction to all volunteers across the centers. The slide-tape presentation of the study includes prompts to promote interaction between the volunteer and the clinician at specific points.

The DCCT slide-tape is also designed to be shown to prospective participants who have successfuly proceeded through the eligibility screen and are being invited to join the study. In this case, the program should be presented as a final review of the study. Only the portion of the program covering the post-randomization phase of the DCCT needs to be shown. This ought to be done just prior to the final consent procedures.

This media overview of the eligibility and post-randomization phases of the DCCT is planned ideally for a single volunteer (and family) and a center staff member. It may be shown to small groups of volunteers. Because the program does prompt a question and answer type of discussion at a number of points, a smaller number of viewers will allow for a more adequate discussion. This presentation is not intended for viewing by mass size audiences.

There are 12 stops for discussion, including the conclusion, during the slide-tape show. Each stop occurs after a specific unit of information has been presented. At these stops, the major points should be emphasized and an assessment of the volunteer's understanding of the content should be undertaken. At this time, misunderstandings can be corrected. Suggestions for discussion at each stop follow.

INTRODUCTION: Following any initial procedures at the first visit, a brief and informal knowledge assessment might be conducted, specifically focused upon any sensitive content in the program. For example, knowledge of potential complications might be evaluated. In the case of adolescents, the parents might be asked what the child knows about complications of diabetes. The program then needs to be presented sensitively, allowing ample opportunity for discussion.

STOP 1: Introduction to the concept of stops

Emphasize the value of discussion and asking questions.

STOP 2: The two research questions

1. Check volunteer's understanding of the questions.

2. Check volunteer's awareness of the controversy over the value of trying to attain blood glucose goals near nondiabetic levels . . . What has the private doctor told the volunteer about this? . . . What does the volunteer believe?

STOP 3: The two research groups - randomization

1. Check volunteer's understanding of having two treatment groups with different treatments.

2. Emphasize that group assignment will be made by a process of randomization . . . there is no choice.

STOP 4: Eligibility criteria - general

If the volunteer has not been asked about proximity to the clinic, relocation plans, pregnancy plans, age, or duration of insulin dependent diabetes, this would be an appropriate time to do so . . . Explanations for these criteria might be given.

STOP 5: Eligibility screening process and Consent #1

1. Discuss the consent to be screened form; be sure that the volunteer understands that this consent form is not for participation in the study, but consent for screening . . . that he/she cannot be considered for the study unless this first process is carried out.

2. Ask volunteer about convenience of coming to the clinic and review clinic hours and degree of flexibility.

3. Discuss whether or not the option of inpatient screening is available at this clinic.

4. This consent for screening extends for four months.

STOP 6: Eligibility examinations and volunteer's handbook

1. Elicit questions about the specific examinations.

2. Elicit questions about confidentiality and emphasize this concept.

3. Emphasize the point that if the volunteer is found to be ineligible on any examination, he/she will be disqualified from participating in the study and will not receive any further tests . . . emphasize that being disqualified does not mean that anything is wrong with the volunteer, but simply that he/she does not fit the strict description of participants required by the study protocol.

4. Explain handbook briefly, telling participant that he/she will receive a copy following the slide-tape show.

STOP 7: Second consent and randomization

1. Emphasize that the consent form is an agreement to participate in the DCCT for two or more years; that the person should feel he/she knows what will be expected of him/her and that he/she feels

comfortable in doing those things . . . this needs to be strongly emphasized in the second viewing, prior to actual signing of the consent form.

2. Emphasize the random assignment to groups; check the volunteer's comprehension of this concept . . . this needs to be strongly emphasized during the second viewing, with some discussion on whether or not the participant could accept an assignment to either of the groups including a discussion of any problems the volunteer thinks he/she might have in accepting assignment to either of the groups.

STOP 8: Standard group procedures

Determine the volunteer's understanding of the standard care group treatment program . . . what will be done and for how long.

STOP 9: Experimental group procedures

1. Determine the volunteer's understanding of the experimental group treatment program . . . what will be done and for how long.

2. Determine whether the volunteer understands the differences in the treatment programs between the groups.

STOP 10: Complications

Determine what the volunteer has been told and/or believes about complications of diabetes; this area needs to be treated very sensitively without arousing any anxieties in the volunteer.

STOP 11: Tests and record keeping for both groups, data analysis

1. Point out that more detail on the tests will appear in the Volunteer's Handbook and can be discussed again.

2. Elicit questions from the volunteer.

3. Review the ways the study could end . . . this is especially important to review during the second viewing . . . e.g., expected to stop for review in two years with the possibility of continuing for eight more years; one treatment program proves superior early on; one treatment program proves problematic early on . . . but participant commitment is for the duration of the study.

4. Emphasize confidentiality in the use and analysis of data which are offered by the participants.

END: Risks and benefits, closing

1. Determine whether or not the volunteer understands the risks and benefits of participation . . . and whether the volunteer can think of any other personal risks and benefits to participation.

2. Elicit any questions about the program.

7.4 VOLUNTEER'S INFORMATION HANDBOOK

At the conclusion of the first clinic visit, the patient will be given the Volunteer's Information Handbook and the Manual of Tests, Terms, and Special Procedures to take home and to read. These two documents have been written in language that the younger patients as well as the adults will understand. The documents provide information on the background of the blood glucose controversy; the questions the trial is designed to answer; the general nature of a clinical trial and the specific characteristics of the DCCT. In addition, the documents provide information on the eligibility criteria, on the differing techniques which treatment groups will employ, and on the procedures used at baseline and at followup to detect the early appearance or progress of any of the complications of diabetes that are being studied. The documents provide a discussion of the patient's safety during the trial, of the patient's responsibilities during the DCCT, of the overall risks and benefits of participating in the trial, and of the costs covered by the DCCT.

The Coordinating Center will stock each clinic with a supply of these documents during the recruitment stage of Phase II and III. One of the responsibilities of the Trial Coordinator will be to maintain an adequate number of these documents.

7.5 VOLUNTEER'S UNDERSTANDING QUESTIONNAIRE

This Questionnaire is based on the information given in the DCCT Slide Presentation and the Volunteer's Information Handbook. The purpose of the Questionnaire is to document the level of the patient's understanding of the goals and conduct of the trial. There are presently two versions of this Questionnaire; Version A (DCCT Form 045) and Version B (DCCT Form 046). Both versions contain the same questions but the questions are in a different sequence in Version B. The Questionnaire is designed to be difficult.

This form is to be completed at the visit at which the Informed Consent for Randomization (DCCT Form 032) is signed. The patient should:

1. be given a pencil with an eraser with which to complete the form;

2. be allowed as much time as he/she needs to complete the form;

3. complete the form himself/herself, without help from another person and without looking at the Volunteer's Information Handbook.

When the patient has completed the Questionnaire, the Trial Coordinator should review the questions with him/her to clarify any items to which the patient gave an incorrect answer. Do not change any of the responses which the patient gave, however.

If the patient gives the wrong answer to any one of the questions, he/she cannot be randomized, but must come back another day to retake another version of the Questionnaire. The patient may benefit from viewing the orientation audiovisual presentation or by re-reading the Volunteer's Information Handbook. The patient should be encouraged to ask questions.

If the patient fails to answer all the items on the retesting, the patient's suitability for randomization will be based on the judgment of the Principal Investigator. A copy of each Questionnaire should be mailed to the Coordinating Center in the weekly batch.

Table 7.1

Sequence of Procedures in the
Informed Consent Process

1. Patient's initial contact with clinic staff

   a) Recruitment Flyer mailed or given to subject

2. Initial Clinic Visit

   a) Screening Interview employing Initial Clinic Visit Form (DCCT Form 001)

   b) Oral discussion with subject

   c) Presentation of DCCT Slide Presentation with ongoing discussion

   d) Volunteer's Information Handbook, Manual of Diabetes Tests, Terms and Special Procedures, and 1st Informed Consent for Screening distributed for study and discussion at home

3. Second Clinic Visit

   a) Discussion with subject and "significant other" of Volunteer's Information Handbook, Manual of Diabetes Tests, Terms and Special Procedures, and 1st Informed Consent; repeat slide show if requested

   b) If 1st Informed Consent signed:

      i) explanation and commencement of compliance and adherence tasks

      ii) commencement of screening tests

4. Evaluation Visits (see Table 6.3).

5. Eligible Subjects

   a) Return to clinic

   b) 2nd Informed Consent discussed with patient and copy sent home for study and discussion

Table 7.1 (Continued)

Sequence of Procedures in the
Informed Consent Process

6. Eligible subjects who wish to volunteer

   a) Return to clinic for further discussion

   b) Take Volunteer Understanding Questionnaire (DCCT Form 045 or 046) requiring 100% correct answers (test may be administered twice)

   c) Sign 2nd Informed Consent for Randomization

7. Return for Randomization

CHAPTER 8

ENTRANCE CRITERIA AND RANDOMIZATION PROCEDURES

Investigators at each participating clinical center will determine by a series of screening interviews and examinations whether a potential study participant is eligible for inclusion in the DCCT. Each clinical center will recruit individuals for the primary prevention and the secondary intervention trials.

The required information from the history and physical exam, local laboratory procedures, central laboratory procedures, and the following evaluations: ophthalmologic, renal, neurologic, cardiovascular, psychological, dietary and compliance/adherence, must be on hand at the Coordinating Center before a subject can be randomized. The Coordinating Center will notify the clinic when a subject appears to satisfy the eligibility criteria.

For a complete discussion of the randomization visit including visit preparation, features of the visit and forms to be completed, see Chapter 6.

8.1 ELIGIBILITY CRITERIA

The following conditions must be satisfied for a subject to be considered eligible for the Phase III study.

8.1.1 Eligibility Criteria Applicable to All Subjects

1. Age greater than or equal to 13 years and less than 40 years at time of randomization and at or beyond the Tanner Stage II level of pubertal development. Refer to the description of the Tanner Stages in Table 8.1.

2. An HbA_{1c} value greater than three standard deviations above the mean of a sample of non-diabetic persons. The DCCT sampling protocol established this value as 6.55 using the methodology of the Central Hemoglobin A_{1c} Laboratory. This criterion is based on the first measurement obtained during the evaluation process and exclusion on its basis is applicable for a period of six months. If, in the opinion of the investigator, the value is clearly inconsistent with self blood glucose measurements or local HbA_{1c} values, a second measurement can be obtained within two weeks of notification of the first value.

3. Informed consent from participants 18 years or older. Informed consent from participants aged less than 18 years and, additionally, informed consent from the parent or guardian.

4. Serum creatinine less than or equal to 1.2 mg/dl, or, at investigator's discretion, creatinine clearance greater than or equal to 100 ml/min/1.73m^2.

8.1.2 For Subjects Without Retinopathy

1. Duration of IDDM for at least one year but less than or equal to five years.

2. Absence of diabetic retinopathy or other ocular lesions which would confound the assessment of retinopathy or other aspects of ocular status based on central grading of stereo fundus photographs.

3. Visual acuity of 50 letters (20/25 Snellen equivalent) or better in both eyes (best corrected) using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity charts and protocol.

4. Less than 40 mg. albumin/24 hour on a four-hour standardized urine collection.

8.1.3 For Subjects With Minimal Background Retinopathy

1. Duration of IDDM for at least one year but less than or equal to 15 years.

2. Presence of at least one microaneurysm in either eye with or without other diabetes related lesions, but less retinopathy than would characterize either eye as P2 (Diabetic Retinopathy Study (DRS) Group 3) or worse based on central grading of stereo fundus photographs.

   Classification of eyes is based on Diabetic Retinopathy Study (DRS) criteria. Eyes with new vessels are worse than P2. Eyes without new vessels which meet any one of the three criteria listed below will be classified as P2. Standard photos referred to below are those of the Modified Airlie House Classification.

   a) Each of the following three lesions is definitely present in at least two of Fields 4 through 7:
      Soft exudates - SE
      Venous beading - VB
      Intraretinal microvascular abnormalities - IRMA

b) Two of the above three lesions are present in at least two of Fields 4 through 7 and Hemorrhages/Microaneurysms (HMa) are present in all four fields, equaling or exceeding standard photograph 2A in at least one of them.

c) IRMA are present in all four of these fields and equal or exceed standard photograph 8A in at least two of them.

3. Visual acuity of 45 letters (20/32 Snellen equivalent) or better in both eyes (best corrected) using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity charts and protocol.

4. Less than or equal to 200 mg. albumin/24 hour on a four-hour standardized urine collection.

8.2 EXCLUSION CRITERIA

In order to be eligible for this study, the subject must be free of the excluding diseases and conditions itemized below. For some of these diseases, the diagnosis can be made on objective grounds. In other cases, it will not be possible to follow rigid criteria, and the diagnosis must rest upon the considered judgment of the examining physician. Hospital records will be used as extensively as possible to document the historical material reported by the subject. Some of these conditions will exclude the subject permanently from the study. Other conditions may only temporarily exclude, and the subject may be reconsidered for eligibility for the study at some later date. See Chapter 6 for procedures for restarting a subject.

8.2.1 Exclusion Criteria Applicable to All Subjects

1. Clinical characteristics of IDDM but subjects with more than five years duration of IDDM are excluded if their centrally measured basal or stimulated C-peptide is greater than .2 pmol/ml. Subjects with five years or less duration of IDDM are excluded if their centrally measured stimulated C-peptide is greater than .5 pmol/ml or basal C-peptide is greater than .2 pmol/ml. The pre-sustacal specimens are considered stimulated if the centrally measured pre-sustacal blood glucose is greater than 150 mg/dl.

2. Previous treatment for IDDM with either three or more daily injections of insulin or with an insulin infusion pump except for periods of less than four weeks to manage an intercurrent illness or to determine optimal blood glucose control. An exception will be made for women who used intensive therapy only during a pregnancy and who will have been on one or two injections of insulin for at least the year prior to randomization.

3. Insulin Resistance: Requirement of a total of more than two units per kilogram of body weight except during intercurrent illnesses lasting less than one month.

4. Three or more documented episodes of diabetic ketoacidosis requiring hospitalization during the 12 months prior to the time of randomization.

5. Women who are pregnant or who plan or desire a pregnancy within two years of the time of randomization.

6. Hypertension

   a) Subjects who required treatment of hypertension during the two years prior to the time of examination are ineligible for the trial.

   b) In adults, sitting blood pressure, setting arm at level of the heart, greater than 140 systolic or 90 diastolic without treatment at the time of the eligibility history and physical examination.

   c) In adolescents, sitting blood pressure, setting arm at level of the heart, greater than the 95th percentile above the mean for proper category of age and sex as defined in the Report of the Task Force on Blood Pressure in Children.[1] blood pressure greater than 140/90 with the exception of females aged 13 years in whom the upper limit is 135/87.

7. Lipids

   a) History of treatment for hyperlipidemia not secondary to diabetes.

   b) Serum cholesterol greater than three standard deviations above the mean for sex and age as defined in the Lipid Research Clinic Population Studies Data Book, Volume I of the Prevalence Study (see Table 8.2). This is a permanent exclusion with one exception: If the subject has an elevated TSH, he/she can be reconsidered for eligibility after treatment.

   c) Calculated LDL-cholesterol greater than 190 mg/dl when total serum cholesterol is below the mean plus three standard deviations but greater than 265 mg/dl.

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[1] Pediatrics, Volume 59, Supplement 1, 1977.

8. Renal disorders

a) Active urinary tract infection defined as any infection of the kidney, ureters, bladder, or urethra, with or without symptoms, that results in pyuria (greater than or equal to 2-4 WBC/hpf) and the following culture results:

i) Outpatients

- Single culture of greater than or equal to 10^5/ml of one organism, OR

- Two (2) cultures of greater than or equal to 100 colonies/ml Candida species

ii) Inpatients (noncatheterized)

- Same as outpatients.

iii) Inpatients (catheterized)

- Single culture with one or two organisms, either of which is greater than or equal to 10,000 colonies/ml, OR

- Single culture of greater than or equal to 100 colonies/ml Candida species.

b) Exclusions based on evaluation of urinary sediment:

i) Over five red blood cells (RBC) per HPF outside the menstrual period in women, or any number of RBC casts prompt renal work up for nondiabetic nephropathy. Subject would not be acceptable pending work-up and treatment.

ii) White blood cell casts indicate UTI and exclude subject pending work-up and treatment of infection.

iii) Cellular, granular, broad or waxy casts suggest nondiabetic renal disease and should prompt work-up for nondiabetic kidney disease.

iv) Hyaline and other casts (up to 10-20 per HPF) or less than or equal to 10,000 (Addis count) per 12 hour urine collection do not indicate disease. They are more common during dehydration or intercurrent illness.

v) Epithelial cells, more often seen in females, are normal findings.

9. History of alcohol or drug abuse or dependence during the five years prior to randomization:[2]

   a) Diagnostic criteria for Alcohol Abuse

      i) Pattern of pathological alcohol use: need for daily use of alcohol for adequate functioning; inability to cut down or stop drinking; repeated efforts to control or reduce excess drinking by "going on the wagon" (periods of temporary abstinence) or restricting drinking to certain times of the day; binges (remaining intoxicated throughout the day for at least two days); occasional consumption of a fifth of spirits (or its equivalent in wine or beer); amnesic periods for events occurring while intoxicated (blackouts); continuation of drinking despite a serious physical disorder that the individual knows is exacerbated by alcohol use; drinking of non-beverage alcohol.

      ii) Impairment in social or occupational functioning due to alcohol use: e.g., violence while intoxicated, absence from work, loss of job, legal difficulties (e.g., arrest for intoxicated behavior, traffic accidents while intoxicated), arguments or difficulties with family or friends because of excessive alcohol use.

      iii) Duration of disturbance of at least one month.

   b) Diagnostic criteria for Alcohol Dependence

      i) Either a pattern of pathological alcohol use or impairment in social or occupational functioning due to alcohol use:

         Pattern of pathological alcohol use: need for daily use of alcohol for adequate functioning; inability to cut down or stop drinking; repeated efforts to control or reduce excess drinking by "going on the wagon" (periods of temporary abstinence) or restricting drinking to certain times of the day; binges (remaining intoxicated throughout the day for at least two days); occasional consumption of a fifth of spirits (or its equivalent in wine or beer); amnesic periods for events occurring while intoxicated (blackouts); continuation of drinking despite a serious physical disorder that the individual knows is exacerbated by alcohol use; drinking of non-beverage alcohol.

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[2] From the American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders (Third Edition)(DSM-III), USA, 1980, pp.163-179.

Impairment in social or occupational functioning due to alcohol use: e.g., violence while intoxicated, absence from work, loss of job, legal difficulties (e.g., arrest for intoxicated behavior, traffic accidents while intoxicated), arguments or difficulties with family or friends because of excessive alcohol use.

ii) Either tolerance or withdrawal:

Tolerance: need for markedly increased amounts of alcohol to achieve the desired effect, or markedly diminished effect with regular use of the same amount.

Withdrawal: development of Alcohol Withdrawal (e.g., morning "shakes" and malaise relieved by drinking) after cessation of or reduction in drinking.

c) Other substance

Three criteria distinguish nonpathological substance use from substance abuse: a pattern of pathologic use; impairment in social or occupational functioning caused by the pattern of pathologic use; and duration of a pattern of use of at least one month.

Substance dependence generally is a more severe form of substance use disorder than substance abuse and requires physiological dependence evidenced either by tolerance or withdrawal.

The substances which have diagnostic criteria listed in the DSM III are alcohol (see above), barbiturates or similarly acting sedatives or hypnotics, opioids, amphetamines or similarly acting sympathomimetics, cannalis, cocaine, phencyclidine (PCP) or similarly acting arylcyclohexylamine, and hallucinogens. The DSM III also has an expanded general discussion of substance abuse and dependence.

10. Any non-diabetic condition that potentially limits life expectancy or that will interfere with participation in the study.

11. Residence at a distance from the clinic that presents a likely impediment to complete followup or a planned permanent move outside of North America.

12. Any form of hemoglobinopathy or hemolytic process which interferes with reliable assessment of diabetic control with conventional assays for glycosylated hemoglobin (e.g., sickle trait).

13. Diabetic Neuropathy - Subjects requiring or requesting treatment for diabetic neuropathy at the time of entry into the trial.

14. Previous or current endocrine disorder other than diabetes, corrected primary hypothyroidism, or functional menstrual disorders. Persons with corrected hyperthyroidism with greater than two years of an euthyroid state at the time of randomization and no past or present ophthalmopathy are eligible to be in the DCCT.

15. Obesity defined as a body weight greater than 130% of the ideal body weight as defined by the 1983 Metropolitan Height and Weight Tables for Men and Women and adjusted for frame size (see Chapter 6). Tables are taken from the data of the 1979 Build Study, Society of Actuaries and Association of Life Insurance Medical Directors of America, 1980 (see Table 8.3).

16. Chronic disease requiring prescription medication for more than a total of four months during the twelve months prior to randomization. (See Tables 8.4 and 8.6 for a detailed list of disqualifying diseases and excluding medications. Table 8.5 is a list of allowable conditions and Table 8.7 is a list of drugs which are not exclusions.)

17. Major electrocardiographic abnormalities or clinical history of ischemic (coronary) heart disease or subjects with symptomatic peripheral vascular disease. Specifically, exclusions include:

    a) Symptomatic coronary heart disease (e.g., angina, myocardial infarction, congestive heart failure);

    b) Symptomatic peripheral vascular disease (e.g., intermittent claudication, presence or history of gangrene of the foot or toe, loss of both pedal pulses in the same foot and/or loss of either groin pulse);

    c) History of myocardial infarction;

    d) Resting EKG suggestive of coronary heart disease or myocardial infarction including heart block or complete left bundle branch block.

18. History of epilepsy or seizures (not caused by hypoglycemia) requiring medication during the five years prior to randomization.

19. Psychological and Behavioral Criteria

    a) Psychological problems such as psychotic, neurotic or personality disorders and conditions which will interfere with the ability to maintain complete followup and adhere to the Protocol, or

    b) A recent pattern of behavior that, in the opinion of the Principal Investigator, indicates a high likelihood of non-compliance, e.g., missed appointments during the pre-randomization phase or inability to follow other instructions

such as those detailed for the Pre-Randomization Behavioral Tasks in Chapter 20.

20. Siblings, parents, children, spouses, or other household members (a) of subjects who have been randomized into Phase II or III, or (b) of clinic staff members. Clinic staff members are also excluded.

21. Current participation in any other clinical trial or any study which may interfere with participation in this trial. Past participation in the following type studies excludes subjects:

    a) Patients previously treated more than twice daily or in intensive treatment with nasal insulin for more than one month are permanently excluded because this is a form of MDI.

    b) Patients getting any form of immunosuppression or immunomodulation therapy for diabetes are also permanently excluded since these could affect the natural history of insulin dependance or the long term renal implications of diabetes. Short term (under four weeks) use of corticosteroids is not an exclusion since this could be given for a variety of reasons. Gamma globulin, cyclosporin, cyclophosphomide, azathiaprine, plasmapheresis, methotrexate and antithymocyte globulin are all considered forms of immunotherapy.

    c) Patients being treated with aldose reductose for approximately four weeks are permanently excluded from participation in the DCCT because of its unknown effects on the natural history of diabetes or its complications.

    Patients previously enrolled as controls for the above studies are eligible.

22. Any condition or use of any medication which will interfere with the application of treatment as outlined in the Protocol.

23. For adolescents, history of or demonstrated failure to maintain normal growth and development two years prior to randomization for any reason, i.e., growth velocity less than the third percentile of normal for age, sex and pubertal stage according to the National Center for Health Statistics Physical Growth Percentiles, *Adapted from: Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM: Physical growth: National Center for Health Statistics percentiles. AM J CLIN NUTR 32:607-629, 1979. Data from the National Center for Health Statistics (NCHS) Hyattsville, Maryland (see Figure 8.1). If previous reliable growth records are not available, failure to maintain growth at a rate of at least 4 cm. or 1.60 inches per year during the previous six months unless pubertal stage (i.e., menarche in females and Tanner IV in males) indicates that growth is complete.

24. Hypoglycemia

    a) More than two hypoglycemic seizures and/or comas during the previous two years.

    b) More than one hypoglycemic episode in the past two years resulting in cerebral impairment (e.g., coma, severe confusion, seizure) before the development of warning symptoms of hypoglycemia while awake (e.g., excessive sweating, tremors, etc.).

25. The presence of significant chorioretinal scars, optic atrophy, retinal degeneration, or other conditions which might confound the assessment of ocular status.

26. Aphakia in one or both eyes or prior ocular surgery other than strabismus or lid surgery.

27. Intraocular pressure greater than or equal to 23 mm of mercury in one or both eyes, or glaucoma requiring medication.

28. Rubeosis iridis in one or both eyes.

29. Myopia of greater than 7 diopters in one or both eyes.

30. Chronic requirement for any ocular medication.

31. The inability to obtain adequate quality stereo fundus photographs.

32. Prior photocoagulation.

8.2.2 Exclusion Criteria for Subjects Without Retinopathy

The presence of diabetic retinopathy manifested by any one of the following lesions on central grading of stereo fundus photographs or clinical exam.

1. Microaneurysms

2. Hemorrhages

3. Hard exudate

4. Soft exudate

5. Intraretinal microvascular abnormalities (IRMA)

6. Venous caliber abnormalities

7. Arteriolar abnormalities

8. New blood vessels or fibrous proliferation

9. Vitreous or pre-retinal hemorrhage

10. Retinal edema

8.2.3 Additional Exclusion Criteria for Subjects With Minimal Background Retinopathy

1. The presence of diabetic retinopathy sufficient to categorize either eye as P2 or worse based on central grading of stereo fundus photographs (see Chapter 8).

2. Macular edema, defined as definite thickening of the retina within one disc diameter of the center of the macula (even if the visual acuity is not yet reduced), as assessed by stereo fundus photography.

8.3 RECRUITMENT AND RANDOMIZATION PROCEDURES

8.3.1 Recruitment

It is not necessary that individuals be referred to the study by a physician; subjects may refer themselves. Each subject must agree, however, that all diabetes care will be provided by the DCCT clinical center health care team.

A recruitment program will be initiated by the DCCT whereby each clinical center will employ recruitment strategies selected among various options best suited to that clinic. These strategies may include advertisement in the mass media of the trial's need for volunteers. (See Chapter 4 for more details regarding recruitment.)

8.3.2 Patient I.D. Numbers

Each subject who completes an initial eligibility screening visit (i.e., DCCT Form 001 completed) will be assigned a Patient Identification Number. The patient identification number will be constructed such that the high order two digits (e.g., the numbers 04 in patient number 04002) denote the collaborating clinic number, and the low order three digits (in this case numbers 002) denotes the order in which a given subject is screened within each clinic (see Chapter 6 for details on Patient ID Numbers and the Patient Initials Identifier). Once a patient is assigned a number, the number should be permanent unless the patient is restarted in the eligibility screening process after deemed temporarily ineligible.

The clinics have been assigned the following numbers to distinguish one clinic from another:

01 Case Western Reserve University
Cleveland, OH 44106

02 Children's Hospital of Philadelphia
University of Pennsylvania
Philadelphia, PA 19104

03 Cornell University
New York, NY 10021

04 Henry Ford Hospital
Detroit, MI 48202

41 University of Michigan
Ann Arbor, MI 48109

05 Joslin Diabetes Center, Inc.
Boston, MA 02215

06 Massachusetts General Hospital
Boston, MA 02114

07 Mayo Foundation
Rochester, MN 55905

08 Medical University of South Carolina
Charleston, SC 29425

09 International Diabetes Center
Minneapolis, MN 55416

10 University of Iowa
Iowa City, IA 52242

11 University of Minnesota
Minneapolis, MN 55455

12 University of Missouri at Columbia
Columbia, MO 65212

13 University of Pittsburgh
Pittsburgh, PA 15213

14 University of Tennessee
Memphis, TN 38163

15 University of Texas
Dallas, TX 75235

16 University of Toronto
Toronto, Ontario, Canada M5G 2C4

17 University of Washington
Seattle, WA 98144

18 University of Western Ontario
London, Ontario, Canada N6A 5A5

19 Vanderbilt University
Nashville, TN 37232

20 Washington University
St. Louis, MO 63110

21 Yale University
New Haven, CT 06510

22 Albert Einstein College of Medicine
Bronx, NY 10461

23 Northwestern University
Chicago, IL 60611

24 University of California, San Diego
San Diego, CA 92103

25 University of Maryland
Baltimore, MD 21201

26 University of New Mexico
Albuquerque, NM 87131

27 University of South Florida
Tampa, FL 33612-4799

8.3.3 Purposes of Randomization

Random allocation to a treatment group assures that the assignment of treatment is not influenced by the subject's condition or any inadvertent or intentional bias. The justification for randomization is that it makes the probability negligible that systematic differences between subjects receiving each treatment will exist. It also permits the application of statistical measures and tests for differences.

8.3.4 The Master Randomization List

Although the recruitment goal was 55 subjects within each of 21 original (Phase II) collaborating clinics and 40 within each of the six Phase III clinics, a provision has been made for the eventual recruitment of more than these quotas in any one clinic. Thus, if one clinic encounters difficulty in reaching its goal, one or more of the other clinics could augment its enrollment to counterbalance the deficit.

Prior to Phase III, the Coordinating Center generated randomization sequences and prepared detailed randomization procedures for its staff to follow. At the time of randomization, the Coordinating Center will specify the treatment (standard or experimental) to be assigned to each eligible subject.

8.3.5 Specific Randomization Procedures

All eligibility data will be forwarded to the Coordinating Center for review prior to the beginning of the treatment. The clinic should adhere to the steps for submission of eligibility specimens and photographs to the central units as closely as possible in order to avoid randomizing ineligible subjects.

Appropriate forms should be mailed to the Coordinating Center within one week prior to randomization; laboratory specimens, EKG's, fundus photographs and fluorescein angiograms should be processed in a timely fashion.

After a subject has completed the evaluation laboratory tests, the behavioral tasks and the two-week diary and appears eligible, the Coordinating Center must approve the subject's eligibility based on the eligibility and baseline tests and procedures described in Chapter 6 and listed in Table 6.4, criteria described in this chapter, and the DCCT Eligibility and Exclusion Report (DCCT Form 038).

After the Coordinating Center has notified the clinical center that the subject fulfills the eligibility criteria, the clinic coordinator confirms a randomization appointment with the subject. At this point, the concept of randomization and the Second Informed Consent are again reviewed with the subject.

On the day of randomization, the Quarterly Clinic Visit Form (DCCT Form 021) is completed to document baseline values and the subject's experience since the baseline medical history and physical examination. If the subject still agrees to participate, the Principal Investigator has reviewed and approved the subject's eligibility, and DCCT Form 011, Randomization Report is completed, the clinic representative will telephone the Coordinating Center and the subject will then be randomized. Randomization will be accomplished by assigning to that subject the next available treatment allocation. The randomized treatment assignment will then be disclosed to the clinic representative.

Each subject will be randomized to one of two groups: Standard or Experimental.

The regimen randomly assigned to each subject should then be instituted as soon as possible with a maximum of four weeks for hospitalization to initiate the experimental therapy according to the protocols for metabolic control (see Chapter 9).

It is important to note that as soon as the treatment assignment is announced, the subject is officially randomized. If it is found later that the wrong assignment was disclosed to the clinic personnel, the assignment will stand as issued once it is disclosed to the patient. The period of followup begins that very day, even if treatment is not actually initiated until several days later. Furthermore, each subject will always be included in the assigned treatment group in all statistical analyses regardless of the eventual therapeutic course. Thus, subjects who fail to comply with, or who are unable to complete the assigned treatment regimen, or who are assigned to the standard group but later undergo more intensive management, will nevertheless be included in the originally assigned group for statistical analysis.

8.3.6 Ineligible Subjects Who Are Randomized

It is possible that there will be subjects who will be randomized and subsequently found to have been ineligible. Upon detection of the improper randomization, the Coordinating Center will inform the Principal Investigator. Since all randomized subjects will be retained in all statistical analyses, improperly randomized subjects should continue to be treated and managed according to the Protocol except in the rare case that continued treatment under the Protocol would jeopardize the welfare of the subject.

It is imperative that the number of ineligible but randomized subjects be minimized. Such subjects by definition will likely respond differently to the two treatment regimens and may dilute any statistical differences which might exist as a result of the therapies. Thus, a small number of improperly randomized subjects may undermine the scientific validity of the trial. For this reason, if there is any doubt as to the eligibility of an individual subject, do not randomize the subject until the Coordinating Center has been consulted.

8.3.7 Treatment Deviations

A therapeutic deviation refers to any subject originally assigned to the standard group who later undergoes intensive therapy or a subject originally assigned to the experimental group who, for whatever reason, discontinue the experimental treatment modalities and use one or two injections of insulin daily. Such subjects will be included in the original treatment group in all statistical analyses regardless of the

circumstances under which therapy is administered. If true benefit is received from either protocol, however, the presence of treatment deviations among the subjects in either group will also dilute the statistical differences between the groups. Thus, as with the ineligible subject who is randomized, a small number of therapeutic deviations may also undermine the scientific validity of the trial (see Chapter 11).

One of the principal functions of the Data, Safety, and Quality Review Group will be to review periodically the accumulated data with respect to the therapeutic benefits and adverse effects of each of the two treatment regimens. If it is determined that either therapy is superior, the trial will be stopped. The study group will be notified so that subjects are informed. Until then, it is preferable that all subjects assigned to receive a specific therapy not deviate.

8.3.8 Patient's Transfer During Screening

Screening can last four months. Patients, although asked early on if they anticipate a move, can have abrupt life changes that necessitate a transfer to another DCCT clinic. If that occurs, the clinic should officially transfer the patient (see Chapter 24) to the randomizing clinic. Credit for the randomization will be given to the receiving clinic; credit for recruitment and all the completed screening tests will be given to the original clinic.

Table 8.1

Description of Tanner Stages of Pubertal Development

Reproductive Organs and Secondary Sex Characters in Girls

Breasts: For descriptive purposes, the adolescent development of the breasts may be divided into five stages on their superficial appearance. The time at which a girl reaches (i.e., enters) each of these stages is usually indicated by the abbreviations B2, B3 etc.

Stage 1 (B1). This is the infantile stage which persists from the time that the effects of maternal oestrogen on the breasts in the neonatal period disappear until the changes of puberty begin.

Stage 2 (B2). The "bud" stage. The breast and papilla are elevated in a small mound and there is an increase in the diameter of the areola. This appearance is the first indication of pubertal change in the breast.

Stage 3 (B3). The breast and areola are further enlarged to create an appearance rather like the small adult breast with a continuous rounded contour.

Stage 4 (B4). The areola and papilla enlarge further to form a secondary mount projecting above the contour of the remainder of the breast.

Stage 5 (B5). The typical adult breast with smoothed rounded contour. The secondary mound present in stage 4 has disappeared.

Pubic Hair: Pubic hair development may also be described in five stages as follows:

Stage 1. The infantile stage in which there is no true pubic hair but there may be a downy vellus comparable to that on the abdominal wall.

Stage 2. Sparse growth of long slightly pigmented hair which appears first on either the labia or the mons pubis.

Stage 3. The hair is considerably darker, coarser and more curled. It spreads sparsely over the pubic symphysis.

Stage 4. The hair is adult in character but covers a smaller area than in most adults. It has not spread on to the medial surface of the thighs.

Stage 5. The hair is distributed in the inverse triangle, characteristic of the adult female. It has spread to the medial surfaces of the thighs but not to the linea alba or elsewhere above the base of the triangle.

Reproductive Organs and Secondary Sex Characters in Boys

Pubic Hair: The development of pubic hair in boys is described in five stages according to the same criteria used for girls. In most men, the pubic hair spreads beyond the pattern described in stage 5 and some authors have used stage 6 to indicate the spread higher on the abdominal wall. However, as the hair seldom reaches its fully adult distribution before the age of 20, stage 6 need not be regarded as a stage of pubertal development. As in the case of the girls, stage 2 is omitted because reliable data were not obtained.

Penis and Scrotum: The development of the genitalia has been divided, for descriptive purposes, into five stages (Tanner, 1962):

Stage 1 (G1) is the pre-adolescent stage and persists from birth until the pubertal development of the testes has begun. The general appearance of the testes, scrotum and penis changes very little during this period although there is some overall increase in the size.

Stage 2 (G2) is shown by enlargement of the testes and scrotum with some reddening and change in texture of the scrotal skin. The attainment of this stage is usually the first external evidence that puberty has begun.

Stage 3 (G3) the penis has increased in length and to a lesser extent in breadth. There has been further growth of the testes and scrotum.

Stage 4 (G4) the length and breadth of the penis have increased further and the glans has developed. The testes and scrotum have further enlarged with darkening of the scrotal skin.

Stage 5 (G5) the genitalia are adult in size and shape.

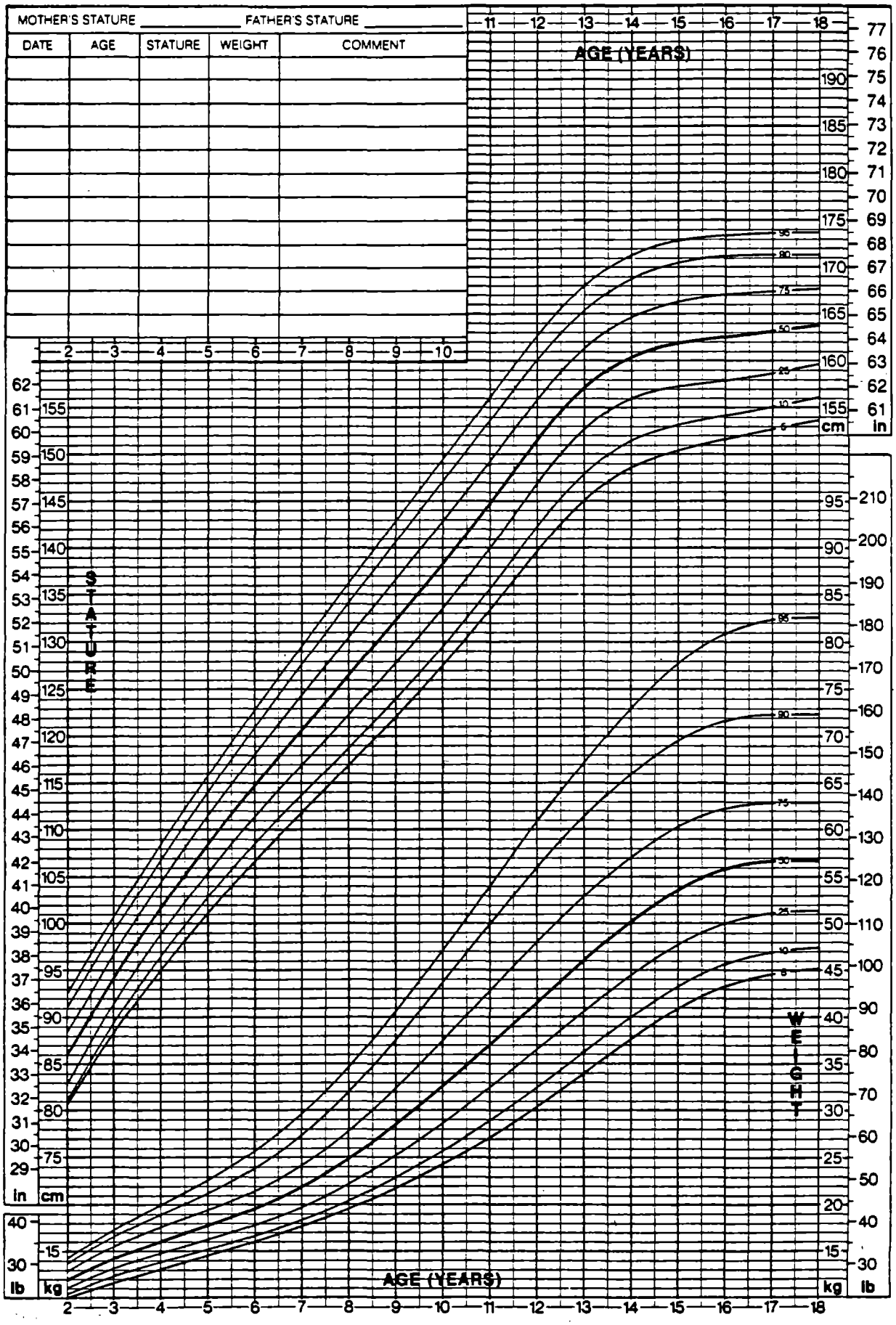
GIRLS: 2 TO 18 YEARS PHYSICAL GROWTH NCHS PERCENTILES*

Figure 8.1a

NAME _____ RECORD # _____

MOTHER'S STATURE _____ FATHER'S STATURE _____

DATE	AGE	STATURE	WEIGHT	COMMENT



Ross Growth & Development Program

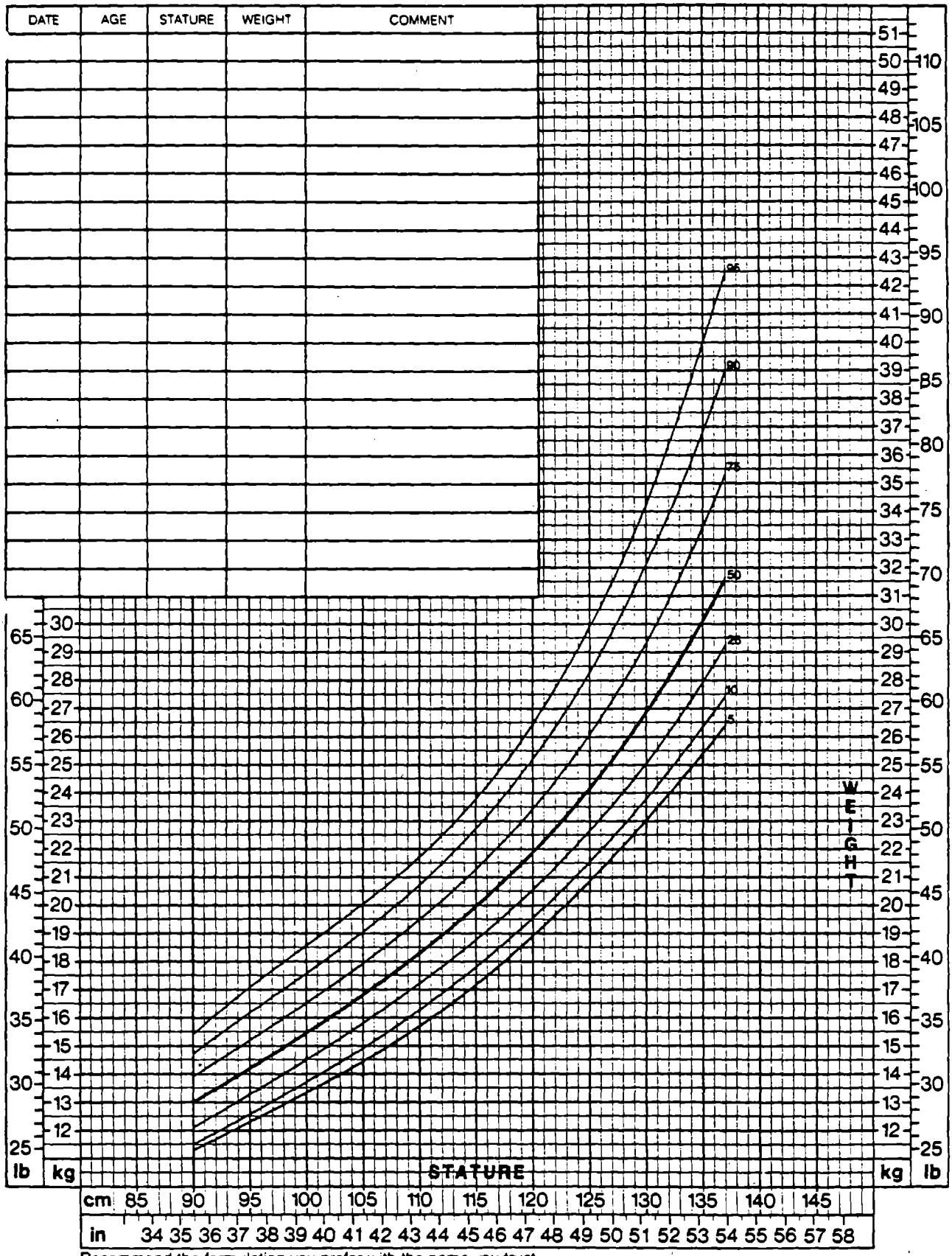
*Adapted from: Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. Am J CLIN NUTR 32:607-629, 1979. Data from the National Center for Health Statistics (NCHS) Hyattsville, Maryland.

GIRLS: PREPUBESCENT PHYSICAL GROWTH NCHS PERCENTILES*

Figure 8.1b

NAME _____ RECORD # _____

DATE	AGE	STATURE	WEIGHT	COMMENT



*Adapted from Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. AM J CLIN NUTR 32:607-629, 1979. Data from the National Center for Health Statistics (NCHS), Hyattsville.

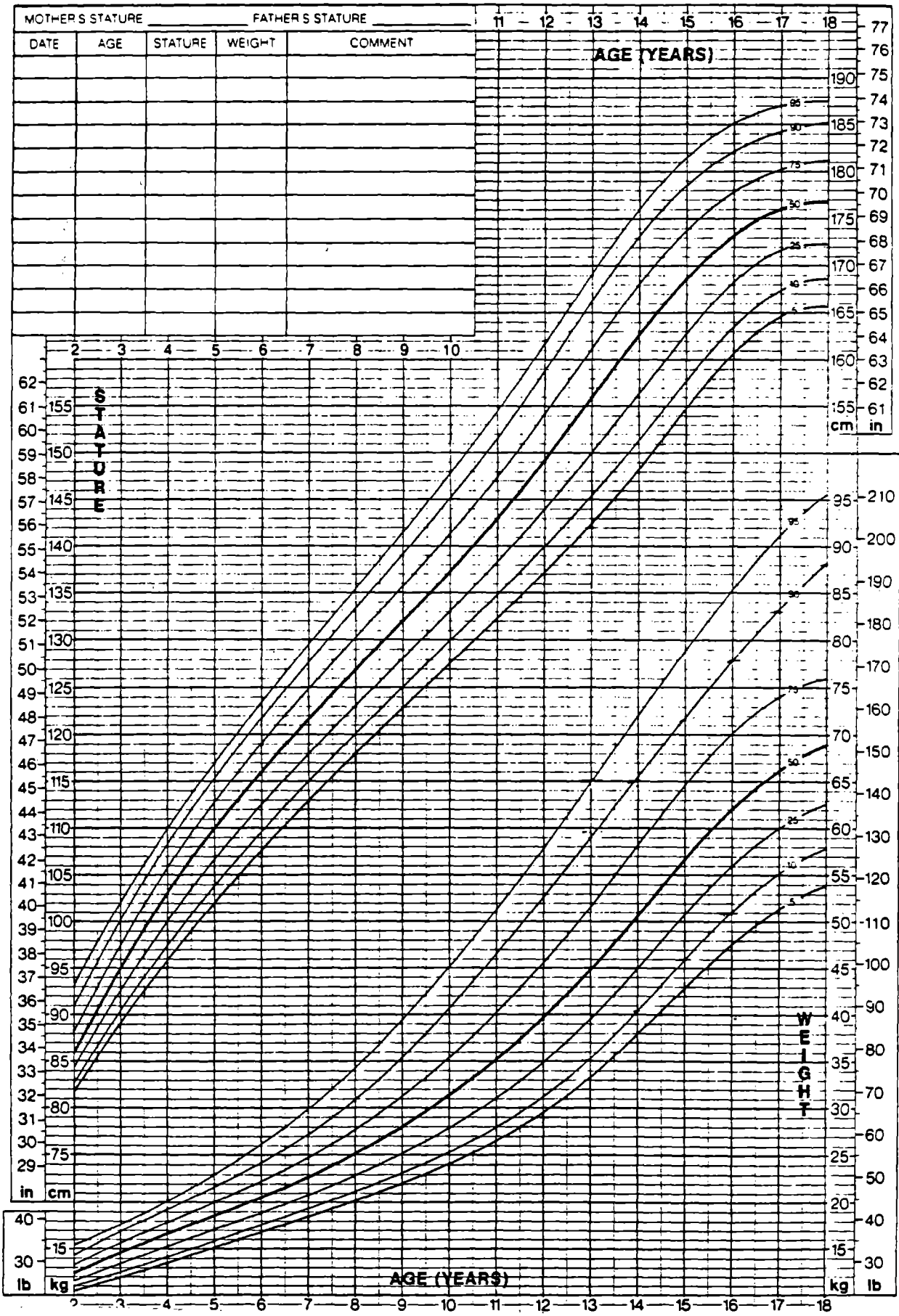
BOYS: 2 TO 18 YEARS PHYSICAL GROWTH NCHS PERCENTILES*

Figure 8.1c

NAME _____ RECORD # _____

MOTHER'S STATURE _____ FATHER'S STATURE _____

DATE	AGE	STATURE	WEIGHT	COMMENT



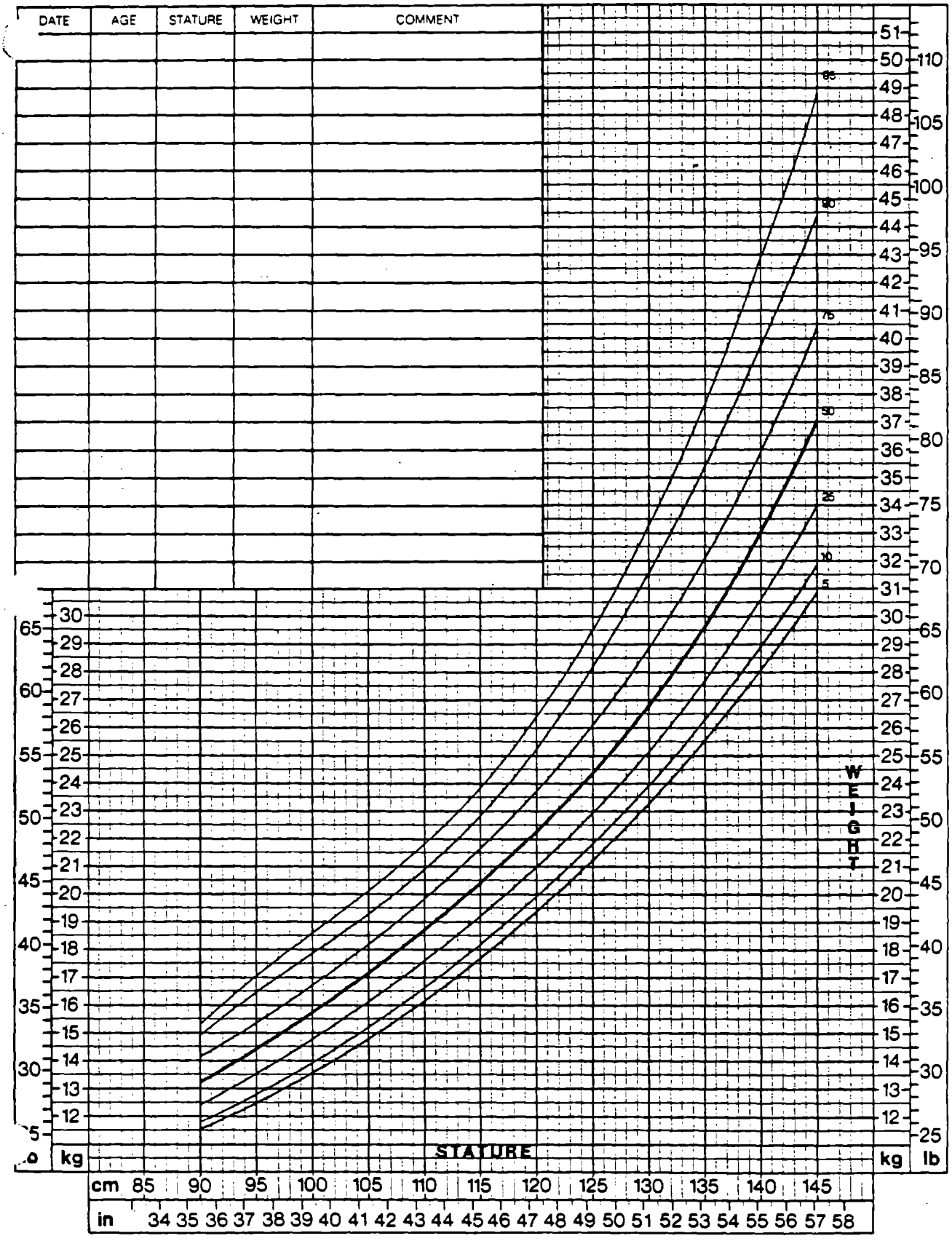
Ross Growth & Development Program

*Adapted from Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. AJCN 1979;32:607-629. Data from the National Center for Health Statistics (NCHS), Hyattsville.

BOYS: PREPUBESCENT PHYSICAL GROWTH NCHS PERCENTILES*

NAME _____ RECORD # _____

DATE	AGE	STATURE	WEIGHT	COMMENT



Adapted from Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. AM J Clin Nutr 32:607-629, 1979. Data from the National Center for Health Statistics (NCHS), Hyattsville, Maryland.

Table 8.2a

Plasma Total Cholesterol (mg/dl)*

MALES (white)

AGE	MEAN	S.D.	MEAN + 3 S.D.
10-14	157.6	23.86	229
15-19	149.9	26.70	230
20-24	166.5	29.70	256
25-29	182.2	36.15	291
30-34	192.2	34.61	296
35-39	201.3	38.53	317

MALES (black)

AGE	MEAN	S.D.	MEAN + 3 S.D.
10-19	160.4	25.30	236
20-29	178.5	36.44	288
30-39	191.6	37.36	304

*From the Lipid Research Clinic Population Studies Data Book, Volume 1, The Prevalence Study - Visit 1, U.S. Department of Health and Human Services, Public Health Service, NIH Publication No. 80-1527, July 1980.

Table 8.2b

Plasma Total Cholesterol (mg/dl)*

FEMALES (white)

AGE	MEAN	S.D.	MEAN + 3 S.D.
10-14	159.6	22.84	228
15-19	157.6	27.36	240
20-24	171.7	31.66	267
25-29	175.8	28.07	260
30-34	179.0	32.47	276
35-39	186.4	31.40	281

FEMALES (black)

AGE	MEAN	S.D.	MEAN + 3 S.D.
10-19	165.0	28.33	250
20-29	177.3	33.58	278
30-39	185.0	35.13	290

*From the Lipid Research Clinic Population Studies Data Book, Volume 1, The Prevalence Study - Visit 1, U.S. Department of Health and Human Services, Public Health Service, NIH Publication No. 80-1527, July 1980.

Table 8.3a

Obesity* Tables - MEN

Height	FRAME Small	Medium	Large
5'1"	164 pounds	170 pounds	181 pounds
5'2"	166	173	184
5'3"	169	176	187
5'4"	172	179	191
5'5"	174	182	195
5'6"	177	186	200
5'7"	181	190	204
5'8"	184	194	209
5'9"	187	198	213
5'10"	190	202	218
5'11"	194	206	222
6'0"	199	211	228
6'1"	203	216	233
6'2"	208	220	239
6'3"	213	226	246

*Defined as a body weight greater than 130% of the ideal body weight as defined by the 1983 Metropolitan Height and Weight Tables taken from the data of the 1979 Build Study, Society of Actuaries and Association of Life Insurance Medical Directors of America, 1980. These figures assume stocking feet and 5 pounds of indoor clothing.

Note that 1 pound = 0.454 kilogram.

Table 8.3b

Obesity* Tables - WOMEN

	F R A M E		
Height	Small	Medium	Large
4'9"	132 pounds	143 pounds	155 pounds
4'10"	134	146	159
4'11"	136	149	162
5'0"	139	152	166
5'1"	142	156	170
5'2"	146	160	174
5'3"	150	164	179
5'4"	154	168	183
5'5"	158	172	188
5'6"	162	176	192
5'7"	166	179	197
5'8"	170	183	201
5'9"	174	187	205
5'10"	177	191	209
5'11"	181	195	213

*Defined as a body weight greater than 130% of the ideal body weight as defined by the 1983 Metropolitan Height and Weight Tables taken from the data of the 1979 Build Study, Society of Actuaries and Association of Life Insurance Medical Directors of America, 1980. These figures assume stocking feet and 3 pounds of indoor clothing.

Note that 1 pound = 0.454 kilogram.

Table 8.4

Disqualifying Diseases

Subjects with a history or obvious manifestation of the following conditions will not be allowed into the trial unless evidence is presented that the condition is no longer active or present (no treatment for greater than five years prior to randomization):

1. Disorders of the heart -- cardiac dysrhythmias (including paroxysmal atrial tachycardia and WPW syndrome), congenital heart disease, rheumatic heart disease, valvular heart disease, ischemic heart disease, pericardial disease, cardiomyopathies, cardiac tumors and unusual forms of heart disease.

2. Disorders of the vascular system -- complicated arteriosclerosis (angina, coronary heart disease, claudication), hypertensive vascular disease (cardiomegaly, renal failure, cerebrovascular disease), diseases of aorta (e.g., coarctation, etc.), untreated hypertension.

3. Disorders of the respiratory system -- hypersensitivity pneumonitis, severe asthma (greater than three episodes per year requiring corticosteroid therapy -- mild asthma will not be excluded), chronic bronchitis, emphysema, bronchiectasis, lung abscess, broncholithiasis, infiltrative diseases of the lungs (e.g., sarcoidosis, silicosis, histiocytosis-X, etc.), neoplasms, primary pulmonary hypertension, pulmonary thromboembolism, cor pulmonale, adult respiratory disease syndrome, cystic fibrosis.

4. Diseases of the kidneys and urinary tract -- acute and chronic renal failure, glomerular diseases, nephrotic syndrome, history of recurrent urinary tract infections (greater than three times in past two years), obstructive uropathy, recurrent nephrolithiasis, cystic diseases of the kidneys, congenital and hereditary disorders of the kidney and urinary tract.

5. Diseases of alimentary tract -- cystic fibrosis, ciliac disease, and active giardiasis, carcinoma of stomach, colon and rectum, Crohn's disease, and ulcerative colitis.

6. Disorders of the hepatobiliary system -- genetic derangements of hepatic metabolism (excluding Gilbert's disease), disturbances of bilirubin metabolism, chronic active hepatitis, cirrhosis, liver tumors, active diseases of gallbladder and bile ducts.

7. Disease of pancreas (excluding diabetes) (e.g., pancreatitis, cancer).

8. Disorders of the hematopoietic system -- untreatable anemia (e.g., megaloblastic, sideroblastic, aplastic) associated with chronic

systemic disease, hemolytic anemias associated with hemoglobinopathies, polycythemia vera, agnogenic myeloid metaplasia, methemoglobinemia, platelet disorders, disorders of blood coagulation factors, diseases of the spleen and reticuloendothelium system (e.g., the leukemias, lymphomas and multiple myeloma).

9. History of neoplasia except benign lesions of the skin or subcutaneous fat (e.g., Wilm's tumor, pheochromocytoma). Basal cell carcinoma of skin and carcinoma in situ of cervix will be considered exclusion criteria.

10. Disorders of the nervous system -- symptomatic peripheral neuropathies other than diabetes, diabetic neuropathy requiring treatment, cranial nerve diseases (e.g., malignant tumors, brainstem syndromes, bulbar palsy, spinal cord diseases), cerebrovascular diseases, inflammatory diseases traumatic diseases of the brain, epilepsy (seizure-free for greater than five years while off medications for one year will be allowed into trial), neoplastic diseases of the brain, meningitis and encephalitis, multiple sclerosis and other demyelinating diseases, metabolic diseases of the nervous sytem, degenerative diseases of the nervous system, paralysis agitans (Parkinson's disease) and any progressive disorders of the nervous sytem, mental retardation disorders.

11. Psychiatric disorders -- the psychoses (e.g., manic-depressive and schizophrenic syndrome), drug and/or alcoholic addiction, personality disorders, bolemia and anorexia nervosa.

12. Diseases of the striated muscle -- myopathic paralyses, progressive muscular dystrophies, myasthenia gravis, dermatomyositis, polymyositis, etc.

13. Disorders of bone -- medullary carcinoma of the thyroid, Pagets' disease metabolic bone diseases, neoplasms, etc.

14. Disorders of the joints and connective tissues -- rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, inherited and other disorders of connective tissue (PAN, SLE, scleroderma, etc.), etc.

15. Nutritional deficiencies -- vitamin deficiency states.

16. Previous or current Endocrine disorders (e.g., pituitary, adrenal, etc.) other than diabetes, corrected primary hypothyroidism, and functional menstrual disorders.

17. Metabolic disorders (e.g., amino acid metabolism, storage diseases, errors in membrane transport, carcinoid syndrome, hemochromatosis, porphyrin metabolism disorders, hepatolenticular disorders, glycogen storage disorders, galactosemia, amyloidosis), hyperlipidemia Type I and severe IIA (greater than 99th percentile).

Table 8.5

Allowable Conditions

1. Cardiac finding not associated with an untoward outcome (e.g., innocent flow murmur, S4 heart sounds, mitral value prolapse).

2. Vascular conditions which might be permitted include Raynaud's disease (in absence of underlying scleroderma), chronic lymphedema, venous varicosities.

3. Respiratory conditions such as "hay fever", allergic rhinitis, chronic sinusitis, nasal polyposis, vasomotor rhinitis.

4. Although orthostatic and functional proteinuria have no untoward outcome, persons with these conditions cannot be enrolled into the study unless their morning recumbent urinary albumin excretion is below 34 mg/four hours. A history of pre-eclampsia and eclampsia (toxemias of pregnancy) will not be an exclusion.

5. Alimentary disorders such as chronic dyspepsia (without pathological condition to account for it), hiatal hernia or other non-malignant esophageal disorders, diverticulosis, hemorrhoids and anal lesions (fissures or ulcers). Gastritis, peptic ulcer disease, irritable bowel syndrome and asymptomatic cholelithiasis will not exclude. History of hepatitis without symptoms or abnormal liver function tests during the last five years, and cholecystectomy.

6. Treated iron deficiency anemia in multiparous women without evidence of other source of bleeding (e.g., G.I. tract), treated pernicious anemia.

7. A history of headaches (e.g., migraine, vascular, cluster) will not exclude a subject. Meniere's disease, Bell's palsy, trigeminal neuralgia and hearing loss will not exclude, unless caused by a tumor. Absence of seizures greater than five years off anticonvulsive therapy, except those clearly related to hypoglycemia. See exclusion criteria regarding hypoglycemic seizures.

8. A psychoneurosis will not be an excluding condition if in the judgment of the Principal Investigator the subject is able to comply with the requirements of the study.

9. Cured parathyroid adenomas, treated pseudogout and gout, and treated testicular and ovarian disorders.

10. A localized non-progressive disorder of a muscle (e.g., atrophy, absence, rupture or hemorrhage).

11. Chronic arthralgias, traumatic arthritis, Tietze's syndromes and degenerative joint diseases.

12. Lipid disorders, mild Type IIA, mild Type IIB (cholesterol less than 99th percentile), Types IV and V, would be allowed.

13. Menstrual irregularities may not exclude; pregnancy will exclude. Subjects with menstrual irregularities should have pregnancy or a specific ovarian-pituitary disorder eliminated as a cause of the irregularity.

14. Subjects with mild clinical signs or symptoms of neuropathy (e.g., mild postural hypotension, paresthesias, occasional mild leg cramps or pain, absent deep tendon reflexes, mild weakness, etc.) will not be excluded from the trial. Persons with any neurological abnormalities will be evaluated by a neurologist to exclude persons with alcoholic, inherited or nutritional neuropathies, as well as persons with multiple sclerosis, atherosclerotic related neuropathies and other neurological diseases.

Table 8.6

Definite Drug Exclusions - Current Usage

1. Chronic steroid usage (more than one month/year in preceding five years).

2. Oral antidiabetic agents (e.g., Diabinese, Dymelor, Orinase, Tolbutamide, Tolinase).

3. Antidiuretics (diabetes insipidus) (e.g., DDAVP, Diapid Nasal Spray, Pitressin).

4. Antineoplastics (e.g., antibiotic derivatives, anti-estrogens, antimetabolites, cytotoxic agents, hormones).

5. Antiparkinsonism drugs.

6. Bone metabolism regulator (e.g., Calcimar, Didronel, Vitamin D) (pharmacologic doses).

7. Digitalis preparations.

8. Quinidine.

9. Anti-anginal agents.

10. Dopamine receptor agonists (e.g., Parlodel).

11. Hormones (e.g., ACTH, anabolics, corticoids, glucocorticoids, gonadotropins, hypocalcemics (Calcimar), mineralocorticoids, vasopressin).

12. Immunosuppressants (e.g., Imuran, etc.).

13. Narcotic detoxification drugs (e.g., Methadone, etc.).

14. Antithyroid preparations (e.g., PTU, Tapazole).

15. Beta-blocker drugs (e.g., Corgard, Inderal, Lopressor).

16. Anti-hypertensive agents (e.g., Aldactazide, Aldactone, Aldomet, Apresoline, Catapres, Demi-Regroton, Demser, Diucardin, Diulo, Diuril, Enduron, Esidrix, Eutonyl, Harmonyl, HydroDIURIL, Hygroton, Inderide, Ismelin, Loniten, Metahydrin, Minipress, Moderil, Naqua, Naturetin, Nipride, Oretic, Raudixin, Rau-Sed, Regroton, Renese, Saluron, Serpasil-Apresoline, Ser-Ap-Es, Unitensen, Zaroxolyn, etc.).

17. Antifibrinolytic agents (e.g., Amicar).

18. Anti-inflammatory agents (e.g., steroids, steroid combinations).

19. Chelating agents (e.g., BAL, Cuprimine, Desferal).

20. Dapsone for dermatitis herpetiformis or leprosy.

21. Psychostimulants (e.g., Cenalene, Deaner, Desoxyn, Menic, Metrazol, Parnate, Pertofrane) during the previous year.

22. Sympatholytics (e.g., Bellergal, Regitine).

23. Antihyperlipidemic agents (e.g., Atromid-S, Choloxin, Levoid, Lorelco, Nicolar, Nico-Span, Questran, Colestid).

24. Parasympathomimetics.

Table 8.7
A Partial List of
Drugs Which Are Not Exclusions*

1. Oral contraceptive agents. Replacement premarin when used to treat primary ovarian failure or menopause.

2. Intermittent anti-infective agents and prophylaxis anti-tuberculous preparations.

3. Intermittent diuretics for cyclic edema (e.g., ethacrynic acid, mercurials, potassium sparing, thiazides, thiazide and combinations). Others: Diamox, Diula, Dyrenium, Hydromox, Lasix, Spironolactone, Zaroxolyn, etc., unless used to treat hypertension during the last five years.

4. Intermittent use of steroid aerosol sprays and steroids for asthma (less than or equal to two courses per year for a maximum of four weeks in past year).

5. Anti-asthma agents (e.g., Vanceril Inhaler).

6. Bronchodilators (e.g., sympathomimetics, xanthine deriviatives.

7. Intermittent ergot compounds for migraine (e.g., Ergotrate Maleate, Methergine).

8. Histamine H2 receptor antagonist -- Tagamet (intermittent and chronic use).

9. Parasympatholytics and non-absorbable antibiotics (anti-acid).

10. Sedatives (e.g., barbiturates, non-barbiturates).

11. Sympathomimetics (e.g., Benzedrine, amphetamines, Neo-Synephrine).

12. Intermittent tranquilizers (e.g., benzodiazepine, butyrophenones, chlordiazepoxide, hydroxyzines, meprobamate, Molindone HCL, phenothiazines, thioxanthenes, etc.), tricyclic antidepressants.

13. Anti-acne agents, including oral and topical antibiotics.

14. Intermittent aspirin, antihistaminics, phenacetin, prostaglandin inhibitors, during the last year.

15. Psoriasis and dandruff creams and shampoos.

16. Thyroxine, thyroid extract, Proloid, etc.

17. Steroid creams.

*The local investigator should make a judgment regarding randomization of subjects using these drugs.

Chapter 9

MEDICAL MANAGEMENT PROCEDURES

9.1 INTERVENTION STRATEGY IN THE STANDARD GROUP

The Standard Treatment regimen is meant to approximate within the context of a clinical trial conventional, "non-intensive" treatment of IDDM as it is carried out in typical subjects by experienced health care teams, including those of the participating centers.

9.1.1 Intervention Strategy

The recommended intervention strategy for the standard group is defined in terms of two sets of aims.

1. First Priority: To achieve absence of symptoms attributable to glycosuria or hyperglycemia; absence of ketonuria; maintenance of normal growth and development and ideal body weight; and freedom from frequent or serious hypoglycemia. The treatment team will be expected to intervene if any of the above priority one aims are not being met using their best judgment as health care providers. Such intervention will take the form of dietary reinforcement or change of type and dose of insulin within the recommended limit of two injections per day and within the standard schedule of clinic visits and monitoring procedures described below.

2. Second Priority: Even if the first priority aims are being met, intervention will be required when the HbA_{1c} exceeds two standard deviations above the mean value currently prevailing in insulin-dependent diabetic populations.[1] No intervention will be required if the first priority aims are being met and the HbA_{1c} value is at or below the mean plus two standard deviation levels of current insulin-dependent diabetics (i.e., 13.11). No intervention will be permitted with the object of raising the

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[1] This mean value, as determined from the Phase II Central Hemoglobin A_{1c} Laboratory's measurement of 205 blood specimens from a random sample of IDDM subjects from the 21 original participating clinical centers is 8.95 with a standard deviation of 2.08, using pre-incubated samples and a high performance liquid chromatograph (HPLC) technique. The upper action limit is 13.11.

HbA_{1c} level solely for the purpose of this study.

In the STANDARD GROUP, HbA_{1c} results will be routinely masked. HbA_{1c} analyses will be done in the Central Biochemistry Laboratory every three months. All values below the upper action limit will be reported to the investigator as "within acceptable limits" in an individualized format that can be shown or sent to the patient. Values exceeding the upper action limit will be reported to the investigator within two weeks of the time the blood sample is obtained as an "Alert" mandating treatment change according to the protocol. The actual HbA_{1c} value will be provided when it exceeds the upper action limit, and repeat HbA_{1c} analyses will thereafter be carried out as frequently as every month in the Central Biochemistry Laboratory until the value is brought below the upper action limit. No HbA_{1c} assays are to be routinely carried out in the local DCCT laboratory. However, in the event of a marked discrepancy between the reported HbA_{1c} and the clinical condition of the patient or the occurrence of a major intercurrent event which, in the investigator's judgment necessitates an interim HbA_{1c} analysis, an additional sample should be promptly sent to the Central Biochemistry Laboratory. At the same time, if deemed necessary by the investigator, an interim HbA_{1c} should be obtained at the local DCCT laboratory on an urgent basis.

It is anticipated that both the first and second priority aims can be met by adjustment of diet, insulin and exercise during regular (three monthly) clinic visits based on history, physical examination, urine testing and HbA_{1c} measurements. Self blood glucose monitoring is not deemed to be necessary to achieve these aims and is not to be encouraged. Indeed, self blood glucose monitoring in this group might adversely affect the outcome of the trial by reducing the difference in glucose levels between the Standard and Experimental Treatment Groups. Since self blood glucose monitoring is permitted at the patient's request, patient/staff interactions should not reinforce blood glucose monitoring in this treatment group. To avoid this, the following is recommended.

During routine clinic visits, it is important to carefully ascertain whether the patient is symptomatic and to assess growth prior to the review of urine or blood tests.

1. If the patient is asymptomatic, growing normally and urine tests are negative for ketones, then he/she is meeting primary priority aims and should be congratulated. Self blood glucose monitoring data (if being obtained) can be reviewed but, with one exception, should not be used to alter treatment. Exception: If blood glucose monitoring reveals consistent patterns of asymptomatic hypoglycemia (e.g., blood glucose consistently is less than 50 mg/dl before lunch), then the treatment regimen should be adjusted. Remember: Unacceptable hyperglycemia should be detected by glycohemoglobin measurements. Self blood glucose monitoring is not to be used by the investigator for the express purpose of lowering glycohemoglobin or blood glucose levels when first and second treatment priorities are being met.

2. If the patient is symptomatic or (in children) not growing, the timing and frequency of hyper- or hypoglycemic symptoms should be carefully assessed by history. Urine testing should be reviewed and correlated to the patient's complaints. Only then should blood glucose records (if being done at the patient's request) be examined. All of these data can be employed to adjust the treatment regimen within Protocol guidelines (e.g., up to two daily injections of insulin). At discharge from the clinic, the patient should be asked to keep track of symptoms and to record results of three to four daily urine tests to determine whether the recommended adjustments have been effective. Blood glucose testing should not be introduced or encouraged. The effectiveness of the adjustments should be determined by follow-up telephone contact within seven to fourteen days. The glycohemoglobin obtained during the clinic visit should be available by this time. If still symptomatic, further adjustments can be made based on history and urine testing. If two or three telephone consultations fail to resolve the problem, the patient should be seen back in the clinic. The treatment regimen should be reviewed, urine tests examined and another glycohemoglobin level obtained. Once again, blood glucose testing should not be encouraged or introduced at this juncture. However, if (after several visits) the patient persistently fails to meet either a first priority or second priority aim, then the treatment team must modify the standard treatment protocol as required to meet these priority aims (see Chapter 11, Modification of Treatment).

3. If the patient is asymptomatic but glycohemoglobin exceeds upper action limits, telephone contact is mandated. History of symptoms and urine testing data should be carefully reviewed. Adjustments in the treatment regimen can be made based on this information with follow-up procedures as outlined above. Markedly elevated glycohemoglobin levels in the face of aglycosuria mandates a review of urine testing techniques at the time of the next clinic visit.

4. If the patient is asymptomatic, growing normally and has glycohemoglobin levels below the upper action limit, he/she is meeting both first and second priority aims. A letter to the patient with the glycohemoglobin report, indicating that he/she is doing well, is recommended.

9.1.2 Insulin

Insulin will be administered as one or two injections per day. Mixtures of short-acting, intermediate-acting, and/or long-acting insulin may be employed as needed. Pork, mixed beef/pork or human insulin may be used.

9.1.3 Glucagon

At the start of treatment, each patient and a family member or friend should receive instruction on the proper use of glucagon to counteract severe hypoglycemia. Glucagon kits should be given to each patient.

9.1.4 Diet

The diet guidelines are designed to provide an acceptable healthy diet for both the Standard and Experimental Treatment Groups. An individualized meal plan which provides for the total nutritional needs of the patient will be an integral part of the treatment regimen. The meal plan will be quantitative in nature with individualization of amounts of food and of identifiable times of food consumption. The meal plan will be compatible with the remainder of the therapeutic regimen, e.g., with the insulin schedule and exercise patterns.

The meal plan will be designed to promote normal growth and development in adolescents and maintain ideal body weight in adults. It should be adaptable to the individual patient's needs with regard to cost, food availability, beliefs, cultural influences, particular tastes, and educational background. The American Diabetes Association's prudent fat diet employing exchange lists is a suitable basis for the initial dietary prescription on entry into the study, but it may be modified as necessary. Reinforcement of the dietary program will be carried out by the dietitian every six months.

In patients with persistent hypercholesterolemia (see Section 10.4.7), the prescribed cholesterol content of the diet will be lowered to less than 300 mg/day with a polyunsaturated to saturated fat ratio of approximately 1.0, and no more than 10% of calories as saturated fat. The diet will be modified when necessary to meet the requirements of other medical conditions.

Modifications of the basic diet considered necessary for maximal efficacy of the experimental treatment regimen are included in Section 9.2.4. In all other respects, the diets are structured so as not to provide any other significant dietary differences between the two groups.

9.1.4.1 Dietary Goals for all Subjects

A modified ADA diet or its equivalent will be observed.

1. Calories -- sufficient calories will be provided to achieve and maintain 90-120% of ideal body weight and/or provide for normal growth and development.

2. Carbohydrate -- 50% of total daily calories should be given as carbohydrate with 45-55% being an acceptable range. Simple sugars should supply no more than 25% of the carbohydrate calories.

3. Fat -- 30% of the total calories should be given as fat with an upper acceptable limit of 35%. Cholesterol should be no more than 600 mg/day and a polyunsaturated:saturated ratio of one is desirable with 0.8 the acceptable lower limit.

4. Protein -- "no less than the RDA for protein" which for adults is .8 grams per kilograms, .84 grams per kilograms for ages 15 to 18, and 1 gram per kilogram for ages 11 to 14.

5. Fiber -- to be encouraged from natural food sources without the use of pharmacologic fiber supplements.

6. Ethanol -- moderation. To be discussed individually.

The guiding principles of dietary therapy in diabetes including regularity and consistency of meals and avoidance of simple sugars will be observed.

9.1.4.2 Specific Recommendations for Standard Treatment Group

In order to achieve the first and second priority aims for the Standard Treatment Group, the following guidelines are suggested:

1. Consistency of meals -- meals should be similar (plus or minus 20%) in caloric content and carbohydrate content from day-to-day in order to prevent either hypoglycemia or symptomatic hyperglycemia secondary to a mismatch between calories and insulin.

2. Regularity -- since the majority of the standard group is taking some form of intermediate acting insulin as a part of its regimen, meals should be regular in their timing to prevent hypoglycemia from delayed feeding. In addition, the use of rapidly acting insulins makes the need for regularity of meals (approximately 15-45 minutes after the insulin injections) mandatory.

3. Snacks -- the use of once or twice per day intermediate acting insulins often requires a snack before dinner and/or before bedtime to "cover" the anticipated peaks of the insulin. If hypoglycemic reactions occur before lunch or before bedtime in regimens where rapid acting insulin is used once or twice/day respectively, either poor timing of the regular insulin or excessive doses of rapid acting insulin may be at fault. Inclusion of a snack at those times is usually not necessary if the timing and/or dosage of the insulin is properly adjusted.

4. Weight maintenance -- overtreatment with insulin is often the cause of weight gain above ideal body weight. The inclusion of three to four snacks per day to prevent hypoglycemia and the treatment of recurrent hypoglycemic reactions both increase the daily caloric intake. If weight gain (greater than 20% ideal body

weight) occurs in the standard group, the insulin regimen and diet should be reviewed with the patient at the regular office visit. Elimination of one or two snacks and/or the gradual decrease in caloric intake at meals (e.g., 10%) in conjunction with a decrease in the insulin dosage will serve to eliminate hypoglycemia and promote weight loss. Weight loss (less than 90% of ideal body weight) may be an indication that metabolic control is significantly abnormal and represents a deviation from a primary goal. Adjustment of insulin and diet are required to attain ideal body weight (90-120%).

9.1.4.3 Education

1. Screening -- During the screening and eligibility period, the dietitian should interview candidates, obtain a three-day food record as mandated for the behavioral tasks (Chapter 20), and obtain a diet history (Chapter 16). Other tools may be used by the dietitian to assess each candidate's present level of education and potential ability to learn and to implement the dietary recommendations necessary for the experimental group.

2. Post-randomization -- After randomization into the standard group, an educational consultation with the dietitian is required. Each standard group patient should achieve at least education level 1 (survival skills.[2] at the end of six months. Follow-up visits for dietary reinforcement and continuing education are required every six months. However, patients may be scheduled to see the dietitian quarterly or more often if it is needed to achieve their goals. At the end of the second year, patients are required to meet education level 2 (home management)[3] Progress toward achievement of education goals should be documented in each patient's DCCT record.

Dietary management has deliberately not been rigidly standardized. The dietitians may use any forms, pre-tests, post-tests, educational approaches and educational materials that are deemed suitable for each patient. It is expected that the educational materials used will not contain statements which are at cross-purposes to the protocol. Most importantly, such materials should not refer to normalization of blood glucose.

Dietary management is not being formally studied during this trial. (Note: the overall, usual composition of the diets in the standard and experimental treatment groups is being tracked with the diet history described in Chapter 16.) Food diaries and other

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[2] American Diabetes Association/American Association of Diabetes Educators. Guidelines for Diabetes Care. (1981), pp. 26-28.

[3] Ibid, pp. 29-35.

data acquired in the process of diet therapy will not be collected nor stored centrally. However, observations, experiences and insights that are noted by the dietitian should be reported to the principal investigator. Dietitians may also submit these observations and any suggestions to the DCCT nutrition coordinator.

9.1.5 Exercise

Specific exercise prescriptions are not required. Exercise will be encouraged according to the individual's interests and physical fitness. Scrupulous adjustment of insulin delivery and diet to the exercise pattern will be emphasized to ensure safety.

9.1.6 Self Monitoring

Standard group patients should be instructed to monitor their diabetes at home at least once a day. Urine tests three to four times a day is the preferred method. Second-voided specimens are recommended. At the discretion of the investigator, 24-hour urine collections for quantitative glucose determinations may also be requested.

Routine self blood glucose monitoring more than once a day should not be recommended unless the patient fails to meet the first priority treatment goals of the standard regimen, i.e., absence of symptoms attributable to glycosuria or hyperglycemia, absence of ketonuria, maintenance of normal growth and development and ideal body weight, and freedom from frequent or serious hypoglycemia.

Patients already performing self blood glucose testing at the time of entry should be encouraged to employ urine testing instead as the standard method of monitoring. Similarly, patients already performing urine testing who later seek to change to blood testing should be encouraged to continue urine testing as the standard method of monitoring. Patients who at any point insist on self blood glucose testing should be instructed that more than one test per day is not required for study purposes other than on sick days or during intercurrent events. They should be reminded that such tests are not for the purpose of achieving any day-to-day blood glucose targets. Rather, these tests are for the purpose of alerting the patient to the presence of asymptomatic hypoglycemia when blood glucose is less than 60, or to the necessity of testing urine for ketones when blood glucose is greater than 240.

Persistently negative urine glucose tests or blood glucose tests less than 60 mg/dl are indications for review of the treatment regimen so as to minimize the risk of hypoglycemia.

The results of urine or blood glucose testing will be used to change the treatment regimen if the patient exhibits symptomatic hyperglycemia, ketosis, or failure to grow and develop normally, or if the HbA_{1c} exceeds the upper action limit.

Self blood glucose monitoring is not to be encouraged unless necessary to achieve first or second treatment priorities. However, if self blood glucose monitoring is employed by the patient, it should be used only to ensure that first priority aims are being met. It should neither be used nor instituted at the election of the investigator for the express purpose of lowering HbA_{1c} or blood glucose when first and second treatment priorities are being met.

Blood glucose levels above 240 mg/dl, or urine glucose 2% or greater, or intercurrent illness are indications for urine ketone testing.

9.1.7 Problematic Issues for Standard Subjects Performing SBGM

When a patient consistently tests blood more than once a day on his/her own, the DCCT staff should seek the reasons for doing so. If these reasons include a desire to or a practice of adjusting insulin or diet so as to lower blood glucose to some specific target of the patient's, he/she should again be reminded of the hypothesis, premises and objectives of the trial. Efforts should be made to reinforce the patient's understanding of the research plan and to solicit the patient's continued participation in that plan.

When standard group patients seek interpretation by the DCCT staff of home urine or blood glucose test results, these results should be discussed within the context of the first priority standard treatment goals, i.e., avoidance of symptomatic hyperglycemia or ketosis, avoidance of hypoglycemia, and maintenance of a HbA_{1c} below the upper action limit. The primacy of the latter as an assurance of overall patient safety should be stressed. Patient concern over any particular home monitoring result or series of results should be deflected so long as those results do not reflect symptomatic hyperglycemia, ketosis or hypoglycemia. No "correct" or "approved" average blood glucose value should be communicated to the patient either directly or indirectly.

Self blood glucose testing materials sufficient for purposes of carrying out the goals of the DCCT should be provided by the DCCT to standard group patients who request such materials. This would usually be limited to blood glucose strips read by comparison with a color chart in numbers sufficient for one test per day. Larger quantities of strips and/or meters should only be provided by the DCCT when required in order to meet the first priority treatment goals for the standard group. Thus, patients who are meeting these goals and who HbA_{1c} is below the upper action limit should not be provided extra strips or meters at their request. This should be made clear to patients on entering the study. It is recognized that this might constitute a problem in the case of patients who were already testing blood more than once per day on a

routine basis prior to entering the trial. However, it is hoped that those who were doing so in a relatively casual, nonfeedback manner would welcome the relief from the necessity of testing so often. Those patients testing often and using the values for adjusting insulin should, of course, not be recruited into the trial.

9.1.8 Clinic Visits

Patients in the standard treatment group will be seen at three-month intervals and will be assessed by: history, emphasizing symptoms of glycosuria; physical examination, with particular emphasis on growth in adolescents and children; review of patient-recorded home urine tests; a home blood glucose collection consisting of 7 samples will be analyzed at the CBL; blood sample drawing for CBL analysis of HbA_{1c} and, at the discretion of the investigator, fasting or random plasma glucose.

9.1.9 Educational Program

An educational program will be provided to ensure that a complete cycle of the subject matter is covered every two years (hygiene, foot care, urine testing, injection techniques, insulin reactions, management of intercurrent illness, etc.). The educational program will also include reinforcement of participation in the clinical trial (see Section 9.5).

9.1.10 Protection of Subjects

In the event that a patient in the standard group cannot be successfully managed by the intervention strategy outlined above, i.e., persistently fails to meet either a first or second priority aim, then the investigator must modify the standard regimen. Such modifications may include the use of more frequent subject-staff outpatient contact, more intensive dietary instruction, and hospitalization for metabolic control. These modifications will be reviewed by the Treatment Committee. If more than two injections or an insulin pump is considered necessary to achieve first and second priority aims, prior permission of the Treatment Committee must be obtained. So long as any modification is only for the purpose of achieving the first and second priority aims in Section 8.1.1, it will not constitute a deviation from the standard treatment protocol (see Section 12.3 for the definition of deviation from the standard treatment protocol).

9.2 INTERVENTION STRATEGY IN THE EXPERIMENTAL GROUP

The experimental treatment regimen is designed to achieve and maintain control of blood glucose as near normal as possible in the absence of significant hypoglycemia. Therefore, in addition to meeting the criteria stipulated for the standard regimen, the intensity of treatment in the experimental regimen is directed toward specific additional targets.

9.2.1 General Guidelines

1. Aims: The aim in the experimental treatment group is to achieve and maintain as near normal glycemic control as possible in the absence of significant hypoglycemia.

   For Plasma Glucose:
   Fasting and preprandial levels: 70-120 mg/dl
   3:00 a.m.: 65 mg/dl or above
   Postprandial plasma levels:
   less than 180 mg/dl (90-120 minutes after meal)

   For HbAlc: The goal will be to maintain the HbA_{1c} level within two standard deviations of the mean for a sample of people without diabetes. A value more than two standard deviations will be an upper limit dictating more aggressive treatment.[4]

   In the EXPERIMENTAL GROUP HbA_{1c} values will be UNMASKED. The required monthly HbA_{1c} analysis will be done in the Central Biochemistry Laboratory, and the individual values will be reported to the investigator within two weeks of the time the blood sample is obtained. No HbA_{1c} assays will be performed in the local DCCT laboratory.

   For Hypoglycemia: The goal will be no episodes of hypoglycemia which require assistance or which are associated with altered mental status, even if self-treatment is successful; and fewer than four mild episodes per week, i.e., without significant mental impairment and easily self-treated.

2. Discussion: The guidelines for responding to blood glucose determinations in this group are extensively discussed in the sections detailing the pump and MDI treatment protocols.

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[4] This mean value, as determined from the Phase II Central Hemoglobin A_{1c} Laboratory's measurement of 124 blood specimens from a random sample of non-diabetic subjects from the 21 original participating clinical centers, is 5.05 with a standard deviation of 0.50, using pre-incubated samples and a high performance liquid chromatograph technique. The upper action limit is 6.05.

One of the aims in this treatment group is to keep the glycosylated hemoglobin level within two standard deviations of the mean for the non-diabetic population. A value more than two standard deviations above the mean for a sample of non-diabetic persons will be an upper action limit dictating more aggressive treatment. However, it should be noted that an equally (if not more) important goal is to avoid any episode of hypoglycemia which requires assistance or is associated with altered mental status. In general, by employing the methods outlined we hope to be able to achieve both treatment goals. However, patients who persistently have mild elevations in glycohemoglobin (i.e., between two to three standard deviations above the mean for a sample of non-diabetic persons) may be particularly difficult problems for the following reasons:

a) In many cases, this glycohemoglobin level represents a marked improvement over pre-study values and may represent the "best" that this subject can do. While more agressive treatment is mandated, this should be approached in a positive manner. The staff needs to guard against giving the impression that the patient is not doing well.

b) In this setting, more aggressive treatment may result in increased problems with hypoglycemia and little or no change in glycohemoglobin. Remember, recurrence of moderate to severe hypoglycemia mandates an analysis of the problem.

c) While closer attention should help lower glycohemoglobin, it is important that this not be interpreted as harassment which would be counterproductive. Once again, patience and a supportive attitude on the part of the staff is critically important.

9.2.2 Insulin

Intensive insulin delivery will be carried out in one of two ways:

1. Insulin may be delivered by continuous subcutaneous infusion employing a pump and consisting of a basal infusion rate coupled with preprandial doses (pump, CSII).

2. Insulin may be administered as three or more subcutaneous injections of insulin daily (MDI).

3. Pork, mixed beef/pork, or human insulin may be employed.

The choice of insulin delivery method shall rest with the DCCT treatment team and the individual subject. Either pump or MDI may be tried first and the alternate method employed if treatment goals are not met. For purposes of data analysis, subjects treated by pump only, subjects treatment by MDI only, and subjects treated by both pump and MDI

will constitute a single group whose outcomes will be compared to those of the Standard Treatment Group.

9.2.2.1 Pump Treatment Protocol

1. General Considerations: The strategy behind subcutaneous insulin pump therapy is to provide appropriate and adjustable amounts of insulin preprandially with major meals and an infusion of insulin primarily directed at maintaining overnight basal requirements. It is useful for both educational purposes and for adjusting treatment regimens to view basal insulin replacement and premeal insulin doses as distinct entities.

   a) Hospitalization: Required for all patients for orientation to pump treatment.

   b) Injection Sites: Anterior abdominal wall is the preferred site, although others, such as thighs, may be employed. Sites should be rotated every one to two days. Routine preparation of site includes cleansing with alcohol, Betadine, etc., before insertion of needle. Certain patients may be more susceptible to site infections, presumably due to staphylococcal colonization. More frequent site rotation and cleansing with hexachlorophene may help alleviate problems. If patients report pain and erythema while using one insulin preparation, this may be resolved by switching to an alternative preparation.

   c) Diet: Within the limits of the recommended dietary prescription, individualization to correspond, as much as possible, to usual eating habits is encouraged. In particular, careful attention to timing as well as content of meals during the initial orientation to pump treatment is important.

   d) Prepump Insulin Treatment: On the day prior to start of pump treatment, patients can be maintained on their usual treatment regimen or be given multiple daily injections of short-acting insulin.

2. Selection of Initial Insulin Doses: A variety of methods has been employed. Listed below is a generally acceptable regimen:

   a) Total Dose: Equal to the patient's usual outpatient daily insulin dosage.

   b) Basal Infusion Dose: 30-50% of total dose given as an hourly infusion rate over 24 hours.

c) Total Pre-meal Bolus Dose: Total dose minus Basal infusion dose distributed as follows:

Pre-breakfast:	25-40%
Pre-lunch:	20-25%
Pre-supper:	25-35%

Bolus doses of insulin are usually given 15-30 minutes before the meal.

d) Snacks and Snack Doses: Approach to between-meal snacks has varied. Morning snacks are only rarely required, midafternoon snacks are commonly employed and all should receive bedtime snacks. Snacks are particularly useful if there is a long interval between meals (greater than or equal to six hours). Small supplemental insulin doses (5-10% of total pre-meal dose) are often employed to cover snacks but some investigators find this unnecessary.

e) Alternative methods such as determining 24-hour insulin requirements using a closed-loop insulin infusion system are acceptable.

3. Initial Adjustment Period:

a) Blood Glucose Monitoring: Minimal requirements during initial adjustment of doses are: before and 90-120 minutes after each meal, before bedtime snack, midnight, and 3:00 a.m. Blood samples may be obtained from an indwelling intravenous catheter, heparin lock or by finger stick. Self blood glucose monitoring by the patients will also be performed to compare with laboratory results. Once the patient's training in self blood glucose measurement has been satisfactorily accomplished, his/her values may be used exclusively for further adjustment of the treatment regimen.

b) Adjustment of Basal Infusion Rate: Most insulin pumps at present can be programmed to deliver multiple basal rates. However, under most circumstances, a single 24 hour rate is sufficient to maintain adequate insulin delivery overnight. The basal infusion rate is adjusted to obtain target glucose levels before breakfast (70-120 mg/dl) and to avoid hypoglycemia at 3:00 a.m. (usual overnight nadir of blood glucose). In general, the daytime basal rate is not altered because of postprandial hyper- or hypoglycemia since these problems usually reflect the adequacy of the premeal bolus dose. The basal rate is increased by 10-15% per day to achieve the above goals. In patients switched directly from conventional to pump treatment, a basal rate which appeared adequate on day one is often found to be insufficient on day two. Presumably, this reflects a carry-over effect of intermediate or long-acting insulin.

Occasionally, it is difficult to obtain target, pre-breakfast blood glucose levels without unacceptably low 3:00 a.m. values. If this occurs, two modifications in insulin can be tried: (1) reduce or eliminate the pre-bedtime snack bolus dose if one is being given, or (2) switch to a variable basal rate program.

c) Adjustment of Premeal Insulin Doses: Premeal insulin doses are adjusted to eliminate excessive postprandial hyperglycemia (more than or equal to 180 mg/dl) and to avoid hypoglycemia before the next meal. Doses are adjusted by one or two units, based on the prior day's experience. The goal is to determine how much insulin is required by the patient for his/her usual breakfast, lunch, and supper. The amount of insulin required for a given meal will be influenced by a number of factors, including premeal blood glucose level, size and content of the meal and the amount of anticipated postprandial exercise. Insulin meal dose adjustments to compensate for the premeal blood glucose level can be performed in two ways. In the first instance, patients are given a fixed premeal insulin dose with an algorithm for supplementing or reducing this dose based on the degree of deviation of the premeal blood glucose from the target value. Although theoretically sound, patients may develop the practice of administering the prescribed premeal insulin dose and not supplementing. A second approach utilizes a variable insulin dose schedule which is directly determined by the premeal self blood glucose monitoring result. Patients are advised that they can not determine the appropriate premeal insulin dose until they self monitor. An example of one such schedule is shown in Table 9.1. When the amounts of insulin required for a particular meal are substantially larger or smaller, the size of the incremental adjustment is also proportionally larger or smaller. In the latter case, increments of less than one unit may also be employed. The variable insulin dose schedule will be modified with experience for each patient and need not vary linearly with blood glucose. It is also likely to change with time.

Common Pitfalls:

- In some patients, control of post-meal hyperglycemia can only be obtained at the expense of hypoglycemia before the next meal. In this situation, redistribution of calories to include a between-meal snack with or without a small supplemental dose or earlier initiation of the premeal bolus (i.e., 30-40 minutes) may be helpful.

- Mild premeal hypoglycemia is not an indication to omit the premeal bolus. Instead, the dose should be reduced (as indicated in the above schedule) and given immediately with or right after eating.

- Between-meal hypoglycemia should be treated with five to ten grams carbohydrate supplement in order to avoid post-hypoglycemic hyperglycemia.

d) Patient Education: A major purpose of the initial hospitalization is to incorporate the patient into the "team" which will be striving to keep his/her blood glucose values as close to normal as possible. Each must obtain the technical skills in the management of the infusion device and demonstrate the ability to measure blood glucose levels accurately. These are confirmed by simultaneous laboratory determinations which should be routinely performed at monthly clinic visits using the patient's meter. Even more importantly, each must become proficient in using the monitoring data to alter his/her own treatment regimen. At the start, the rationale for initial selection of basal and premeal doses should be carefully explained. Subsequently, specific attention must be paid to involve the patient in the decision-making process. By discharge, the patient should be the primary person making these decisions.

e) Other Requirements Prior to Discharge:

i) Patient and family will be instructed in the treatment of hypoglycemia, including the use of glucagon. Patients will be discharged with glucagon kits.

ii) Review of "sick day" management and ketosis.

iii) Specific instructions will be given on how to reach the on-call treatment team.

4. Outpatient Followup:

a) Guidelines concerning frequency of self blood glucose monitoring telephone contacts and clinic visits are given in Sections 9.2.7 and 9.2.8. Clinical visits and telephone contacts are most frequent during the initial weeks of outpatient pump treatment to adjust for changes in diet and exercise, to extend the learning process and to develop further the relationship between patients and staff.

b) Adjustment of doses due to changes in diet: A goal of the initial hospitalization was to determine insulin requirements for the patient's usual meals. During outpatient pump treatment, meal size and content is likely to be much more variable. A goal of this phase of treatment is to determine the dosage adjustments required for unusually large or small meals. An empirical approach is to start with small adjustments (one to two units) which are then modified by experience, i.e., postprandial excursions. Demonstrations of how timing and content of meals influence blood glucose fluctuations should be used to reinforce dietary principles and compliance.

c) Adjustments for exercise: Hypoglycemia may occur with variable degrees of exercise in individual patients. Hypoglycemia due to planned postprandial exercise can usually be prevented by reducing the preceding preprandial bolus dose by one-third to one-half the usual amount. In some patients, reducing the basal infusion rate and/or providing extra carbohydrate may also be required. Exercise performed before breakfast may or may not require a decrease in the basal infusion rate. Rarely, in patients whose work involves vigorous activity, a variable basal rate (i.e., lower during the day and higher during the night) may be employed. Simply removing the pump for activities such as swimming is also acceptable as long as the time interval is no longer than four hours from the last preprandial bolus. However, if the time interval is prolonged and/or it overlaps with a regular meal, then rapid acting insulin should be given by injection to cover the meal. All adjustments for exercise need to be individualized and should be based on blood glucose measurements.

d) Adjustments of "usual" dose: Changes in the basal infusion rate and usual premeal bolus doses should also be expected. For example, many women experience such changes depending on the phase of their menstrual cycle. The basal rate should be adjusted according to daily fasting and weekly 3:00 a.m. blood glucose levels during the initial adjustment period. The need for alteration in the "usual" preprandial dose will be apparent by repeated patterns of high or low blood glucose before the next meal. For example, the repeated need for supplemental insulin before supper due to high blood glucose values indicates that the lunch dose should be increased.

e) Acute decompensation: Several investigators have suggested that patients on pump treatment may be more susceptible to the development of ketosis/ketoacidosis. Certainly, interruption of the infusion because of needle dislodgement, catheter leakage or occlusion, or battery failure places the patient at risk because only rapid acting insulin is being infused. The key to minimizing this problem is early recognition. If a premeal blood glucose value is unexpectedly elevated (greater than 240 mg/dl), patients should check their urine for ketones and check the pump to insure that the system is functioning properly. The needle should be pulled out and the flow of insulin checked by observing its emergence from the tip. The needle should be inserted in a new subcutaneous site.

   i) If the urine is free of ketones, supplemental insulin is given according to the preprandial variable dosage schedule. Blood glucose must then be rechecked before the next meal.

   ii) If there is acetonuria but the patient is asymptomatic, then an extra one or two units above the usual supplement should be given. In addition, the patient must recheck blood and urine tests before the next meal.

The on-call treatment team member must be contacted if, after these maneuvers, blood glucose and urine ketones remain unchanged or are rising. At this point, the entire infusion system including syringe, insulin and catheter should be changed. Patients should contact the on-call treatment team member immediately if symptomatic.

A pump runaway situation with discharge of the controls of the syringe/reservoir is a potential danger of pump treatment. If this occurs or is even suspected, patients should disconnect the pump at once. They should check their blood glucose and eat. They should also call in immediately.

f) Persistent failure to achieve experimental group aims: By employing the above procedures, it is anticipated that most patients should be able to achieve the target aims of the experimental group. However, maintenance of near normal glycemic control over prolonged periods is central to the success of the study. It cannot be emphasized too much that the key to obtaining this goal is continued close contacts between patients and staff. Such contacts should provide positive reinforcement and encouragement to the patients. Once stabilized, monthly outpatient visits and weekly telephone contacts should be sufficient. Indeed, if the patient is doing well, more frequent contact would probably be counter-productive. On the other hand, if the patient consistently fails to meet the aims of this group, closer attention is mandatory. The following may be helpful:

i) Careful review of technical skills regarding operation of pump and blood glucose monitoring procedures.

ii) More frequent blood glucose monitoring to include two-hour postprandial determinations.

iii) Confirm accuracy of patient's results by comparing blood glucose values determined by the patient at home with levels from capillary blood samples collected at the same time and measured in the laboratory.

iv) More frequent (one to two per week) clinic visits with more intensive dietary counseling. Review and reinforce concepts of insulin adjustments for premeal glucose, diet and exercise.

v) Ascertain whether intercurrent psychosocial problems may be interfering with adherence/compliance. Intervene where possible and appropriate.

vi) Consider hospitalization for readjustment of doses and reeducation.

It should be noted that patience and a supportive attitude may be particularly helpful. Problems which might at first appear insurmountable often work themselves out in a reasonable period of time.

9.2.2.2 Multiple Daily Injection Treatment Protocol

1. General Considerations:

The considerations for use of MDI are essentially the same as those outlined for use of an insulin pump (see previous section). Regular insulin boluses will be given prior to each meal and when necessary prior to a major snack. The basal infusion will be mimicked as follows: An injection of intermediate-acting insulin may be given at bedtime or with the supper dose. An injection of long-acting insulin may be given once a day (at supper) or split (at breakfast and supper).

Specifically:

a) Hospitalization: Required for all patients for introduction to MDI and dose selection.

b) Injection Sites: Anterior abdominal wall is the preferred injection site. Routine preparation of site includes cleansing with alcohol, Betadine, etc., before insertion of needle. Suitable indwelling catheters may also be used.

c) Diet: Within the limits of the recommended dietary prescription, individualization to correspond as much as possible to usual eating habits is encouraged. In particular, careful attention to timing as well as content of meals during the initial orientation to MDI treatment is important.

d) Pre-MDI Insulin Treatment: On the day prior to start of MDI treatment, patients can be maintained on their usual treatment regimen or be given multiple daily injections of short-acting insulin.

2. Selection of Initial Insulin Doses:

a) Total Dose: Equal to the patient's usual outpatient daily insulin dosage.

b) "Basal" Dose: If long-acting insulin is used to provide basal coverage, 40-60% of total dose is given as Ultralente prior to supper. This may be mixed with the short-acting pre-supper insulin. If the Ultralente dose is split, half is given with breakfast and half with supper. If intermediate-acting insulin is used to provide basal coverage, 20-30% of the total dose is given as intermediate-acting insulin prior to bedtime.

c) Total Pre-Meal Bolus Dose = (total dose minus basal dose) distributed as follows:

Pre-breakfast:	25-40%
Pre-lunch:	20-25%
Pre-supper:	25-35%

Bolus doses of insulin are usually given 15-30 minutes before the meal.

d) Snacks and Snack Doses: The approach to provision of and coverage for between-meal snacks has varied. Morning snacks are only rarely required; midafternoon snacks are commonly employed, and all should receive pre-bedtime snacks. Snacks are particularly useful if there is a long interval between meals (greater than six hours). Snacks (particularly the bedtime snack) generally do not require supplemental insulin administration. Small supplemental insulin doses (5-10% of total pre-meal dose) are employed by some investigators to cover snacks.

e) Alternative methods, such as determining 24-hour insulin requirements using a closed-loop insulin infusion system, are acceptable.

3. Initial Adjustment Period:

a) Blood Glucose Monitoring: Minimal requirements during initial adjustment of doses are: before and 90-120 minutes after each meal, before bedtime snack, midnight, and 3:00 a.m. Blood samples may be obtained from an indwelling intravenous catheter, heparin lock or by finger stick. Self blood glucose monitoring by the patients will also be performed to compare with laboratory results. Once the patient's training in self blood glucose measurement has been satisfactorily accomplished, his/her values may be used exclusively for further adjustment of the treatment regimen.

b) Adjustment of Basal Dose: The long-acting dose is adjusted to obtain target glucose levels before breakfast (70-120 mg/dl) and to avoid hypoglycemia at 3:00 a.m. (usual overnight nadir of blood glucose). In general, the long-acting insulin dose is not altered because of postprandial hyper- or hypoglycemia since these problems usually reflect the adequacy of the premeal bolus dose. The long-acting insulin dose is increased by 10-15% per day to achieve the above goals. In patients switched directly from conventional to MDI, several days may be required before adequate fasting plasma glucose concentrations can be achieved, presumably reflecting a delay in achieving "steady-state" insulin concentrations with a change in the long-acting insulin dose.

Occasionally, it is difficult to obtain target, prebreakfast blood glucose levels without unacceptably low 3:00 a.m. values. If this occurs, reduction or elimination of the pre-bedtime snack bolus dose (if one is being given), or an increase in the size of the evening snack is often helpful. Conversely, an unacceptably high 3:00 a.m. plasma glucose value, which therefore results in an unacceptably high pre-breakfast value, frequently results from too large a bedtime snack or insufficient pre-supper short-acting insulin rather than insufficient long-acting insulin.

c) Adjustment of Premeal Insulin Doses: Premeal insulin doses are adjusted to eliminate excessive postprandial hyperglycemia (more than or equal to 180 mg/dl) and to avoid hypoglycemia before the next meal. Doses are adjusted by one or two units, based on the prior day's experience. The goal is to determine how much insulin is required by the patient for his/her usual breakfast, lunch, and supper. The amount of insulin required for a given meal will be influenced by a number of factors, including premeal blood glucose level, size and content of the meal and the amount of anticipated postprandial exercise. Insulin meal dose adjustments to compensate for the premeal blood glucose level can be performed in two ways. In the first instance, patients are given a fixed premeal insulin dose with an algorithm for supplementing or reducing this dose based on the degree of deviation of the premeal blood glucose from the target value. Although theoretically sound, patients may develop the practice of administering the prescribed premeal insulin dose and not supplementing. A second approach utilizes a variable insulin dose schedule which is directly determined by the premeal self blood glucose monitoring result. Patients are advised that they can not determine the appropriate premeal insulin dose until they self monitor. An example of one such schedule is shown in Table 9.1. When the amounts of insulin required for a particular meal are substantially larger or smaller, the size of the incremental adjustment is also proportionally larger or smaller. In the latter case, increments of less than one unit may also be employed. The variable insulin dose schedule will be modified with experience for each patient and need not vary linearly with blood glucose. It is also likely to change with time.

Common Pitfalls:

- In some patients, control of postmeal hyperglycemia can only be obtained at the expense of hypoglycemia before the next meal. In this situation, redistribution of calories to include a between-meal snack with or without a small supplemental dose or earlier initiation of the premeal bolus (i.e., 30-45 minutes) may be helpful.

- Mild symptomatic premeal hypoglycemia is not an indication to omit the premeal bolus. Instead, the dose should be reduced

(as indicated in Table 9.1) and given immediately with or right after eating.

- Between-meal hypoglycemia should be treated with five to ten grams carbohydrate supplement in order to avoid post-hypoglycemic hyperglycemia.

d) Patient Education: A major purpose of the initial hospitalization is to incorporate the patient into the "team" which will be striving to keep his/her blood glucose values as close to normal as possible. Each must obtain the technical skills in the use of the glucose measuring devices and demonstrate the ability to measure blood glucose levels accurately (confirmed by simultaneous laboratory determinations). Even more importantly, each must become proficient in using the monitoring data to alter his/her own treatment regimen. At the start, the rationale for initial selection of basal and premeal doses should be carefully explained. Subsequently, specific attention must be paid to involve the patient in the decision-making process. By discharge, the patient should be the primary person making these decisions.

e) Other Requirements Prior to Discharge:

i) Patient and family will be instructed in the treatment of hypoglycemia, including the use of glucagon. Patients will be discharged with glucagon kits.

ii) Review of "sick day" management and ketosis.

iii) Specific instructions will be given on how to reach the on-call treatment team.

4. Transition to Outpatient Status:

Assuming that variability due to exercise and diet will be greater in the outpatient than in the inpatient setting, upon discharge it is usually safer to instruct patients to decrease the amounts of insulin required for their usual diet (i.e., X, Y, Z and A in the previous example) by one unit. This recommendation is based on the premise that (a) until patients become adept at adjusting their insulin doses, they are at greater risk of hypoglycemia, and (b) it is more desirable to adjust the insulin dose schedule in the outpatient setting so as to bring slightly "high" preprandial glucose values down rather than slightly "low" preprandial glucose values up. Patients will contact the clinic daily until a stable program has been achieved. At this time, patients will review the alterations in the pre-meal bolus doses that they made on the previous day. During this transition period, patients will be instructed not to alter the long-acting insulin dose without prior consultation with the clinic.

9.2.3 Diet

The diet guidelines are designed to provide an acceptable, healthy diet for both the standard and experimental groups. An individualized meal plan which provides for the total nutritional needs of the patient will be an integral part of the treatment regimen. The meal plan will be quantitative in nature with individualization of amounts of food and of identifiable times of food consumption. The meal plan will be compatible with the remainder of the therapeutic regimen, e.g., with the insulin schedule and exercise patterns.

The meal plan will be designed to promote normal growth and development in adolescents and maintain ideal body weight in adults. It should be adaptable to the individual patient's needs with regard to cost, food availability, beliefs, cultural influences, particular tastes, and educational background. The American Diabetes Association's prudent fat diet employing exchange lists is a suitable basis for the initial dietary prescription on entry into the study, but it may be modified as necessary. Reinforcement of the dietary program will be carried out by the dietitian every six months.

In patients with persistent hypercholesterolemia (see Section 8.2.1 - 5b), the prescribed cholesterol content of the diet will be lowered to less than 300 mg/day with a polyunsaturated to saturated fat ratio of approximately 1.0, and no more than 10% of calories as saturated fat. The diet will be modified when necessary to meet the requirements of other medical conditions.

Modifications of the basic diet considered necessary for maximal efficacy of the experimental treatment regimen are included in Section 9.2.3.2. In all other respects, the diets are structured so as not to provide any other significant dietary differences between the two groups. Compliance with the dietary recommendations is expected. However, the major goal of the experimental intervention is to attain the target blood glucose levels. If subjects in the experimental group are attaining their blood glucose goals, the dietary goals should be considered as secondary goals. The secondary (diet) goals should not be pursued if it is at the expense of the primary goals.

9.2.3.1 Dietary Goals for all Subjects

A modified ADA diet or its equivalent will be observed.

1. Calories -- sufficient calories will be provided to achieve and maintain 90-120% of ideal body weight and/or provide for normal growth and development.

2. Carbohydrate -- 50% of total daily calories should be given as carbohydrate with 45-55% being an acceptable range. Simple sugars should supply no more than 25% of the carbohydrate calories.

3. Fat -- 30% of the total calories should be given as fat with an upper acceptable limit of 35%. Cholesterol should be no more than 600 mg/day and a polyunsaturated:saturated ratio of one is desirable with 0.8 the acceptable lower limit.

4. Protein -- "no less than the RDA for protein" which for adults is .8 grams per kilograms, .84 grams per kilograms for ages 15 to 18, and 1 gram per kilogram for ages 11 to 14.

5. Fiber -- to be encouraged from natural food sources without the use of pharmacologic fiber supplements.

6. Ethanol -- moderation. To be discussed individually.

The guiding principles of dietary therapy in diabetes including regularity and consistency of meals and avoidance of simple sugars will be observed. The specific recommendations that follow are directed at ensuring the success of MDI and insulin pump therapy in attaining the target blood glucose goals.

9.2.3.2 Specific Recommendations for Experimental Treatment Group

1. Consistency of meal size and composition and adjustment of preprandial dose.

   The matching of insulin dose to preprandial blood glucose concentration and size of meal is unique to MDI and pump therapy. Patients must be carefully instructed in determining insulin bolus size for a given meal. Widely varying meal sizes (in either total caloric or carbohydrate content) from day-to-day make adjustment of preprandial boluses difficult. The use of a strict ADA exchange diet is in general not necessary although an understanding of the carbohydrate-protein-fat content of foods is important in determining size of the preprandial bolus.

   a) Although some patients will adjust the size of the meal depending on the preprandial blood glucose concentration and hold the preprandial bolus constant, most subjects should be taught to adjust the preprandial bolus.

   b) The adjustment of bolus size on the basis of the meal size and content becomes second nature to most experimental pump/MDI patients. However, the new pump/MDI patient must be taught a variable dose insulin scale for diet as he is taught a variable scale for preprandial glucose.

      Adjustment must be individualized during in-patient programming of MDI or pump therapy and can be made on the basis of

i) Carbohydrate content - approximately one unit for every 15 to 20 grams of carbohydrate.

ii) The amount of protein and fat is less significant than the amount of carbohydrate but should be taken into account.

iii) Exercise - the dose of insulin given for a meal will vary depending on the duration and intensity of any planned postprandial exercise.

iv) Systems of insulin adjustment that are complex and time-consuming or requiring weighing of foods are not necessary and should be discouraged unless they are being used by the subjects prior to the trial.

2. Regularity of meals

Although use of the pump or MDI may provide somewhat increased flexibility of meal times, meals must still be reasonably regular in their timing to avoid the effect of previous meal boluses on the next meal. In addition, the timing of the preprandial injection before the meal is often overlooked as a critical variable in maximizing the efficacy of the pump or MDI.

Since pump therapy and MDI with ultralente no longer have intermediate acting insulins as part of the regimens, meals and snacks do not necessarily need to be taken at specific times to cover the anticipated peak activity of different injections. This would seem to provide increased flexibility in the timing of meals. However, the success of all pump and MDI regimens to date has been based on carefully structured meal patterns (e.g. plus or minus one hour). MDI regimens that include intermediate acting insulins may have to include snacks to cover the anticipated peaks of activity.

The following guidelines should be followed:

a) Teach all patients initially to keep meals on a very regular pattern.

b) As subjects meet blood glucose goals, they will begin to experiment with changing the timing of meals. This should be anticipated and dietary reinforcement provided to restrict the variability of meal times. However, if blood glucose goals are maintained despite the increased variability, the subject should not be reprimanded since the flexibility of meal timing is thought to be an important positive attribute by pump patients and will contribute to overall adherence.

c) If blood glucose goals are not being met, excessive variability in the diet or inappropriate timing of preprandial boluses might be the cause and should be addressed.

3. Weight maintenance diets

Careful attention should be paid to weight maintenance diets. Even diabetic subjects who are well-schooled in diabetic diets note a tendency to gain weight while on MDI or insulin pumps. This was particularly evident during Phase II of the DCCT. Since insulin is administered to attain euglycemia, glycosuria and the attendant caloric drain that may have been present during conventional therapy are eliminated. With the more efficient utilization of caloric intake, weight gain is a constant risk. The initial diet prescription should be adjusted to compensate for this effect. Careful review of diet is mandated if an unacceptable increase in weight occurs during experimental treatment regimens.

Possible criteria for initiating a weight loss intervention program include elevations in either blood pressure or low density lipoprotein (LDL), patient concern and failure to meet treatment goals as described below:

Patient concern: Defined as a patient uphappy about his/her body weight and desiring help with weight loss. It is important that it is the patient who is concerned about his weight, not the physician, dietitian, and/or nurse clinician.

Development of hypertension (140/90) secondary to weight gain

Elevation in LDL cholesterol Confirmed by repeat determination

Patients in whom weight gain is producing adverse effects on adherence: Patients who are upset about their weight may fail to adhere to treatment recommendations in an effort to lose weight. These patients should be helped in an appropriate manner (see below).

Patients in whom weight gain is associated with failure to meet the goal for their treatment condition: Inappropriate eating and weight gain may be associated with failure to meet the study goals for HbAlc. In these cases, weight control should be encouraged.

However, the use of Very Low Calorie (VLCD) or Liquid Protein Diet have the following restrictions:

Diets of 800 kcal (VLCD) or less are not allowed in the DCCT. The use of a liquid formula (protein) diet is not encouraged. If a center desires to use such a diet, a request must be submitted to the treatment committee for consideration. There is no data that describe the use of these diets in IDDM. Furthermore, there is no evidence that

such diets improve long term weight loss. If a patient is on a diet of less than 800 cal/day or is on a liquid formula diet these modifications from protocol should be noted on Form 21.

Based on the extensive literature on weight control, the following guidelines are recommended for patients who meet the criteria specified above for initiating weight loss efforts. The goal should be to produce steady weight loss and maintenance, rather than rapid weight loss followed by regain. To accomplish this, patients should be instructed to follow an ADA type of diet, with their calorie goal reduced by 500 calories/day or 15-20% of the normal calorie intake. This degree of caloric restriction should produce an approximate weight loss of 1 lb/week. Calorie goals should not be set at below 800 cal/day.

The calorie restriction should be coupled with instruction to increase daily exercise. Numerous studies have shown that the combination of diet plus exercise produces larger weight losses than diet or exercise alone. Moreover, patients who develop an exercise habit are most likely to achieve long-term weight control. The type and duration of exercise recommended will depend on the patient. However, for weight loss it should be noted that exercises that are long in duration and moderate in intensity, such as walking, are recommended. A 150 lb. person who walks 1 mile uses 100 calories. Therefore, a 150 lb. patient who develops an exercise program in which he/she walks 2 miles/day on 5 days/week would be expending an additional 1000 calories/week in exercise.

In teaching patients to modify their diet and exercise, it is both more efficient and more effective to work with small groups of patients than to see patients individually. It is also recommended that patients be seen frequently (once/week) for prolonged periods of time (approximately 15 weeks). To accomplish this, it may be helpful to refer patients to ongoing behavioral weight control programs (perhaps available in the psychology, psychiatry or nutrition departments) or to groups such as Weight Watchers. However, to ensure that the weight loss program is consistent with the DCCT Protocol preference should be given to programs based within DCCT institutions. Alternatively, the psychologists or nutritionists associated with the DCCT may wish to develop an intervention for these patients.

4. Snacks

In the absence of MDI regimens that include intermediate-acting insulins, snacks are not mandatory. Many patients have snacks in their diet as part of the previous diet prescription and, given a choice, would prefer not to have frequent snacks.

a) Dietary history should determine the number of snacks in diet as well as the number of snacks the subject would prefer.

b) Except for the night-time snack which is preferred by many investigators as a safeguard against hypoglycemia, no particular snack is mandatory.

c) If weight gain above ideal body weight occurs, elimination of snacks might be all that is necessary to correct the weight gain.

d) Subjects must be individually instructed in the amount of insulin necessary to cover snacks. In general, some insulin (depending on blood glucose, size of snack and exercise) is necessary.

5. Concentrated sweets

All diabetic patients on pump or MDI regardless of their stated attitudes and expectations regarding the pump will experiment with increased concentrated sweets. Although blood glucose control after dietary indiscretions can be more effectively controlled with the pump or MDI, blood glucoses will still fluctuate more widely than in the absence of concentrated sweets. Such dietary indiscretions must be anticipated and discouraged.

6. Treatment of hypoglycemia

Acceptable therapy for hypoglycemic episodes has been outlined elsewhere in the Manual of Operations. The warning signs of hypoglycemia often occur immediately before a meal. There are several possible treatments in such a situation.

Ideally, check preprandial blood glucose, if it is low (less than 70):

a) Ingest some portion of meal (equivalent to 10 grams of simple carbohydrate) immediately and give the preprandial bolus of insulin (determined by blood glucose concentration). Eat remainder of meal at specified interval after bolus.

b) Treat reaction with 10 grams of simple carbohydrate (not part of planned meal). Give preprandial bolus predicted on blood glucose concentration after hypoglycemic symptoms abate, and eat at specified interval after injection.

9.2.3.3 Education

Many diabetic patients have misconceptions about MDI and pump therapy. In general, individuals believe that these therapies will make their care effortless and in particular, that the regularity and consistency of diet and restriction of simple carbohydrate can be dispensed with. In order to address these common misconceptions, the following guidelines are proposed:

1. Screening -- During the screening and eligibility period, the dietitian should interview candidates, obtain a three-day food record as mandated for the behavioral tasks (Chapter 20), and obtain an diet history (Chapter 16). Other tools may be used by the dietitian to assess each candidate's present level of education and potential ability to learn and to implement the dietary recommendations necessary for the experimental group.

2. Post-randomization -- After randomization into the experimental group, no diet intervention is necessary until the patient has been hospitalized for orientation. During this admission, the patient should be allowed to select his/her own diet, including the number of snacks. A night-time snack is recommended. Any significant deviation from the recommended diet will require consultation with the dietitian.

   Patient teaching should focus primarily on matching the insulin doese to preprandial blood glucose concentration and size of meal. To help attain target blood glucose goals, the patient should understand:

   a) the carbohydrate-protein-fat content of foods in order to

      i) be consistent with meal size and composition, and

      ii) adjust the preprandial bolus when the carbohydrate content of the meal varies,

   b) how to adjust insulin dosage and/or food intake for planned exercise,

   c) appropriate treatment of hypoglycemia, and

   d) appropriate timing of meals and timing of preprandial boluses.

In addition, each experimental group patient should achieve at least education level 2 (home management)[5] by the end of six months. Additional topics of concern to these patients should also be addressed, such a tendency to gain weight, snacks, concentrated sweets, increased incidents of hypoglycemia, etc. Follow-up visits for dietary reinforcement and continuing education are required every six months, however it is anticipated that experimental group patients will visit the dietitian monthly during the first six months in order to achieve their goals. At the end of the second year, patients are required to meet education level 3 life-style)[6] Progress towards achievement of education goals should be documented in each patient's DCCT record.

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[5] American Diabetes Association/American Association of Diabetes Educators, Guidelines for Diabetes Care (1981), pp. 29-35

[6] Ibid, pp. 36-39.

Dietary management has deliberately not been rigidly standardized. The dietitians may use any forms, pre-tests, post-tests, educational approaches and educational materials that are deemed suitable for each patient. It is expected that the educational materials used will not contain statements which are at cross-purposes to the protocol. Most importantly, such materials should not emphatically assert that normalizing blood glucose will prevent diabetic complications.

Dietary management is not being formally studied during this trial. (Note: the overall, usual composition of the diets in the standard and experimental treatment groups is being tracked with the diet history described in Chapter 16.) Food diaries and other data acquired in the process of diet therapy will not be collected nor stored centrally. However, observations, experiences and insights that are noted by the dietitian should be reported to the principal investigator. Dietitians may also submit these observations and any suggestions to the DCCT nutrition coordinator.

If the diet fits the basic requirements outlined, patient teaching should focus on:

1. Variable insulin dose schedule for different size meals and snacks. Actual portion sizes (rather than food models) should be used.

2. Timing of preprandial boluses for meals.

3. Treatment of hypoglycemia.

4. A challenge with 25-30 grams of simple carbohydrate in the inpatient setting to demonstrate the effect of concentrated sweets on blood glucose should be carried out.

See Section 9.5 for teaching objectives for the experimental group subjects.

9.2.4 Exercise

Specific exercise prescriptions are not required. Exercise will be encouraged according to the individual's interest and physical fitness. Scrupulous adjustment of insulin delivery and diet to the exercise pattern is based on self blood glucose monitoring data and should be emphasized to ensure safety.

9.2.5 Urine Tests

Urine tests for ketones will be required when the blood glucose exceeds 240 mg/dl or an intercurrent illness develops. Other urine tests for glucose and acetone may be obtained at the discretion of the investigator to supplement, but not substitute for, blood glucose measures.

9.2.6 Blood Glucose Monitoring

Self blood glucose monitoring will be performed a minimum of four times a day, to include three preprandial and one bedtime sample. A 3:00 a.m. sample will be obtained once a week and repeated the next night if the value is less than 65 mg/dl. The clinic staff is to be notified promptly if the repeat value is also less than 65 mg/dl. Postprandial samples for self monitoring will be obtained at least every three months concurrent with collection of the home capillary blood samples for central data analysis. In the event that the intervention aims are not being met, more frequent self monitoring of pre- and postprandial glucose profiles will be required. Patients may also be asked to bring blood glucose samples collected at home for analysis in the local DCCT laboratory in order to validate the accuracy of patient reports. For measurements of blood glucose performed at home, the use of a reflectance meter is required. For measurements of blood glucose performed away from home, the use of visually determined estimates is permitted.

9.2.7 Clinic Contacts

Patients will be seen every week initially until the desired treatment goals have been achieved. They will be seen at least monthly thereafter. A system for ready availability of professional staff must be devised by each center, possibly including occasional nighttime or weekend clinics. Telephone contacts will be made daily for the first week, then weekly thereafter.

9.2.8 Protection of Subjects

If intensification of treatment for the purpose of achieving the experimental group HbA_{1c} goal results in repeated severe hypoglycemia that cannot be prevented by adjusting insulin dose or mode of delivery, diet, exercise, or subject reeducation, then the blood glucose and HbA_{1c} targets must be raised to a level consistent with subject safety. This is considered a modification of the experimental treatment regimen and as such will be reviewed by the Treatment Committee.

9.3 GENERAL PROCEDURES TO MAXIMIZE ADHERENCE TO PROTOCOL

The hypothesis of the DCCT will be explained as thoroughly and frankly as possible. The subject will be recruited into a research alliance with the investigator. The equal importance of participating in the Standard or the Experimental Treatment Group will be emphasized before informed consent is sought and reemphasized periodically thereafter. The positive aspects of participating in the DCCT will be emphasized. These include regular and sophisticated surveillance for complications, early stop points, and rapid transfer of results to subjects regarding whichever (if either) treatment protocol proves to be superior with regard to the development or progression of complications.

One person will be clearly identified in each of the professional disciplines (physician, nurse-clinician, dietitian, consultants) who will primarily relate to the subject in his or her area of diabetes management. A backup individual for coverage when the primary care giver is not available will also be identified. Alternate professionals should be identified and periodically introduced. As much as possible, equalization of secondary health care benefits in the Standard and Experimental Treatment Groups should be practiced.

Periodic structured group meetings will be held to provide feedback from the DCCT to the subjects and to encourage the latter to voice questions, concerns, or suggestions regarding the trial. All DCCT subject activities will be conducted with the utmost courtesy, convenience, efficiency, brevity, and openness. Transportation, parking, maintenance of meal patterns, child care, etc., will all be facilitated whenever possible. Of necessity, this will be dependent upon local resources available to the investigators.

9.4 PRODUCTS AND DEVICES

The Treatment Committee will review all new products and devices using predetermined criteria to determine if they should be used by the study subjects. All such products and devices must be approved by the Treatment Committee before they can be used in a clinical center. Any product or device approved by the Treatment Committee and meeting all criteria for use in the DCCT can be used on DCCT subjects, even if it is only available to a subset of the DCCT centers.

The approved products or devices are all listed on the Supplies Order Form (DCCT Form 068). The Minutes of recent Treatment Committee meetings will contain updated information on action with respect to new products and devices.

9.5 TEACHING OBJECTIVES

The Trial Coordinators have developed separate educational objectives for the standard group and the experimental group patients (Appendix B). These are teaching objectives for the patients selecting MDI/pen pump, and for those selecting pump therapy. Another set of objectives assesses the experimental group subjects' knowledge about self blood glucose monitoring.

The appropriate objectives should be reviewed with the subject following randomization and periodically thereafter. No forms are required to document these reviews.

Table 9.1

Variable Insulin Dosage Schedule*

Blood Glucose (mg/dl)	Breakfast (units)	Lunch (units)	Supper (units)	Bedtime Snack (units)
≤50	5	3	5	0
51-100	7	5	7	0
101-150	8	6	8	0
151-200	9	7	9	1
201-250	10	8	10	2
251-300	11	9	11	3
greater than 300	12	10	12	4

*NOTE: The above is only an example.

Chapter 10

DEFINITIONS AND MANAGEMENT OF INTERCURRENT EVENTS

10.1 INTRODUCTION

Intercurrent events are occurrences (illnesses, accidents, etc.) which have an impact on or are related to subject safety, treatment efficacy, or other study relevant conditions.

Designated intercurrent events have been placed into one of three categories that refer to the time frame for reporting the event to the Coordinating Center. In later paragraphs, the time frames are given for each category as well as the events that are subsumed.

All Category 1 and 2 intercurrent events (see below) are to be documented and reported to the Coordinating Center using the DCCT Form 020 (Notification of Intercurrent Events) in a timely fashion. In the case of hypoglycemia, Form 083 (Notification of Hypoglycemic Intercurrent Event) and Form 092 (Further Details of Hypoglycemic Event) must also be completed. For the purpose of reporting intercurrent events to the Coordinating Center, the following categories describe the time frame for such reporting. Each event is designated to one of these categories.

Category 1: The event should be reported by telephone to the Coordinating Center immediately upon documentation of the event by the Principal Investigator. As soon as details relevant to completing DCCT Form 020 are available, these should be transmitted to the Coordinating Center by telephone, with follow-up mailing of the form within 24 hours. Category 1 events are definite catastrophic hypoglycemia and suspected catastrophic hypoglycemia. All deaths must be reported to the Coordinating Center or a member of the Executive Committee.

Category 2: If the patient is treated in the hospital by the clinical center, reporting of the event on DCCT Form 020 should be done when the patient is discharged from the hospital or as soon as the center obtains the details of treatment at another hospital.

If treated outside the hospital, reporting on DCCT Form 020 should be done at the time of diagnosis or initiation of treatment or as soon thereafter that adequate clarifying details of the event are available. In some cases, this may require that reporting be delayed until after a period of brief followup or treatment. In any case, the reporting of such an event should occur no later than the next quarterly visit. Category 2 events are listed in Table 10.6

Category 3: The event should be reported on the DCCT Form 021, Quarterly Visit, at the next quarterly visit, unless hospitalization is required for treatment, in which case the event becomes a Category 2 event. Category 3 events are listed in Table 10.7.

Intercurrent events may be reported by the patient or someone reporting for the patient to the clinic staff.

The Morbidity/Mortality Classification Committee will periodically review the DCCT Form 020 and other data to provide a uniform classification of those intercurrent events that may be statistical endpoints for data analyses but do not terminate the patient's participation in the trial.

This chapter is in two parts:

1. Sections 10.2 through 10.6 present the definitions of those intercurrent events which are important outcomes of the trial. The frequency of these events will be tabulated in the statistical analysis of the study results. The clinical centers are required to report each occurrence of each of these events to the Coordinating Center.

2. Section 10.7 discusses guidelines for the management of certain intercurrent events. The definitions in Sections 10.2 and 10.3 are for purposes of ascertainment and are not intended to direct clinical management.

10.2 DEFINITIONS OF DIABETIC INTERCURRENT EVENTS (CATEGORY)

10.2.1 Ketoacidosis (Category 2)

The diagnosis of ketoacidosis as a DCCT event requires each of the following four criteria to be satisfied:

1. A symptomatic diabetic state such as polydypsia and polyuria with or without nausea;

2. The presence of

   a) serum ketones or

   b) large/moderate ketones in urine;

3. At least one of the following:

   a) arterial blood pH less than 7.30 or

   b) venous blood pH less than 7.25 or

   c) serum HCO'3" less than 15 mEq/L.

4. Treatment within a health care facility.

10.2.2 Hyperglycemic, Hyperosmolar, Nonketotic Coma (Category 2)

The diagnosis of a hyperglycemic, hyperosmolar, nonketotic coma as a DCCT event requires each of the following criteria to be satisfied:

1. A symptomatic state characterized by central nervous system manifestations.

2. Plasma glucose greater than 500 mg/dl.

3. Plasma bicarbonate greater than 20 mEq/L.

4. Serum osmolality greater than 330 mOsmoles/L.

5. Absence of significant ketonemia or ketonuria.

10.2.3 Hypoglycemia

Two levels of hypoglycemia are distinguished -- catastrophic and severe.

1. Catastrophic Hypoglycemia (Category 1)

   At least one of the following catastrophes must have occurred:

   a) death,

   b) neurological insult requiring hospitalization,

   c) myocardial infarction,

   d) injury to the patient requiring hospitalization,

   e) injury to another person requiring hospitalization.

Evidence for a relationship between the catastrophic event and hypoglycemia may consist of the following, in decreasing order of certainty:

   i) A catastrophe in conjunction with a blood glucose less than 50 mg/dl determined in a health care facility.

   ii) A catastrophe in conjunction with a finger stick blood glucose less than 50 mg/dl determined by non-medical personnel.

iii) A catastrophe in conjunction with one or more manifestations of severe hypoglycemia, e.g., confusion, irrational or uncontrollable behavior, convulsions or coma reversed by oral carbohydrates, subcutaneous glucagon or intravenous glucose.

iv) A catastrophe in conjunction with prodromal symptoms of hypoglycemia, such as sweating, palpitation, anxiety, hunger or blurred vision remembered by the patient as occurring shortly before the event occurred.

The final determination of catastrophic hypoglycemia will be made by the Morbidity/Mortality Classification Committee.

2. Severe Hypoglycemia (Category 2)

At least one of the following clinical manifestations of severe hypoglycemia, which the patient was unable to treat himself/herself, must have occurred:

a) memory loss

b) confusion,

c) uncontrollable behavior,

d) irrational behavior,

e) unusual difficulty in awakening

f) suspected seizure

g) seizure

h) loss of consciousness.

For such an episode to be counted as severe hypoglycemia, either the blood glucose must have been measured and found to be less than 50 mg/dl or the clinical manifestations must have been reversed by oral carbohydrates, subcutaneous glucagon or intravenous glucose. When neither of the latter two criteria is fulfilled, such an episode will be considered as suspect severe hypoglycemia if the patient recalls typical prodromal symptoms and there is no other apparent explanation for the clinical manifestations. Hypoglycemia that is less than severe may be too variable in symptomatology to be reliable and therefore will not be documented as an intercurrent event. However, hypoglycemia of this type will be summarized for the seven days preceding the quarterly visit.

10.2.4 Ketosis (Category 3)

The diagnosis of ketosis as a DCCT event requires each of the following criteria to be satisfied:

1. A symptomatic diabetic state such as polydypsia and polyuria with or without nausea;

2. Large/moderate ketones in the urine;

3. Active management by the health care team (defined by a temporary change in insulin dosage);

In addition, if any of the following blood value(s) are measured, they should exceed the following limits in order to differentiate ketosis from ketoacidosis:

a) arterial blood pH greater than 7.29

b) venous blood pH greater than 7.24

c) HCO'3" greater than 15 mEq/L.

10.3 PHOTOCOAGULATION POLICY AND OCULAR INTERCURRENT EVENTS

The Study Group adopted thresholds so that any subject who passes them will be assured of timely appropriate treatment and/or increased monitoring. The Central Ophthalmologic Reading Unit (CORU) issues a report to the Principal Investigator and ophthalmologist when a subject's photographs indicate the occurrence of proliferative or non-preproliferative diabetic retinopathy or clinically significant macular edema (DCCT Form 071, Observation of Proliferative or Nonproliferative Diabetic Retinopathy, or DCCT Form 094, Observation of Clinically Significant Macular Edema). Photocoagulation should be carried out in any eye which develops high risk characteristics and should be considered in any eye detected at the CORU as having significant macular edema as defined in the Early Treatment Diabetic Retinopathy Study findings published in the December 1985 issue of Archives of Ophthalmology. If the DCCT ophthalmologist believes that photocoagulation should be considered for any eye that does not have high risk characteristics or clinically significant macular edema, consultation from the Ophthalmic Committee should be sought. A full set of color photographs of both eyes should be taken, copies made and a set of copies sent to each member of the Committee together with DCCT Form 076 (Request for Ophthalmic Committee Consultation). The Committee may agree with a proposal to photocoagulate one eye of a patient with PDR or severe P2 retinopathy in each eye. All situations will be considered on a case-by-case basis. When the CORU unmasks a patient's eye status, the notification should be recorded by the clinic on DCCT Form 020.

Ophthalmic definitions of the intercurrent events for use in the DCCT are as follows:

Loss of Vision (Category 2)

Loss of vision is defined as less than 20/200 (ETDRS Visual Acuity Charts) in either or both eyes.

DRS High Risk Characteristics (Category 2)

1. New vessels on or within one disc diameter of the optic disc (NVD); moderate or severe (equal to or greater in extent than those in standard photograph 10A) with or without vitreous or pre-retinal hemorrhage.

2. New vessels other than NVD (new vessels "elsewhere" - NVE); moderate or severe (equal to or greater than 1/2 disc area in extent in any single standard photographic field) with vitreous or pre-retinal hemorrhage (in any field).

3. NVD; mild (less than standard photo 10A) with vitreous or pre-retinal hemorrhage (in any field).

If vitreous and/or pre-retinal hemorrhage is present and the ophthalmologist believes sufficient new vessels (greater than or equal to 1/2 disc area of NVE or any definite NVD) have been obscured by this hemorrhage that the preceding definition of high risk characteristics have been fulfilled, then this occurrence is considered a high risk characteristic event.

Other Ocular Diseases (Category 2)

These are ocular diseases other than retinopathy that may influence visual acuity or medical treatment for more than three months.

Pan-Retinal (Scatter) Photocoagulation (Category 2)

Full Scatter Treatment -- Full scatter treatment consists of 1200 to 1600 five hundred micron lesions as specified in Section 10.7.13.2. This form of treatment should be applied to all eyes developing High Risk Characteristics.

Mild Scatter Treatment -- Mild scatter treatment consists of 400 to 650 five hundred micron lesions spaced one burn width apart covering a similar area as full scatter. This treatment is not recommended routinely for the DCCT until its efficacy is established by the ETDRS.

Macular Photocoagulation: (Category 2) Focal treatment of discrete leakage as specified in Section 10.7.13.4. Grid treatment of diffuse leakage or nonperfusion.

Pre-Proliferative Characteristics (Category 2)

Progression in the past year of three or more steps on the DCCT retinopathy scale to moderately severe non-proliferative diabetic retinopathy (Level 50, defined below) in either eye.

Progression to very severe nonproliferative diabetic retinopathy (Level 55, defined below) in either eye.

The DCCT classification of retinopathy includes two levels of severe nonproliferative retinopathy and approximates the ETDRS category P2. Less severe eyes at this level are placed into DCCT Level 50 and more severe eyes are placed into DCCT Level 55.

The definitions of these levels involve four lesions at specified levels considering photographic fields 3 through 7, and for convenience, these are hereafter termed "P2 lesions", soft exudates (SE) present in at least two fields, intraretinal microvascular abnormalities (IRMA) present in at least two fields, venous beading (VB) present in at least two fields, and hemorrhages/microaneurysms (H/Ma) equaling or exceeding those in standard photo #2A in at least one field.

Eyes qualify for Level 50 if any of the following conditions is met, considering fields 3 through 7:

1. H/Ma equal or exceed standard photo #2A in at least four fields;

2. VB is present in at least two fields; or

3. SE is present in at least two fields, IRMA are present in at least two fields, and H/Ma equal or exceed those in standard photo #2A in at least one field.

Eyes qualify for Level 55 if any of the following conditions is met, considering fields 3 through 7:

1. IRMA equal or exceed those in standard photo #8A in at least two fields;

2. VB is definitely present in at least two fields, and two other P2 lesions are also present;

3. H/Ma equal or exceed those in standard photo #2A in at least four fields, and two other P2 lesions are also present; or

4. All four P2 lesions are present.

Proliferative Retinopathy Less Than DRS High Risk Characteristics (Category 2)

Clinically Significant Macular Edema (Category 2)

"Clinically significant macular edema" designates edema which is threatening vision and refers to any of the following characteristics:

1. Thickening of the retina at or within 500 microns of the center of the macula.

2. Hard exudates at or within 500 microns of the center of the macula, if associated with thickening of the adjacent retina.

3. A zone or zones of retinal thickening one disc area or larger in size, any part of which is within one disc diameter of the center of the macula.

10.4 CARDIOVASCULOR INTERCURRENT EVENTS

10.4.1 Myocardial Infarction (MI) (Category 2)

Myocardial infarction (MI) is classified as acute or non-acute and each of these classes is further designated as definite or suspected using criteria presented in Table 10.1. The diagnosis of acute MI depends on the availability of ECGs and/or enzymes measured within 72 hours after (a) arrival in the hospital or (b) the onset of symptoms of a cardiac event occurring in the hospital. The ECG series will be assigned the highest category for which criteria are met, i.e., first, "evolving diagnostic," then "diagnostic," then "equivocal," then "other." The ECGs will be sent to the Central ECG Reading Unit where they will be coded using the Minnesota Code, detailed definitions of which are given in Table 10.2. The various combinations of enzyme results will be classified as "abnormal," "equivocal," "incomplete" or "normal" by criteria which are given in Table 10.3. A definition of "prolonged cardiac pain" is given in Table 10.4

1. Acute Myocardial Infarction -- A definite or suspected acute myocardial infarction is diagnosed on the basis of the presence or absence of chest pain, ECG findings, and/or enzyme changes as defined in Tables 10.1 - 10.4.

2. Non-acute Myocardial Infarction -- A non-acute or "old" myocardial infarction can, in principle, have occurred either before randomization and not been recognized on the local ECG reading or after randomization without appropriate concurrent investigation to yield evidence which meets the criteria for definite or possible acute myocardial infarction.

A definite or suspected non-acute myocardial infarction is diagnosed on the basis of presence or absence of chest pain, ECG findings, and/or enzyme changes as defined in Tables 10.1 - 10.4

Both definite and suspected non-acute MI are further subdivided according to whether or not either was present before randomization. Definite or suspected non-acute MIs classified by the Central ECG Reading Unit from the baseline assessments before randomization will be designated as "pre-study" events. Note that eligibility is determined by a local reading. Definite or suspected non-acute MIs diagnosed for the first time on an ECG recorded after randomization will be designated as "study" events. Only study events will be counted in comparisons of the incidence of myocardial infarction between the experimental and standard groups.

The criteria for definite and possible acute and non-acute MIs are summarized in Table 10.1.

10.4.2 Angina Pectoris (Category 2)

To have a definite diagnosis of clinical angina, a patient must have all three of the following characteristics of chest pain or pressure:

1. The location of the pain includes the sternum at any level.

2. The pain or discomfort usually occurs during a form of exertion or stress.

3. The pain or discomfort on most occasions lasts at least 30 seconds and disappears in ten minutes or less from the time the subject rests or decreases his intensity of exertion or stress.

The pain or pressure may also be located in the left chest, and may radiate to the arms and/or to the jaw. Meals may be considered a form of cardiovascular stress.

10.4.3 Arrhythmia (Category 2)

The following types of arrhythmia are to be reported to the Coordinating Center documented by an ECG:

1. atrial fibrillation

2. atrial flutter

3. atrial tachycardia

4. junctional tachycardia

5. ventricular tachycardia

6. ventricular fibrillation

7. ventricular premature complexes

   a) multifocal

   b) runs of three or more

   c) six or more per minute

8. second degree AV block

9. complete AV block

The official DCCT classification of the arrhythmia will be made by the Central ECG Reading Unit.

10.4.4 Congestive Heart Failure (Category 2)

The DCCT diagnosis of congestive heart failure (CHF) can be made in either of the following two circumstances:

1. The presence of at least two major manifestations of CHF or

2. The presence of one major and at least two minor manifestations.

Major Criteria:

1. paroxysmal nocturnal dyspnea

2. distended neck veins (not supine)

3. rales with unexplained dyspnea

4. cardiomegaly and pulmonary hilar congestion on x-ray, or increasing heart size

5. acute pulmonary edema

6. increased venous pressure

7. hepatojugular reflex

Minor Criteria:

1. bilateral ankle edema

2. night cough

3. dyspnea on ordinary exertion

4. hepatomegaly

5. pleural effusion

6. tachycardia

10.4.5 Hypertension (Category 2)

The development of hypertension in a DCCT patient after randomization will be defined as the measurement of either a systolic pressure greater than or equal to 140 mm Hg or a diastolic pressure greater than or equal to 90 mm Hg on two consecutive occasions within one month, without any anti-hypertensive medication having been taken within two weeks of either measurement. This applies to adolescents and adults, except that the upper limit in females aged 13 years is a systolic blood pressure of 135 mm Hg and a diastolic pressure of 87 mm Hg. The measurements are to be made exactly according to the procedure defined in Chapter 18 of the Manual of Operations. The initial diagnosis of hypertension should be documented on the Intercurrent Event Form (DCCT Form 020).

10.4.6 Cerebrovascular Accident (CVA) (Category 2)

A definite cerebrovascular accident is diagnosed when two criteria are present.

1. One or more of the following symptoms and/or one or more of the following signs:

   a) Carotid arterial system: weakness or numbness in contralateral limbs, contralateral homonymous hemianopsia, dysphasia, or agnosia.

   b) Vertebral-basilar artery system: weakness of single or multiple limbs, numbness of face (especially the mouth), diplopia, dysphagia, dysarthria, homonymous hemianopsia, ataxia, nystagmus, or altered consciousness.

2. Symptoms and signs persist over 24 hours.

CVA with permanent neurological deficit is diagnosed when there is a persistent abnormality of central nervous system function manifesting itself either on neurological examination or by persistent disability that interferes with normal daily activities.

CVA without permanent neurological deficit is diagnosed when the abnormality is not persistent.

10.4.7 Transient Ischemic Attack (Category 3)

1. Criterion number 1 (above) is satisfied (include episodes of vertigo and nausea for vertebro-basilar system).

2. Symptoms and signs persist for at least 10 minutes but for less than 24 hours.

10.4.8 Peripheral Ischemia (Claudication) (Category 3)

Dull leg pain (or cramp, tightness), usually brought on by continuous walking, and relieved within ten minutes by stopping exercise. The site is one or both calves and/or hips and thighs. It does not start at rest. It is possible to confuse these symptoms with symptomatic diabetic neuropathy. In that case, a joint determination of the cause of pain is to be made by the neurologist and diabetologist.

10.4.9 Hyperlipemia (Category 2)

1. Hypercholesterolemia -- defined as a Central Biochemistry Laboratory (CBL) reported serum LDL cholesterol > 160 mg/dl. Two consecutive elevated levels one month apart are required. When the second report is positive, the clinic will receive the values for total cholesterol, triglycerides, HDL cholesterol, and calculated LDL cholesterol from these two measurements as well as from all previous measurements. The DCCT Form 020 should be filed with the Coordinating Center and the procedure outline in Section 10.7.10 should be followed. If the second part is negative, none of the previous values will be provided and the routine schedule of annual measurements should be resumed.

2. Hypertriglyceridemia is defined as CBL reported persistent elevation of serum triglycerides over 500 mg/dl. Two consecutive elevations within one month are required. When the second report is positive, the DCCT Form 020 should be filed with the Coordinating Center indicating central unit notification.

   See Figure 10.1 for a sample of a hyperlipemia alert from the Coordinating Center.

10.5 RENAL INSUFFICIENCY (CATEGORY 2)

When alerted by the central laboratory that serum creatinine is ≥2.0 mg/dl, draw a local sample within one month, and if this is also ≥2.0 mg/dl in the absence of ketonemia, this is indicative of renal insufficiency.

10.6 OTHER INTERCURRENT EVENTS

10.6.1 Infections

1. Infusion Catheter Infection (Category 2): Any infection at the site of the infusion catheter which requires oral or parenteral antibiotics or surgical incision or drainage.

2. Urinary Tract Infection (Category 3): Any infection of the kidney, ureters, bladder, or urethra, that results in symptoms of upper or lower tract infection, such as flank pain, fever, low back pain, dysuria, or frequency of urination and a midstream, clean catch urine culture yielding the following results:
Outpatients:

   - Single culture of clean-catch urine with a colony count greater than or equal to 20,000/ml.

   OR

   - Two cultures of greater than or equal to 100 colonies/ml Candida species

   In the absence of symptoms, two cultures with colony counts of greater than 100,000 of a single organism are required to indicate infection. With gram positive organisms or fungi lower colony counts may be significant in the absence of symptoms. Pyuria will generally be present in active infection but alone would not indicate infection.
Inpatients: (noncatheterized)

   - Same as outpatients.
Inpatients: (catheterized)

   - Single culture with one or two organisms, either of which greater than or equal to 10,000 colonies/ml OR

   - Single culture of greater than or equal to 100 colonies/ml Candida species.

3. Post-operative Wound or Deep Infections: (Category 3) Pus or serous drainage with local signs of inflammation. Include deep infections where superficial signs may be minimal, e.g.,

osteomyelitis following orthopedic surgery. A positive culture is one where exudate or tissue yields a pure culture of one species or, when mixed flora is expected, (e.g., bowel surgery) results of cultures should be reported as mixed, e.g., anaerobic/aerobic, and a predominant type of organism described, e.g., mixed gram negative.

4. Gangrene: (Category 3) Dry gangrene is necrosis of tissue of the toes or foot in which darkening or blackness develops and no sensation is present in the affected area. If infection of skin and/or subcutaneous tissues is present, a diagnosis of wet gangrene is made.

5. Cutaneous or Mucocutaneous Infection: (Category 3) Purulent or serous drainage and a pure culture of one organism are needed. If the site normally is rich in normal flora, e.g., mouth, vagina, then the Gram stain or KOH prep and the culture both must be used to confirm the diagnosis. Furunculosis, impetigo, and cellulitis are included under this heading.

6. Lower Respiratory Tract: (Category 3) (Includes pneumonia and tracheobronchitis)

   Pneumonia: (Category 3) The following signs should be present: Temperature greater than 99.6 degrees F (37.5 degrees C), purulent sputum, increased breath sounds, and rales. Patients must have an abnormal chest X-ray reported as consistent with the diagnosis of pneumonia. The etiological agent should be demonstrated by culture of purulent sputum or serologically using paired sera.

   Tracheobronchitis: (Category 3) Cough, purulent sputum, and normal chest X-ray are minimal criteria for this diagnosis.

7. Upper Respiratory Tract with Fever: (Category 3) Any three of the first five signs and symptoms and fever suffices to make this diagnosis. Rhinorrhea, nasal obstruction, sore throat, cough, sneezing and temperature greater than or equal to 99.6 degrees F (37.5 degrees C). Include sinusitis or otitis media in this category.

8. Gastroenteritis with Fever: (Category 3)

   a) Loose stools three times per day for greater than or equal to two days and,

   b) Temperature greater than 99.6 degrees F (37.5 degrees C) during the first two days of illness, AND

   c) Either the isolation of an enteric pathogen, or illness occurring in conjunction with an outbreak of known viral origin.

10.6.2 Amputation (Category 2)

Surgical or traumatic resection of the lower extremity or part of the lower extremity.

10.6.3 Major Accident (Category 2)

An event which produces serious injury to the patient or to other persons whether or not hospitalization is required.

10.6.4 Psychiatric Disease Requiring Treatment (Category 2)

1. A definite intercurrent event should be recorded only if the psychiatric illness involves an episode of treatment by a mental health professional (psychiatric social worker, psychologist, or psychiatrist) and a primary diagnosis of psychiatric illness is made.

   Psychiatric illness is defined and reported using diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders III published by the American Psychiatric Association.

   a) Outpatient treatment includes evaluations and/or treatment in an emergency room, office or while on a medical/surgical inpatient service for a primary medical problem.

   b) Inpatient treatment means hospital admission to a psychiatric service for a primary psychiatric diagnosis and treatment by a mental health professional.

   Specify diagnosis and treatment provided.

2. A probable intercurrent event may be specified when criteria for treatment and/or diagnosis are unclear or not verifiable, e.g., treatment by a mental health professional when records about specific diagnoses are not obtainable and the patient's report is insufficient to document the nature or severity of the problem. Specify diagnosis and treatment provided.

3. Available records should be used to document the occurrence of an event. In either case, the decision is to be made by the behavioral scientist on the DCCT site.

10.6.5 Pregnancy (Category 2 on the Form 020)

The diagnosis of pregnancy can be made for DCCT purposes by either:

1. Two positive serum or urine pregnancy tests in a patient who has missed only one period or

2. One positive serum or urinary pregnancy test in a patient who has missed more than one period.

Once the diagnosis of pregnancy in a DCCT patient has been transmitted to the Coordinating Center, a further indication of the outcome of the pregnancy will be required. This information is to be transmitted via the DCCT Forms 020 (Intercurrent Event) and 106 (Details of Pregnancy and Outcome). The following outcomes will be clearly distinguished in safety reports:

1. Abortion

   a) spontaneous

   b) induced

2. Live birth -- birth weight (grams) _____

   -- gestational age (wks) _____

   -- Apgar score _____

   a) discharged alive

      i) with congenital malformation;
      specify _____

      complications _____

      ii) without congenital malformation

      a) with complications, specify _____

      b) without complications

   b) neonatal death

      i) congenital malformation;
      specify _____

      ii) other;
      specify _____

3. Still birth (greater than 20 weeks) -- birth weight (grams) _____

   a) congenital malformation;
   specify _____

b) other;
specify _____

10.6.6 Neuropsychological Deterioration (Category 2)

Neuropsychological deterioration will be defined as having occurred whenever the neuropsychologists have rated a patient's functioning as having become "substantially worse" (rating 5) since the last examination. The Coordinating Center will notify the Principal Investigator who should complete a DCCT Form 020.

10.6.7 Psychosocial Adverse Reactions (Category 3)

The following reportable intercurrent events are disruptions in personal life:

1. Among unmarried adolescents (≤17 years of age), legal separation or divorce of parents; among married individuals, legal separation or divorce.

2. For individuals who are fully employed, major adverse change in occupational status, i.e., demotion or being fired by the employer.

3. For full-time students, expulsion, dropping out or quitting school.

No other psychosocial reactions should be reported as intercurrent events.

10.6.8 Failure to Maintain Growth and Development (Category 3)

1. Failure to maintain at least the same rate of linear growth as shown prior to entering the study or at least 4 cm per year.

2. Failure to progress at a normal rate through the stages of sexual maturation.

3. Failure to maintain a normal weight-for-height ratio on the standard growth grid.

10.6.9 Imprisonment (Category 3)

Incarceration for more than one month of an experimental group patient or for more than three months of a standard group patient, thereby preventing protocol mandated followup.

10.7 MANAGEMENT OF INTERCURRENT EVENTS

Participation in the DCCT trial will in no way jeopardize the provision of appropriate treatment for intercurrent illnesses. Although specifics for the management of all possible intercurrent illnesses cannot be realistically set forth, the highest standards of care will be followed and liberal use will be made of appropriate consultants.

Patients will be encouraged to contact the DCCT clinical center at the onset of symptoms suggesting any intercurrent illness. In addition, a 24-hour on-call system will be available to respond to all types of patient emergencies. Whenever possible, intercurrent illnesses requiring hospitalization will be managed at the DCCT clinical center with active involvement by the DCCT physician responsible for the patient's diabetes care. This will enable the study protocol to be followed as closely as possible without compromising treatment of the intercurrent illness.

Detailed guidelines are provided here for the management of patients with ketoacidosis, hypoglycemia, and pregnancy because of the special relevance of these conditions to IDDM. Additional guidelines are provided for the management of patients requiring surgery and patients with infection, myocardial infarction, renal insufficiency, hypertension, hyperlipidemia, cancer, and psychiatric disorders.

10.7.1 Diabetic Ketoacidosis

10.7.1.1 General Considerations

The incidence of diabetic ketoacidosis should be minimized or eliminated in patients of both the standard and experimental treatment groups by stressing the importance of immediately contacting the DCCT center at the first sign of a problem. The "on-call" physician should be called at the onset of symptoms of nausea or vomiting, for undue hyperglycemia, or for ketonuria. The importance of checking the urine for ketones when not feeling well, or when hyperglycemic, should be strongly emphasized. Pump-treated patients need to check the infusion system carefully at such times (see pump treatment protocol). Early intervention, including intravenous rehydration in the outpatient clinic, may abort an episode of diabetic ketoacidosis.

It is particularly important that diabetic ketoacidosis be managed (if possible) at the DCCT center under the supervision of one of the

Trial physicians. If this is not possible, the responsible DCCT physician should remain in close contact with the medical facility that is utilized. All patients should be admitted to the intensive care unit for careful monitoring during the initial phase of treatment. If such an episode occurs at an outlying hospital, the patient should be seen at the DCCT center as soon as possible after discharge.

Each episode of ketoacidosis (including those not treated at the DCCT center) should be carefully documented with regard to the following:

- precipitating causes

- maximum glucose, BUN, creatinine

- minimum arterial pH, pCO'2", bicarbonate

- duration of ketoacidotic event (date/time of onset of symptoms to date/time of normalization of pH and bicarbonate)

- adverse sequelae with particular reference to nephropathy, peripheral vascular disease, or retinopathy.

In the Standard Treatment Group, recurrent diabetic ketoacidosis (greater than two episodes per year) is a mandatory indication for intensifying treatment (see Chapter 9). In the Experimental Treatment Group, recurrent diabetic ketoacidosis should be an indication for trying the alternate experimental treatment approach, i.e., from multiple daily injection to pump therapy, or vice versa. If recurrent ketoacidosis persists, then deviation from the experimental protocol is mandatory.

10.7.1.2 Management

1. Initial Investigations: A rapid but careful history and physical examination should be performed with special attention to possible precipitating causes; for example, infection, myocardial infarction, or pump malfunction. Blood should be obtained for determination of glucose, ketones, BUN, creatinine, electrolytes, calcium, phosphate, amylase, and complete blood count. Arterial blood for pH and blood gases should be obtained. Cultures and gram stain of materials from suspected sites of infection should be performed promptly. An ECG should be performed.

2. Intravenous Fluids: Rehydration should be initiated immediately. One or two liters of isotonic electrolyte solution (10 to 20 ml/kg body weight in children) should be given during the first hour to improve circulatory volume. For patients in shock, other volume expanders may occasionally be required. Following this, slower progressive rehydration

should be carried out at a rate of 300 to 500 ml/hour, depending on the initial state of dehydration and the patient's progress as documented by blood pressure, pulse rate, central venous pressure when needed, and urine output. This repletion fluid may be either isotonic or hypotonic with added sodium bicarbonate as needed. Only hypotonic solutions should be given when the serum sodium exceeds 145 mEq/L. Glucose should be added to the repletion solutions when the plasma glucose falls to less than 300 mg/dl; the aim being to maintain subsequent plasma glucose concentrations between 200 and 250 mg/dl.

3. Insulin: Continuous intravenous infusion of physiologic doses of insulin is the preferred method of administration. A loading dose of 0.1 units/kg by bolus injection should be followed by a sustaining infusion of 0.1 units/kg/hour or, in adults, 10 units/hour. An acceptable alternative to intravenous insulin infusion is an initial intravenous bolus dose of 0.1 units/kg and hourly injections of 0.1 units/kg intramuscularly or subcutaneously. If the plasma glucose has not decreased by at least 100 mg/dl after two hours, then the insulin infusion rate should be doubled. If the plasma glucose does not decrease in the next two hours, then the insulin dose should be increased by an order of magnitude; for example, one unit/kg/hour. Insulin infusion is continued until both hyperglycemia and ketoacidosis have been corrected, using intravenous glucose to maintain plasma glucose between 200 and 250 mg/dl. Ketoacidosis can be considered corrected when plasma bicarbonate returns to normal, or the calculated anion gap returns to normal even if bicarbonate has not, or when ketones have disappeared from the plasma. Once hyperglycemia and ketoacidosis have been corrected, the patient can be maintained on continuous intravenous insulin at rates of one to two units/hour with appropriate amounts of glucose until oral intake is assured. Thereafter, patients should be returned to the therapy of their assigned group as soon as is feasible, allowing for any interval therapy necessitated by a precipitating intercurrent illness. In pump-treated patients, the pump should be carefully checked to determine whether a system failure contributed to the development of the ketoacidosis.

4. Bicarbonate: Treatment with intravenous bicarbonate is given for severe metabolic acidosis. Clinical indications include coma, hypotension not quickly responding to vigorous fluid replacement, super-imposed respiratory acidosis due to hypoventilation, or hyperkalemia causing electrocardiographic abnormalities. Chemical indications include an arterial pH of less than 7.10 and/or a plasma bicarbonate of less than five mEq/L. Sodium bicarbonate should be given by careful intravenous injection or by addition to fluids which are being infused rapidly. The amounts should be sufficient to raise the pH above 7.0 quickly and then to above 7.1. A dose range of 50

to 200 mEq may be required. Treatment effects must be monitored by repetitive measurement of arterial pH and blood gases. Plasma potassium must also be measured frequently to avoid hypokalemia during aggressive bicarbonate treatment.

5. Potassium: If the patient is hypokalemic on admission (serum potassium less than 3.5 mEq/L), then 30 to 40 mEq of potassium should be added to each liter of the initial intravenous fluids. Thereafter, potassium should be administered at a rate of approximately 20 mEq per hour until normokalemia has been achieved. If the patient is normokalemic on admission (serum potassium 3.5-5.5 mEq/L), then 20 to 30 mEq of potassium should be added to each liter of intravenous fluids. If the patient is hyperkalemic on admission (serum potassium greater than 5.5 mEq/L), then no potassium is added to the initial fluids but is added to subsequent fluids as soon as the serum potassium has decreased to less than 5.5 mEq/L. It may be expected that the average patient will require approximately 10 to 20 mEq of potassium per hour during overall treatment of ketoacidosis in order to maintain normokalemia. Approximately half the potassium may be administered as the chloride salt and half as potassium phosphate.

6. Monitoring Procedures: The patient should be weighed on admission and p.r.n. to ascertain volume status. Blood glucose by Dextrostix or Chemstrips should be measured hourly. Plasma glucose should be measured every two hours. Arterial pH and blood gases should be measured with a frequency dependent on the severity of the initial state of acidosis and dependent on the vigor of bicarbonate administration. Plasma electrolytes should be measured every two to four hours. Repeated clinical evaluations should be carried out to search for precipitating causes of ketoacidosis. Mental status and neurological examination should be carefully monitored for evidence of increasing intracranial pressure or cerebral edema. Immediate computerized axial tomography of the brain and neurologic consultion should be obtained if cerebral edema is suspected. Electrocardiograms should be repeated if plasma potassium falls below 3.5 mEq/L.

10.7.2 Hypoglycemia

Diagnostic efforts to identify the cause of a serious episode or of multiple mild episodes of hypoglycemia should be undertaken. If hypoglycemia is not found to be due to an inappropriate combination of insulin, food intake and activity, then other causes (such as adrenal, pituitary, or autonomic dysfunction) must be sought by suitable diagnostic testing.

Treatment of hypoglycemia varies with the ability of the patient to recognize the symptoms and respond accordingly. Mild hypoglycemia associated with symptoms such as hunger, headache, shakiness, rapid pulse, perspiration, etc., may be relieved by the oral ingestion of 5 to 10 grams of a simple carbohydrate in any readily available form, such as a sugar containing soft drink or orange juice. This is usually sufficient to elevate the blood sugar within 15 to 20 minutes and alleviate all symptoms. If the patient fails to improve in this time, the dose should be repeated. Overfeeding is to be discouraged so as to avoid gross hyperglycemia.

Individuals experiencing dizziness, lethargy, belligerence or confusion usually require assistance. Moistened sugar cubes, honey, or specially prepared emergency sources of glucose many be administered orally so long as the patient is not comatose. However, patients may refuse to take such feedings, or they may be completely unconscious or convulsing. Under these circumstances, glucagon can be administered subcutaneously. A dose of one mg is usually sufficient to restore consciousness. However, the patient's family should also prepare to arrange for emergency service in case the glucagon injection should be ineffective. Once the patient responds and becomes rational, an oral feeding should be provided. Continued observation with a repeated feeding in two to four hours is essential.

Patients unresponsive to glucagon should be seen by a physician and intravenous glucose administered. The most effective way of treating severe hypoglycemia by health professionals is the intravenous administration of 50% glucose. A dose of 20 cc in any patient, regardless of age or weight, is sufficient to normalize plasma glucose. A major problem associated with IV therapy is overdosage. The entire 50 cc ampule of 50% glucose in water, regarded as a unit dosage by health professionals in emergency vehicles and those staffing emergency rooms, is not required.

Patients usually respond to IV therapy within a few minutes and should be observed until they are fully responsive and well-oriented. A repeat dose of IV glucose may be required if the patient's symptoms begin to recur. Eventually, oral feeding should be provided, and if well-tolerated, the stable asymptomatic patient can be sent home. A responsible person should be available for continued observation and for retreatment at home, if necessary. Occasionally, prolonged confusion, disorientation, nausea, or vomiting may be experienced; these patients should be observed by health professionals and, if necessary, hospitalized until these symptoms have disappeared.

All episodes of hypoglycemia requiring assistance in treatment must be reported to the DCCT physician on call.

A sample set of instructions to be given to a subject when he is randomized is presented in Figure 10.2.

10.7.3 Infection

A subject may have a clinically significant infection if he or she has symptoms or signs of local inflammation, a temperature of greater than 99.6 degrees Fahrenheit, has symptoms capable of producing dehydration (example nausea and vomiting) or symptoms of prostration. Under these circumstances, the patient should contact the covering physician at the clinical center and depending on the type, severity and effects of the infection, appropriate treatment will be instituted on an outpatient or in hospital basis. In addition to the usual clinical and laboratory criteria for determining if hospitalization is required for a particular infection, the development of symptoms of uncontrolled diabetes or moderate to severe ketonuria on two successive fractional urine tests requires more intensive clinical and laboratory assessment with possible hospitalization.

10.7.3.1 Standard Treatment Group

During acute infections, subjects may have to augment their usual insulin therapy with subcutaneous injections of Regular insulin. With more protracted infections, further adjustments in insulin therapy will be necessary. In either situation, more frequent patient physician interaction will be required. If hospitalized, more intense insulin replacement (e.g., intravenous insulin) may be instituted to obtain metabolic stabilization.

10.7.3.2 Experimental Treatment Group

Subjects on the insulin pump or multiple daily injections (MDI) will be provided with specific guidelines directed at increasing insulin administration in response to hyperglycemia resulting from infection. In addition to increasing the frequency of home glucose monitoring, which they will all be routinely doing, urine testing for ketones will be initiated. It is, however, recognized that the glycemia goals outlined for this group may not be desirable or achievable during the period of acute infection. If hospitalized, intravenous insulin may be transiently required to attain metabolic stabilization.

10.7.3.3 Documentation

Infections that occur during the clinical trial can be divided into two broad categories:

1. Those that occur as a side effect of the new treatment (pump-infusion site), and

2. Infections in general that occur in both treatment groups.

The first category simply documents the experience of those treated with the insulin infusion apparatus as regards cutaneous infection. In the second category, the infections of interest are those of the urinary tract, those associated with peripheral vascular disease, post-operative infections, upper and lower respiratory tract infections, cutaneous (non-infusion site) and mucocutaneous infections, gastroenteritis.

Verification, evaluation and documentation of infections are expected to meet normal diagnostic standards of each study institution. Specifically, Gram's stain and culture of exudate should be done on all suspected sites of infection, and, when indicated, anaerobic or fungal cultures should be included. Blood cultures should be obtained when clinically indicated; cultures of urine should be done quantitatively.

Specific infections or conditions should meet the definitions of these disorders listed previously. Inquiry about infection will be made at each outpatient visit.

10.7.4 Psychiatric Events

Emotional disorders unrelated to diabetes or to the DCCT may arise during the course of this study. The occurrence of certain emotional problems may also be affected by the experimental intervention and thus may represent a study outcome measurement. In order to insure both the safety of the study participants, and reduce the adverse effect that problems might have on the completion of the Protocol, the following recommendations are made:

1. Each center should have appropriate consultants for the management of emotional disorders available for both the adolescent and adult populations. The therapist, while a consultant to the study, will have as his primary goal the well-being of the subject and will thus serve as a patient advocate.

2. Subjects identified as having symptoms of psychiatric or psychologic disorders will be referred to a consultant for evaluation and therapy. Intercurrent emotional problems will not necessarily lead to a deviation from the study protocol. However, if the Principal Investigator and the consultant decide that the patient's judgment is seriously affected or that the risk of suicide exists, deviation from the experimental treatment protocol is allowable. It is also allowable should major drug addiction or alcoholism develop. In all such instances, the intensity of blood glucose control should be lessened sufficiently so as to eliminate the aggravated risk of hypoglycemia. Should any of the above circumstances lead to deterioration of metabolic control beyond that which has been defined as acceptable for the Standard Treatment Group, then additional measures (as defined in Chapter 8.1) should be taken to restore the patient to an acceptable metabolic state.

3. If the Principal Investigator and the consultant decide that the mode of therapy or participation in the study is itself causing or exacerbating the emotional problem, the subject may be transferred to inactive status. Any subject who attempts suicide with insulin may be transferred to inactive status. (See Chapter 11 of this Manual for procedures to follow.)

4. In rare instances, persistent non-adherence may itself be a manifestation of serious underlying emotional problems. Therefore, after all other remedial efforts have failed, any subject who is not meeting the treatment goals, standard or experimental, should be discussed with the therapist. If an emotional problem is thought to be the cause of chronic poor adherence, appropriate evaluation and treatment should be instituted.

10.7.5 Myocardial Infarction

All subjects with suspected or proven acute coronary insufficiency will be admitted to a coronary care unit in the care of a cardiologist. In both the standard and experimental groups, changes in insulin requirement will undoubtedly occur and more frequent blood glucose monitoring (at least every four hours) will be required.

With regards to specific recommendations for the experimental group, it is recognized that the plasma glucose treatment goals will be relaxed in order to avoid any possibility of hypoglycemia. In general, for those subjects on insulin infusion pumps, it would be desirable to discontinue insulin pump therapy in favor of standard insulin replacement. However, if the Principal Investigator or DCCT designate of the clinical center personally supervises the use of the insulin infusion pump throughout the intercurrent event, continued insulin replacement using this technique is permissable.

10.7.6 Renal Insufficiency

Reduction in renal function may result from diabetic nephropathy, from diabetes-associated hypertension with nephrosclerosis, from repeated bouts of urinary tract infection with or without papillary necrosis, or from completely non-diabetes related renal diseases.

Prophylactic measures which should be employed include: 1) avoidance of significant, prolonged dehydration; 2) vigorous treatment of hypertension with drug regimens that do not in themselves lead to reduction in GFR; 3) prompt treatment of urinary tract infections with appropriate antibiotics for a sufficient period of time and with follow-up cultures to assure that the infection has been eradicated; 4) treatment of neurogenic bladder dysfunction to prevent stasis; 5) surveillance and treatment for any condition leading to upper or lower urinary tract obstruction.

If proteinuria appears or a rise in serum creatinine is observed appropriate diagnostic steps should be taken. Particular emphasis should be given to a search for reversible causes of renal dysfunction.

If persistent proteinuria is thought to be due to diabetic nephropathy, serum creatinine and creatinine clearance should be measured at least every six months. The patient should be referred to the nephrology service when serum creatinine exceeds 2.0 mg/dl or creatinine clearance falls below 40 ml/minute. If any significant degree of dietary protein restriction is prescribed, this should be coordinated with the patient's diabetic dietary program.

As creatinine clearance falls, the liability to hypoglycemia may increase for at least three reasons: 1) decreased appetite, 2) decreased degradation of insulin, 3) an ill-defined lesion in hepatic gluconeogenesis.

For patients in the Standard Treatment Group, a reduction in total insulin requirement may be anticipated. In addition, it may be beneficial to increase the amount of short-acting insulin relative to the amount of intermediate-acting insulin. Self blood glucose monitoring may have to be substituted for urine testing as serum creatinine increases.

For patients in the Experimental Treatment Group, a reduction in the basal infusion rate (pump patients) or in the dose of long-acting insulin (MDI patients) may be anticipated. The scale for preprandial insulin doses may have to be adjusted downward. If the cause of the renal insufficiency is non-diabetes related and no retinopathy is clinically apparent, treatment goals in the experimental group may be maintained, but with extra regard for safety.

In the Experimental Treatment Group, if renal insufficiency of any cause progresses to the point where chronic dialysis is needed, it may be necessary to deviate from the Protocol so as to lessen the risk of hypoglycemia. Blood glucose monitoring should be readily available during the dialysis procedure.

If renal transplantation is performed, and glucocorticoid therapy is given, the recommendations for adjustment of insulin dosage given in Chapter 9 should be followed. In such patients, the experimental and standard treatment protocols, respectively, should be maintained unless other indications for deviations arise.

10.7.7 Cancer

Adjustment in insulin therapy in both the standard and experimental groups will be required in response to changing nutritional states and effects of treatment.

10.7.8 Surgery

Goals during surgery and the perioperative period are the avoidance of hypoglycemia or marked hyperglycemia, i.e., plasma glucose concentration of approximately 200-250 mg/dl. A variety of methods have been used to achieve these goals. Most utilize either a reduced dose of intermediate-acting insulin given subcutaneously, supplemented postoperatively with short-acting insulin, or a continuous intravenous insulin infusion. A suggested outline for these methods is as follows:

10.7.8.1 Standard Treatment Group

1. Approximately one-half of the patient's customary intermediate-acting insulin is injected subcutaneously on the morning of surgery. In the absence of the need for fluid restriction, an intravenous infusion of 5% dextrose is initiated at a rate of 80-100 cc/hour (i.e., 4-5 grams/hour). When available and feasible, plasma glucose levels are monitored every one to two hours during the operation, and the glucose infusion is adjusted to maintain plasma glucose concentrations between 200-250 mg/dl. Following completion of surgery, a plasma glucose concentration is obtained in the postoperative recovery room. Small amounts of supplemental insulin are given to restore the plasma glucose to the desired range if necessary. If the patient is able to resume eating shortly after the operation, then a second dose of subcutaneous insulin is given as required. If a prolonged period of fasting is anticipated, approximately five to ten units of short-acting insulin are added to each 1000 cc of D5W and run at approximately 100 cc/hour. The amount of insulin is varied subsequently, depending on the resultant plasma glucose concentration.

2. An alternative approach is to omit all long-acting insulin on the morning of surgery. Instead, a continuous intravenous infusion of insulin at a rate of approximately one unit/hour is initiated. A separate infusion of D5W is also initiated at a rate of approximately 80-100 cc/hour. Plasma glucose concentrations are measured at one to two hour intervals during the operative period and the glucose infusion adjusted to maintain plasma glucose concentrations in the desired range. If the patient resumes eating shortly after the operation, approximately one-quarter of the patient's usual dose of intermediate-acting insulin is given subcutaneously and the intravenous insulin infusion discontinued approximately one hour later.

10.7.8.2 Experimental Treatment Group

If the patient is utilizing a pump and if the trial physician both considers it appropriate and will supervise its use, then the pump may continue to be employed during surgery. If not, the pump should be discontinued and the patient given intravenous insulin and glucose as outlined in number 2 above to maintain the plasma glucose concentration at approximately 250 mg/dl. If the pump is to be utilized, the basal rate should be reduced by approximately 50% the night before and an intravenous glucose infusion started on the morning of surgery to minimize the chance of hypoglycemia. On the day of surgery, the pump is kept in the basal mode throughout the operative and perioperative period. Due to the stress of surgery (e.g., increases in counter-insulin hormones), it is anticipated that plasma glucose concentrations will rise. Nevertheless, plasma glucose should be measured at one to two hour intervals and supplemental glucose infused (50-100 cc/hour of D5W) to maintain plasma glucose at approximately 200-250 mg/dl.

If the patient is being maintained on MDI or insulin prior to surgery, then he should receive approximately one-half of his customary dose of long-acting insulin the evening before surgery with the short-acting insulin dose being omitted on the day of surgery. Plasma glucose should be monitored when feasible at hourly intervals and supplemental glucose and insulin infused as outlined above. When the patient is able to resume eating, he should restart both his normal basal and pre-meal insulin doses. The intermediate or long-acting insulin should be taken at the customary times.

10.7.9 Pregnancy

In any patient actively attempting to become pregnant, the physician should aim for the blood glucose and glycohemoglobin goals stipulated in the experimental treatment protocol (Chapter 9).

Whenever a subject in either the Experimental or the Standard Treatment Groups misses her period by more than one week and pregnancy is a clinical possibility, she should have a serum or urine pregnancy test. If the result indicates pregnancy, then the patient should be offered immediate hospitalization for evaluation of blood glucose control and normalization of her glucose levels.

Goals for normalization of blood glucose in pregnancy are:

Fasting level	70-100 mg/dl
One hour postprandial level	140 mg/dl
Mean of 24-hour profile	80-90 mg/dl

In striving for these goals, episodes of hypoglycemia which require assistance from others in their treatment or which are associated with altered mental status, even if successfully self-treated, must be avoided.

The optimal insulin delivery system should be offered to each pregnant patient in order that the above blood glucose levels be attained. Therefore, in the standard treatment group, either multiple daily injections or insulin infusion pump therapy may be initiated, if necessary. Self monitoring of blood glucose should be taught to all such patients. The dietary program should be adjusted to meet currently advocated requirements during pregnancy. In general, a minimum of 30 Calories/kg is needed. Redistribution of meals may be required so as to obviate any tendency to morning fasting ketosis. It is imperative that an immediate line of communication be opened with the obstetrician of the patient's choice, whether that individual is within the DCCT clinical center or is a community physician. Management of blood glucose control should remain the primary responsibility of the Principal Investigator who should work in concert with the obstetrician. Patients admitted to the hospital for improvement of blood glucose control to meet the above standards should be under the care of the Principal Investigator. Patients admitted for management of obstetrical problems should be under the care of the obstetrician, if possible in the same institution as the DCCT clinical center. In such instances, the Principal Investigator should continue to maintain his/her role in blood glucose management.

Pregnant patients will be seen by the ophthalmologist each trimester to ensure that retinopathy does not progress to an unacceptable level during the gestational period. This is mainly a concern for women who already have developed some retinopathy, but all pregnant women will be seen in order to avoid unmasking. No photographs or other data will be taken at trimester visits other than those regularly scheduled.

During labor and delivery, blood glucose should be maintained at 80-100 mg/dl by appropriate IV infusion of glucose and insulin. Blood glucose monitoring should be performed hourly for this purpose.

Prior to active labor, the following glucose and insulin infusion rates are suggested as guidelines for maintenance of blood glucose:

Blood Glucose	Glucose Infusion	Insulin Infusion
less than 60 mg/dl	10 gm/hr	-
60-100 mg/dl	5 gm/hr	-
100-140 mg/dl	- (normal saline)	-
140-180 mg/dl	0	3% of usual daily dose as regular insulin per hour
greater than 180 mg/dl	0	6% of usual daily dose as regular insulin per hour

During active labor (three contractions per 10 minutes), glucose requirements average 2.5 mg/kg/min, and insulin infusion is usually not

needed. All of the above recommendations must be tailored to the individual patient's needs.

If labor is to be induced electively in the morning, the patient being treated with multiple subcutaneous insulin injections should receive her bedtime dose of intermediate insulin. The patient being treated with subcutaneous pump delivery should receive her usual nighttime basal rate. In the morning, intravenous glucose and insulin infusions should then be given as outlined above. If labor is induced non-electively later in the day, glucose and insulin infusion requirements may be affected by any prior administration of subcutaneous insulin and must be estimated individually.

If cesarean section is performed, patients should be managed as outlined above for the induction of labor. Whenever possible, elective cesarean sections should be performed first thing in the morning.

Premature labor should be managed in the same manner as outlined above for spontaneous labor.

During the immediate postpartum period, insulin requirements may drop precipitously and remain low for up to four days. Thereafter, insulin requirements usually return to the patient's prepartum range. Blood glucose control may then be restored to DCCT non-pregnant standards. Patients should then be returned to the treatment regimen, standard or experimental, to which they had been originally assigned. For nursing mothers, the dietary regimen should allow for increased caloric and mineral needs.

10.7.10 Management of Hyperlipemia

Since primary hereditary forms of hyperlipemia will, in general, have been excluded prior to acceptance into the Trial, the development of hyperlipemia during the study will likely be secondary to another disorder or diabetes.[1]

1. Management of Hypertriglyceridemia: Hypertriglyceridemia should be treated by reduction of total caloric intake if the patient is above ideal weight. A reduction in the fat proporation of the caloric intake may also be efficacious. If these methods are ineffective and serum trigylcerides continue to exceed 500 mg/dl, appropriate drug therapy may be considered.

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[1] Hyperlipemia exceeding the alert levels in Section 10.4.9 is not very likely to be due to decompensated diabetes unless hemoglobin Alc is > 13%. In such cirucumstances, measures which bring hemoglobin Alc below 13% are likely to result in reduction in hyperlipemia to below the alert levels.

2. Management of hypercholesterolemia:

1. All DCCT subjects, irrespective of serum lipids levels, are to be instructed in the Step 1 Diet of the National Cholesterol Education Program. This consists of an intake of saturated fat < 10% of calories, total fat < 30% of calories, and cholesterol < 300 mg per day.[2]

2) In the event of a confirmed, persistent level of LDL cholesterol > 160, the following procedure should be followed:

a) Hypothyroidism should be sought by appropriate testing, and, if discovered, should be treated with thyroxine.

b) If not hypothyroid, the subject should be referred to the Study Dietition for dietary evaluation. If the subject is found not to be adhering to the Step 1 diet, he/she should be thoroughly reinstructed in this diet with reinforcement at quarterly visits. Total cholesterol, triglycerides, HDL cholesterol and calculated LDL cholesterol should be rechecked at six months. If LDL cholesterol is then < 160 mg/dl, the subject should continue on the Step 1 Diet and LDL cholesterol should be rechecked at the ensuing annual visit. If the repeat LDL cholesterol after six months on the Step 1 Diet is still > 160 mg/dl, the subject should then be instructed in the Step 2 Diet. This consists in a further reduction in saturated fat to < 7% of calories, and in dietary cholesterol to < 200 mg/day. If on the first dietary evaluation, the subject is found to have been adhering to the Step 1 Diet, he/she should then be immediately instructed in the Step 2 Diet as described above.

c) If after six months on the Step 2 Diet, LDL cholesterol is < 160 mg/dl, the subject should continue on the Step 2 Diet and LDL cholesterol should be rechecked at the ensuing annual visit. If LDL remains > 160 mg/dl, consideration should be given to drug therapy.

d) The decision to use drug therapy is an individual one to be taken at the DCCT Clinic. An LDL cholesterol > 190 mg/dl is, in itself, a reasonable indication for drug therapy. Other factors which should be taken into consideration in deciding to initiate drug therapy include the concurrent presence of one or more of the following additional risk factors for coronary heart disease: family history of premature coronary heart disease, smoking, hypertension, HDL cholesterol < 35 mg/dl,

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[2] Adherence to this diet acknowledges the possible greater need of all IDD patients to be protected from hypercholesterolemia. It will decrease the confounding effect of dietary inequalities in the two treatment groups and allow clearer determination of the effects of the Standard and Experimental Treatment Regimens on serum lipid levels.

evidence of cerebral vascular or peripheral vascular disease. If drug therapy is elected, the currently available drugs should be tried in the following sequence:

1) Bile acid resine or Nicotinic Acid
2) Lovastatin
3) Gemfibrozil; Probucol

A combination of bile acid resins and other drugs may also be efficacious. Regardless of which drugs are used, efforts to maximize adherence to the Step 2 Diet should continue. On drug therapy, initial follow up of LDL cholesterol is recommended at 4-6 weeks and subsequent follow up at 3-6 month intervals. These levels should be measured at the Central Biochemical Laboratory. The goal of treamtment is to lower LDL cholesterol to < 160 mg/dl.

Monitoring for adverse drug effects should be conducted at suitable intervals as determined by the Clinic staff using local laboratory facilities.

10.7.11 Glucocorticoid-Requiring Illness

Insulin requirements will vary in both the Standard Treatment Group and the Experimental Treatment Group depending on the schedule of steroid administration.

10.7.11.1 Standard Treatment Group

If the steroid is given as a single morning dose, it will frequently be necessary to increase both the morning intermediate- and short-acting (when present) insulin without altering the evening insulin dose. When not previously utilized, morning short-acting insulin may need to be given. If the steroids are given in doses divided throughout the day, the total daily insulin dosage will likely increase, and patients on a single morning insulin dose may require an additional evening injection. If the steroid is being administered every other day, then the insulin requirements may be greater on the day of steroid ingestion.

10.7.11.2 Experimental Treatment Group

If the steroid is being given as a single morning dose, then an increase in only the pre-meal bolus may be required with a disproportionate increase being needed early in the day. If the steroid is given in divided doses, then an increase in both pre-meal and basal dose will probably be necessary. If the steroid is being administered every other day, then the insulin requirements may be greater on the day of steroid ingestion.

10.7.12 Hypertension

1. Goal of Therapy:

Blood pressures are to be measured at quarterly visits and, if indicated, during intercurrent events. Therapy should be initiated at either a systolic of 140 or a diastolic of 90 mm Hg. If a BP elevation is found on any routine visit, the subject should return for a second BP reading within one month. A BP $\geq$ 140/90 on a second reading is an indication for therapy. A BP reading $\geq$ 160/105 must be repeated within 48 hours so that therapy can be initiated immediately, if this level is confirmed. The goal of therapy is to maintain the BP < 140/90.

More intensive efforts to control hypertension may be indicated than in the non-diabetic population in view of the propensity to renal and other arteriosclerotic disease in diabetic patients with hypertension.

The hypertension treatment goals should be the same in the standard and experimental groups. In the case of the standard group, treatment and followup of hypertension should be arranged in a manner that does not increase the intensity of blood glucose management.

2. Diagnostic Evaluation:

Usual Practice for screening for reversible causes of hypertension is recommended.

3. Therapy:

Because of the potential hazard to the patient of persistently elevated blood pressure levels, achievement of a normal blood pressure (BP $\leq$ 140/90) should be achieved within three months. Patients should return at 2 - 4 week intervals to achieve this aim. Henceforth, BP levels should be checked only at quarterly visits. BP checks at more frequent intervals should be discouraged unless specifically indicated or requested by the patient in order to avoid treatment bias between standard and experimental groups. When indicated home blood pressure monitoring is allowed.

If the BP is $\geq$ 140/90 but < 160/105, non-pharmacologic therapy should be employed initially, consisting of reinforcement of the perscribed ADA diet aiming at achieving ideal body weight with the addition of moderate sodium restriction (2g or 88 eMq Na^+ diet) and encouragement of physical activity. If the blood pressure does not fall into an acceptable range after 4 - 6 weeks, then pharmacologic therapy should be added. A BP $\geq$ 160/105 should be treated initially with both non-pharmacologic and pharmacologic therapy.

NOTE - The stepped care approach recommended in NIH Publication No. 84-1088 should not be automatically adhered to in patients with diabetes mellitus. In particular, in DCCT patients, beta blockers should be considered drugs of last choice.

FIRST DRUG

a) If the patient is considered volume overloaded, than a low dose (25 - 50mg) of a thiazide-type diuretic is an appropriate first drug. If there is impaired renal function (serum creatinine > 2.0 mg/dl), then metolazone (2.5 - 5 mg) or a loop diuretic such as furosemide (40 - 80 mg) are the diuretics of choice. Potassium levels should be monitored and supplements may be required. If used, they should be employed with caution.

b) Other first line drugs would include a calcium channel blocker (nifedipine, verapamil, diltiazem), a peripheral alpha blocker (prazosin) or a centrally acting adrenergic inhibitor (clonidine, alpha methyldopa or guanabenz).

c) If blood pressure control is not acceptable with one drug, then another first line drug may be substituted.

SECOND DRUG

If the blood pressure remains unacceptable with these first line drugs, than one of the agents noted above but not initially utilized should be added.

THIRD DRUG

d) If necessary, a vasodilator such as hydralazine or minioxidil (especially with renal insufficiency) could be added.

e) Angiotensin converting enzyme (ACE) inhibitors may also prove to be effective. However, the exact role of ACE inhibitors in patients with proteinuria is not clear at this time. Because there is some preliminary evidence that these drugs may alter the amount of proteinuria and the progression of renal insufficiency, their inconsistent use may obscure valuable renal endpoint data. Their use may mask the ability to differentiate between study groups and they may affect proteinuria independent of the antihypertensive effect. These drugs otherwise should be added only after other drug combinations are found to be ineffective or side effects are intolerable. Because they may produce hyperkalemia when renal insufficiency and hyporeninemic hypoaldosteronism occurs, potassium levels need to be checked frequently. Use of ACE inhibitors requires prior review by the Treatment Committee.

f) Beta blockers should be used as a last resort because of their ability to mask signs and symptoms of hypoglycemia, i.e., they should be used only after all other drug combinations have been tried. IF BETA BLOCKERS ARE USED, A PROTOCOL DEVIATION IS MANDATED.

g) All of the drugs have side effects and some of these may be particularly bothersome to diabetic patients (e.g., exacerbation of impotence) and those should be kept in mind. In addition, some of the agents can induce laboratory abnormalities (e.g., change in potassium, cholesterol) and thus care should be taken that in treating one cardiovascular risk factor another is not induced or exacerbated.

10.7.13 Treatment of Eyes with Argon Laser Photocoagulation in the DCCT

10.7.13.1 Treatment of Eyes at the Time of First Observation of High Risk Characteristics

Usually the occurrence of high risk characteristics (HRC) will be noted initially by the ophthalmologist during the ophthalmoscopic examination at a follow-up visit. In such cases, fundus photographs of the seven standard fields in both eyes should be taken and DCCT Form 027 completed. If HRC are noted at a nonscheduled follow-up visit, only the visual acuity portion of DCCT Form 027 need be completed, but complete photographic documentation is required.

If no previous scatter treatment has been given, full scatter should be initiated. If less than full scatter has been given previously, full scatter should be completed by adding lesions between old burn scars and extending treatment peripherally. If full scatter has already been given, additional scatter between scars, peripheral to the previous treatment and/or posterior to previous treatment to within one disc diameter of the macula, and/or other photocoagulation treatment at the discretion of the treatment ophthalmologist may be given.

In the event the clinical center ophthalmologist is reluctant for any reason to proceed with full scatter treatment in the presence of high risk characteristics, he/she should consult the Ophthalmic Committee so that the case may be reviewed and recommendation made.

If high risk characteristics are observed in both eyes simultaneously, the eye to be treated first is chosen at the discretion of the treating ophthalmologist. No more than four weeks should elapse between the time of treatment of the first eye is completed and the treatment of the second eye is initiated.

10.7.13.2 Scatter Treatment Regimens Recommended for DCCT (adapted from ETDRS)

1. Treatment Parameters

   a) A standard Argon Laser should be used for application of treatment where possible. Krypton red may be used if adequate treatment is not possible using argon. The following parameter apply to routine treatment with the argon laser.

   b) The 500-micron spot size should be used throughout.

   c) An exposure time of 0.1 seconds should be used.

   d) Power settings should be adjusted to obtain a moderately intense white lesion which does not spread appreciably larger than 500 microns. If unable to obtain an adequate burn after increasing the power to one watt, the exposure time and/or power may be increased at the discretion of the treating ophthalmologist.

   e) Burns should be applied to the retina starting at points on an oval defined as two disc diameters above, below, and temporal to the center of the macula and 500 microns from the nasal half of the disc margin and extending peripherally to the equator.

   f) Placement of burns directly on or over normal retinal vessels should be avoided.

2. Full Scatter

   a) A minimum of 1200 lesions and a maximum of 1600 lesions should be applied during the first treatment session (a session may be a series of treatment episodes). However, should an eye fail to respond within four to six weeks of complete therapy, additional treatment may be applied between scars peripheral to previous treatment, and/or a posterior to previous treatment to within one disc diameter of the center of the macula, at the discretion of the treatment ophthalmologist.

   b) The applications should be scattered uniformly throughout the area defined in 1.e) above. All burns should be placed one-half burn diameter apart.

   c) Treatment should be divided into a minimum of two treatment episodes no less than two weeks apart or three or more treatment episodes no less than four days apart and should be completed in five weeks. No more than half the maximum number of full scatter burns (800) should be applied in any episode.

d) Treatment may be extended anterior to the equator as long as the spacing of burns is 1/2 burn diameter apart.

e) If full scatter treatment is applied at the same episode as focal treatment of macular edema, the focal treatment should be done first and the scatter treatment should be applied to nasal quadrants. At least two weeks but not more than five weeks should elapse before completion of the scatter temporally.

10.7.13.3 Local Photocoagulation for NVE as Part of Treatment of High Risk Characteristics

New vessels elsewhere (NVE) are defined as neovascularization on or anterior to the retina and located at least one disc diameter from the disc margin. All NVE which are outside of the papillomacular bundle and one disc diameter from the center of the macula may be treated when observed. Lesions which cannot be readily differentiated between surface NVE or intraretinal microvascular abnormalities (IRMA) may be considered as NVE and treatment as such.

1. Treatment Parameters

   a) Spot size from 200 to 1000 microns may be used.

   b) Exposure time 0.1 to 0.5 seconds.

   c) Power adjusted to obtain a moderately intense whitening of the retina.

2. Flat Patches of Neovascularization covering less than or equal to two disc areas of retina (an area of retina with a diameter of approximately one and a half diameters) may be treated as follows.

   a) The entire patch should be covered with confluent treatment, including the retina between the new vessels.

   b) Confluent treatment should be continued past the edges of the patch for 500 microns but should not impinge upon the papillomacular bundle nor come closer than 500 microns from the disc margin or one disc diameter from the center of the macula.

   c) Treatment over normal retinal vessels which may cause occlusion of those vessels should be avoided.

   d) If adequate confluent treatment is not feasible because of chorioretinal scars, preretinal hemorrhage, elevation of part of the NVE patch, large retinal vessels and/or if small NVE patches are so numerous and so close together that such

treatment would lead to confluent scars <4 disc areas in extent, limited "full scatter-type" treatment may be used instead.

3. Flat networks covering more than two disc areas of retina.

   a) Limited "full scatter-type" treatment (that is, burns placed 1/2 burn diameter apart) should be applied over the entire area involved, spacing 500-micron spot size burns 1/2 burn width apart and extending treatment for at least one disc diameter beyond the border of the involved area in all directions.

   b) Confluent treatment may be applied at the discretion of the treatment ophthalmologist.

   c) Treatment should not impinge upon the papillomacular bundle nor come closer than 500 microns from the disc margin or one disc diameter from the center of the macula.

4. New vessel networks elevated greater than or equal to 1/4 disc diameter from the retina.

   a) Patches less than or equal to two disc areas in size may be treated as described below:

      i) The base of origin of new vessel patch and surrounding retina should be treated with confluent lesions covering an area not to exceed 3000 microns in diameter.

      ii) Treatment should not impinge upon the papillomacular bundle, nor come closer than 500 microns to the disc margin or one disc diameter to the center of the macula.

      iii) Treatment over normal retinal vessels as to cause occlusion of these vessels should be avoided.

   b) Patches >2 disc areas in size should be treated as in 3.a) above.

5. The following lesions may or may not be treated:

   a) New vessels the size of the largest retinal arteriole crossing the disc margin in this eye.

   b) New vessels accompanied by fibrous proliferation.

   c) New vessels over old treatment scars.

6. Vitreous and/or preretinal hemorrhage.

a) If vitreous or preretinal hemorrhage occurs from a patch of NVE during treatment, the treater may use any combination of spot size, exposure time or power setting judged necessary to stop the hemorrhage. However, if the treater believes that more treatment may merely aggravate the bleeding by causing tissue shrinkage which holds the leaking source open, treatment of the bleeding spot is not required.

b) If within 24 hours of completion of any treatment, vitreous and/or preretinal hemorrhage occurs in an eye which has NVD present less than standard photograph 10A or NVE less than or equal to 1/2 disc area, this hemorrhage should not be considered as contributing to a "high risk event." However, if in the opinion of the treater, the hemorrhage is of such magnitude as possibly to preclude application of full scatter treatment within the next 12 months, and if he/she therefore believes such treatment is necessary, then this even may be considered a "high risk characteristics event" and the treatment applied.

7. If, during followup, additional treatment of a previously treated patch of NVE or treatment of new patches of NVE is required, strong burns, especially with small spot sizes, should be avoided over previous burn scars. In addition, if additional confluent treatment would result in >4 disc areas of treatment, limited "full scatter-type" treatment may be applied.

10.7.13.4 Treatment of Macular Edema

Eyes should be considered for treatment of macular edema once clinically significant macular edema has been detected at the CORU or if the eye is already being treated for HRC. If treatment is to be performed for macular edema following or at a regular follow-up visit, the visual acuity portion of DCCT Form 027 should be completed even if this is not an annual exam. If treatment is to be applied at a non-scheduled follow-up visit, only the visual acuity portion of DCCT Form 027 need be completed, and photographic documentation is not necessary if the clinic has been notified by the CORU previously. Under no circumstance should treatment of macular edema be considered an emergency. Photographic confirmation of clinically significant macular edema at the CORU is an absolute prerequisite for consideration of treatment. The following sections adapted from the ETDRS should serve as guidelines for macular edema treatment.

1. Identification of Treatable Lesions

a) A fluorescein angiogram should be used to identify the lesion to be treated. These include discrete points of retinal hyperfluorescence or leakage (most of which will presumably be microaneurysms), areas of diffuse leakage

within the retina (microaneurysms, IRMA, or diffusely leaking retinal capillary bed), and retinal avascular zones. All such lesions which are within two disc meters of the center of the macula and greater than or equal to 500 microns from the center of the macula should be treated.

b) It is recommended that a projector or a stereo viewer be utilized to study either the positive or negative fluorescein angiogram at the time of treatment. Photographs taken at a sufficiently early phase in the transit to identify clearly the treatable lesions within two disc diameters of the center of the macula should be projected on a screen behind the patient or placed in a stereo viewer mounted over or next to the slit lamp oculars of the photocoagulation.

c) Treatment of lesions may be carried out as described below.

2. Treatment of localized edema: Discrete leakage with or without circinate rings.

a) Treatable lesions in this setting include microaneurysms which fill and/or leak and other points of focal leakage such as intraretinal microvascular abnormalities (IRMA) or capillaries seen on the fluorescein angiogram at a distance of 500 microns or more from the center of the macula and within two disc diameters of the center of the macula. Microaneurysms and punctate hemorrhages less than 125 microns in longest diameter which do not fill with fluorescein and which are 500 microns or more from the center of the macula and outside the papillomacular bundle may be treated. Blot hemorrhages (greater than 125 microns) should not be treated.

b) Microaneurysms and/or other focal points of leakage into the retina further than two disc diameters from the center of the macula which fill and/or leak (whether they are located in Field 2 or outside of it) may be treated at the discretion of the ophthalmologist. Treatment is recommended if these lesions leak prominently and are associated with retinal thickening and/or hard exudate rings which extend into the area of the retina within two disc diameters of the center of the macula.

c) Treatment closer than 500 microns from the center of the macula is optional. However, if macular edema persists and the patient is able to read fewer than 40 letters correctly at four meters, corresponding to a visual acuity worse than 20/40, treatment should be considered for leaks which are 300 to 500 microns from the center of the macula unless there is perifoveal capillary dropout and the treating ophthalmologist believes that such treatment would destroy the remaining perifoveal capillary network.

d) Treat as outlined below:

i) Spot sizes from 50 to 500 microns may be used, depending upon the location. Within 500 microns from the center of the macula, 50 to 100 micron spot sizes are recommended. No more than 50 burns which produce lesions of 500 micron spot sizes may be placed within two disc diameters of the center of the macula.

ii) In general, exposure time should be limited to 0.1 seconds but if while treating within 500 microns of the center of the macula the treater believes this exposure time is too long. 0.05 second exposure may be used.

iii) Power should be varied to obtain an endpoint of whitening around the microaneurysm or leaking site without excessive spreading of the burn.

iv) For microaneurysms greater than or equal to 40 microns, an attempt should be made to obtain actual darkening or whitening of the microaneurysm itself.

v) Usually it is preferable to treat individual microaneurysms with 100 to 200 micron spot sizes initially in order to obtain some whitening of the surrounding retina. Subsequent treatment can be given with 50 to 100 micron spot size in order to obtain darkening or whitening of the aneurysm without excessive "take" and damage to Bruch's membrane.

vi) Clumps of microaneurysms may be treated with larger spot sizes (200-500 microns), although additional subsequent treatment to individual microaneurysms with 50 to 100 micron spots in order to obtain darkening or whitening of the microaneurysm is recommended.

vii) Confluent treatment in the papillomacular bundle greater than 500 microns in diameter should be avoided. The papillomacular bundle is defined as the area of the retina bounded by lines from the superior and inferior disc margin to a 1000 micron diameter circle centered on the center of the macula.

viii) Treatment of nerve fiber layer retinal hemorrhage should be avoided, although leaks in hemorrhages and hemorrhages thought to be obscuring microaneurysms may be treated.

3. Treatment of Diffuse Edema: Diffuse leakage and/or avascular zones with or without circinate rings.

   a) Areas of diffuse leakage (IRMA or dilated capillaries) and/or areas of capillary dropout should be identified, as well as any focal leaks on the fluorescein angiogram that appear to be contributing to the macular edema.

   b) Treat any focal leaks or areas as outlined above in the section describing treatment of localized edema - 10.7.13.4.2.

   c) Treat areas of diffuse leakage or capillary dropout (except areas of soft exudate that prevent laser "take") as specified below:

      i) Place 200 micron burns of mild to moderate intensity in these areas, leaving at least one burn width between lesions but deviating from even spacing to cover more completely areas of intensive leakage and dropout, and sparing as much retina as possible in areas of more sparse leakage and areas of normal perfusion.

      ii) This treatment may be extended above, below, and temporally to the inner limits of peripheral scatter treatment if necessary.

      iii) Treament should not be applied within 500 microns of the center of the macula.

Table 10.1

Summary of Diagnostic Criteria for Nonfatal MI

Prolonged Cardiac Pain	ECG Findings	Enzymes	Diagnosis
Present	Evolving Diagnostic	Abnormal	Definite Acute MI
		Equivocal	Definite Acute MI
		Incomplete	Definite Acute MI
		Normal	Definite Acute MI
	Diagnostic	Abnormal	Definite Acute MI
		Equivocal	Suspected Acute MI
		Incomplete	Suspected Acute MI
		Normal	Definite Nonacute MI
	Equivocal	Abnormal	Definite Acute MI
		Equivocal	Suspected Acute MI
		Incomplete	Suspected Acute MI
		Normal	Suspected Nonacute MI
	Absent, Uncodable, or Other	Abnormal	Definite Acute MI
		Equivocal	Suspected Acute MI
		Incomplete	Suspected Acute MI
		Normal	No MI
Not Present	Evolving Diagnostic	Abnormal	Definite Acute MI
		Equivocal	Definite Acute MI
		Incomplete	Definite Acute MI
		Normal	Definite Acute MI
	Diagnostic	Abnormal	Definite Acute MI
		Equivocal	Suspected Acute MI
		Incomplete	Definite Nonacute MI
		Normal	Definite Nonacute MI
	Equivocal	Abnormal	Suspected Acute MI
		Equivocal	Suspected Acute MI
		Incomplete	Suspected Nonacute MI
		Normal	Suspected Nonacute MI
	Absent, Uncodable, or Other	Abnormal	Suspected Acute MI
		Equivocal	No MI
		Incomplete	No MI
		Normal	No MI

Table 10.2

Definitions of ECG Types

1. Evolving Diagnostic ECG

An evolving pattern on serial ECGs of ECG changes within lead groups (i.e., anterior (V1-V5); lateral (I, avL, V6); inferior (II, III, avF). Two or more ECG recordings during the hospitalization are needed for this classification. New Q waves must persist on all subsequent tracings. One or more of the following criteria must be met:

a) No Q code in one ECG record followed by a record with a diagnostic Q code (Minnesota Code 1-1-1 through 1-2-5 plus 1-2-7). or

b) An equivocal Q code (Minnesota Code 1-2-8 or any 1-3 code) and no major ST segment depression in one ECG record followed by a record with a diagnostic Q code plus a major ST segment depression (Minnesota Code 4-1 or 4-2). or

c) An equivocal Q code and no ST segment elevation in one ECG record followed by a record with a diagnostic Q code plus an ST segment elevation (Minnesota Code 9-2). or

d) An equivocal Q code and no major T wave inversion in one ECG record followed by a record with a diagnostic Q code plus a major T wave inversion (Minnesota Code 5-1 or 5-2). or

e) No Q code and neither 4-1 nor 4-2 followed by a record with an equivocal Q code plus a 4-1 or a 4-2. or

f) No Q code and no 9-2 followed by a record with an equivocal Q code plus a 9-2. or

g) No Q code and neither 5-1 nor 5-2 followed by a record with an equivocal Q code plus a 5-1 or a 5-2.

2. Diagnostic ECG

   a) Minnesota Code 1-1-1 through 1-2-5 plus 1-2-7 for Q and QS patterns. or

   b) Minnesota Code 9-2 for ST segment elevation plus a major T wave inversion (Minnesota Code 5-1 or 5-2).

3. Equivocal ECG

   a) Q and QS patterns 1-2-8 through 1-3-6. or

   b) ST junction and segment depression 4-1 through 4-3. or

   c) T-wave items 5-1 through 5-3. or

   d) ST segment elevation item 9-2.

4. Other ECG

   All other findings, including normal.

5. Uncodable ECG

   a) Missing lead.

   b) Baseline drift greater than 1 in 20, if it obscures ST-T wave.

   c) Muscle tremor artifact giving more than 2 mm peak-to-peak oscillation.

   d) Other technical errors making Q-wave measurements impossible, such as extreme lack of centering, or marked clipping.

6. Absent ECG

   No ECG available for coding.

Table 10.3

Definitions of Enzyme Criteria

Enzymes will be considered for the categories of "abnormal" or "equivocal" only if (a) the upper limit of normal for the laboratory making the determination is recorded and (b) the enzyme has been measured within 72 hours after arrival at the hospital or after an in-hospital CHD event (whichever is later).

1. Abnormal Cardiac Enzymes

Enzymes will be classed as "abnormal" if all the following criteria are met:

a) Total CPK is at least twice the upper limit of normal (ULN). and

b) Either CPK-MB is "present" (if laboratory uses criteria of "present" and "absent"), or CPK-MB (heart fraction) or total LDH or SGOT are at least twice the ULN. and

c) There is no known non-ischemic cause (defibrillation, surgery, liver disease, injections, etc.) for the elevated enzymes.

2. Equivocal Cardiac Enzymes

Enzymes will be classed as "equivocal" if the following criteria are met:

a) The criteria for "abnormal" enzymes are not met

AND

At least one of total CPK, CPK-MB (heart fraction), total LDH, or SGOT is above the ULN, or CPK-MB is "present" (if laboratory uses criteria of "present" or "absent"). or

b) The first two criteria for "abnormal" enzymes are met but there is a non-ischemic cause for elevated enzymes.

3. Normal Cardiac Enzymes

Enzymes will be classed as "normal" if they meet the criteria for consideration as "abnormal" or "equivocal" but do not meet any of the criteria for these categories.

4. Incomplete Cardiac Enzymes

Enzymes will be classed as "incomplete" if they do not meet the criteria for consideration as "abnormal" or "equivocal".

Table 10.4

Definition of Prolonged Cardiac Pain

Pain having the following characteristics:

1. It occurs anywhere in the anterior chest, left arm, or jaw, and may also involve the back, shoulder, right arm, or abdomen on one or both sides.

2. It has a duration of more than 20 minutes. (See item 4 below for an exception.)

3. There is no definite non-cardiac cause of chest pain (all cases of non-cardiac chest pain to be reviewed by physician panel).

4. If additional doses of nitrates or calcium blockers were self-administered before medical care was sought without obtaining relief of the pain, this is considered sufficient evidence of prolonged cardiac pain without documentation of duration.

Table 10.5

Plasma Total Cholestrol (mg/dl)*

MALES (white)

AGE	MEAN	S.D.	MEAN + 2 S.D.
10-14	157.6	23.86	205.3
15-19	149.9	26.70	209.3
20-24	166.5	29.70	225.9
25-29	182.2	36.15	254.5
30-34	192.2	34.61	261.4
35-39	201.3	38.53	278.36

MALES (black)

AGE	MEAN	S.D.	MEAN + 2 S.D.
10-19	160.4	25.30	211.0
20-29	178.5	36.44	251.4
30-39	191.6	37.36	266.3

*From the Lipid Research Clinic Population Studies Data Book, Volume 1, The Prevalence Study - Visit 2, U.S. Department of Health and Human Services, Public Health Service, NIH Publication No. 80-1527, July 1980.

Table 10.5 (Continued)

Plasma Total Cholestrol (mg/dl)*

FEMALES (white)

AGE	MEAN	S.D.	MEAN ± 2 S.D.
10-14	159.6	22.84	205.3
15-19	157.6	27.36	212.3
20-24	171.7	31.66	235.0
25-29	175.8	28.07	231.9
30-34	179.0	32.47	243.9
35-39	186.4	31.40	249.2

FEMALES (black)

AGE	MEAN	S.D.	MEAN ± 2 S.D.
10-19	165.0	28.33	221.7
20-29	177.3	33.58	244.5
30-39	185.0	35.13	255.3

*From the Lipid Research Clinic Population Studies Data Book, Volume 1, The Prevalence Study - Visit 2, U.S. Department of Health and Human Services, Public Health Service, NIH Publication No. 80-1527, July 1980.

Table 10.6

Category Two Intercurrent Events

Diabetic Intercurrent Events

Ketoacidosis
Hyperglycemic, hyperosmolar, nonketotic coma
Definite severe hypoglycemia
Suspected severe hypoglycemia

Ocular Intercurrent Events
Loss of vision
High risk characteristics (HRC)
Other ocular diseases
Photocoagulation

Cardiovasular Intercurrent Events
Definite acute myocardial infarction
Suspected acute myocardial infarction
Angina pectoris
Arrhythmia
Congestive heart failure
Initial diagnosis of hypertension
CVA with permanent neurological deficit
CVA without permanent neurological deficit

Renal Intercurrent Events
Renal insufficiency

Other Intercurrent Events
Infusion catheter infection
Amputation (traumatic)
Amputation (surgical)
Major accident not requiring hospitalization but requiring medical attention
Major accident requiring hospitalization
Overnight hospitalization
Psychiatric disease requiring treatment
Other

Pregnancy Related Intercurrent Events
Pregnancy
Abortion (spontaneous)
Abortion (induced)
Live birth
Discharged alive with congenital malformation
Discharged alive without congenital malformation
Neonatal death with congenital malformation
Neonatal death with other complications
Still birth with congenital malformation
Still birth with other complications

Table 10.6 (Continued)

Category Two Intercurrent Events

Central Unit Notification
Notification of pre-proliferative or proliferative characteristics
Notification of clinically significant macular edema
Notification of hypercholesterolemia
Notification of hypertriglyceridemia
Notification of neuropsychological deterioration

Table 10.7

Category 3 Intercurrent Events

Transient ischemic attack
Peripheral ischemia (claudication)
Urinary tract infection
Post-operative wound or deep infection
Gangrene
Cutaneous or mucocutaneous infection
Lower respiratory tract infection
  including pneumonia and tracheobronchitis
Upper respiratory tract infection with fever
Gastroenteritis with fever
Psychosocial adverse reaction
Failure to maintain growth and development
Imprisonment
Minor outpatient surgery or incidental trauma
Intercurrent endocrine events

Figure 10.1

Sample Safety Threshold Alert Memo
from the DCCT Coordinating Center

Clinic ____

Effective July 1, 1988

The Central Biochemistry Laboratory has reported that Patient ID _____, ____, has a calculated serum LDL cholesterol greater than 160 mg/dl. The specimen, accession number _____, was collected _____.

This patient should have an additional serum LDL cholesterol assessment within one month of this notification. If both levels are elevated, you will be notified and an intercurrent event form should be filed.

Figure 10.2

Sample Set of Instructions for
Management of Low Blood Glucose Reactions
(Hypoglycemia or "Insulin Reactions")

1. Always carry four glucose tablets on your person, keep four glucose tablets at your bedside, and keep four glucose tablets in your car.

2. If you are certain that you are feeling "low", take two glucose tablets at once. If you are not feeling right but are uncertain whether you are "low", measure your blood glucose. If it is less than 80, take two glucose tablets. If you are uncertain and it is not possible to measure your blood glucose, it is safer to take two glucose tablets than to wait.

3. If you do not feel better 15 to 20 minutes after taking two glucose tablets, check your blood glucose again. If it is less than 80, take an additional one or two glucose tablets.

4. If for some reason glucose tablets are not available when you are "low", take 20 grams of carbohydrate as six ounces of orange juice, six ounces of pop such as Coke or gingerale, four lumps of sugar, ten Life Savers, 1 1/2 ounces of milk chocolate, or other candy.

5. If you are going to engage in planned strenuous exercise such as running, swimming, bicycling, walking rapidly, or playing basketball or tennis, be sure to follow your prescription for adjusting that day's insulin dose.

6. If you are going to engage in unplanned strenuous exercise, take two glucose tablets or an equivalent carbohydrate snack before starting the exercise.

7. Whether engaging in planned or unplanned exercise, always have glucose tablets or another source of carbohydrate available in case your blood glucose becomes low during the exercise.

8. If you exercise strenuously in the evening, be absolutely certain to check your blood glucose at bedtime. If it is less than 120, eat an extra large snack. Remember, exercise can cause a low blood glucose reaction several hours afterwards, especially during the night when you are fasting.

9. If you have a low blood glucose reaction just before you are about to drive your car, do not start until you have treated your reaction and have rechecked your blood glucose. Do not begin to drive until your blood glucose is at least 80-100.

10. If you are eating out and driving to the restaurant yourself, do not take regular insulin at home. Measure your blood glucose and draw up the correct pre-meal dose of insulin. Take the syringe with you and give yourself the insulin when you get to the restaurant. If your blood glucose is less than 80 before leaving, have a small snack before you even drive to the restaurant.

11. If you are driving long distance from city to city, have plenty of extra snacks in the car. Stop and check your blood glucose every two hours. If it is less than 80, take a 10 gram carbohydrate snack (for example, one fruit exchange). If it is less than 60, take two glucose tablets.

12. If you are driving alone and feel even a slight reaction coming on, or if anyone else in the car suggests you may be "low", immediately pull over and take two glucose tablets. Never try to make it to wherever you are going before treating a suspected reaction.

13. Never argue with someone who tells you that you are "acting low" or "acting funny". Assume you are "low" and treat yourself or accept treatment if it is offered by another. Remember, safety first.

CHAPTER 11

CHANGES IN TREATMENT OR FOLLOW-UP SCHEDULE

While the success of the DCCT depends heavily on the extent to which patients adhere to the directions of the Protocol, it is recognized that circumstances will arise in which patients will become unwilling or unable to follow the directions. The term "change in treatment or follow-up schedule" is used in a broad sense to include several types of events such as a modification, deviation, change in assigned follow-up schedule, transfer to inactive status, and loss to followup.

This chapter presents definitions of these several types of changes and establishes a terminology by which to refer to them. Table 11.1 indicates the two main categories into which these events are classified, namely events related to the procedures or goals of treatment specified for patients assigned to one or the other of the treatment groups, or events related to the measurements of the major outcome assessments. Inability to obtain measurements of outcome variables may result in loss to followup.

Failure to follow the Protocol in either of these two major categories may be offically sanctioned by the appropriate study committee or it may occur spontaneously despite efforts to prevent it (unsanctioned).

Under no circumstances can a patient in the DCCT be formally transferred from one treatment group to the other. For the purposes of statistical analysis, all subjects remain in the treatment group to which they were assigned at the time of randomization. Any alteration in a subject's treatment regimen or follow-up schedule from that outlined in the Protocol or Manual of Operations represents either a modification of treatment, a deviation from treatment, a modification of outcome visit schedule, or a transfer to inactive status, as discussed below.

11.1 MODIFICATION OF TREATMENT

A modification of treatment is any change which makes the treatment regimen differ from that outlined in Chapter 9 for the standard group and for the experimental group. Specifically, in the standard group, modifications include, but are not limited to, the implementation of more frequent staff-patient contact, more intensive dietary instruction, more intensive monitoring or hospitalization to meet first or second priority aims for the standard group (as outlined in Chapter 9 of the Manual). It is not a modification from treatment if a standard group patient who performs blood glucose monitoring once daily additionally checks a second

blood glucose on occasion prior to exercise for safety reasons. However, this is a modification of treatment if the patient consistently checks the blood glucose twice daily and uses the value for a purpose other than safety reasons. It is not a modification of treatment for the standard group patient who monitors urines three to four times per day and, in addition, one blood glucose per day. This is allowed by the treatment protocol for the standard treatment group. In the experimental group, modifications include raising the glycemic goals because of repeated severe hypoglycemia.

Modifications are required in certain situations and allowable in others. The Quarterly Visit Form (DCCT Form 021) allows for reporting of the initiation of modifications as well as termination of these modifications. When a modification in treatment is needed, it should be carried out by the DCCT clinic and reported on the next Quarterly Visit Form. The Treatment Committee will review modifications at their meetings. The primary purpose of this review will be to determine whether therapeutic methods differing from those outlined in the Manual of Operations are occurring studywide or at individual centers. If any particular modification is widespread and appears justified, a change in treatment as outlined in the Manual of Operations may need to be considered by the Treatment Committee.

There is one important exception to this policy and procedure. This is the use of more than two insulin injections per day or of an insulin pump in a standard group subject in order to meet priority one and two aims. This particular modification requires prior approval of the Treatment Committee. This approval should be obtained from the Chairman of the Treatment Committee who will consult with the members of the Treatment Committee if he/she feels it is necessary. Such an intensification of therapy would rarely, if ever, be required on an emergency basis.

11.2 DEVIATIONS FROM TREATMENT PROTOCOLS

11.2.1 Definition of Deviation from Treatment

Deviations from treatment are clearly defined. They are:

1. Deviation from the experimental treatment protocol is defined as withdrawal from the intensive methods of insulin delivery set forth in Chapter 9. It is not a deviation from treatment for an experimental group patient whose prescribed regimen consists of three injections per day, but who takes only two injections daily on most days because a given blood glucose value calls for a pre-prandial dose of "0" units. As long as the prescribed regimen is consistent with a MDI regimen as stated in the Protocol, this is not a deviation.

2. Deviation from the standard treatment protocol is defined as institution of insulin delivery by pump or multiple daily

injections for any purpose other than meeting the first and second treatment priorities set forth in Chapter 9.

11.2.2 Deviations from Experimental Treatment

Deviations from the experimental treatment may be carried out for the following reasons:

1. Inability to prevent recurrent severe hypoglycemia despite manipulations within the experimental treatment.

2. Major sequelae of hypoglycemia such as an accident which jeopardizes the patient or others, or alters the ability of the subject to continue on intensive methods of insulin delivery.

3. Psychiatric disorder or sociopathic behavior affecting judgment or causing risk of suicide.

4. Substance abuse.

5. Inaccessibility of subject to management by DCCT staff or other qualified personnel.

6. Recurrent diabetic ketoacidosis after trial on both CSII and MDI.

7. Blindness.

8. Any serious intercurrent illness (example: malignancy with short life expectancy).

9. Unavoidable chronic use of beta-blocking drug for intercurrent illness.

10. Adoption of a hazardous occupation.

11. Patient insistence.

11.2.3 Treatment Policy

The magnitude of allowable change from the goals of blood glucose control will vary in individual circumstances. The greater the risk of serious hypoglycemia, the less the DCCT physician should strive for the blood glucose and HbA_{1c} targets set for the experimental group. Similarly, the less the patient can be relied on to adhere to the experimental treatment program or the less the DCCT physician can directly supervise the patient's management, the less he/she should strive for the blood glucose and HbA_{1c} targets set for the experimental group. However, the DCCT physician should always attempt to achieve a degree of control as close to the experimental treatment goals as can be

safely and reasonably implemented and at least the criteria for acceptable care which have been set for the standard treatment group.

In the event that a patient insists on change from the experimental treatment, the investigator should discontinue the use of those treatment techniques to which the patient objects. However, with the patient's concurrence, the investigator should continue to strive for the blood glucose and HbA_{1c} goals of the experimental treatment with whatever techniques remain available to him/her.

11.2.4 Deviations from the Standard Treatment

Deviations from the standard treatment may be carried out in the following two situations:

1. Pregnancy or purposely pursuing conception.

2. Patient insistence. The patient's right to change treatment for any reason should always be honored gracefully.

subsection 'Completion of DCCT Forms 003, 021

For individuals who deviate, Forms 003 and 021 should be completed by checking the current form of insulin delivery and completing those questions pertaining to the current form of insulin delivery.

11.2.5 Treatment Policy

In that situation where the patient absolutely insists on a program of management more stringent than that of the standard treatment regimen, the following is recommended. Each investigator should determine, on an individual basis, whether it would be in the best interests of the patient for that investigator to continue personal management of the patient's blood glucose control in this circumstance. If the investigator elects to continue such management personally, he/she should determine with the patient the techniques to be used and the blood glucose and/or HbA_{1c} target levels to be sought. If the investigator elects not to continue such management personally, he/she should assist the patient in obtaining from another physician the type of blood glucose control desired by the patient.

In either case, the DCCT should continue to provide the same monitoring of clinical status and HbA_{1c} levels and the same surveillance for microvascular and macrovascular complications. If another physician has assumed management of blood glucose control, that physician should be provided with the same HbA_{1c} report from each three-month DCCT clinic visit that is prepared for standard patients. That physician should also be notified promptly of any changes in outcome that pass the safety thresholds defined in Chapter 6.

DCCT Form 022, Notification of Deviation from Assigned Treatment or Goals, is to be completed whenever a randomized patient or his/her DCCT physician seeks a deviation from the Protocol-specified regimen of the treatment group to which the patient is randomized. Except in emergency situations, all such deviations must be approved beforehand by the Treatment Committee or its Chairman.

11.3 UNSANCTIONED CHANGES OR DEVIATIONS FROM ASSIGNED TREATMENT

Unsanctioned changes from assigned treatment may occur either as a result of a patient's conscious or unconscious decision to disregard the recommendations of DCCT staff, or a DCCT staff member's disregard of the Protocol. In the latter case, the Protocol only permits unsanctioned changes from assigned treatment when the need for change is perceived as sufficiently urgent to require action before the Treatment Committee has an opportunity to review the request for change.

A patient's departure from instructions given by DCCT staff falls into the general category of non-compliance (or non-adherence) which is discussed in Chapter 20. Adherence is defined for the purposes of the DCCT as "the extent to which the patient's behavior, in terms of taking medications, following diets, executing other lifestyle changes and attending DCCT visits, coincides with clinical prescriptions." While this definition implies that non-adherence behavior which exceeds the prescription of the provider as well as that which falls short of it, non-adherence is most commonly understood to denote the latter response and Chapter 20 deals with this aspect of the matter. However, in the standard group of the DCCT, behavior which exceeds the physician's instructions with respect to the fact and frequency of self blood glucose monitoring and to the frequency of insulin injections can be envisioned and might be encountered. Similarly, in the experimental group, over-zealous pursuit of normal blood glucose levels by the subject in a manner beyond that prescribed and at the expense of safety could occur.

Such unsanctioned changes from Protocol are most likely to occur in the standard group if patients have access to literature which promotes or provides instructions in the use of multiple daily injections and/or self blood glucose monitoring or promotes frequent self blood glucose monitoring with immediate routine adjustment to insulin doses. In particular, DCCT materials relating to these activities should not be made available to patients assigned to the Standard Treatment Group.

11.4 MODIFICATION OF OUTCOME VISIT SCHEDULE

The failure of a patient to undergo an endpoint measure (quarterly HbA_{1c} or Profilset, semiannual fundus photography, or annual follow-up testing or visit) does not constitute a deviation or require a transfer to inactive status. Each missed endpoint measure should be reported on DCCT Form 014, Notification of Missed Clinic Visit). Subsequent missed visits should also be reported on DCCT Form 014 until such time as the subject is transferred to inactive status or resumes the Protocol-specified visit schedule. Transfer to inactive status should be avoided whenever possible and applies only when a subject will not be returning for ANY participation in the study.

11.4.1 Sanctioned Failure to Obtain Endpoint Determinations

There are some intercurrent events, such as hypoglycemia and pregnancy, that cause a cancellation or postponement of endpoint determination for ANS, neurobehavioral testing, and renal studies.

11.4.2 Unsanctioned Failure to Obtain Endpoint Determinations

This category embraces patient non-adherence to requested attendance at regularly scheduled endpoint examinations or patient refusal to undergo certain procedures at such visits. If the guidelines for achieving visit compliance outlined in Chapter 20 are followed carefully, no major problems should be encountered among patients who remain under clinical care for their diabetes at the DCCT centers. However, patients who have been transferred to the care of other physicians, either because of geographic relocation or because of sanctioned changes from the treatment study protocol, may be reluctant to continue attending the DCCT center for procedures which they do not perceive as essential for the overall care of their diabetes. Each and every reasonable approach to the facilitation of such visits should be taken. This may frequently need to include reimbursement (or in some cases preimbursement) for the cost of transportation, either to the original DCCT center or, in the case of patients who have relocated, to the nearest DCCT center.

11.5 TRANSFER TO INACTIVE STATUS

Transfer to inactive status is defined as a temporary or permanent moratorium on subject participation in the study in its entirety. Transfer to inactive status is allowable in the following situations:

1. When in the judgment of Principal Investigator and mental health consultants, any manner of participation in the study could no longer be considered informed or would be directly injurious to the subject's well-being.

2. Catastrophic injury or illness resulting in coma, dementia, blindness, or inability to monitor diabetic retinopathy adequately.

3. Complete inaccessibility to metabolic management or to monitoring of endpoints (for example, long-term imprisonment).

4. Subject withdraws consent for continued participation in the trial.

All investigators should be sure that in appropriate cases any DCCT subjects who are in the inactive status category are encouraged and given every opportunity to return to the study as active participants at any time.

11.5.1 Procedure for Request for Transfer to Inactive Status

At the earliest knowledge of a patient requiring or anticipating transfer to inactive status, the investigator should contact, by telephone, the Chairman of the Clinic Monitoring Group, who will discuss the matter with other members of the Group. DCCT Form 016, Application for Transfer to Inactive Status, should be filed with the Coordinating Center as soon as possible. The Treatment Committee will review all cases of transfer to inactive status at their regular meetings.

11.6 LOSS TO FOLLOWUP

The criteria for assignment to the category of Loss To Followup can only be fulfilled retroactively at the end of the study. This term will signify the unavailability of the final glucose profile, HbA_{1c} determination and fundus photographs at the end of the study. A subject who misses two successive evaluations of the principal outcome measure, i.e., fundus photographs for retinopathy, and these missed visits are unsanctioned, will be designated as lost to followup until he/she resumes evaluation. The DCCT Form 014 should be completed for each visit missed.

11.7 SUMMARY

1. Modification of treatment:

   a) Report on DCCT Form 021.

   b) No need to contact Treatment Committee unless planning to initiate intensive insulin therapy in a standard group patient.

2. Deviation from treatment regimen:

a) Report on DCCT Form 022.

b) Contact Chairman of Treatment Committee.

c) Standard patient on more than two injections of insulin or an insulin pump; experimental patient on less than three injections of insulin daily.

3. Modification of outcome visit schedule:

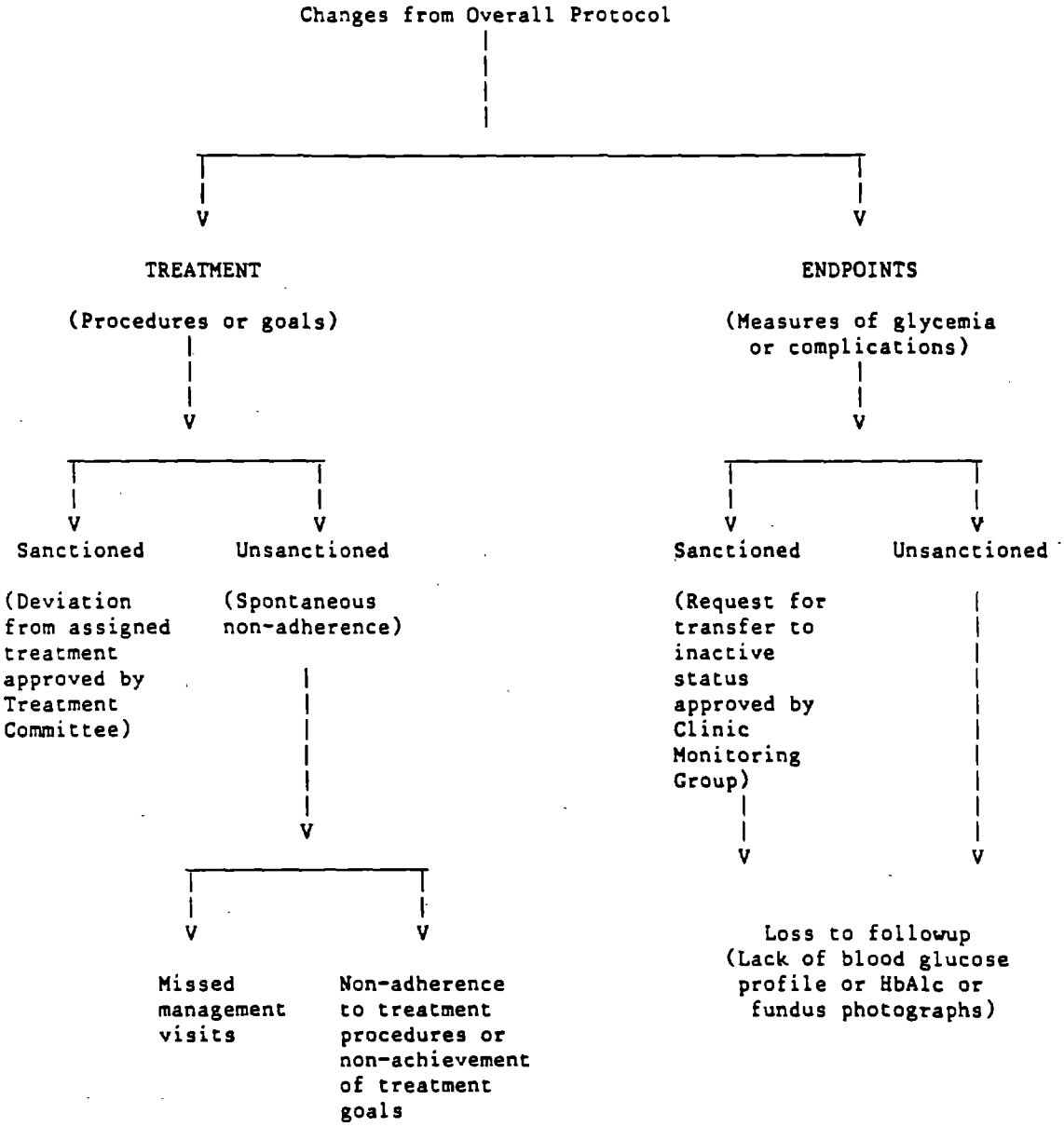
a) Report on DCCT Form 014.

4. Transfer to inactive status:

a) Apply for transfer on DCCT Form 016.

b) Contact Chairman of Clinic Monitoring Group.

Table 11.1


Changes from Overall Protocol
TREATMENT
(Procedures or goals)
Sanctioned
(Deviation from assigned treatment approved by Treatment Committee)
Unsanctioned
(Spontaneous non-adherence)
Missed management visits
Non-adherence to treatment procedures or non-achievement of treatment goals
ENDPOINTS
(Measures of glycemia or complications)
Sanctioned
(Request for transfer to inactive status approved by Clinic Monitoring Group)
Unsanctioned
Loss to followup
(Lack of blood glucose profile or HbAlc or fundus photographs)

CHAPTER 12

LABORATORY SPECIMENS

12.1 INTRODUCTION

This chapter presents procedures for collecting those laboratory specimens that require patient instructions and/or more than normal preparation by the staff to collect the specimen. Urine glucose testing performed by patients is described in Section 12.2 and techniques for self blood glucose monitoring are given in Section 12.3. The remainder of the chapter is devoted to the standardized procedures used in this trial for collecting specimens for endpoint analysis. These specimens include serum and urine for renal studies (Section 12.4) and for the glomerular filtration rate determination (Section 12.5); the 24-hour urine collection for measurement of dietary protein (Section 12.6); the capillary blood glucose collections (Section 12.7); the C-peptide test (Section 12.8); and lipids (Section 12.9). Chapter 15 of this Manual presents details of specimen processing, labeling and mailing.

12.2 URINE GLUCOSE TESTING

12.2.1 General Guidelines

Both first and second void urines can provide useful information. First void urines may give a reasonably good indication of the average level of sugar in the blood during the interval since the patient last urinated. Some physicians prefer second void urine testing and recommend that only fresh urine (that is, urine recently formed by the kidneys) be tested for sugar. A fresh specimen may give a reasonably good indication of sugar in the blood at the time the test is made. A fresh specimen of urine is obtained in the following manner:

1. Empty your bladder 20 to 30 minutes before you are going to do the test. Discard this urine.

2. Drink a glass of water.

3. In 20 to 30 minutes, or as soon as you are able, empty your bladder again. Test a part of this urine for sugar.

   If necessary, one hour may lapse between the first and second times the bladder is emptied; a wait longer than one hour is undesirable.

12.2.2 Methods

Several methods have been used to measure urine glucose levels. Since the glucose oxidase method is both specific and convenient, it is preferred by many practicing diabetologists. Others feel, however, that this method is not sufficiently quantitative and, therefore, advocate the measurement of total reducing substances in the urine. Either method is acceptable in the present trial with the selection being determined by patient and physician preference.

12.2.2.1 Glucose Oxidase Method (Test Tape)

1. Lift top lid and by pulling straight up, withdraw approximately 1 1/2 inches of tape. While keeping a slight tension on tape, close lid and hold. Tear tape by pulling straight out.

2. Dip 1/4 inch of tape into specimen, remove immediately and wait one minute. Yellow color indicates urine is sugar (glucose) free.

3. Then immediately compare the darkest area while holding tape on white area above color chart. If tape indicates 1/2 percent or higher, wait one additional minute and make final comparison.

12.2.2.2 Total Reducing Substances: Clinitest Methods

1. General: A number of substances found in urine, such as salicylates and penicillin, react positively with Clinitest but are not present in most cases in sufficient quantity to interfere with the test. Ascorbic acid, nalidixic acid, cephalosporins and probenecid in large quantities may cause false positive results. Metabolites of some sulfa drugs and methapyriline compounds may interfere at levels below 1/2 percent (1.5 g/dl). They are not known to interfere at 1/2 percent or higher. Reducing sugars other than glucose will react positively with Clinitest. These include lactose, fructose, galactose, and pentoses.

2. Procedures: Clinitest 2-Drop Method

   a) Collect urine in clean container. With dropper in upright position, place 2 drops of urine in test tube. Rinse dropper with water and add 10 drops of water to test tube.

   b) Drop tablet into test tube. Watch while complete boiling reaction takes place. Do not shake test tube during boiling, or for the following 15 seconds after boiling has stopped.

   c) At the end of this 15-second waiting period, shake test tube gently to mix contents. Compare color of liquid to 2-Drop Color Chart. Ignore sediment that may form in the bottom of

the test tube. Ignore changes after the 15-second waiting period.

d) Record the percent result which appears on the color block that most closely matches the color of the liquid. Color Chart results for the 2-Drop Method range from negative to 5%.
IMPORTANT: Urine containing more than 5% sugar may cause a very rapid color change during the boiling and 15-second waiting period. Observe the solution closely during this time to detect "pass-through" color changes. Should these occur, the color will pass rapidly through green, tan and orange to a dark greenish brown. In this case, record the result as over 5% sugar, and do not compare final color to the 2-Drop Color Chart.

3. Procedures: Clinitest 5-Drop Method

a) Collect urine in clear container. With dropper in upright position, place 5 drops of urine in test tube. Rinse dropper with water and add 10 drops of water to test tube.

b) Drop tablet into test tube. Watch while complete boiling reaction takes place. Do not shake test tube during boiling, or for the following 15 seconds after boiling has stopped.

c) At the end of this 15-second waiting period, shake test tube gently to mix contents. Compare color of liquid to 5-Drop Color Chart. Ignore sediment that may form in the bottom of the test tube. Ignore changes after the 15-second waiting period.

d) Record the percent result which appears on the color block that most closely matches the color of liquid. Color Chart results for the 5-Drop Method range from negative to 2%.
IMPORTANT: Urine containing more than 2% sugar may cause a very rapid color change during the boiling and 15-second waiting period. Observe the solution closely during this time to determine "past-through" color changes. Should these occur, the color will pass rapidly through green, tan, orange to a darkish greenish brown. In this case, record the result as "over 2% sugar" and do not compare final color to the 5-Drop Color Chart.

4. Limitation of Clinitest Procedure: Clinitest is not specific for glucose and will react with sufficient quantities of any reducing substances in the urine. Failure to observe the reaction at all times can lead to erroneously low results if the "pass-through" phenomenon is missed. Low specific gravity urines containing glucose may give slightly elevated results and urines with high specific gravity may give slightly lowered results. The metabolites of some sulfa drugs and methapyriline compounds may interfere with the sensitivity of Clinitest. These substances are not known to interfere at glucose levels of 1/2 percent (0.5 g/dl)

or higher. High protein concentrations extend boiling time, increase foaming and may make visual comparison difficult.

12.2.2.3 Urine Acetone

1. General: This test is based on the development of color ranging from buff-pink for a negative reading to maroon when acetoacetic acid and acetone react with nitroprusside. Normal urine specimens ordinarily yield negative results with this test. Detectable levels of ketone may occur in urine during physiological stress conditions such as fasting, pregnancy and frequent strenuous exercise. In diabetic ketoacidosis, starvation, or with other abnormalities of carbohydrate or fat metabolism, ketones may appear in urine in large amounts.

2. Procedures:

   a) Collect urine in clear container.

   b) Place acetest tablet on a clean surface, preferably on a piece of white paper.

   c) With dropper in upright position, place one drop of urine on tablet.

   d) Compare color of acetest tablets to color chart at 30 seconds.

   e) Record as negative, small, moderate or large depending on the color.

3. Limitation of Procedure: Positive results may occur with highly pigmented urine specimens. Urines containing bromsulfalein or very high quantities of phenylketones may give false positive results as will urine preserved with 8-hydroxyquinoline. L-dopa metabolites may give an atypical reaction which could be interpreted as a positive test. The acetest is specific for the detection of acetoacetic acid and acetone. It is about ten times more sensitive to acetoacetic acid than acetone and will not react with beta hydroxybuturic acid (which is the ketone body present in greatest concentration normally). Acetest tablets have prolonged stability in unopened containers and if stored below 30 degrees C. Once open, the acetest tablets have decreased stability and they must be recapped promptly after removing the tablet, particularly to protect them from exposure to moisture.

12.3 BLOOD GLUCOSE TESTING

12.3.1 General Introduction

Reflectance meters will be used for measuring blood glucose by the experimental group whenever possible. When this is not feasible, then visual interpretation of strip will be allowed. Although both dextrostix and chemstrips are adequate when used with a meter, only chemstrips provide sufficient discrimination when used visually.

12.3.2 Blood Letting

1. Wipe finger to be punctured with an applicator saturated with alcohol. Allow to dry.

2. Puncture distal portion of digit. Free flow of blood may be enhanced by placing hand in warm water before fingerprick is performed. Some patients feel puncturing on lateral portion of digit is less painful. Puncture site should be rotated so as to avoid scarring. Puncture may be made using either single pronged lancets or small hypodermic needles. Automated spring-operated devices (Autolet, Monojector, Penlet, Metoclix, Hemolet) makes puncturing the finger relatively painless.

3. After puncture, hold the pricked finger in a position with palm facing down until a large landing drop of welled blood has formed. Bring strip to finger and transfer the blood by lightly touching the reagent area of the strip to the drop. Be sure to cover the reagent area completely. Do not smear.

12.3.3 Visual Interpretation Using Chemstrips

1. After placing blood on strip, start timing immediately.

2. Wait exactly 60 seconds. Then, using moderate pressure, wipe off blood with a clean, dry cotton ball. Lightly wipe the strip two more times using the clean sides of the cotton ball. Wipe all blood or cotton residues from the test area.

3. Wait one additional minute. Then match the two colors of the reagent area to the color blocks on the vial label. If the two colors on the reagent strip match one of the color blocks, then the value of that specimen is close to the stated value for the block.

4. At times the closest match may be one reagent pad corresponding to one blood glucose concentration, and the other pad corresponding to the next higher (or lower) value. In such cases, the blood glucose can be estimated as falling about in the middle of these

two values. Thus, for example, if the blue pad matches the bottom blue of 180 mg/dl and the green pad matches the top green color corresponding to 240 mg/dl, the blood glucose concentration can be considered as being around 210 mg/dl.

5. If the color values on the strip are approximately 240 mg/dl or more, wait one more minute for a final reading.

6. The color reaction at two minutes (less than 240 mg/dl) and three minutes (over 240 mg/dl) are endpoints and will be stable when stored under proper conditions (protected from direct sunlight, heat and excessive humidity). Strips can be dated and saved.

12.3.4 Visual Interpretation Using Visidex

1. After placing blood on strips, start timing immediately.

2. Wait exactly 60 seconds. Keep the strip level while timing. At the end of 60 seconds, quickly wash the reagent pads with water from a wash bottle or tap (faucet) sufficiently to remove the blood. Do not overwash.

3. Gently blot once on a lint-free paper towel.

4. Immediately compare the reactive green pad to the nearest matching green color block. If the green pad matches or is darker than 180 mg/dl (10 mmol/L), color block, wait an additional 30 seconds from wash time (90 seconds total elapsed time), then compare the other reactive pad to the orange color blocks and read the results. If the color falls between any two blocks, estimate result.

12.3.5 Use of Accuchek-bG Reflectance Meter for Reading Chemstrips

1. Calibration: Insert correct Calibration Strip. Close door. Press (ON/OFF) to turn ON; wait for and verify 888. Open door. Insert unused Chemstrip bG under strip guide. Close door; wait for 000. Open door and remove unused Chemstrip bG; place strip on flat work surface.

2. Testing: Prick finger as above; obtain a large hanging drop of blood. Bring Chemstrip bG to finger and cover both test zones with blood. DO NOT SMEAR. Press timer. Wait for 60 and first beep (one minute). Wipe Chemstrip bG with cotton ball. Insert Chemstrip bG under strip guide. Wait for 120 and second beep (two minutes). Close door. Read blood glucose value. Press ON/OFF to turn OFF. Open door. Remove Chemstrip bG.

12.3.6 Use of Glucometer Reflectance Meter for Reading Dextrostrips

1. Calibrations:

a) General. The Glucometer may be calibrated using a wet calibration chip. The former is preferred.

b) Wet Calibration Method.

i) Low Calibration Procedure.

- Turn the GLUCOMETER ON
- If low cal. does not appear, press the cal. button to activate the calibration process.

- Remove a DEXTROSTIX Reagent Strip from the bottle and immediately replace and tighten the bottle cap.

- Make sure the Test Chamber Lid is closed and press the time button. CAUTION: Test Chamber Lid appears slightly raised with strip in place. This is normal. Do not force lid closed.

- At the sound of the first buzzer, quickly apply a large drop of DEXTRO-CHEK Calibrator (Low) to the reagent pad of the DEXTROSTIX Reagent Strip (cover reagent pad generously). Keep DEXTROSTIX level to avoid spilling the solution. Allow reaction to continue until buzzer sounds (60 seconds).

- Immediately wash the reacted reagent pad for about two seconds with a sharp stream of water from the DEXTRO System Wash Bottle. Direct the stream of water across the entire reagent pad and blot gently on a lint-free paper towel. Do not wash under a faucet or tap.

- Lift the Test Chamber Lid and insert the reagent strip to the end of the Strip Guide with the reagent pad face down.
CAUTION: FOR ACCURATE READINGS, THE REAGENT PAD MUST COVER THE OPTICAL WINDOW.

- Gently close the Test Chamber Lid (do not force) and press the read button, high cal. will appear on the display panel replacing low cal.

- Lift the Test Chamber Lid, dispose of the used strip and close the lid. Begin the High Calibration Procedure.

ii) High Calibration Procedure - Repeat steps 3 through 9 using the DEXTRO-CHEK Calibrator (High) and a fresh DEXTROSTIX Reagent Strip. At Step 9, after pressing the read button, mg/dl or mmol/l will appear on the display

indicating that calibration has been established. Next run a Control Test.

c) Calibration Chip Method

i) Low Calibration Chip Procedure - Turn the GLUCOMETER ON.

- If low cal. does not appear on the display, press the cal. button to activate the calibration process.

- Make sure the Test Chamber Lid is completely closed and press the time button. The buzzer will sound followed by a 60 second digital countdown period.

- During countdown, remove Low Cal Chip from its container.

- At the sound of the second buzzer (end of 60 second countdown), lift the Test Chamber Lid and insert the Low Cal Chip securely in place.

- Gently close the Test Chamber Lid (do not force) and press the read button; high cal. will appear on the display panel replacing low cal.

- Remove the Low Cal Chip and close the lid. Begin the High Calibration Procedure. Do not discard the Low or High Cal Chips used in this procedure. Store in the holder provided.

d) High Calibration Chip Procedure - Repeat steps 3 through 6 using the High Cal Chip. At step 6, after pressing the read button, mg/dl or mmol will appear on the display indicating that calibration has been established. Next run a Control Test. CAUTION: KEEP THE LOW AND HIGH CAL CHIPS CLEAN AND DRY. AVOID SCRATCHING OR MARRING THE SURFACE.

2. Control Test: A control test should be run after each calibration. It is recommended that a control test be performed at least once a day.

i) Control Procedure: - Remove a DEXTROSTIX Reagent Strip from the bottle and immediately replace the bottle cap.

- Make sure Test Chamber Lid is closed (gently) and press the time button.

- At the sound of the first buzzer, quickly apply a large drop of Control Solution to the reagent pad of the DEXTROSTIX Reagent Strip (cover reagent pad generously). Keep DEXTROSTIX level to avoid spilling the solution. Allow reaction to continue until buzzer sounds (60 seconds).

- Immediately wash the reacted reagent pad for about two seconds with a sharp stream of water from the DEXTRO System Wash Bottle. Direct the stream of water across the entire reagent pad and blot gently on a lint-free paper towel. Do not wash under a faucet or tap.

- Lift the Test Chamber Lid and insert the reagent strip to the end of the Strip Guide with the reagent pad face down.

- Gently close the Test Chamber Lid (do not force) and press the read button. The Control Test result will appear within seconds on the display.

- Lift the Test Chamber Lid, dispose of the used strip and close the lid.

3. Blood Glucose Test Procedures.

- Remove a DEXTROSTIX Reagent Strip from the bottle and immediately replace and tighten the cap.

- Wipe the finger to be punctured with an applicator saturated with alcohol. Allow the alcohol to dry.

- After performing a finger puncture, allow a drop of blood to form and wipe it away with a clean, dry cotton ball.

- Allow another drop of blood to form. Make sure the Test Chamber Lid is closed (gently) and press the time button.

- At the sound of the first buzzer, quickly apply a large drop of blood sufficient to cover the entire reagent pad of the DEXTROSTIX Reagent Strip (cover pad generously). Keep DEXTROSTIX level to avoid spilling the drop of blood. Allow reaction to continue until the buzzer sounds (60 seconds).

- Immediately wash the blood off of the reacted reagent pad for about two seconds with a sharp stream of water from the DEXTRO System Wash Bottle. Direct the stream of water across the entire reagent pad and blot gently on a lint-free paper towel. DO NOT WASH UNDER A FAUCET OR TAP.

- Lift the Test Chamber Lid and insert the reagent strip to the end of the Strip Guide with the reagent pad face down.

- Gently close the Test Chamber Lid (do not force) and press the read button. The blood glucose concentration value will appear within seconds on the display.

- Record blood glucose result.

- Lift the Test Chamber Lid, dispose of the used strip and close the lid.

- Turn off GLUCOMETER, unless another test is to be performed.

12.4 CREATININE AND ALBUMIN IN SERUM AND URINE

The measurements of creatinine and albumin in serum and urine must be considered together within one protocol used in determining renal function. Measurement of creatinine in serum and urine, appropriately collected over a defined period of time, will allow calculation of the patient's creatinine clearance. Coupling these values with the albumin levels in the same serum and urine specimens will provide a relative index of the urinary excretion of albumin.

One organizational difficulty with this protocol encompasses the needs to determine eligibility with respect to albumin excretion and to utilize the same measurement for baseline values (if the patient is accepted into this study). Since the protocol for this study is complex, the following explanation assumes that one carefully managed collection procedure can be utilized to send specimens to the CBL both for eligibility and for baseline measurment (see Table 15.1).

Ideally, the protocol is begun in the morning after the patient has had his or her breakfast and first injection of insulin. However, testing is allowed anytime day or night. It is important that the person be in a resting and relaxed state. The patient's condition should satisfy the treatment goals set forth for the Standard Treatment Group. In both morning and afternoon testing sessions, the usual snack is allowed. In addition, the patient will be asked to drink copious amounts of water during the testing protocol. Any symptomatic hypoglycemia which the patient or anyone else must treat with food is cause to abort the collection and the studies must be scheduled for another visit on another day. The test should not be done when the patient is actually ill. Questions regarding individual circumstances should be referred to the CBL.

First ask the patient to void, discard this specimen and record the time of voiding. During the course of the protocol, the patient will be asked to drink 250 ml of water every half hour. Any time during the second two hours of the four-hour protocol, draw 10 ml of blood into a red-topped tube and promptly separate the serum. Divide the serum into two appropriately labeled containers and freeze. Send one aliquot to the CBL for determination of creatinine and albumin.

After four hours (and sooner if the patient wishes to void during the course of the study) ask the patient to void, measure the volume of urine voided during the course of the study and record the time of voiding at the end of the study. This time and time noted at the beginning of the study can be used to determine the duration of the study. Make all collections on ice, and mix all collected urine. Transfer 4.6 ml (see

side of tube) of urine to each of five appropriately labeled containers. Freeze all specimens and retain one frozen aliquot in the clinical center. Send the remaining four aliquots for creatinine and albumin determinations to the CBL. The extra containers will be stored in the CBL at -70 degrees C for possible reprocessing of specimens at a future time.

12.5 GFR

12.5.1 Background Information

1. Preparation to Implement GFR Procedure

   First thing is to notify your radiation safety board that you will be attempting to carry out this procedure. An official of this board will stipulate what are the local rules.

2. ^{125}I-sodium Iothalamate -- availability and other pertinent information.

   All orders for ^{125}I-Iothalamate are placed by Andrew Levey, M.D. of Tufts University, Boston, Massachusetts. In order for you to receive an order, you must have on file at the Coordinating Center the name and address of the local individual who is responsible for receiving the radioisotope.

   The sole supplier of Glofil in the United States at the present time is Isotex Inc., Box 909, Friendswood, Texas, 77546, phone (713) 482-1231. The material is synthesized on a monthly schedule and is available in 5 ml aliquots (1.0 mCi). It is stored at 4^{o}C in its lead container in a suitable nuclear medicine area and its shelf life and expiration date is 45 days from the date of production. This information is stated on the label that appears on the outside of each Golfil box. is 60 days. The limit to Glofil's usable life is a function of the chemical instability of the isotopic label which is slowly released as free ^{125}-I from the iothalamate molecule. As this free ^{125}-I accumulates, the clearance of Glofil deviates from the true Glomerular Filtration Rate (GFR). The material should not be used past the manufacturer's expiration date.

   The iothalamate is drawn up in a 1.0 ml plastic syringe with a 25 gauge x 5/8 inch needle. The total activity in the dose for all patients should be 35 micro curie. Remember, however, that 0.03-0.04 ml is left in the needle hub when the shot is given so the total activity is not equal to the activity administered to the patient. The syringe weight/activity before and after the shot is not measured and no standard solution of the iothalamate is required. The iodine-allergic patient should not be given the iothalamate.

Technologists handling the iothalamate should take all safety precautions to protect both the patient and themselves from unnecessary radiation exposure. Technologists should wear appropriate gamma ray sensitive fill badges and follow their exposure levels; the iothalamate should be stored and delivered in shielded containers. ^{125}-I emits low energy gamma radiation with a maximum energy of 36 KeV and lead will shield the user very effectively (1 mm of lead will stop 99.96% of the radiation from a ^{125}-I source. The syringes may be handled briefly, while the shot is given to the patient, without shielding. Gloves need not be worn unless dose leakage or other unsafe conditions arise. All syringes, needles, empty isotope bottles and any other radioactive trash should be disposed of via established contaminated refuse protocols (consult local radiation safety and/or disposal regulations); as a rule of thumb, any isotope decays to less than 1% of its original activity in 7 half-lives. This is 420 days for ^{125}-I. Small amounts of ^{125}-I may be disposed of by flushing with large amounts of water down the drain in approved disposal sinks. Consult your local radiation safety departments for further information.

3. Super Saturated Potassium Iodide (SSKI)

Super saturated potassium iodide is taken by the patient at least 30 minutes prior to the test. The SSKI prevents thyroid uptake of any free ^{125}-I; this protects the patient and eliminates error in GFR determination due to the additional elimination route for the isotope. The patient with a true iodine allergy should not be given SSKI and should not be tested.

4. Sources of Excess Variability

It must be remembered that among other things:

a) Patients may have mistakenly collected only portions of their timed urines, either by discarding some of the urine or by not emptying the bladder completely, thus reducing the apparent urine flow rate.

b) Patients have had apparent urine retention problems which were not noted in their charts and which made complete voluntary collection of timed urines impossible.

c) Collection times may not be recorded exactly. Times must be recorded at the completion of the void. A one or two minute error can cause a 10% error in flow rate. A method should be worked out whereby the subject signals the technician or reads a digital clock at the end of the void.

d) General laboratory problems may produce variability in sample counts.

5. Unacceptable Results

In cases where the urine output remains below 1 ml/min, the GFR results are not valid. In any case where the urine collection volumes are not complete, the GFR results are not valid. In any case where some other isotope contaminates the patient samples and its interference cannot be subtracted or allowed to decay to background, the GFR results are not valid. In certain cases of sample contamination (e.g., fecal contamination of urine), the GFR is not valid. Slight discoloration of urine by blood due to menstruation is allowable; severe contamination is to be avoided.

However, in all cases, send all available information to the laboratory for analysis.

12.5.2 Detailed Procedures

12.5.2.1 General Principles

The validity of GFR determinations is enhanced by following several important rules. Accurate timing of urine collections and careful measurement of urine volume is essential. The length of the timed urine collections may vary. The times are recorded at the end of each urine collection and before the blood is drawn. Blood samples are drawn immediately following each urine collection period.

The GFR procedure will be performed on all consenting subjects at baseline, the third annual visit and at study end. Baseline testing will be done any time before randomization. Annual visit windows open 21 days before the scheduled visit and remain open until the start of the next annual visit window.

The procedures described here detail the GFR determination using ^{125}-iodine iothalamate (^{125}-I) solution. At times (e.g., third annual followup), the 4-hour study for determination of albumin and creatinine levels will be done in conjunction with the iothalamate study. Information is provided for coordinating the two studies.

All bloods may be saved at room temperature and processed at the end of the study. Urine should be kept refrigerated for 4-hour studies. It is not necessary to refrigerate urine collected for the iothalamate study as the determinations are not affected by the growth of bacteria. Urine aliquots must be removed and volume measured before pooling for use in 4-hour renal tests which ends 240 minutes after "U-Pre" void (see description below). Aliquots will be included with the next routine shipment to the Central Biochemistry Laboratory (CBL).

1. Preparation for procedures:

   a) Each female patient must have a blood pregnancy test done within 72 hours prior to the injection of iothalamate solution. A positive result will be reason enough for canceling the procedure.

b) Due to possible blocking effects and potential adverse interactions, non-steroidal anti-inflammatory agents (e.g., aspirin, Motrin, Advil) should be discontinued at least 48 hours prior to the procedure. These medications may resume immediately following the test. Tylenol and codeine may be substituted during this period. Anti-hypertensives and diuretics should be discontinued for 24 hours prior to the test.

c) The test should be canceled if the patient has a known allergy to iodine.

d) To avoid inadvertent protein loading that would inhibit accurate interpretation of results, a low protein diet will be followed prior to the study. There should be no more than 15 grams of protein for breakfast or 25 grams of protein for lunch the day of the study. The local dietitian should work with each subject in adjusting the home diet or in arranging for appropriate meals to be served at the site of the test. Insulin doses should be adjusted for the changes in diet as needed.

2. Morning prior to clinic visit:

a) The study should be postponed if a sympomatic urinary tract infection (UTI) is known to exist. Acute intercurrent illness or a positive pregnancy test will cause postponement of the study.

b) Vigorous exercise is to be avoided on the day of the study.

c) Fluorescein angiography should not be performed on the same day as the GFR procedure due to discoloration of the urine.

d) It is best to start the water load (see next section) at home if the patient lives close to the clinic.

3. Arrival at clinic:

a) Measure height and weight. Record on the worksheet.

b) An oral water load of 10 ml/kg body weight is begun (complete within 30 minutes). If water load is begun at home, instruct the patient to take 5 mg/kg water (two 8-ounce glasses of water) at home. Then provide the patient another 5 mg/kg after he/she arrives at the clinic. After each voiding, the urine volume is measured and equivalent volume of water plus 100 ml is ingested. No other beverages may be substituted for the strict water load. Liquid (e.g., D5-W) should not be infused as part of the water load.

c) Patient voids and urine is saved. Label "U-Pre". Record clock time under "T-Pre" on worksheet. Obtain two 1.8 ml aliquots.

Discard remainder. Note that, where applicable, the collection for 4-hour renal study starts immediately following "U-Pre" void.

d) The administration of 5 drops of SSKI is done orally. The solution may be mixed with up to 20 ml of water.

e) A heparin lock or a 3-way stop-cock infusion set is inserted in a large antecubital vein and blood samples taken. An infusion set is not to be used for water loading.

f) Draw 10 ml of blood for iothalamate test; centrifuge and prepare two 1.8 ml aliquots of serum in cryotubes, label as "B-Pre". The processing of the blood may be done now or at the completion of the study. The blood may sit at room temperature until processed. If serum volume is low, prepare 1 full aliquot (1.8 ml) for the CBL and retain remainder as backup. Do not draw additional blood to increase volume of backup.

All appropriate tubes for any other simultaneous biochemistry measurements must be drawn at this time, prior to the radioisotope injection. This would include a 10 ml collection for the 4-hour renal collection to obtain 2 equal aliquots in 4.6 ml Nunc tubes. In the event that biochemistry samples are drawn after the isotope injection, a statement to this effect must be included with the samples when mailed.

g) After background serum and urine samples ("U-Pre", "B-Pre") are obtained, and at least 30 minutes post-SSKI (minimum of 45 minutes if a full breakfast or lunch has just been ingested), ^{125}I-Iothalamate is injected subcutaneously in the deltoid region. This will be provided in unidose syringes as a sterile, pyrogen free solution containing approximately 35 microcuries per dose. The entire volume (approximately 0.2 cc) will be injected subcutaneously at one site. Injection technique: all injections will be made subcutaneously in the upper arm with a 25 gauge 5/8 inch needle.

4. Equilibration period:

a) Patient should remain sedentary throughout the study. Light activity is acceptable.

b) Smoking will not be allowed during the study.

c) Allow at least 60 minutes to pass after injection of ^{125}-I. Continue the water load during this time. The load should be approximately 10 ml/kg during this hour or three to four 8 oz glasses.

d) Although the patient may void multiple times during this 60 minute period, the first clearance period will not begin until at least 60 minutes have transpired since the injection and the

urine flow rate is at least 3 ml/min. If the patient voids more than once during the period, all urine is saved and pooled for measurement of flow rate during the equilibration phase. If flow rate is less than 3 ml, water is continued until flow rate is greater than 3 ml in the subsequent void, i.e., another three 8 oz glasses of water should be drunk over the 30 minute interval. Any urine collected during the 60+ minutes is saved for the 4-hour renal test where appropriate. This urine is not needed for the determination of GFR.

The urine is saved for the 4-hour renal pooled collection.}

e) The timed collections start with the first void at least 60 minutes after the ^{125}-I injection with a flow rate of at least 3 ml/min. This urine is not needed for the iothalamate study. The patient must empty his/her bladder with each void.

f) Record time at end of urine collection as "T-0" on the worksheet.

All times will be recorded to the nearest minute using a digital clock. The recording of the urine sample times is the most critical; all times are recorded based on the momemt of completion of the urine collections, not the blood samples. A method should be worked out whereby the subject signals the technician or reads a digital clock at the end of the void.

g) Immediately following the "T-0" voiding, a blood sample is taken and labeled as "B-0"; two 1.8 ml aliquots of serum are prepared as above.

5. Collection period:

a) Spontaneous voiding (approximately every 30 minutes); maintain urine flow rate $\geq$3 ml/min. After each void, urine volume should be measured and an equal amount of water drunk. If less than 300, add 100 ml to load. Administer extra water if the flow rate is <3 ml/min but do not discontinue the study. Always record all information and attempt to complete the study. The calculations of GFR can be performed on partial studies when necessary.

The length of time between the urine collections will vary as they are based on spontaneous voiding. Note that subjects with lower GFR will excrete the water load more slowly than subjects with normal GFR. There is no maximum duration for the procedure. Total time will vary depending on the time needed to obtain 4 samples; however, no less than 20 minutes and preferably more than 30 minutes should elapse between voids in order to reduce the variability of the measurement by increasing the likelihood of complete emptying of the bladder.

For collection periods less than 20 minutes, the urine should be pooled with the next collection thus creating a pool of urine to be treated and aliquoted as one collection period.

If the 4-hour study collection concludes before the iothalamate test, note time and volume at the conclusion of the 4-hour renal protocol.

b) At the next voiding, the urine is collected and labeled as "U-1"; two 1.8 ml aliquots are saved. Remainder is saved for 4-hour renal if appropriate.

c) The time is recorded as time "T-1".

d) Coincident with time 1 voiding, a second blood sample is taken and labeled as "B-1"; prepare serum as above.

e) This sequence of timed urine and blood collections is repeated for times 2, 3 and 4. The water load continues throughout this stage.

f) The procedure should be stopped if the patient vomits.

g) The blood sugar should be measured at the beginning of the iothalamate GFR procedure. If symptomatic hypoglycemia exists or if the blood sugar is less than 90, the patient should be fed. One hour should pass before re-measurement. If the blood sugar is 90 or more, without symptomatic hypoglycemia, the test may proceed. Half way through the procedure (approximately two hours in), the blood sugar should be measured again. If the blood sugar is less than 90, the patient should be fed. If at any time the blood sugar drops below 55 or symptomatic hypoglycemia occurs, the test should be stopped. If at least three post-equilbration urine collections have been completed, the test will be considered complete and all samples should be sent to the CBL noting that the study was terminated prematurely. If less than three collections were completed, the test should be rescheduled for another day and no samples should be sent to the laboratory.

6. <u>End study</u>:

a) Remove infusion catheter.

b) The subject is encouraged to maintain a high urine output and to void frequently to minimize radiation exposure to the bladder.

c) Continue to collect urine for the 4-hour study where appropriate. These tests end 240 minutes after "T-Pre". Under extreme circumstances, the iothalamate study may take longer than the 4-hour renal test. When this occurs, the pooled collection (4-hour study) stops but timed collections

(iothalamate study) continue until four collection periods have been completed.}

d) Any medications discontinued prior to the study may be reinstated at the completion of the procedure.

e) Blood is separated by centrifugation; serum is placed in labeled vials (B-Pre, B-0, B-1, B-2, B-3 and B-4); urine is similarly placed in labeled vials (U-Pre, U-1, U-2, U-3 and U-4). All vials are placed in mailers provided and sent to the CBL. See "Specimen Preparation for Transport" in Section 12.5.3 below.

f) Nursing mothers are counseled to refrain from breast feeding for 24 hours following the procedure.

12.5.3 Specimen Preparation for Transport

1. All urine should be refrigerated throughout the study. It is not necessary to refrigerate urine unless iothalamate and 4-hour study are performed simultaneously. All bloods may be processed together at the end of the procedure. Bloods may remain at room temperature until processed.

2. Urine is aliquoted into labeled 1.8 ml cryotubes TO THE LINE Retain one backup tube for each collection. (Tubes will be labeled U-Pre, U-1, U-2, U-3, and U-4.) Measure the volume and record the time of all voidings. Collection U-0 is not analyzed and should not be mailed to the laboratory.

3. All blood is separated by centrifugation as usual.

4. Serum is aliquoted into labeled 1.8 ml cryotubes TO THE LINE Retain one backup tube for each collection. (Tubes will be labeled B-Pre, B-0, B-1, B-2, B-3, and B-4.) Each serum tube sent should contain 1.8 ml of serum; the backup tubes can contain less. It is not necessary to draw additional blood to increase volume of backup.

5. If 4-hour study test is performed, 5 aliquots of the well mixed 4-hour urine collection are placed into 4.5 ml cryotubes. Four aliquots are sent to the Central Biochemistry Laboratory (CBL); one is retained for backup. Note on the mailing list that these samples were collected in conjunction with the GFR and therefore contain some radioactivity. See Cahpter 12.4 for more detail.

6. Freeze all serum and urine aliquots at -20°C.

7. Ship to CBL with next routine shipment.

a) It is not necessary to label tubes or mailers as containing radioactive material.

b) Any serum or urine sample stored locally should be marked as containing radioactive material or stored separately as per local regulations.

c) Include the mailing list. Note in the comment section of mailing list whether the 4-hour renal was done in conjunction with GFR or whether irregularities such as hypoglycemia occurred during the procedure.

d) Backup samples are to be saved for one year before being discarded. The remaining radioactivity should be small enough to allow disposal with regular trash. Check local regulations.

12.6 24-HOUR URINE COLLECTION

For the proper evaluation of tests on a timed urine specimen, it is essential that a complete and accurate collection be made. The following instructions apply to the collection of a 24-hour timed urine specimen.

1. Be sure that the patient understands the procedure. All urine passed during the collection period must be saved.

2. Reagents:

    1. Redistilled Water
    2. Glacial acetic acid (AR grade) to be obtained locally.

    Preparation:

    1. In a 250 ml or larger volume graduated cylinder, add about 200 ml distilled water.
    2. Add 12.5 ml of glacial acetic acid with caution. Always add acid to water!
    3. Add water to the 250 ml mark of the cylinder.
    4. Pour the 250 ml into the emtpty urine container and mix thoroughly. Store tightly covered.
    5. Larger volumes of the 5% acetic acid may be prepared and stored. Stable for one year at room temperature.

    Procedure:

    1. Record the entire volume of sample including the 250 ml of 5% acetic acid. Do not subtract the 250 ml from the volume.
    2. When a patient uses 2 containers, mix both volumes together thoroughly before aliquoting into tubes.
    3. Remember, mix all specimens thoroughly before aliquoting!
    4. Keep urine containers in a safe place out of reach of children. If acid spills, rinse with copious amount of water.

5. Direct patients to refrigerate urines during and after collection, but it is not critical when using this preservative.

3. Have the patient empty the bladder at a specified time (e.g., 8:00 a.m.). DISCARD THIS URINE. Record the date and time. This is the beginning of the collection period.

4. Collect all urine passed during the 24 hours specified.

5. Have the patient empty the bladder at whatever time is necessary to complete the timed collection (e.g., a 24-hour collection, the next morning at 8:00 a.m.). SAVE THIS SPECIMEN. Start with an empty bladder and finish with an empty bladder.

6. Keep the collected urine refrigerated during the entire collection period.

7. Return the entire urine collection to the clinic upon completion.

8. Measure total volume.

9. With a disposable pipette, aliquot a portion of the well-mixed urine into two 4.5 ml tubes. Do not fill above the 4.5 ml mark. Freeze both aliquots.

10. Send one tube to the CBL and retain one in the clinic as backup.

12.7 CAPILLARY COLLECTIONS FOR BLOOD GLUCOSE PROFILES

12.7.1 Preparation

1. Remove profilset (Profilset) from refrigerator.

2. Remove test tube to be used (prelabeled by clinic with sampling times) and warm to room temperature (this can be done with hands).

3. Mark actual time and date of collection on test tube.

4. Wash hands thoroughly with warm water.

5. Tear open alcohol wipe (do not remove).

6. Remove Autoclix-Lancet, pull off the protective cap while turning.

7. Open warmed test tube and storage tube containing capillaries.

8. Remove a capillary for use and close the storage tube.

12.7.2 Sample Taking

1. Remove alcohol wipe and swab the fingertip.
2. Make a skin puncture with Autoclix-Lancet.
3. Remove the first blood drop with the alcohol wipe.
4. With the second drop of blood, fill the capillary tube end to end while holding it in the horizontal position. Be sure there are no air bubbles.
5. If a quality control specimen is needed, fill a duplicate capillary and process in the same manner. If the wrong finger stick is quality controlled, the patient should report this to the Trial Coordinator, who should advise the Coordinating Center as to which finger stick was actually quality controlled.

12.7.3 Preparation of the Sample

1. Holding the blood filled capillary in a horizontal position, clean the capillary with an alcohol wipe or fingers. (Be careful no blood is drawn out of the tube with the alcohol wipe.)
2. Insert the capillary completely filled with blood into the test tube.
3. Close cap tightly on the test tube.
4. Mix the tube containing the capillary until there is no more blood visible in the capillary.
5. Leave the capillary in the test tube.
6. Check time and date of collection on test tube and return it to the profilset.
7. Return profilset to refrigerator.
8. The profilset contains 10 dilution tubes. Seven are used in collecting the profile; the remaining three can be used for quality control or as backup for collection problems.

12.7.4 Caution

1. Do not take internally.

2. Keep out of reach of children.

12.8 C-PEPTIDE TESTING

C-peptide testing should be scheduled as the first assessment during a morning visit to the clinic because the patient must arrive at the clinic in a fasting state (see Table 6.3, the Evaluation Module Schedule and Chapter 15). To avoid possible hypoglycemia, it is recommended that the test meal be administered no later than the patient's usual time of breakfast.

In preparation for C-peptide testing, the patient should receive nothing by mouth on the night prior to testing in order to be fasting for eight hours.

On the morning of the scheduled C-peptide test, the patient should not take his/her usual insulin injection.

As soon as the patient arrives at the clinical center, blood glucose should be checked by reflectance meter. If the blood glucose is <250, proceed with the test. If the blood glucose is >250 but <400, proceed only if urine ketones are negative. If blood glucose is >400 or if blood glucose is >240 and moderate or greater ketonuria are present, the test should be rescheduled. Next, a blood sample should be obtained by venipuncture for measurement of C-peptide, glucose, creatinine and cholesterol. The sample should consist of 10 ml and be placed in a red-topped tube. The separated serum is divided into two aliquots and frozen.

Immediately following the collection of the blood sample, the patient should ingest the test meal which is to be consumed within ten minutes. The test meal will consist of a commerical mixed meal, Sustocal (TM), Mead-Johnson. The amount to be ingested should be calculated as follows:

Amount Required = 20% of total daily caloric requirement[1] with a maximum of 360 calories (12 ounces or 360 ml of Sustocal).

The test meal consists of one calorie per ml.

A second blood sample will be obtained by venipuncture in 90 minutes after the ingestion of the test meal. It should consist of 10 ml of blood placed in a red-topped tube. The separated serum is divided into two aliquots and frozen.

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[1] Daily caloric requirement is calculated as 30 calories per kilogram body weight.

Both blood samples should remain on ice or in the refrigerator at four degrees C until the blood can be centrifuged and the plasma frozen.

Immediately following the second blood sample, the patient will take his/her usual morning insulin dosage and return to his/her usual diabetes care regimen. Patients usually taking a mid-morning snack will omit it on the morning of the testing. Patients will remain under observation in the clinic until they have their lunchtime meal.

12.9 LIPIDS (CHOLESTEROL, TRIGLYCERIDES, HDL CHOLESTEROL)

For this collection instruct the patient to refrain from eating or drinking on the night prior to testing in order to be fasting for eight hours.

The eligibility measurement of cholesterol will be done on the fasting serum specimen also used for the C-peptide test. The baseline specimen for measurement of cholesterol, triglycerides, and HDL cholesterol will be drawn and sent to the CBL two weeks prior to randomization.

Draw blood into a 10 ml red-topped serum tube, separate the serum and freeze the separated serum in two aliquots, one of which is shipped to the CBL.

12.10 ADDITIONAL INFORMATION

For further information, lists of supplies, and directions for processing and shipping specimens, see Chapter 15.

CHAPTER 13

CLINIC OPHTHALMOLOGIC PROCEDURES

13.1 FUNDUS PHOTOGRAPHY

13.1.1 Introduction

In the DCCT, color stereo fundus photographs are required under three circumstances:

1. At the Evaluation Visit a full set of seven fields and lens is required for each eye (see Chapter 6).

2. At each semiannual Endpoint Visit, or

3. Prior to application of photocoagulation treatment at any visit (for development of DRS high risk characteristics, clinically significant macular edema, impending neovascular glaucoma, or any other indication for laser treatment), a full set of photographs of the seven standard fields and lens is required for each eye. If new vessels and/or vitreous or preretinal hemorrhage are present only outside the seven standard fields, an optional Field 8 is required (see Section 13.1.5.1).

At the Evaluation Visit of subjects who are in the primary prevention trial, i.e., subjects with no retinopathy at entry, a fluorescein angiogram (FA) is required with early phase photographs of the eye selected by the procedure described in Section 13.1.6.1. FA will also be done in the primary subjects at five years and at the end of the study.

13.1.2 Photographs Required for DCCT Eligibility

A full set of photographs of each eye (seven color stereo views and lens photo) which meets the requirements for quality specified in this chapter must be submitted to the Central Ophthalmologic Reading Unit (CORU) for grading to establish ocular eligibility of each subject screened for enrollment in the DCCT. Information regarding eligibility is transmitted to the Coordinating Center and is used by the Coordinating Center to issue a treatment allocation for the subject. If the pathological signs visible in the color stereo fundus photographs are either insufficient for entry to the study or too severe for entry to the study, the subject is ineligible. When the CORU staff notify the Coordinating Center staff of ineligibility of a subject on the basis of

the grading of the fundus photographs, the Coordinating Center notifies the clinical center. Any questions regarding the CORU's classification of a particular subject will be transmitted from the clinic to the Coordinating Center to the CORU.

If the identification labeling of the photographs is incomplete or inconsistent with other information, an attempt will be made to resolve the problem by a telephone call from the CORU coordinator to the clinical center coordinator. If the problem cannot be unequivocally resolved, the photographs will be returned to the clinical center. In that event the clinical center has the option of correcting the identification labeling and resubmitting the photographs if resubmission can be accomplished within the time limits for admission to the study.

A fluorescein angiogram is not required for admission to the study, but should be obtained on each subject in the primary prevention stratum (i.e., those without retinopathy detectable on fundus photographs at entry). The fluorescein angiogram need not be obtained at the same time fundus photography is performed, but must be obtained prior to randomization. Primary subjects who refuse to allow a fluorescein angiogram to be done will not be excluded from the study.

13.1.3 Camera and Equipment

Stereo fundus photography is carried out using a modified fundus camera, preferably the Zeiss FF series, but the Topcon or similar camera may be substituted UPON APPROVAL OF THE CORU. Some of the modifications in the following list are described specifically in terms of the Zeiss camera.[1] be followed with the Topcon or other camera (if in doubt, contact your manufacturer's representative and/or the Central CORU).

1. Fundus camera is moved backwards (away from the subject) on its base sufficiently so that its center of rotation corresponds to the pupil of the subject's eye (1).

2. Number 7 aperture (14 mm diameter) in recoss disk modified by adding a central 6 mm diameter opaque disk (referred to as "black dot" by Zeiss). It is further recommended, but not required, that Kodak Wratten filter #81A be added to this aperture.

3. Power supply modified to allow recharging within one to two seconds.

4. Opaque cone removed from film carrier to allow use of entire image.

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[1] Some of the modifications have been made by the manufacturer on the recent models of the Zeiss camera.

5. Fixation target of camera replaced by that provided with the Haag-Streit 900 slit-lamp.

The technique described by Allen (2) is used. The use of the stereo separator is optional for color photographs but strongly recommended for fluorescein photographs. A setting between 2.25 and 2.50 is recommended if the stereo separator is used.

No specific electronic flash setting is specified since this will vary with the model of camera used.

Refer to Appendix 13-A for a discussion of how to obtain satisfactory fundus photographs.

13.1.4 Pupillary Dilation

Adequate dilation of the pupil is important to permit good quality stereo photography. Sufficient time should be allowed for dilation to at least 6 mm, repeating drops, if necessary, to achieve and maintain a pupil of at least this size during photography. Only if repeated instillation of drops and passage of at least 45 minutes after the last drops fail to produce dilation of 6 mm should photographs be taken through a smaller pupil. If the pupils cannot be dilated to at least 4 mm for the Evaluation Visit fundus photography and fluorescein angiography, the subject should not be entered into the DCCT.

13.1.5 Color Photography

13.1.5.1 Seven Standard Fields of the Fundus

The seven standard fields of the fundus (and optional Field 8) are defined below and are illustrated in Figure 13.1 for both the right and left eyes. This description assumes that there are two cross hairs in the camera ocular, one vertical and the other horizontal.

Field 1 - Disc; Center of optic disc at intersection of cross hairs in ocular.

Field 2 - Macula; Center of macula at intersection of cross hairs in ocular.[2]

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[2] In practice, to keep the central gray artifact created by the camera from obscuring the center of the macula, the intersection of the cross hairs should be placed about one-eighth to one-fourth DD nasal of the center.

Field 3 - Temporal to macula; Nasal end of horizontal cross hair at center of macula.

Field 4 - Superior temporal; Lower edge of field tangent to a horizontal line passing through upper edge of optic disc and nasal edge of field tangent to a vertical line passing through center of disc.

Field 5 - Inferior temporal; Upper edge of field tangent to a horizontal line passing through lower edge of optic disc and nasal edge of field tangent to a vertical line passing through center of disc.

Field 6 - Superior nasal; Lower edge of field tangent to a horizontal line passing through upper edge of optic disc and temporal edge of field tangent to a vertical line passing through center of disc.

Field 7 - Inferior nasal; Upper edge of field tangent to a horizontal line passing through lower edge of optic disc and temporal edge of field tangent to a vertical line passing through center of disc.

Field 8 - An optional field outside the seven standard fields taken to document new vessels and/or preretinal or vitreous hemorrhage, if these occur during followup. The area of the fundus photographed should be designated as follows (see Figure 13.1):

ST Superior Temporal quadrant

SN Superior Nasal quadrant

IT Inferior Temporal quadrant

IN Inferior Nasal Quadrant

If the optional field is taken on the boundary between two quandrants, the following designations should be used as appropriate:

S Superior

N Nasal

T Temporal

I Inferior

If two photographs outside the seven standard fields are needed to document both new vessels and preretinal or vitreous hemorrhage, one should be labeled "Field 8a" and the other "Field 8b": Field 8a the first reached going temporally from 12 o'clock and Field 8b the second.

13.1.5.2 Fundus Reflex ("Lens") Photograph

A single, non-stereo fundus reflex photograph should be taken in addition to those required of the seven standard fields. As well as documenting the condition of the lens, the fundus reflex photograph will allow the CORU graders to take opacities of the media into consideration when reviewing photographic quality.

During followup, if fundus photography is not possible because of opacities in the media, a bound-down pupil, previous enucleation, or for any other reason, a fundus reflex photograph should be taken to document the reason.

In order to take the fundus reflex photograph it is necessary to use the +16/+33 diopter setting on the auxillary plus lens system of the camera. The small white knob on the right side of the Zeiss unit is turned until the correct number (+16/+33 or +20/+40 on some cameras, perhaps similar high plus diopter readings on others) appears at the dot. In order to standardize the magnification of these photographs (the object being to fill the photographic field as much as possible with the iris while still maintaining sharp focus) the following procedure should be used:

1. The film-to-lens distance of the camera is increased to its maximum, by turning the large focusing knob so that its upper aspect moves toward the subject. Turn the knob in this direction as far as it will go.

2. The subject's headrest is moved away from the camera until the iris is in crisp focus (approximately one and a half inches further away than when adjusted for taking photographs of the fundus). It is acceptable to move the subject slightly further away, so that the focusing knob may be used for fine adjustment of focus if the photographer wishes. Focus should be on lens opacities when present, otherwise on the pupillary margin.

3. The subject is asked to open his/her eyes very wide, or the lids should be gently retracted if necessary, so that the entire cornea is visible.

4. The photograph is taken.

13.1.5.3 Film Processing, Mounting, and Labeling

Kodachrome 25 Daylight film is recommended and may be processed in routine fashion at any Eastman Kodak Processing Laboratory. A different color film may be used, if necessary, to expedite processing, but only on approval of quality by the CORU. It is important that the processing laboratory correctly orient each transparency in the readymount and correctly number the readymounts. Transparencies processed by Kodak are in the proper position when the frame number is visible and right side up.

The transparencies returned from the processing laboratory are mounted in standard cardboard 2 x 2 inch readymounts. Each readymount is identified on the bottom of the cardboard frame with a label on which is written or printed the accession number, the eye (right or left), and the field. These labels are printed by the Coordinating Center and mailed to the clinical centers for identifying all photographs. An illustration of the proper labeling of a stereo pair is given in Figure 13.2.

The mounted and labeled transparencies should be placed in 9 x 11 inch transparent plastic sheets containing 20 pockets per sheet. The plastic sheets should be constructed so that the pockets open at the side rather than at the top; that is, the OPEN side of the left pocket should face the OPEN side of the right pocket. There is less chance of loss when the transparencies are mounted in this manner because they tend to press against each other and are thus held in place. One sheet should be used for each eye. The transparencies should be mounted so that the pocket openings face to the front, that is, face the person mounting the slides, and the edge with the three holes for a ring binder should be to the left of the mounter. The transparencies of the fundus should be oriented for stereo viewing in an arrangement approximating the anatomic position as illustrated in Figure 13.3.

The sheet identification labels are completed and attached to the front of the plastic sheets. This label includes on the top the accession number, and on the bottom the current clinic number, subject identification number, subject's initials, visit number, eye, date the photographs were taken, and the name and DCCT certification number of the photographer. The visit designation for photographs taken during Evaluation Visit (i.e., eligibility/baseline) is printed as BSLN. If photographs are not all taken on the same date, the dates should be written on the cardboard mount of the left member of each stereo pair, just above the photograph and the date of the last photographic session recorded on the appropriate form and on the label as the "date of photos." The label is placed on the front of the plastic sheet under Field 7 for the right eye and under Field 5 for the left eye as illustrated in Figure 13.3, i.e., as one looks at the front of the plastic sheet, the sheet label is in the bottom right corner and all slide labels are visible. (When sets are graded at the CORU, opaque masks cover the lower portion of the sheet identification labels.)

13.1.5.4 Evaluation Visit Fundus Photographs

A complete set of seven stereo views and lens photo of satisfactory quality for each eye is obtained during the Evaluation Visit. Presence of pathologic changes sufficient to meet eligibility requirements and absence of lesions which are criteria for exclusion are documented by the photographs.

As soon as the fundus photographs taken at the Evaluation Visit are returned from the processing laboratory, the photographs are reviewed in the clinic for quality (see Section 13.3.5.6). Evaluation Visit fundus

photographs must satisfy the following conditions before the treatment allocation can be issued by the Coordinating Center:

1. Field 2 of "good" quality, Field 1 of at least "fair" quality with good focus, and

2. At least four of Fields 3 through 7 of at least "fair" quality, with good focus in at least four of these five fields.

If these two conditions are not met for both eyes, the subject must be recalled to have the necessary photographs retaken. If photographs are taken on different dates, all dates must fall within a two-month time period. Photographs meeting conditions above must be read at the CORU before the treatment allocation can be issued for the subject.

If the only disqualifying deficiency (or deficiencies) for either eye is a Field 2 of less than "good" quality and/or a Field 1 of less than "fair" quality, and if the color Field 2F included with the angiogram for that eye is of "good" quality and/or the color Field 1F is of at least "fair" quality, the CORU staff will include the appropriate field(s) from the angiogram in the color set for detailed grading. In such cases, repetition of the Evaluation Visit color photographs will not be required.

Photographs are labeled and assembled in the plastic sheets as outlined in Section 13.1.5.3. The date of the photographic session and the date of mailing to the CORU is recorded on the DCCT Fundus Photography Form (DCCT Form 025). The photographs and one copy of the DCCT Form 025 are sent to the CORU. The original of DCCT Form 025 is sent to the Coordinating Center. In addition, the Fundus Photograph Mailing List (DCCT Form 042) is completed whenever the clinic mails a package of stereophotographs or angiograms to the CORU.

The Evaluation Visit fundus photographs for each subject are graded for degree of diabetic retinopathy and for photographic quality in the CORU before the treatment allocation is issued by the Coordinating Center. The CORU notifies the Coordinating Center of the degree of retinopathy, whether clinically significant macular edema is present, whether the photographs are of sufficient quality, or whether eligibility is undetermined pending receipt of adequate retakes. In the latter case, direct communication between the CORU and the clinical center occurs concerning the unsatisfactory photography. Exclusion criteria (Chapter 8) may be observed by CORU personnel even when photographic quality is poor. In this event, retakes are not suggested by the CORU. If CORU personnel cannot determine the eligibility of the subject because of poor photographic quality, the clinical center may elect to submit a new complete set of photographs of adquate quality of both eyes. They must be submitted early enough so that the CORU can determine retinopathy status and the Coordinating Center can establish the subject's eligibility within the time limit for eligibility screening.

13.1.5.5 Photographs Prior to Photocoagulation Treatment

If it becomes necessary during the course of the study to apply photocoagulation treatment in either or both eyes (for development of DRS high risk characteristics, clinically significant macular edema, impending neovascular glaucoma, or other indication for laser treatment), stereo views of the seven standard fields must be taken of each eye prior to the initiation of treatment.

In cases where the pertinent retinopathy (such as neovascularization or hemorrhage) occurs only outside of the seven standard fields, special care should be taken to document these lesions in optional Field 8, as described in Section 13.1.5.1.

As for the scheduled Endpoint Visits, the DCCT Fundus Photography Form (DCCT Form 025) should be completed and submitted to the CORU, with the original of the form mailed to the Coordinating Center.

13.1.5.6 Endpoint Visit Fundus Photographs

Stereo views of the seven standard fields and a lens photograph are taken of each eye at each semiannual Endpoint Visit (see Figure 13.1).

The set of available photographs should be labeled and assembled in plastic sheets as outlined in Section 13.1.5.3 and forwarded to the CORU. The DCCT Fundus Photography Form (DCCT Form 025) should be completed and submitted to the CORU with each set of photographs. The original of DCCT Form 025 is mailed to the Coordinating Center.

If any fundus details can be seen through the fundus camera, all seven fields should be photographed, even though no details are visible in some fields. If extensive lens opacities or vitreous hemorrhage make it impossible to see any fundus details with the fundus camera, an attempt should be made to photograph only standard Fields 1 (disc) and 2 (macula); the other standard fields do not need to be taken. If no fundus reflex can be seen with the camera, a single non-stereo photograph of the anterior segment (lens) is taken.

During followup, it is the responsibility of each photographer to review fundus photographs for quality, and to make the decision to perform retakes of some or all fields when the first attempt at photographs is unsatisfactory.

The following criteria should be used to determine when photography should be repeated. If Fields 1 or 2, or more than one of the five remaining fields are partially or totally missing, or if the photographer judges the photographs to be of poor quality for technical reasons that can be corrected (such as poor field definition, focus or stereo or photographic artifacts), the set should be considered unsatisfactory.

In arranging for retakes during followup, the following guidelines should be used. These have been formulated to balance the need for adequate photographs against the risk of inconveniencing the subject unduly.

If the photographer decides that retakes are needed and the subject can return within the same window or before the opening of the next endpoint visit window, only the unsatisfactory fields need be retaken. Sets composed of photographs taken on different dates should have the date each was taken written on the mount of one member of the stereo pair. If selected photographs to remedy the deficiencies can not be retaken before the opening of the next endpoint visit, complete sets of photographs of both eyes should be retaken.

The retake session must be performed no later than the next scheduled quarterly visit. If it is convenient for the subject to return for retakes sooner, this may of course be done. For any photographs retaken, the follow-up visit number entered on DCCT Form 025 is ascertained by comparing the date the latest photographs were taken with the subject's appointment schedule.

During followup, the CORU will continue to formally monitor fundus photographs for quality, and will ask for retakes at least for annual visits when sets submitted are inadequate.

13.1.5.7 Photographic Quality

Each set of fundus photographs should be assessed for quality before the photographs are sent to the CORU. All photographers will be "provisionally certified," and the photographer taking a set of photographs should grade them carefully for quality, using DCCT Form 025 to record the evaluation, before the photographs are sent to the CORU. All photographs are graded in detail for quality at the CORU and feedback is provided to photographers as necessary to help solve any problems that may be found. Photographers who consistently submit photographs of good quality[3] will be "fully certified" and thereafter their photographs may be checked by any member of the clinic staff merely for presence or absence of each field.

The CORU staff carries out only an abbreviated overall quality grading on photographs taken by fully certified photographers. If overall quality is less than "fair" for reasons attributable to photographic technique, a detailed quality grading is carried out, with only the fields and photographic characteristics causing the grade to be lowered recorded on the form. When the grader deems it necessary, comments on the set are returned to the clinical center. If overall quality of

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[3] A sample of photographs of at least ten subjects must have the following distribution of quality: at least two-thirds "fair" or better and not more than 5% "inadequate, unexplained."

photographs taken by any photographer consistently fails to meet study standards, his/her certification will revert to the "provisional" category; all photographs must then be graded in detail for quality and recorded on the DCCT Form 025, both by the photographer and the CORU staff, until problems are resolved and full certification is restored.

In grading photographic quality, a three-step scale is used. The steps, designated "good," "fair," and "poor" are defined below as they apply to a single photographic field:

STEP	FIELD DEFINITION	FOCUS AND CLARITY EFFECT	STEREOSCOPIC
Good	less than one half DD from definition	Crisp (at least centrally)	Satisfactory
Fair	one half to one DD from definition	Fuzzy, but better than standard #14	Less than satisfactory but useful for grading
Poor	More than one DD from definition	Clarity no better than standard #14	Little or no stereoscopic effect

A photograph will be considered "good" if all three characteristics listed above are graded "good"; "fair" if one of the conditions listed as "fair" is present and the other two are "fair" or "good"; and "poor" if one or more of the conditions listed as "poor" is present.

A set of photographs will be graded "excellent," "good," "fair," "acceptable" or "inadequate" according to the criteria listed below:

GRADE

Excellent = E — Beyond meeting criteria for "good," set is outstanding for its high quality.

Good = G — Fields 1 and 2 are of good quality; of remaining five fields (3 through 7) at least two are of good quality and not more than one of poor quality, with good focus in at least four of these five fields.

Fair = F — Field 2 is of good quality, and Field 1 and at least four of Fields 3 through 7 are at least fair in quality, with good focus in at least four of these six fields.

Acceptable, Borderline
Set does not meet criteria for "fair" but is judged to provide adequate documentation of retinopathy and can be graded.

B_1 — From lens photo included with the set, CORU grader confirms that media opacities account for problems in set.

B_2 — In opinion of CORU grader, lens photo does not show substantial opacity, but photographer noted on form that media opacities caused problems.

B_3 — Photographer noted on form that extreme photophobia, poor fixation, excessive tearing or similar condition caused problems.

B_4 — None of above descriptions apply, therefore quality problems in set are unexplained.

Inadequate — I_1, I_2, I_3, I_4

Quality of set is too poor to allow reliable grading. One of four grades is assigned in such cases. These are differentiated just as the four grades for "acceptable, borderline" described above.

13.1.5.8 Duplication and Shipment of Photographs

Clinical centers are required to keep complete copies of all photographs taken at baseline, five years, and the last subject contact (whenever that may be). These would serve as backup for what may be the most important visits, should the need for access to the original photographs rather than the grading data derived from them become important. For all other visits, only the copies currently specified in

the Manual of Operations are required (for fundus photographs and fluorescein angiograms, disc and macular fields of both eyes). Each clinical center should establish a mechanism whereby the ophthalmologist can specify that more complete copies are essential to patient care.

The method of copying (whether to make true copies of the original set sent to CORU or to shoot two sets during the photographic session) is left to the discretion of the clinical center, based upon local conditions and preferences. For patients who are photophobic to the degree that patient cooperation is problematic, photographers are asked to consider taking only one set, perhaps with extra pictures of disc and macula (given their central importance) and any other fields known to be marred, and making copies from the originals.

13.1.6 Fluorescein Angiography

13.1.6.1 Selection of the Eye for Early Phase Photography

It is possible to obtain early phase photographs of only one eye at a single session. The eye should be selected as follows: The right eye is designated for early phase photographs if the subject's birthday is in February, April, June, August, October, or December; the left eye if the subject's birthday is in January, March, May, July, September, or November.

13.1.6.2 Camera and Film

The standard fluorescein fundus photographic equipment available at each clinic may be used. Interference filters, the Allen stereo separator, automatic film transport and an internal timer, which prints on the film the time elapsed since the beginning of the fluorescein injection, are preferred. Kodak Tri X ASA 400 film is recommended. The Allen stereo separator should be set between 2.25 mm and 2.5 mm.

13.1.6.3 Standard Fluorescein Fields

Field 2F: Cross hairs of the fundus camera centered one-half DD temporal to the center of macula.

Field 1F: Temporal edge of the disc is located one-fourth DD from temporal edge of the field. Horizontal cross hair of the fundus camera should pass through the disc between its horizontal meridian and its inferior pole (i.e., no change in vertical adjustment will be required between Field 2F and Field 1F).

The location of these fields is depicted in Figure 13.1.

13.1.6.4 Stereo Color Photographs of Standard Fluorescein Fields

Standard stereo color photographs of Fields 1F and 2F should be taken immediately prior to fluorescein angiography.

13.1.6.5 Fluorescein Injection

Five ml of 10% fluorescein should be injected rapidly into the antecubital or other convenient vein. If a clinic customarily uses 25% fluorescein, this may be substituted, using the volume which is standard at that clinic.

13.1.6.6 Early Phase Photographs (see Figure 13.4)

For early phase photographs the camera is centered on Field 2F. Before the injection of fluorescein, a "test" frame should be taken of Field 2F of the eye designated for early phase photography. This photograph provides a check that the camera and flash are in satisfactory working condition. The test frame need not be submitted. If the photographer wishes to use the first frame for subject identification, he/she may do so.

The Allen stereo separator is turned to the right for the "test" frame. The second photograph is the left side of the first stereo pair and the third photograph is the right side of that stereo pair and so on through the series. The photographs are then in stereo pairs when they are arranged in numerical order in the plastic sheets.

The first photograph of the early phase (with Allen separator turned to the left) is taken at time "0"; that is, at the moment of injection of the fluorescein dye, and the second photograph (with the separator to the right) is taken at the moment the injection is complete. These photographs constitute a stereo pair and are the "control" photographs for this field; the times at which they are taken document the rate of injection.

1. Preferred Early Phase Procedure:

   Ideally, early phase photographs consist of a pair of control photographs followed by a series of 16 exposures taken at one-second intervals, beginning 11 seconds after the start of fluorescein injection. The result is eight stereo pairs following the control pair, completed 26 seconds after the start of injection. At this point, the fundus camera is moved to the second eye as quickly as possible, and a stereo pair of Field 2F is taken.

   The rapid series described for the first eye should be sufficient to obtain at least one stereo pair of the full

capillary phase in most subjects. However, if the photographer is able to observe the transit of fluorescein dye through the vessels of the retina (i.e., if the exciter filter is in the path of the light used to observe the fundus), and determines that in a particular subject the full capillary phase will be missed if the rapid series is terminated at 26 seconds, the photographer is required to wait until the full capillary phase is observed to take the final one or two stereo pair(s) of the rapid series before switching to the second eye. On the other hand, if the photographer observes that in a particular subject the full capillary phase is reached considerably earlier than 26 seconds, then the photographer is required only to complete the stereo pair in progress and then take one more stereo pair as a precaution before switching to the second eye, even if the camera is repositioned sooner than 26 seconds after the beginning of injection. Thus, a stereo pair of Field 2F in the second eye may be obtained shortly after the full capillary phase is observed in the rapid series eye, even if the transit of fluorescein occurs relatively early. The photographer should pay particular attention to the perifoveal capillary net when judging the time of the full capillary phase, making sure that these vessels have displayed the transit of fluorescein dye.

2. Alternative Early Phase Procedures

The procedure for obtaining multiple early phase photographs described above is strongly preferred, but if the photographer is for some reason unable to follow it, particularly if automatic film transport and Allen separator are not available (or if the exciter filter is in the path of the light used to observe the fundus), he/she may elect instead to obtain three stereo pairs during the early part of the fluorescein transit. The major goal is to obtain at least three good quality stereo pairs. One pair should be obtained as the early capillary phase begins, one several seconds later in the full capillary phase, and one several seconds after that. In judging the time of the full capillary phase, the photographer should pay particular attention to the perifoveal capillary net, making sure that these vessels have displayed the transit of fluorescein dye. At this point, the camera is repositioned to the second eye as quickly as possible, and a stereo pair of Field 2F is taken.

13.1.6.7 Mid-Phase Photographs

As soon as the early photographs are completed, a second stereo pair of Field 2F of the eye not designated for the rapid series should be taken approximately 45 seconds after the beginning of injection, followed by a stereo pair of Field 1F.

At this point, the camera is repositioned back to the rapid-series eye, and stereo pairs are taken first of Field 2F (at approximately 60 seconds) and then of Field 1F.

Ideally, the mid phase photographs should be completed within approximately 65 seconds of the start of fluorescein injection. Not every angiography session will allow attainment of this goal. Of course, in subjects where slow circulation or delay in injection has forced a delay in the termination of the rapid series, the mid phase photographs will also be later than normal. However, in no subject should the mid phase photos be completed any later than two minutes after the beginning of injection.

13.1.6.8 Late-Phase Photographs

A final stereo pair of Field 2F in each eye is taken between seven and nine minutes.

13.1.6.9 Obtaining Good Quality and Stereoscopic Effect

In obtaining stereo pairs, care should be taken that at least one member of the pair is of good technical quality. In some cases, it will be possible to obtain good quality in both members, but if this is not the case, the aim should be to obtain good quality in one member and some stereo separation, accepting poorer quality in the second member of the pair if necessary.

13.1.6.10 Evaluation Visit Angiography

When the fluorescein photographs have been processed, they should be reviewed for photographic quality in the clinic (see Section 13.1.6.11). At the beginning of the study, all photographers will be "provisionally certified," and must record the results of their examination of angiogram quality on DCCT Form 026 before the angiogram is sent to the CORU. Photographers who consistently[4] submit fluorescein angiograms of good quality will be "fully certified," and thereafter their angiograms may be checked by a member of the clinic staff simply for the presence or absence of each field.

The eye in which early phase photographs are to be taken is selected by the procedures described in Section 13.1.6.1.

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[4] A sample of photographs of at least ten subjects must have the following distribution of quality: at least 80% "fair" or better and not more than 5% "inadequate, unexplained."

13.1.6.11 Fluorescein Photographic Quality

At the CORU, angiograms taken by provisionally certified photographers receive a detailed quality review, and feedback is provided to photographers as necessary to solve any problems that might arise. After a photographer becomes fully certified, the CORU staff perform only an abbreviated overall quality grading on the angiograms submitted. If overall quality is less than "fair" because of photographic technique, a detailed quality grading is carried out, with only the fields and photographic characteristics causing the grade to be lowered recorded on the form. When the grader deems it necessary, comments on the angiogram are returned to the clinical center.

In grading all fluorescein photograph sets, a three-step scale is used, with steps of good, fair, and poor as defined below (for each individual stereo pair):

STEP	FIELD DEFINITION	FOCUS AND CLARITY EFFECT	STEREOSCOPIC
Good	less than one half DD from definition	Crisp (at least centrally)	Satisfactory
Fair	Greater than or equal to one-half DD but less than one DD from definition	Clarity sufficient to assess any capillary loss	Less than satisfactory but useful for grading
Poor	Greater than or equal to one DD from correct field definition	Clarity insufficient to assess any capillary loss	Little or no stereoscopic effect

A stereo pair will be considered "good" if all three characteristics listed above are graded "good"; "fair" if one of the conditions listed as "fair" is present and the other two are "fair" or "good"; and "poor" if one or more of the conditions listed as "poor" is present.

A set of fluorescein photographs will be graded "excellent," "good," "fair," "acceptable," or "inadequate" according to the following criteria:

GRADE

Excellent = E — Beyond meeting criteria for "good," angiogram is outstanding for its high quality.

Good = G — The following four fields of good quality: Field 2F, first eye, in capillary phase (at least one stereo pair between 11 and 26 seconds -- perifoveal capillary net should be visible, thus in subjects with slow circulation this pair may be somewhat later); Field 2F, second eye, in early phase or 45-120 second phase; and Field 1F, each eye, in 45-120 second phase. The following of at least fair quality: Field 2F, each eye, in 7-9 minute phase and color photos of Fields 1F and 2F, each eye.

Fair = F — The following fields of at least fair quality, with good focus in at least three of these four fields: Field 2F, first eye, in capillary phase or 45-120 second phase; Field 2F, second eye, in early phase or 45-120 second phase; and Field 1F, each eye, in 45-120 second phase. At least one Field 2F, either eye, in 7-9 minute phase, of at least fair quality.

Acceptable, Borderline
Set does not meet criteria for "fair" but is judged to provide adequate documentation of retinopathy and can be graded.

B_1 — From lens photo included with the set, CORU grader confirms that media opacities account for problems in set.

B_2 — In opinion of CORU grader, lens photo does not show substantial opacity, but photographer noted on form that media opacities caused problems.

B_3 — Photographer noted on form that extreme photophobia, poor fixation, excessive tearing or similar condition caused problems.

B_4 — None of above descriptions apply, therefore quality problems in set are unexplained.

Inadequate — I_1, I_2, I_3, I_4

Quality of set is too poor to allow reliable grading. One of four grades is assigned in such cases. These are differentiated just as the four grades for "acceptable, borderline" described above.

13.1.6.12 Film Processing, Mounting, and Labeling

The film may be processed in a local processing laboratory. Any processing procedures which yields good quality negatives may be used for this film. The negatives returned from the processing laboratory should be mounted in standard cardboard 2 x 2 inch readymounts. Each readymount should be labeled on the bottom of the cardboard frame using printed labels supplied by the Coordinating Center on which should be written, if not correctly preprinted, the accession number assigned by the Coordinating Center for the given subject's angiogram.

For each frame, the time in seconds from the start of injection must be recorded on the label affixed to each readymount, unless shown in the photograph itself. An illustration of the proper labeling of a stereo pair is given in Figure 13.5.

The mounted and labeled negatives are placed in an 18 x 11 inch transparent plastic sheet containing 40 pockets per sheet. A 40-pocket sheet like the Bardes Sheet #462042 "Clearlast," available from Bardes Products, Inc., 5225 West Clinton Avenue, Milwaukee, Wisconsin 53223, is strongly recommended. The early phase photographs and late phase photographs should be arranged in time sequence as illustrated in Figure 13.6. The sheet identification label supplied by the Coordinating Center should be completed and attached to the edge of the plastic sheet as indicated.

This sheet identification label is keyed to the accession number on the individual slide labels. It contains the current clinic number, subject identification number, subject's initials, visit number, date the photographs were taken, and the photographer's DCCT certification number. The visit designation for photographs taken at the Evaluation Visit (i.e., eligibility/baseline) fluorescein angiography session is defined as BSLN.

When angiograms are graded at the CORU, opaque masks are used to conceal all but the accession number, so as to avoid any possible grader bias.

13.1.6.13 Duplication and Shipment of Fluorescein Photographs

All fluorescein photographs sent to the CORU must be original negatives. They should be duplicated by the clinical center and the copies (positive or negative at the Principal Investigator's discretion) retained at the clinical center. The original negatives properly mounted, labeled, and assembled in plastic sheets should be forwarded to the CORU with a copy of DCCT Fluorescein Angiography Form (DCCT Form 026) and DCCT Form 026 should be sent to the Coordinating Center in the routine weekly forms mailing. In addition, the Fundus Photograph Mailing List (DCCT Form 042) is completed and distributed whenever the clinic mails a package of stereophotographs or angiograms to the CORU.

13.1.7 Use of Uncertified Photographers in Extenuating Circumstances

Photographs submitted for the DCCT should be taken by certified photographers. Clinical centers are encouraged to have at least two, and preferably all, of their ophthalmic photographers certified for the DCCT (see Chapter 23 for certification procedures).

After the Evaluation Visit, on those rare occasions when a subject who has come a long distance attends the clinic for a visit requiring photographs and all photographers certified for the DCCT (provisionally or fully) are ill or on vacation, the clinical center may have no alternative but to submit photographs taken by an uncertified photographer. The name of the uncertified photographer should be entered on the DCCT photography form, and the space for the photographer's certification number left blank. Special effort should be made to follow the DCCT photography protocol and to obtain photographs of satisfactory quality.

13.2 OPHTHALMIC EXAMINATION

At study entry a complete ophthalmic examination should be performed on each subject to provide baseline information for reference during follow-up. Only a small portion of the information available from such an examination is collected and stored in the DCCT data base. It should be emphasized that the Baseline Ophthalmic Examination and Ocular History and the Endpoint Visit Ophthalmic Examination Forms (DCCT Forms 008 and 027) are not designed to replace the subject record and that, in general, a separate clinical record is required for purposes of subject management.

13.2.1 Anterior Segment Examination

The examination of the anterior segment of each eye is performed at the Baseline Ophthalmic Examination to document the baseline status of the eye and to detect characteristics which render the eye ineligible, and at Endpoint Visit examinations to detect any changes in ocular status during the course of the study which may be attributable to disease or treatment. The examination should be performed in a dimly illuminated room; a slit-lamp biomicroscope should be used in the standard fashion starting anteriorly and working posteriorly.

The corneas are examined and abnormalities in the epithelium, stroma and endothelium are noted (but not recorded on a form). The depth of the anterior chamber is assessed to determine if there is any danger in dilating the pupil. If the angle is thought to be closeable, the eye should not be dilated until appropriate provocative tests are performed. The presence of cells, flare or other abnormality is recorded on the appropriate DCCT form, at the Baseline Ophthalmic Examination. The presence of new vessels on the iris is recorded. If, at the Baseline

Ophthalmic Examination, definite new vessels are present on the iris in either eye, the subject is ineligible for the study. The lens is evaluated after the pupil is dilated and opacities or aphakia are noted; subjects who are aphakic in one or both eyes at the Baseline Ophthalmic Examination are ineligible for the DCCT. The clarity of the lens is assessed. In general, mild to moderate axial, posterior subcapsular opacities (PSC), or 2+ nuclear sclerosis may be expected to reduce visual acuity but not to less than 20/100. Severe PSC or severe nuclear sclerosis or a combination may be expected to reduce acuity to less than 20/100.

13.2.2 Intraocular Pressure

The intraocular pressure is measured in both eyes before the pupils are dilated at the Baseline Ophthalmic Examination. A Goldmann applanation tonometer mounted on a slit-lamp is used for the measurement. To insure a clean tonometer surface, a solution such as phenymercuric borate (Merfen's solution) on a cotton ball is used to clean the tip of the tonometer mechanically, followed by a wipe with sterile water on a cotton ball.

After a brief explanation of the procedure, the subject receives one or two drops of local anesthetic in each eye. A drop of anesthetic is placed on the fluorescein strip and this in turn is touched to the conjunctival surface of the lower lid while the subject looks up. A combination anesthetic-fluorescein drop may be substituted. The subject places chin and forehead firmly in the headrest, and directs his/her gaze straight ahead (with or without a fixation target).

The tonometer is brought into position and the tip illuminated with a wide open slit and blue filter from approximately 45 degrees to the side. A magnification of ten power is recommended. The examiner brings the tonometer prism to within five to ten millimeters of the center of the cornea while looking around the side of the microscope. If the subject has a tendency to blink as the tonometer approaches, the examiner may need to hold the lids apart. Care must be taken to keep from exerting pressure on the globe through the lids as this may affect the accuracy of the measurement. The examiner then looks through the oculars and, with the measuring scale set at one (10 mm Hg), gently brings the tip of the tonometer into contact with the center of the cornea by moving the joy stick forward. At contact the examiner will see a bright yellow-green spot that will break into two separate semicircular arcs. These arcs should be in sharp focus and be of equal circumference above and below the horizontal dividing line. If they are not of equal circumference the joy stick is pulled back, removing the tonometer from the cornea, and the elevation changed in the appropriate direction (towards the larger arc). Only then is the tonometer replaced on the cornea by pushing the joy stick forward. Pulsation of the arcs indicates proper contact of the tonometer. If the arcs start to overlap before pulsation is noted, the joy stick has been pushed too far forward and the examiner should back off slightly. The width of the arcs should be about one-tenth their diameter. If greater, excess fluid should be wiped from the tonometer.

The force applied to the cornea is increased until the inner borders of the two fluorescein arcs just touch each other. The inner border of the arc represents the demarcation line between the cornea flattened by applanation and the cornea not flattened. The joy stick is then pulled back just far enough to lose the image and then moved gently forward again to check the measurement. If the inner borders of the two arcs are still just touching, the measurement is rechecked as before. If the arcs do not overlap enough, the force is increased and again the measurement is rechecked.

The reading taken from the scale is multiplied by ten to convert to intraocular pressure in mm Hg. A measurement of two on the scale corresponds to 20 mm Hg. intraocular pressure. Each scale division between the numbers is equal to 2 mm Hg.

13.2.3 Ophthalmoscopic Examination

13.2.3.1 Baseline Visit

The ophthalmoscopic evaluations of the Baseline Ophthalmic Examination provide comparison with photographic assessment which will be used to develop clinical guidelines from study results. All subjects who are judged to be eligible on the basis of these ophthalmoscopic examinations and who meet other eligibility criteria have fundus photographs for primary prevention subjects and a DCCT fluorescein angiogram, including color photographs of Fields 1F and 2F, taken of each eye and submitted to the CORU for assessment of eligibility. Judgment on the amount of retinopathy present for eligibility screening is made only on the basis of CORU assessment of the fundus photographs and should not be made at the time of the ophthalmoscopic evaluation.

13.2.3.2 Endpoint Visits

At Annual Endpoint Visits, the ophthalmoscopic examination is carried out to detect changes in retinopathy, particularly development of characteristics for which photocoagulation treatment might be considered necessary. It is important that this examination be done in a systematic and thorough fashion.

13.2.3.3 Increased Follow-up Visit Schedule

The CORU will notify the Principal Investigator and the ophthalmologist if any of the following is detected in endpoint visit photographs: any proliferative retinopathy; severe non-proliferative retinopathy; moderately severe NPDR if there has been progression of at least three steps on the DCCT retinopathy index within the past year; or clinically significant macular edema. This notification will trigger an

increased visit schedule by which subjects are seen by the ophthalmologist every three months.

No study forms need be completed at these extra visits, unless High Risk Characteristics (HRC) are noted, in which case the visual acuity on DCCT Form 027 should be completed as well as photographs of both eyes. Once HRC are detected, study visual acuity measurements should be completed at each subsequent quarterly visit. See Manual Chapter 10 for photocoagulation policy and other ocular intercurrent events.

Requests for increased followup for other diabetes related reasons will be considered by the Ophthalmic Committee on an individual basis. Initiate consideration by completing DCCT Form 076, Request for Ophthalmic Committee Consultation.

The presence of ocular symptoms will also trigger an exam by the ophthalmologist. These exams may continue as long as symptoms persist and can be related to diabetic eye disease. To this end, each subject who is seen for symptoms will be contacted before the next scheduled visit to determine if the symptoms have persisted and whether the subject needs to see the ophthalmologist at that visit.

The detection of other ocular conditions not related to diabetic retinopathy should be treated as would be appropriate for non-DCCT subjects. Approval for increased followup is not required, nor are the costs of this care necessarily covered by the DCCT program.

Refer to Chapter 10, Definition and Management of Intercurrent Events, for forms used to initiate an increased follow-up visit schedule.

When photographs are taken at a visit other than a regularly scheduled Endpoint Visit, the Coordinating Center will provide special labels for these upon request.

13.2.4 Indirect Ophthalmoscopy

Indirect ophthalmoscopy is performed to obtain an overall stereoscopic view of the fundus and vitreous including the posterior pole and an anterior view that extends at least to the equator in all quadrants. At the Baseline Ophthalmic Examination particular attention should be paid to any signs of new vessels, vitreous hemorrhage, preretinal hemorrhage, fibrous proliferation, or retinal elevation, that is, for characteristics which would make a subject ineligible for the study (see Chapter 8). The examination should be performed with a head-mounted indirect ophthalmoscope and handheld condensing lens (a 14 or 20D Nikon Aspheric lens is recommended) with the subject sitting or lying down if necessary. If the subject has had a vitreous hemorrhage, the sitting examination should always be done first.

13.2.5 Direct Ophthalmoscopy

Direct ophthalmoscopy is performed to obtain a detailed evaluation of the disc and macula as well as to confirm lesions seen by indirect ophthalmoscopy. Particular attention is placed on evaluating the presence of microaneurysms, or other lesions of diabetic retinopathy. Of particular clinical importance is the identification of new vessels on the disc (NVD) and distinguishing new vessels elsewhere (NVE) from intraretinal microvascular abnormalities (IRMA), as these lesions may indicate that clinical intervention may be necessary. The examination should be performed with a transformer-powered direct ophthalmoscope or a halogen bulb handheld ophthalmoscope.

13.3 BEST CORRECTED VISUAL ACUITY MEASUREMENTS

13.3.1 Introduction

Visual acuity is one of the response variables used in the evaluation of treatment effects in the DCCT.[5] It is therefore essential that a standard procedure be used to obtain visual acuity measurements in each of the participating clinics and that precautions be incorporated in the procedures for obtaining visual acuity measurements so as to minimize the effects of examiner and subject bias.

Visual acuity measurements of each eye are obtained as part of the Baseline Ophthalmic Evaluation prior to randomization and at each annual follow-up visit. In addition, visual acuity (as well as photographs of both eyes) measurements are obtained using standard study procedures in the case that High Risk Characteristics are noted. Once HRC are detected, visual acuity is performed at each quarterly visit (see Section 13.1.2.3). The visual acuity measurements must be obtained by a certified DCCT visual acuity examiner at the beginning of each eye examination before the subject's pupils have been dilated. Visual acuity is documented on either the Baseline Ophthalmic Examination and Ocular History Form (DCCT Form 008) or the Endpoint Visit Ophthalmic Examination Form (DCCT Form 027).

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[5] Albeit a remote one for most subjects, given that they enter the trial with moderate non-proliferative retinopathy, at most, and some have no retinopathy detectable in fundus photographs.

13.3.2 Safeguards to Avoid Bias

Every effort is made to obtain an accurate measure of visual acuity for both eyes of each subject at each follow-up visit. Both examiner and subject bias may affect these measurements. The subject randomized to experimental treatment may be so anxious to believe that experimental treatment is helpful that he/she "tries harder." Alternatively, the subject may become convinced that his/her eyes have been damaged by the experimental or standard treatment and may not try to read the smallest line he/she can see. There is no way to prevent the subject from knowing which treatment group he/she is in; that is, the subject cannot be "masked." Instead the examiner must urge, cajole, and encourage the subject to keep trying to read each smaller line on the chart to ensure that the subject makes a maximal effort with each eye. Furthermore, the refraction (outlined in Chapter 13) should be carried out meticulously without hurrying the subject and each answer should be checked to be certain that the best possible refraction has been obtained for each eye.

It also may not be possible in many cases to "mask" the examiner; that is, to keep the examiner from knowing which group the subject is in until after the visual acuity measurements have been obtained at each visit because of the presence of pumps. Attempts should be made to mask examiners by requesting subjects to hide and turn off pumps during examination, and by supplying external pumps (not attached) to random subjects in the standard group. The subject should be instructed to avoid indicating to the examiner the identity of his/her treatment group. Masking the examiner is the best method of avoiding the effects of examiner bias which, as was true for subject bias, may be in either direction. To accomplish masking of the examiner, at the beginning of the visual acuity examination the examiner is given the subject's lens corrections obtained with subjective refraction at the last examination, but the examiner is not given access to the subject's record or chart or any other information on prior visual acuity or treatment.

A simple way to comply with these procedures is to use a standard Refraction Data Form (DCCT Form 008) which is updated at each examination. This form may be kept separately from the subject's chart. If not kept separately, it may be removed from the chart and given to the visual acuity examiner by another individual. Alternatively, the Clinic Coordinator may record lens corrections from the previous visit in pencil in the appropriate section for distance subjective refraction of the form to be used for the current visit. The individual carrying out the distance subjective refraction would then revise these findings and measure and record best-corrected visual acuity for each eye before proceeding with the other questions on the form.

13.3.3 DCCT Visual Acuity Chart DCCT Adaptation (Modified Baily-Lovie)

The DCCT will use the charts and procedures developed for the Early Treatment Diabetic Retinopathy Study (ETDRS), a multicenter clinical trial of diabetic retinopathy. The chart should be hung so that the lower edge measures between 21 and 33 inches from the floor. Such hanging should provide that the charts are displayed in a plane parallel to the wall and perpendicular to the line of viewing. The charts are supplied by the DCCT Coordinating Center.

The DCCT Refraction Chart R (Figure 13.7) or any other visual acuity chart except DCCT Visual Acuity Chart 1 or 2 may be used to determine the best distance lens correction, at 10 to 20 feet, for each eye. Testing of all subjects begins at four meters. Two DCCT Visual Acuity Charts are used for the measurement of visual acuity, each with a different letter sequence. The right eye will always be tested with Chart 1 (Figure 13.8) and the left eye with Chart 2 (Figure 13.9).

Visual acuity measured at four meters (and at one meter for low vision subjects) may be determined from DCCT Visual Acuity Charts as shown for Charts 1 and 2 in Figure 13.10. The visual acuity equivalents for 20 feet are indicated. Visual acuity measured at one meter may be determined as shown in Figure 13.11.

13.3.4 Illumination of the DCCT Visual Acuity Charts and Room Illumination

Room illumination should be at a level of 50 to 100 foot-candles as measured with a photometer held four feet from the floor and directed toward the ceiling. This is equivalent to the room lighting in most office buildings or schools. Illumination should be within the stated limits at all points along a line from the subject to the chart except for the three-foot segment closest to the chart, where the limit may be exceeded. The chart itself should be illuminated by an incandescent light or other source directed towards the chart in such a way to evenly illuminate it and not create shadows or glare.

13.3.5 Beginning Approximate Refraction

If the subject wears contact lenses and has spectacle glasses as well, he/she should be instructed to refrain from wearing the contact lenses on the day of each examination. In the event that the subject either has no glasses or has forgotten the instructions and has reported for examination wearing contact lenses, these should be removed and at least one-half hour should elapse before refraction and visual acuity testing is done. In this latter event, careful attention should be given to the cornea on slit-lamp examination and any abnormalities should be noted in the subject's clinic record.

If the subject's visual acuity in either eye is less than 4/20 (20/100 equivalent) with the subject's present distance glasses (or without correction, if the subject does not have glasses), retinoscopy and refraction should be carried out by an examiner proficient in these procedures. The lens corrections obtained are used as the beginning approximate refraction in the procedure outline below for determination of best-corrected visual acuity. If the subject's visual acuity is 4/20 (20/100) or better with the subject's present distance glasses, the glasses are measured with a lensometer and these measurements are used as the beginning approximate refraction. If the results of the subjective refraction from a previous DCCT visit are available, these results should be used as the beginning approximate refraction. If the subject's visual acuity is 4/20 (20/100) or better and the subject does not have glasses for distance vision, the beginning approximate refraction is no lens correction or plano.

13.3.6 Subjective Refraction

The frame[6] lens cells are parallel to the anterior plane of the orbits and centered in front of the pupils. The left eye is occluded and the beginning approximate refraction as determined above is placed in the right anterior lens cells with the cylindrical correction anterior. The subject is asked to look at and read any standard chart or DCCT Refraction Chart R to determine the best lens correction. The standard chart at a distance of 10 to 20 feet may be used directly or with a mirror, or a projecto-chart may be used for the refraction. Note that the DCCT Visual Acuity Charts 1 and 2 are not used for this purpose but only to test the visual acuity under the prescribed conditions after the best refraction is determined. A +0.50 sphere is held in front of the right eye and the subject is asked if the vision is improved while looking at the smallest line read well. If the subject responds that it is not improved, he/she is asked if vision is made worse. If vision is improved or there is no change, the sphere in the trial frame is replaced with a sphere that is one-half diopter more plus. The +0.50 sphere is held in front of the right eye again and the subject is asked if the vision is improved or worsened. The process of increasing the plus sphere in the trial frame is repeated until the subject says that the +0.50 sphere held in front of the trial frame makes the vision worse. When this occurs, the +0.50 sphere is removed from in front of the trial frame. By this process the highest plus or least minus sphere that will produce a minimum blurring of the subject's vision is determined.

After determining the highest plus or least minus sphere, the subject is asked to read the smallest line possible. A -0.37 sphere is held in front of the trial frame and the subject is asked if the vision is

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[6] It is permissible to use a phoropter for the subjective refraction. However, the final refraction to be used for visual acuity testing must be placed in a trial frame and the final sphere must be rechecked as described in the last paragraph of this Chapter.

improved. If it is not, the +0.50 sphere is tried again to see if the subject will still accept more plus. If the subject reports that the vision is improved by the -0.37 sphere, the subject is requested to read the smallest line possible. If the examiner is convinced that the vision is improved, the sphere in the trial frame is replaced by a sphere that is 0.25 diopter less plus. Minus spherical power is added by -0.25 diopter increments in the above fashion until the subject shows no further improvement in vision.

For purposes of this discussion only plus cylinder techniques will be presented. If the beginning approximate refraction contains a cylinder correction, changes in cylindrical axis are tested by adding a 0.25, 0.37, or 0.50 diopter cross cylinder, first with the positive axis 45 degrees to one side of the cylinder axis, and then with the positive axis 45 degrees to the opposite side of the cylinder axis. Since neither position may produce a clear image the subject is encouraged to select the position of least blur while fixing on a single round letter on the line above the line on the chart he/she is able to read when the cross cylinder is not held up before the trial frame. If the subject cannot choose between the two positions of the cross cylinder at the beginning of this test, the axis of the cylinder is moved five degrees to 15 degrees, first in one direction and then in the other, with the cross cylinder being checked in each position to confirm that the original axis was indeed correct. If the subject does prefer one position of the cross cylinder to the other and the cylinder in the trial frame is plus, the axis of the cylinder is moved five to 15 degrees[7] axis of the cross cylinder when in the position which the subject said was better. The cross cylinder is tried again with the positive axis 45 degrees to one side of the new cylinder axis and then with the positive axis 45 degrees to the opposite side of the new cylinder axis and the subject is asked which position he/she prefers. If the subject prefers one position to the other, the axis of the plus cylinder is moved toward the positive axis of the cross cylinder. Testing for change of axis is repeated until the subject cannot decide that one position of the cross cylinder is better than the other.

Change in cylinder power is now tested by adding the cross cylinder, first with the positive axis and then with negative axis coincident with the cylinder axis. For this test, the subject is requested to focus attention on a round letter on the lowest line on the chart he/she is able to read. If the subject prefers the positive axis coincident with the cylinder axis, the power of the correcting plus cylinder is increased by an additional plus 0.25 diopter. If the subject prefers the negative axis conincident with the cylinder axis, the total power of the correcting plus cylinder is reduced by 0.25 diopter. The process is repeated until the subject cannot choose one of the cross cylinder positions as better than the other, i.e., until both positions are equally bad. If 1.00 diopter of cylinder should be added, 0.50 diopter

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[7] When the power of the cylinder is low and/or the subject's discrimination is poor, larger shifts will produce more clear-cut answers.

of sphere of opposite sign should be added as well, and, similarly, 0.25 diopter of sphere of opposite sign added for each additional 0.50 cylinder.

If the beginning refraction is a sphere, the presence of astigmatism is tested by arbitrarily placing a 0.25 cylinder at 180 degrees in the trial frame, after having determined the highest plus or least minus sphere producing minimal blurring of vision as described above. The refraction is then continued by using the cross cylinder to test for cylinder axis and power. In this situation, or in any situation when testing for cylinder power with the cross-cylinder technique and when 0.25 cylinder is present, if the preference with cross-cylinder indicates that this 0.25 cylinder should be removed, before doing so rotate the 0.25 cylinder 90 degrees from its original position and test for cylinder power once again. At this point, if additional power is preferred, it should be added. If, on the other hand, the preference is to remove the 0.25, this should be done and the final refraction would be purely spherical.

Example:

Starting refraction: -2.50 + 0.25 axis 37 degrees. Use of the cross cylinder to check cylinder axis indicates that the subject prefers the 37 degrees axis. If on using the cross-cylinder to check cylinder power one finds that the subject wants the 0.25 cylinder removed, rotate the cylinder to 127 degrees and test for cylinder power once again. If additional power is preferred, add it. If the preference is to remove the 0.25 cylinder, this should be done.

If 0.50 or more diopters of cylinder have been added, the cylinder axis should be refined, if possible, by using the cross cylinder as described above.

Minus cylinders may be used instead of plus cylinders to determine the best correction for the power and axis of the cylinder. If minus cylinders are used, the procedure described above must be revised to reflect this change in sign.

When neither the power nor the axis of the cylinder can be improved, the power of the sphere is rechecked by adding +0.37 and -0.37 spheres and changing the spherical power by quarter diopter increments of the appropriate sign until the subject can perceive no improvement in vision. If the sphere is changed at this point, the cylinder should be rechecked. This process is repeated until no further significant lens changes are made. The lens corrections obtained in this way for the right eye are recorded on the examination form in the section for visual acuity measurements as the corrections obtained by subjective refraction for the right eye. The entire process is repeated for the left eye and the lens corrections are recorded on the examination form as the corrections obtained by subjective refraction for the left eye.

If a site other than the actual DCCT refraction lane at four meters and/or a chart other than DCCT Refraction Chart R are utilized for the

refraction, a final check of the sphere, as outline above, should be carried out just prior to the actual visual acuity testing, using the DCCT refraction lane at four meters and DCCT Refraction Chart R and light box. If the refraction with the DCCT refraction is recorded on the form. Similarly, if a phoropter has been used for the subjective refraction, a final check on the sphere, as described above, should be performed with a trial frame using the DCCT refraction lane at four meters and the DCCT Refraction Chart and light box.

13.3.6.1 Refraction for Subjects with Poor Visual Acuity

If it is not possible to perform a subjective refraction at the 10-20 foot distance because the subject's visual acuity in one or both eyes is too poor to see the largest letters on the refraction chart at that distance, then the refraction should be attempted at the one meter distance in the eye(s) in question. If the subjective refraction can be successfully performed at the one meter distance, then a +0.75 sphere should be subtracted from the one meter refraction, in order to make the correction appropriate for the four meter visual acuity test distance. It is the latter correction that should be entered in the appropriate space on the form provided for distance subjective refraction.[8]

Example:

Refraction could not be performed at 10-20 feet in the right eye because the subject could not see any letters on the refraction chart at that distance. When the subject was moved up to one meter, the following was obtained:

+ 2.00 + 1.00 x 180 degrees

In order to make this appropriate for visual acuity testing at four meters, a +0.75 sph. must be subtracted from the above result.

+ 2.00 + 1.00 x 180 degrees

- +0.75 sph

+1.25 + 1.00 x 180 degrees

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[8] NOTE: The visual acuity should always be tested first at the four meter distance, even if the subject could not be refracted at the four meter distance. If the number of letters read correctly at four meters is less than or equal to 20, the visual acuity must also be tested at the one meter distance, in which case the +0.75 sphere should be replaced (see Section 13.3.7 Best-Corrected Visual Acuity Measurements).

This value is entered on the form for distance subjective refraction and used to test the visual acuity at four meters.

Example:

In another subject, the refraction could not be performed at four meters and the following refraction was obtained at one meter in the left eye:

-1.75 + 0.50 x 90 degrees

The appropriate correction for four meter visual acuity testing is:

-1.75 + 0.50 x 90 degrees

- +0.75 sph

-2.50 + 0.50 x 90 degrees

If the subjective refraction cannot be performed at either the four meter or the one meter distance because the subject's visual acuity is too poor to see the largest letter on the refraction chart at both of these distances, then the most recent distance subjective refraction obtained at a previous DCCT visit should be used for visual acuity testing.

13.3.7 Best-Corrected Visual Acuity Measurements

The distance from the subject's eyes to the DCCT Visual Acuity Chart should be 4.0 meters. With the lens correction obtained by subjective refraction in the trial frame, the subject is asked to read DCCT Visual Acuity Chart 1 from the top with the right eye. It is emphasized to the subject that each answer will be scored so that adequate time should be allowed for each letter in order to achieve the best identification.

When the subject cannot read a letter, he/she is encouraged to guess if at all possible. If the subject states that a letter is one of two letters, he/she is asked to choose only one letter and, if necessary, to guess. It may be suggested that the subject fixate eccentrically or turn or shake his/her head in any manner if this improves visual acuity. If the subject employs these maneuvers, care must be taken to insure that the fellow eye remains covered. Only one reading is allowed for each letter. When a subject attempts to read the chart and comes to a level at which he/she cannot even guess, the examiner may stop the test for that eye provided that the subject has previously made some errors which indicate that the best possible acuity level has been reached.

The examiner records each letter identified correctly by the subject as he/she reads the chart by circling the corresponding letter on the appropriate DCCT form for this visit. Letters read incorrectly, or for which no guesses are made, are not marked on this form. Each letter read correctly is scored as one point. The score for each line (including zero if no letters were read correctly on that line) and the total score for that eye must be recorded on the form after the testing has been completed.

If the number of letters read correctly at four meters is less than twenty, the test should be repeated at one meter and both the four- and one-meter totals should be recorded on the appropriate DCCT form for this visit. Both eyes should be tested at four meters before the subject is moved up to the one-meter test distance. Prior to actual testing at one-meter, +0.75 spheres should be added to the correction already in the trial frame to compensate for the new distance. The subject may stand or sit for the visual acuity test at four meters, but must sit for the one-meter distance.

If the subject's visual acuity is so poor that he/she cannot read the largest chart letters when tested at one meter (i.e., the number of letters read correctly at one meter is zero) then the subject's ability to count fingers, detect hand motion, or have light perception should be evaluated. If the examiner is not convinced that the subject can count fingers or detect hand movements, this eye should be tested for light perception (see Chapter 13).

The same procedure for obtaining visual acuity for the right eye is used for the left eye, except that DCCT Visual Acuity Chart 2 is used.

13.3.8 Calculating the Visual Acuity Score

After each measurement of visual acuity, the visual acuity score for the visit is calculated. The visual acuity score is defined as follows:

1. If four or more letters are read correctly at the four-meter test distance, the visual acuity score is equal to the number of letters read correctly at four meters plus 30; or

2. If fewer than four letters are read correctly at the four-meter test distance, the visual acuity score is equal to the number of letters read correctly at one meter; or

3. If no letters are read correctly at either the four-meter distance or the one-meter distance, the visual acuity score is 0.

13.3.9 Proposal for Conversion from Visual Acuity Examination Record Form to Visual Acuity Value

One may obtain a "fractional" visual acuity by noting the last full line read correctly and adding to it the number of letters read correctly beyond this line; for example, if a subject were to read all the letters on the 4/10 line and above and four of five letters on the 4/8 line, the acuity could be expressed as 4/10 + 4 (20/50 + 4).

For purposes of statistical analyses, conversion to Log MAR units may be done. (1) Each line of letters has a corresponding Log MAR value. It is assumed that each letter on the chart has a Log MAR value of 0.02, as each line of five letters has a total value of 0.10. One may therefore arrive at a Log MAR value for each test by the calculation (1.70-0.02N) where N is the total number of letters read correctly. For subjects tested at the four-meter test distance, 30 letters will be considered as having been read correctly prior to testing, in order to have scores attained at four meters and one meter correspond. In the example, by this method, N = (30+39) = 69 and the Log MAR value would be 1.70 - (0.02 x 69) = 0.32. In other words, it is assumed, for scoring purposes, that the subject could read the 30 largest letters at one meter without actually testing this ability.

It should be noted that this method of conversion to Log MAR units has the difficulty of assigning the same 0.02 value to each letter read correctly, no matter which line the letter is from. Therefore, any letter on the 4/6.25 (20/32) line is given the same 0.02 value as any letter on the 4/8 (20/40) line, or any other line for that matter. While some accuracy may be lost by this method, the error is estimated to be small and the advantage of giving some credit for all correct answers probably outweighs this disadvantage.

13.3.10 Testing Light Perception

If the number of letters read correctly at one meter was zero and the examiner is not convinced that the subject can count fingers or detect hand movements, the eye is tested for light perception with the indirect ophthalmoscope as the light source. Room lighting should remain at the level of normal visual acuity testing. The subject should close the opposite eye and occlude it by making a tight seal with the palm around the orbit and the bridge of the nose. The indirect ophthalmoscope light should be in focus at three feet, and the rheostat set at six volts. From a distance of three feet the beam should be directed in and out of the eye at least four times; the subject should be asked to respond when he/she sees the light. If the examiner is convinced that the subject perceives the light, vision should be recorded as light perception, otherwise as not light perception.

13.3.11 Examinations After the Baseline Visit

The lens corrections obtained by subjective refraction at the preceding completed examination should be used as the beginning approximate refraction for the next examination. These results should be recorded in pencil on the appropriate examination forms in preparation for the subject's examination and, if used, on the Refraction Data Form at the end of each examination.

13.3.12 Visual Acuity Required for Eligibility

Eligibility for DCCT requires that the subject read correctly 50 or more letters at the four-meter test distance with each eye, which corresponds to 4/5.0 (20/25) or better vision at the Evaluation Visit, unless the eye has diabetic retinopathy confirmed by the CORU assessment of the Evaluation Visit photographs in which case the eye may have 4/6.5 (20/32) vision (45 letters correct). If less than 50 letters are read correctly with either eye at the Evaluation Visit, the Trial Coordinator should be informed promptly. If retinopathy is not present on the basis of the clinical examination, the subject may not be eligible unless retinopathy is detected on fundus photographs read at the CORU.

If a subject otherwise clincially eligible for the study does not meet the eligibility criteria described above, the vision may be retested no sooner than the following day. If the subject is still ineligible, the subject is temporarily excluded for six months. At the end of six months, the subject may be restarted. See Chapter 6 for procedures for restarting subjects.

Summary of Visual Acuity Requirements for Eligibility

Diabetic Retinopathy Present	Letters correct at Baseline Visit
No	Greater than or equal to 50 (4 meters)
Yes	Greater than or equal to 45 (4 meters)

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2. Allen, L: Ocular fundus photograph. Amer. J. Ophthal. 57:13-28, 1964.

APPENDIX 13-A

POINTERS ON PHOTOGRAPHIC TECHNIQUE

Since the CORU analyzes photographs for quality in terms of (1) field definition, (2) focus/clarity, and (3) stereo effect, the comments presented here on photographic technique are organized under those headings.

FIELD DEFINITION

Color

For color fundus photographs, proper field definition is discussed in Section 13.1.5.1 of the Manual of Operations; for fluorescein angiograms, correct field definition is presented in Section 13.1.6.3. Both are illustrated in Figure 13.1.

Try the following technique for attaining proper definition in Field 4 and other fields. Assuming that Field 4 is being taken, (1) move the camera from the center of the disc upwards until the upper edge of the disc meets the bottom of the vertical cross hair, (2) take note of some landmark at the intersection of the cross hairs (e.g., a small vessel or microaneurysms), (3) swing the camera temporally until this landmark is at the nasal end of the horizontal cross hair (at this point, the lower edge of your field will fall on the same plane as the upper edge of the disc) -- this is the proper position for Field 4. For Field 6, rotate the camera back nasally until the fundus landmark you selected is at the temporal end of the horizontal cross hair. Comparable maneuvers will do the same for Fields 5 and 7.

Fluorescein

Note that for angiographic Fields 1F and 2F the proper field definitions are different from those for Fields 1 and 2.

Field 1F is located such that the temporal edge of the disc is positioned 1/4 DD from the temporal edge of the field. Thus, Field 1F shows more of the nasal field than the standard Field 1. It is important to keep a small amount of the retina visible temporal to the disc to ensure that the entire disc remains in the field. The decision to use this modification was made because some of the earliest microvascular changes visible in fluorescein occur in this area.

Field 2F is centered 1/2 DD temporal to the center of the macula. Often, photographers make the error of centering it nearly on the center of the macula, which is too far nasal. One should not see much or any of the optic disc in Field 2F. This more temporal placement (compared with standard Field 2) includes more of the retinal area temporal to the macula, which is another area where some of the earliest changes visible in fluorescein occur.

Using these field definitions modified for angiography, you will notice that very little if any overlap will occur between Fields 1F and 2F. Since only two fields are taken, this arrangement maximizes the area of retina captured in the pictures.

FOCUS/CLARITY

Perhaps the most common error in fundus photography is poor focus, which can be avoided if the photographer develops a constant awareness of the need to keep the cross hairs in the ocular of the camera in sharp focus by adjusting the ocular as often as necessary. The cross hairs must be in sharp focus at all times -- having the fundus in focus and the cross hairs blurred results in an out-of-focus photograph.

If it is not possible to get the entire photographic field in crisp focus, please concentrate on getting the center of the field in focus, sacrificing a bit on the periphery if necessary. This is especially important in Fields 1 and 2. Frequently the CORU sees photographs showing the fovea to be slightly out of focus while the periphery of Field 2 is in focus. (This may be due to the fact that when the photographer moves to Field 2, having just taken Field 1, he or she does not refocus on the foveal area.)

A common problem is focusing too deep. Photographs which include the disc (Fields 1, 1F, and often 2) sometimes show clear focus on the bottom of the cup, while the retina is slightly out of focus. It appears that some photographers use the disc margin or the granular pattern of the pigment epithelium for focusing. Instead, it is desirable to focus on the fine vascular branches as they approach the macula. If you recall that the depth of focus is greater posterior to the plane of absolute focus than anterior to it, it makes sense to err on the side of focusing slightly up into the vitreous rather than too deep. This should keep both the anterior surface of the retina and the pigment epithelial background in focus. Such a strategy is of special importance when macular edema is present.

In all field except Field 2, when elevated retinopathy is present such that the depth of field cannot encompass both the most posterior detail of retina and the elevated lesion at the same time, it is usually advisable to take one side of the stereo pair focused on the plane of the flat retina (near the anterior surface) and the other side of the pair focused near the top of the elevated structure. It should be remembered, however, that the focus should not be so far anterior that all landmarks below disappear. Some recognition of these must be possible in order to be able to fuse the two sides comfortably when looking at them binocularly.

In Field 2, focus both members of the stereo pair on the small blood vessels near the center of the fovea. When there are elevated structures other than macular edema, they can nearly always be seen in another field because of the overlapping of the fields.

Photographers should periodically determine if their cameras need cleaning, and clean them when necessary. Photos marred by dust on the lenses often provide ambiguous evidence -- we at the CORU cannot tell whether that superficial lightish spot is a soft exudate or a dust spot.

STEREO EFFECT

Adequate dilation of the pupil is important to permit good quality stereo photography. When photographs are taken before dilation is complete or after the pupil has started to come down, the maximum stereo separation cannot be obtained. Sufficient time should be allowed for dilation to at least 6 mm, repeating drops if necessary to achieve and maintain a pupil of at least this size during photography. Only if repeated instillation of drops and passage of at least 45 minutes after the last drops fail to provide dilation of 6 mm should photographs be taken through a smaller pupil. If the pupils cannot be dilated to at least 4 mm for the qualifying visit fundus photographs, the subject should not be entered into the DCCT (see Section 13.1.4).

Many photographers use the Allen stereo separator. If it is used, a setting between 2.25 and 2.50 is recommended (see Section 13.1.3). Please be careful about overriding the separator, i.e., moving the camera too far back toward the first member of the pair when taking the second member.

Please take care in photographing stereo pairs that at least one member of the pair is of good technical quality (by that is meant primarily crisp focus). In most cases, it will be possible to obtain good quality in both members, but if this is not the case, the aim should be to obtain good quality in one member and some stereo separation in the pair, accepting poorer quality in the second member of the pair if necessary.

Figure 13.1

DCCT REFRACTION CHART R

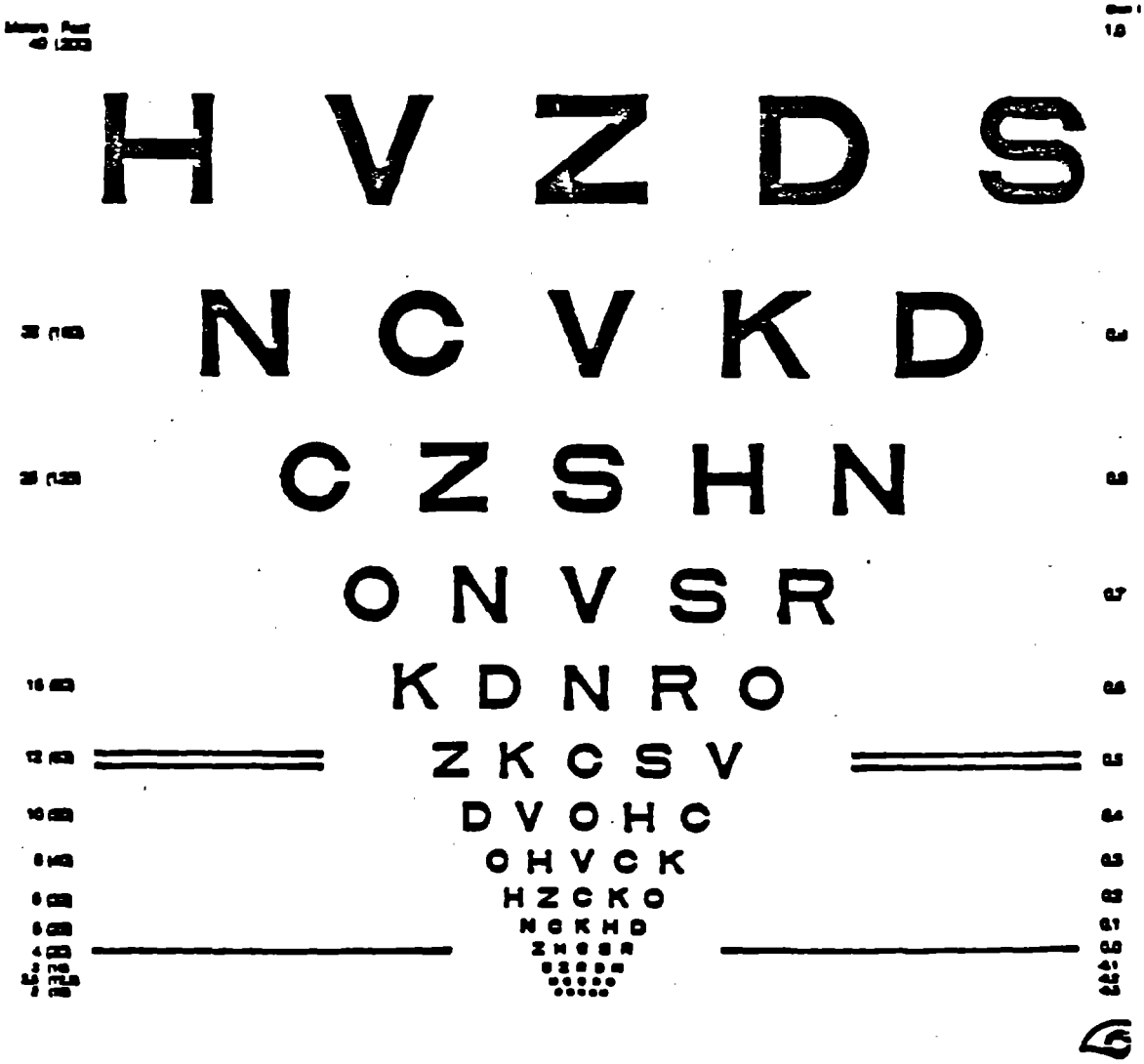


Figure 13.2

DCCT VISUAL ACUITY CHART 1

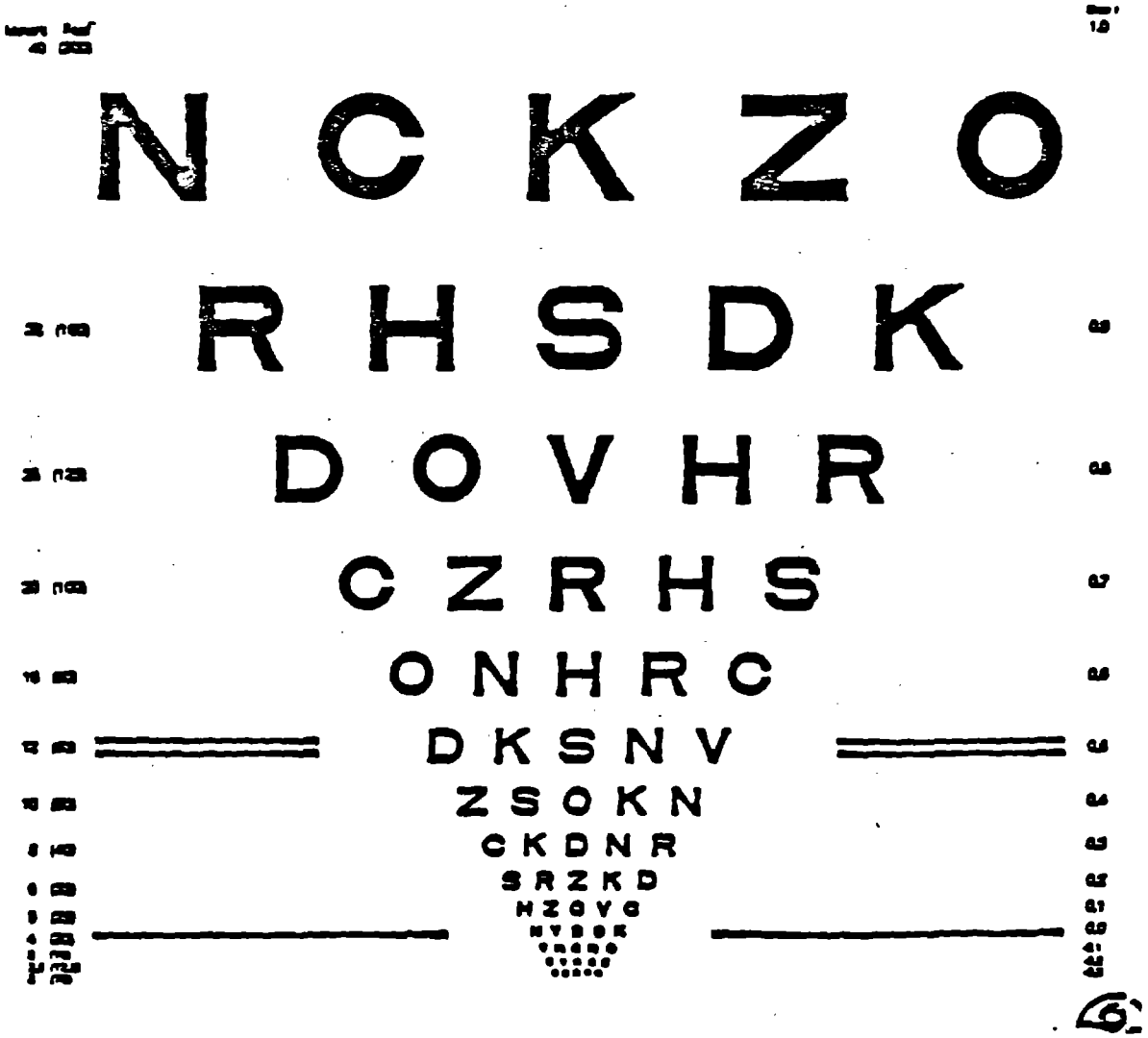


Figure 13.3

DCCT VISUAL ACUITY CHART 2

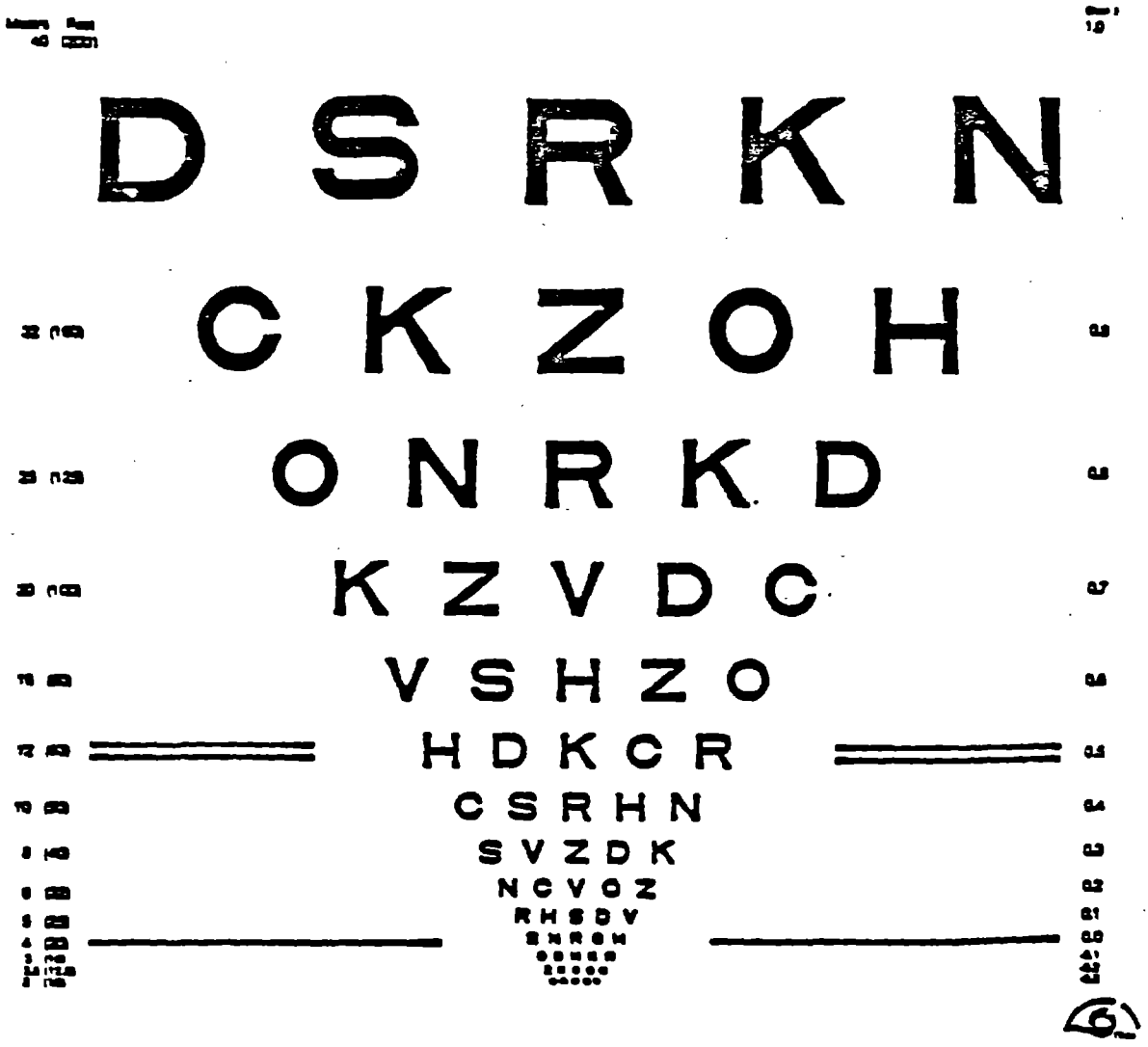


Figure 13.4

VISUAL ACUITY FROM DCCT CHARTS AT FOUR METERS DISTANCE

ACTUAL VISUAL ACUITY	EQUIV. VISUAL ACUITY	LETTERS CHART 1	LETTERS CHART 2	LOG MAR*
4/40	20/200	N C K Z O	D S R K N	1.0
4/32	20/160	R H S D K	C K Z O H	0.9
4/25	20/125	D O V H R	O N R K D	0.8
4/20	20/100	C Z R H S	K Z V D C	0.7
4/16	20/80	O N H R C	V S H Z O	0.6
4/12.5	20/62.5	D K S N V	H D K C R	0.5
4/10	20/50	Z S O K N	C S R H N	0.4
4/8	20/40	C K D N R	S V Z D K	0.3
4/6.25	20/32	S R Z K D	N C V O Z	0.2
4/5	20/25	H Z O V C	R H S D V	0.1
4/4	20/20	N V D O K	S N R O H	0.0
4/3.12	20/16	V H C N O	O D H K R	-0.1
4/2.5	20/12	S V H C Z	Z K C S N	-0.2
4/2	20/10	O Z D V K	C R H D V	-0.3

* See Chapter 12.

Figure 13.5

VISUAL ACUITY FROM DCCT CHARTS AT ONE METER DISTANCE

ACTUAL VISUAL ACUITY	EQUIV. VISUAL ACUITY	LETTERS CHART 1	LETTERS CHART 2	LOG MAR*
4/160	20/800	N C K Z O	D S R K N	1.6
4/125	20/640	R H S D K	C K Z O H	1.5
4/100	20/500	D O V H R	O N R K D	1.4
4/80	20/400	C Z R H S	K Z V D C	1.3
4/63.5	20/320	O N H R C	V S H Z O	1.2
4/50	20/250	D K S N V	H D K C R	1.1
4/40	20/200	Z S O K N	C S R H N	1.0
4/32	20/160	C K D N R	S V Z D K	0.9
4/25	20/125	S R Z K D	N C V O Z	0.8
4/20	20/100	H Z O V C	R H S D V	0.7
4/16	20/80	N V D O K	S N R O H	0.6
4/12.5	20/62.5	V H C N O	O D H K R	0.5
4/10	20/50	S V H C Z	Z K C S N	0.4
4/8	20/40	O Z D V K	C R H D V	0.3

*See Chapter 12.

Figure 13.6

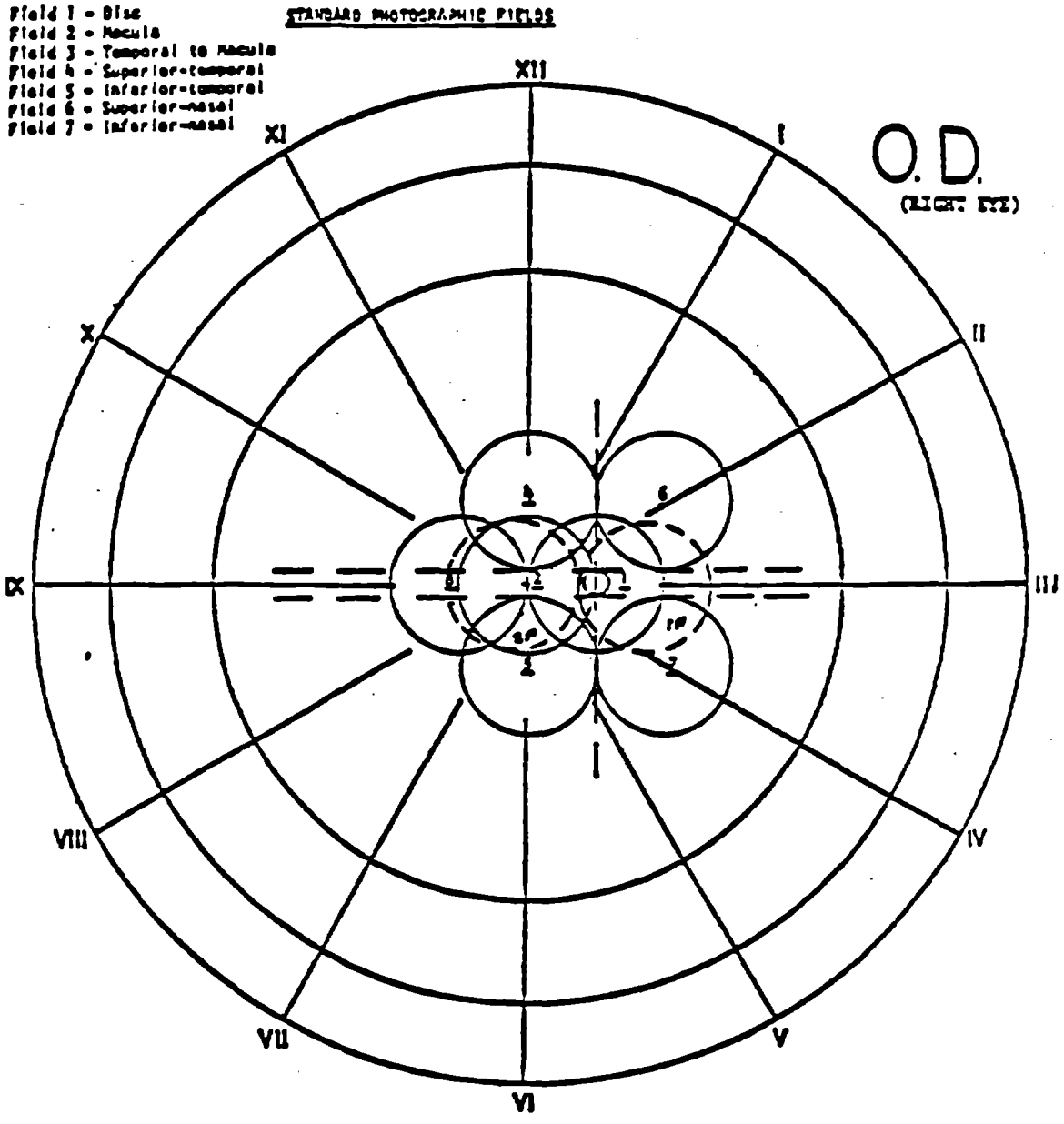

Field 1 - Disc
Field 2 - Macula
Field 3 - Temporal to Macula
Field 4 - Superior-temporal
Field 5 - Inferior-temporal
Field 6 - Superior-nasal
Field 7 - Inferior-nasal
STANDARD PHOTOGRAPHIC FIELDS
O.D.
(RIGHT EYE)
XII
I
II
III
IV
V
VI
VII
VIII
IX
X
XI

Figure 13.6 (Cont'd)

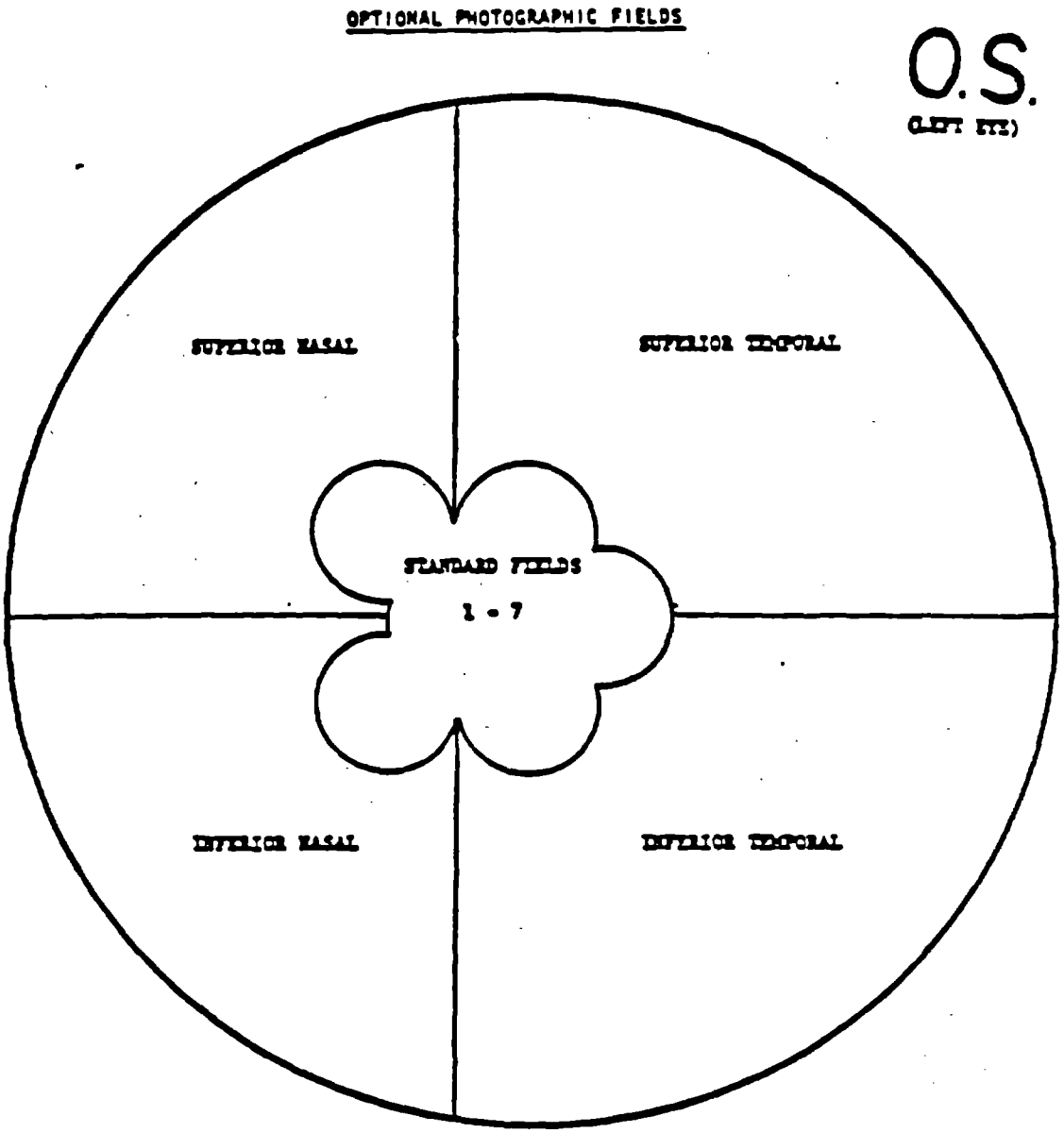


Figure 13.6 (Cont'd)

Field 1 - Disc
Field 2 - Macula
Field 3 - Temporal to Macula
Field 4 - Superior-temporal
Field 5 - Inferior-temporal
Field 6 - Superior-nasal
Field 7 - Inferior-nasal

STANDARD PHOTOGRAPHIC FIELDS

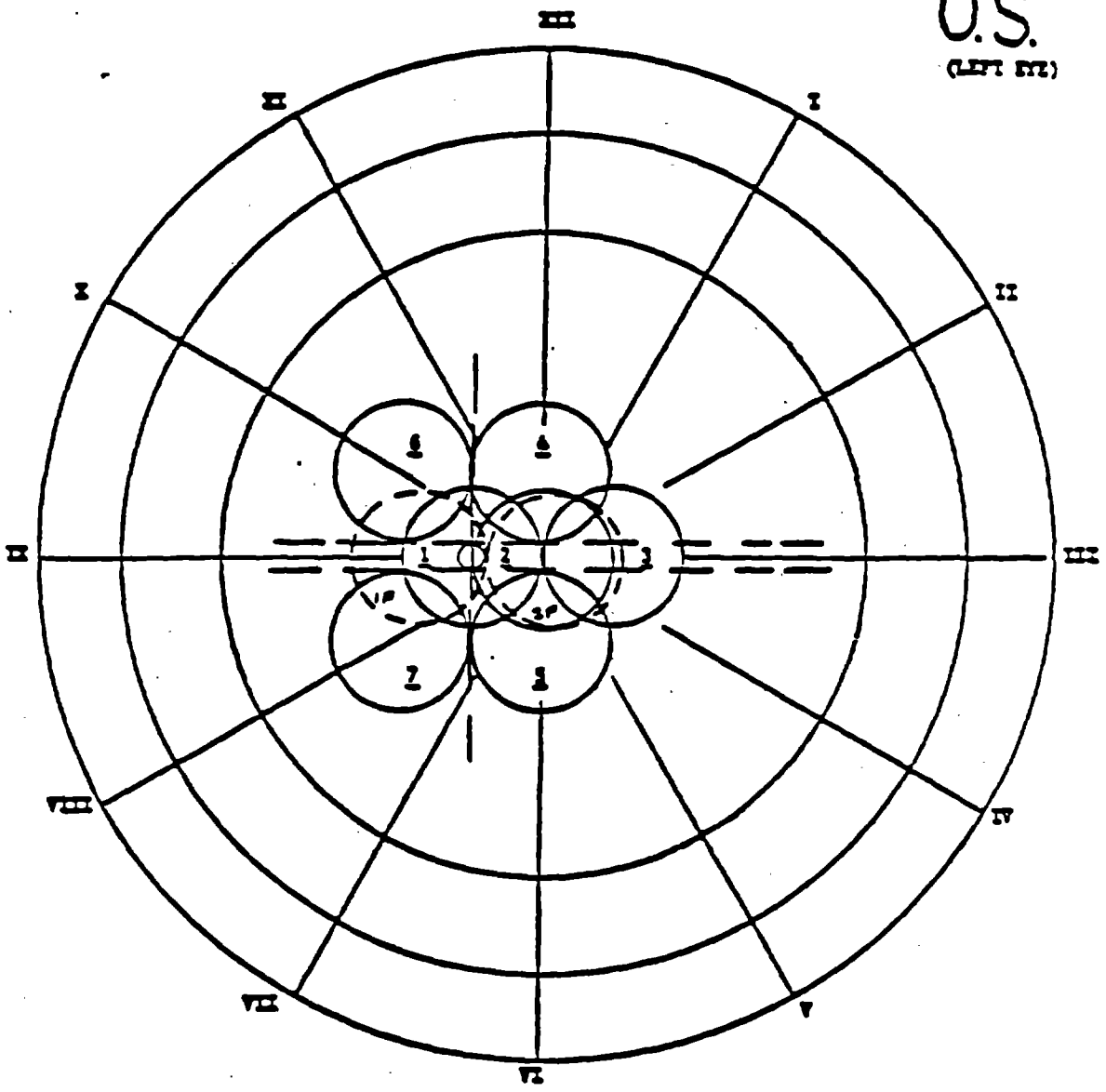


Figure 13.6 (Cont'd)

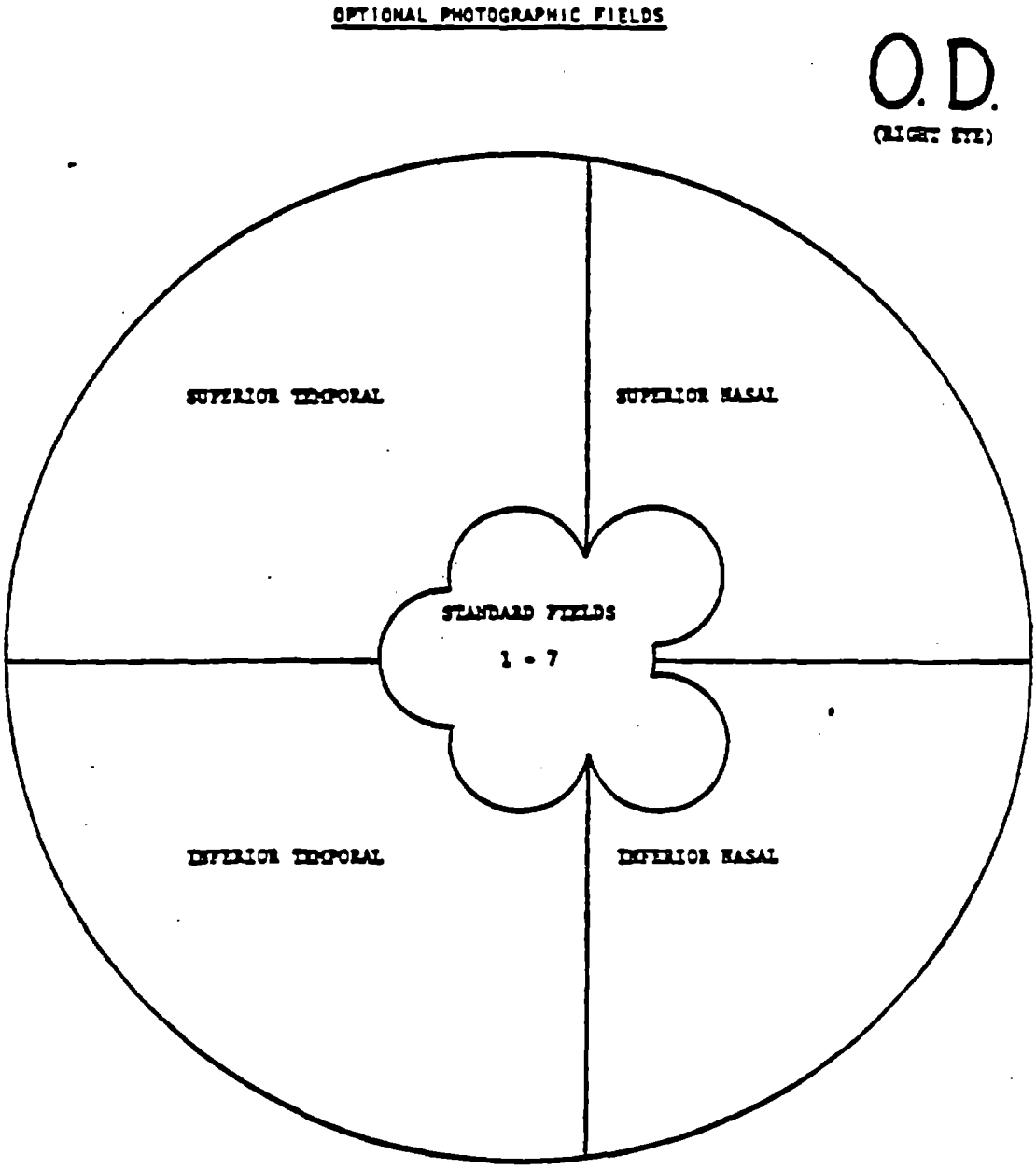
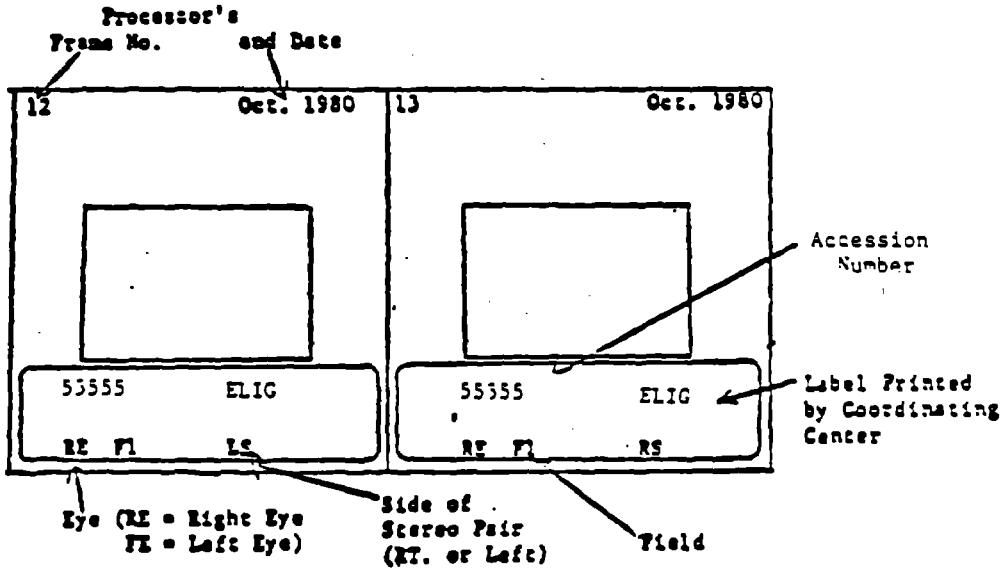


Figure 13.7

IDENTIFICATION LABELS TO BE PLACED ON EACH PAIR OF STEREO COLOR FUNDUS PHOTOGRAPHS



Note: Printed labels are supplied by the Coordinating Center. Labels for each set which may be possibly taken during the study are specifically designated for each patient. These use randomized accession numbers (to allow masking of graders evaluating the photographs). Each accession number corresponds uniquely to a given eye of a given patient at a given visit. Thus, there should be no substitution of labels, and great care taken to ensure accurate labeling.

Figure 13.8

PLACEMENT OF FUNDUS PHOTOGRAPHS IN PLASTIC SHEETS
RIGHT EYE

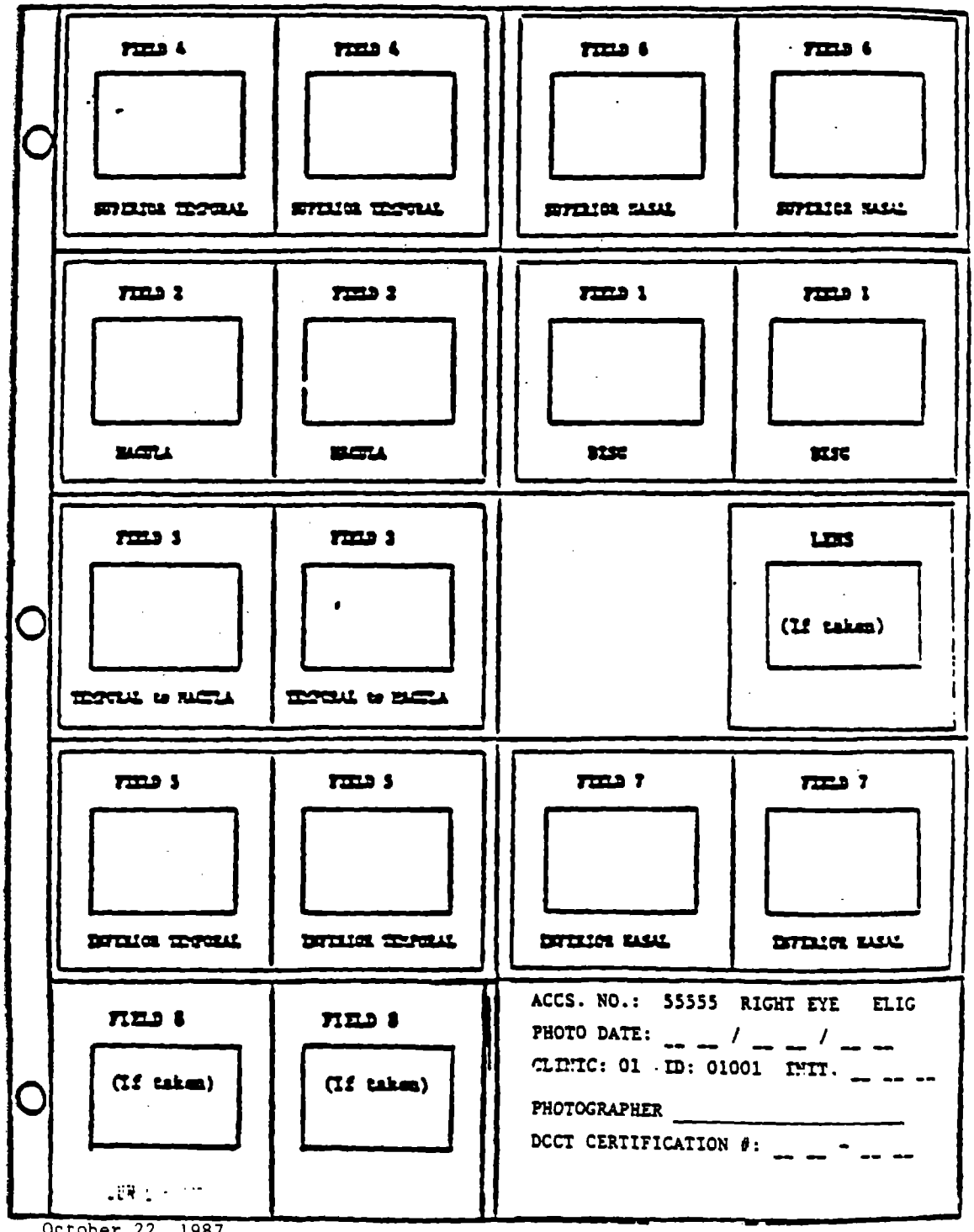


Figure 13.8 (Cont'd)

PLACEMENT OF FUNDUS PHOTOGRAPHS IN PLASTIC SHEETS
LEFT EYE

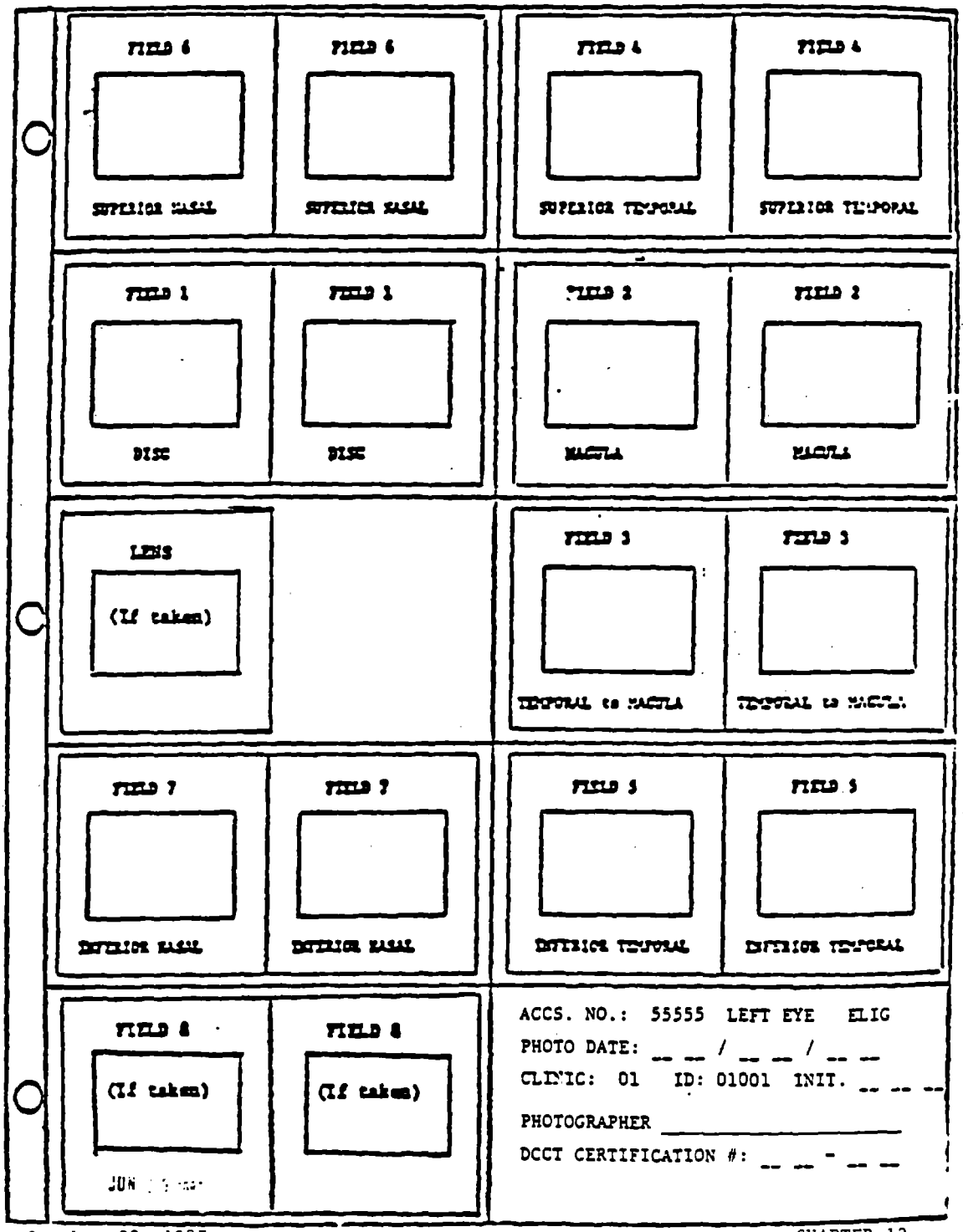


Figure 13.9

SCHEMATIC DIAGRAM:
DCCT FLUORESCEIN ANGIOGRAPHY PROCEDURE

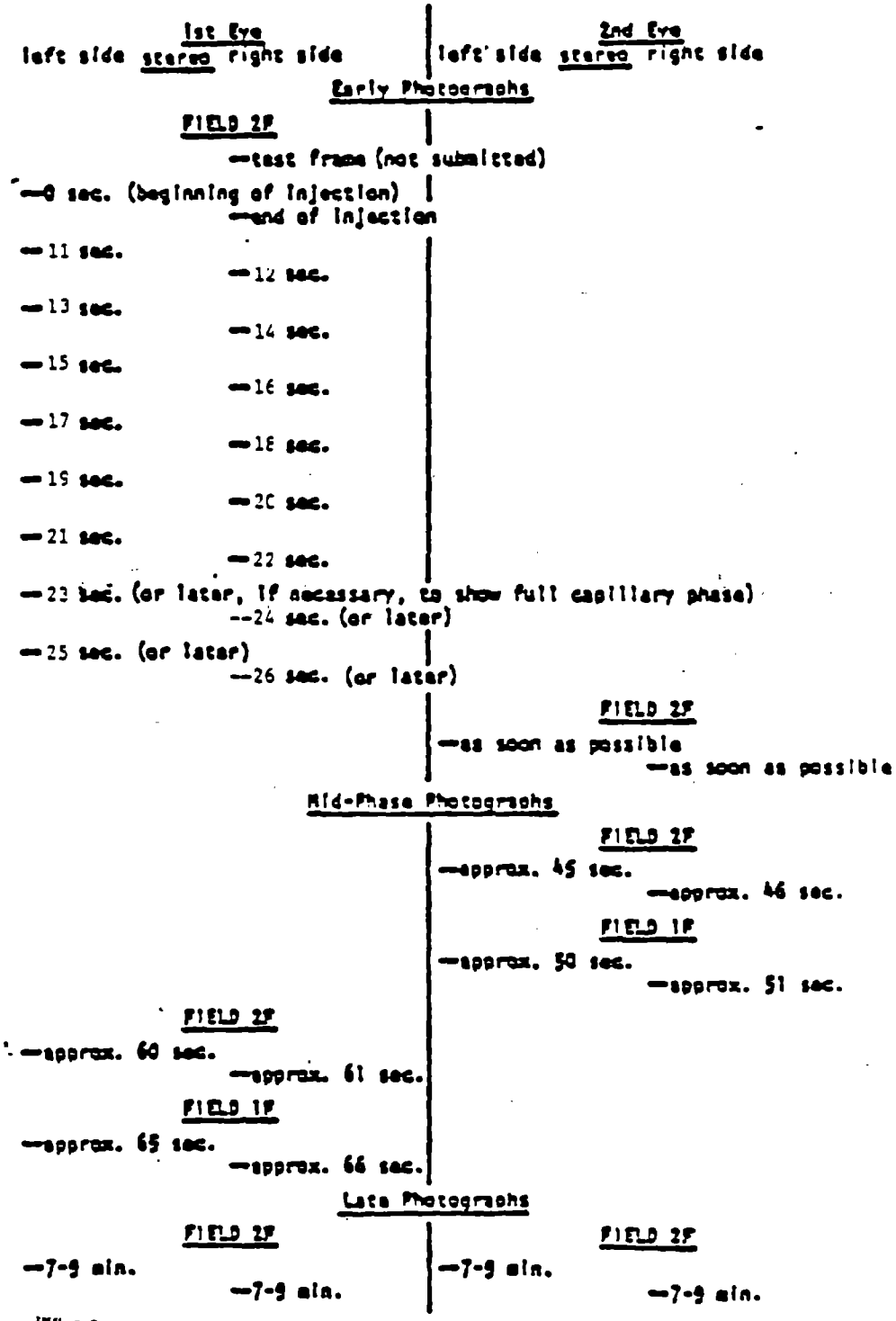
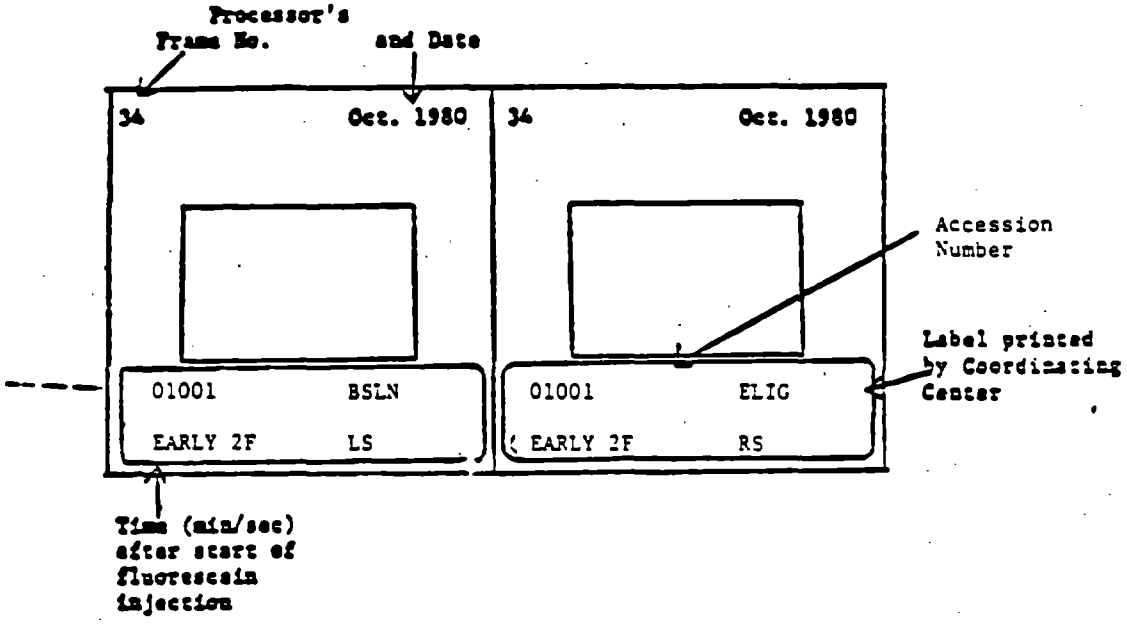


Figure 13.10

IDENTIFICATION LABELS TO BE PLACED ON EACH PAIR OF STEREO PHOTOGRAPHS TAKEN DURING FLUORESCEIN ANGIOGRAPHY



Note: Printed labels are supplied by the Coordinating Center. The time after the start of the fluorescein injection at which a photograph was taken must be written in by clinical center staff if it is not correctly printed on the negative by a timer in the camera. Accession numbers are assigned uniquely to each patient (so as to allow masked grading of the angiogram), thus there should be no substitution of labels and great care taken to ensure accurate labeling.

Figure 13.11

FLUORESCEIN PHOTOGRAPHS

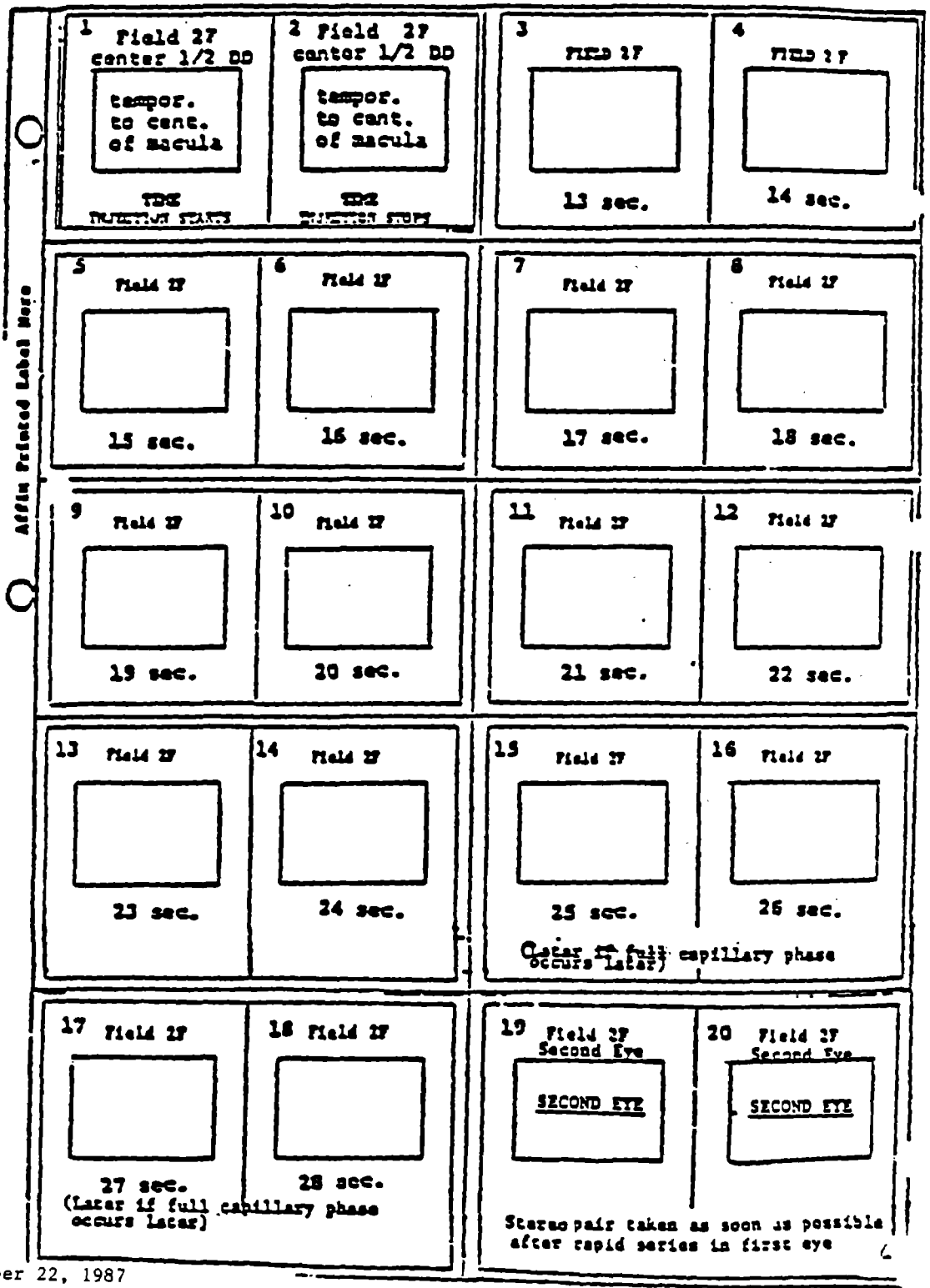
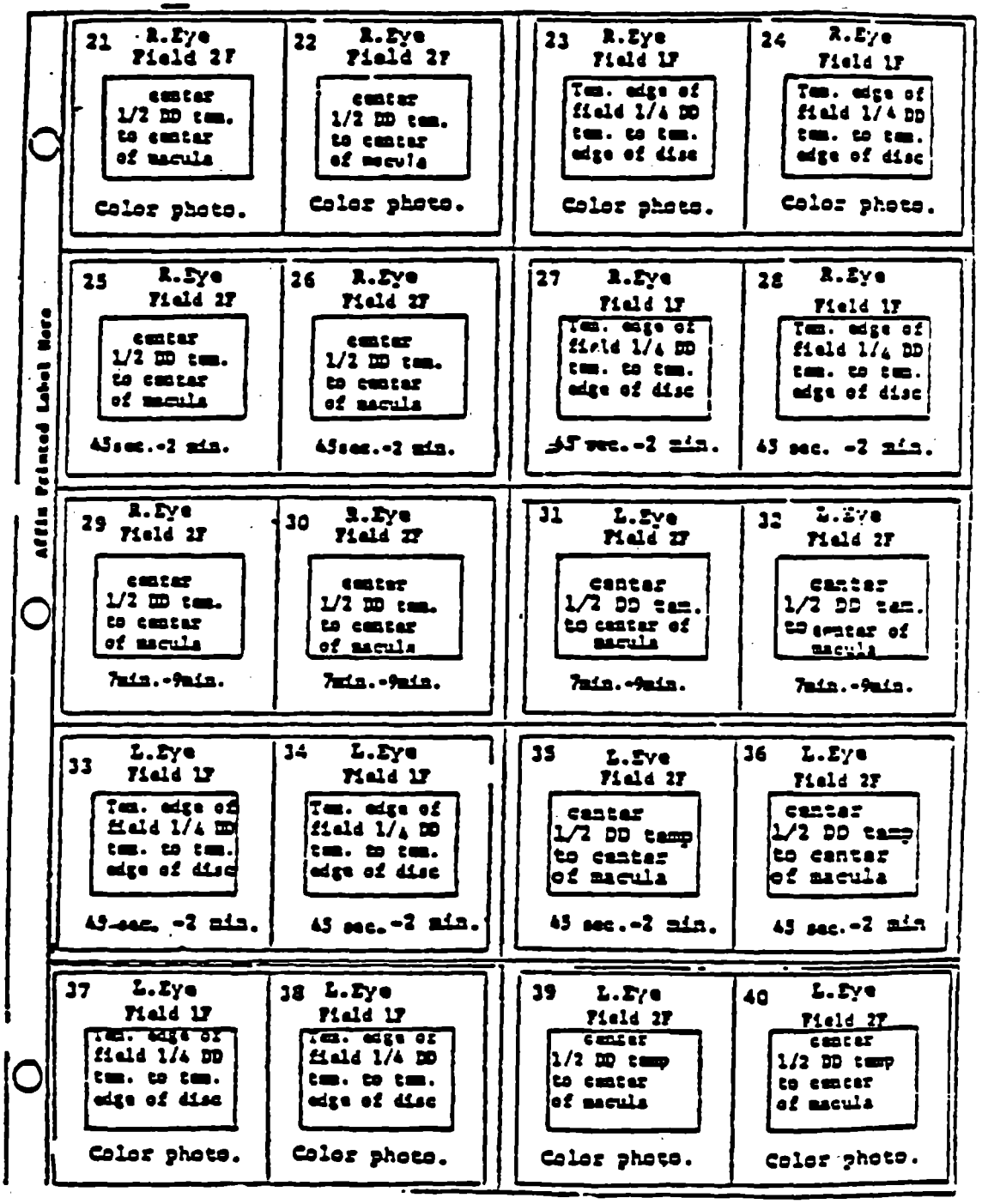


Figure 13.11 (Cont'd)

FLUORESCEIN PHOTOGRAPHS



CHAPTER 14

THE CENTRAL OPHTHALMOLOGIC READING UNIT

14.1 ORGANIZATION

The Central Ophthalmologic Reading Unit (CORU) is a unit of the Department of Ophthalmology in the Medical School of the University of Wisconsin. It is located on the Madison campus of the University of Wisconsin system. Composing the staff of the CORU are the following personnel: Director, Associate Director, Assistant Director, Project Associate (senior grader), Graders, Systems Analyst/Programmer, Biostatistician, Coordinator, and clerical assistants. The CORU functions in the DCCT as a subcontractor of The Biostatistics Center of The George Washington University.

14.2 GOALS

The objectives of the CORU in the DCCT are to perform the following functions:

1. Evaluate color fundus photographs and fluorescein angiograms of subjects submitted for the DCCT to determine ocular eligibility;

2. Grade color photographs in detail using an adaptation of the Modified Airlie House Classification of Diabetic Retinopathy;

3. Grade fluorescein angiograms in detail using an adaptation of the ETDRS Fluorescein Angiography Classification System;

4. Monitor photographs submitted in the DCCT for satisfactory quality, providing feedback and compiling statistics as appropriate;

5. Review the performance of photographers seeking DCCT certifications;

6. Enter grading data into computerized files, edit and summarize the data, and transmit the results to the Coordinating Center;

7. Take measures to assess the quality of the grading programs as they are carried out;

8. Serve as a repository for the photographs submitted in the DCCT, providing safe physical storage and an adequate inventory system;

9. Collaborate with the DCCT Research Group in preparing manuscripts describing ophthalmologic procedures and results.

14.3 ELIGIBILITY ASSESSMENT

Prior to assessment for retinopathy, photographs submitted to establish eligibility are reviewed by a senior grader to be sure that they are of adequate photographic quality. If they are unsatisfactory, a request for retakes is issued to the Coordinating Center, with information also sent to the clinical center furnishing details of the photographic quality observed.

Assuming photographs are satisfactory, retinopathy is then evaluated in detail by two masked, independent graders, using the same procedure and form utilized for follow-up visits as well (described in Section 14.4).

When a grading of record has been determined, a computerized system derives an overall retinopathy level for each eye and determines the overall status of the subject. In cases where retinopathy is judged too severe for entry into the DCCT, a manual review by a senior grader confirms the appropriateness of the finding.

Results of the eligibility assessment are transmitted to the Coordinating Center on a weekly basis using a direct computer-to-computer transfer, with appropriate safeguards against errors in communication.

14.4 DETAILED GRADING OF COLOR FUNDUS PHOTOGRAPHS

Sets of color stereoscopic fundus photographs of each eye taken at the baseline and semi-annual follow-up visits are evaluated for presence and severity of various retinal abnormalities. This grading is performed in duplicate by two graders working independently, with significant differences being resolved if possible through regrading of the problematic lesions, and if necessary through adjudication by a third, more senior grader.

Color detailed grading is carried out under an adaptation of the Modified Airlie House Classification of Diabetic Retinopathy, with the results recorded on DCCT Form 033 (Detailed Color Grading Form).

All editing of data is accomplished using a computerized system that checks for omissions and large discrepancies in the gradings. Regrading and adjudication forms are issued by the computer as necessary, and completed by the original graders or the adjudicator without reference to previous assessments.

Graders are masked to subject ID and clinic as they make their assessments. The order in which photo sets are examined is determined by a randomized reading list arranged so that right and left eyes are not included in the same batch of photographs. The coordinator assembles packets of photos for grading using the reading list as a guide.

Results of the detailed grading are maintained in a computer file. Before transmission of information to the Coordinating Center, completed gradings are further processed to summarize the lesion-by-lesion, field-by-field detail that they contain. Data transfer is accomplished by sending a magnetic computer tape.

14.5 DETAILED GRADING OF FLUORESCEIN ANGIOGRAMS

For primary subjects who enter the DCCT, fluorescein angiograms taken of both eyes at baseline, five years and study termination are evaluated for presence and severity of various retinal characteristics. Grading is performed by a senior staff member specializing in fluorescein interpretation.

Detailed fluorescein grading is done in accordance with a modification of the ETDRS Fluorescein Angiography Classification System, with results recorded on DCCT Form 034 (Detailed Fluorescein Grading Form).

Grading data are edited using a computerized file system that checks for omissions and internal inconsistencies.

The grader is masked to subject ID and clinic. Angiograms are examined in an order specified on a randomized reading list. Packets of angiograms are assembled by the coordinator using the reading list as a guide.

Data from the detailed grading are maintained in a computer file. Before transmission of information to the Coordinating Center, completed gradings are further summarized. Transfer of data is accomplished by mailing a magnetic computer tape.

14.6 PRELIMINARY ASSESSMENT OF FOLLOW-UP COLOR PHOTOGRAPHS

As follow-up visit color photographs are received at the CORU, they are given a preliminary examination for satisfactory quality and for development of retinopathy severe enough to require treatment or at least more frequent observation by the local ophthalmologist.

Any data emanating from this preliminary grading for retinopathy are separate from the information produced by the color detailed grading program. The latter data are to be used for any data analysis; the former are maintained solely to help clinics monitor possible development of retinopathy which may be treatable with laser photocoagulation.

Graders performing the subsequent detailed assessment do not have access to any preliminary evaluation.

14.7 MONITORING OF PHOTOGRAPHIC QUALITY

The CORU program for monitoring photographic quality has two components: (1) an assessment of each photo set received, with feedback to the clinic as appropriate, and (2) a two-step certification program.

As photographs are received at the CORU, each set is assessed for photographic quality. Photos submitted for subject eligibility (which become the baseline photos for those subjects entering the study) are evaluated prior to the detailed grading to determine eligibility. Photographs submitted during followup receive a preliminary examination for photo quality at the same time they are reviewed for development of retinopathy treatable with photocoagulation.

Summaries of the results of the evaluations are sent to the Coordinating Center monthly. Semi-annually, similar summaries are sent to the clinical centers. Occasionally, the CORU mails additional information to the photographers and study ophthalmologists concerning points of the photography protocol.

Before photographers are allowed to submit photos in the DCCT, they are required to send samples of their work for review and approval at the CORU. Extensive comments are returned each time an application is processed. Separate certification is required for color and fluorescein. See Chapter 23 for more details about certification procedures.

When photographers come into the study, they are "provisionally certified," meaning that their work is monitored in detail at the CORU. After they have submitted work of satisfactory quality for a specified period, their certification status is altered to "full," meaning that they no longer have to record a field-by-field quality assessment of their photos. At that time, the CORU as well shifts to a briefer, overall evaluation of the work from those photographers.

Photographers whose work is not generally satisfactory are closely monitored, with suggestions for improvement made as appropriate. For those photographers having problems not remediable in a reasonable period of time, certification for DCCT photography will be revoked.

14.8 HANDLING OF DATA

Data generated by the various grading programs are entered into computerized files, where all editing and further processing is carried out.

Data are entered by clerical assistants using interactive CRT terminals. To check the accuracy of manual entry, a second complete verification entry is made by another data enterer. After that entry is completed, an editing program compares the first and second independent entries, indicating the data fields needing resolution.

As requested by the Coordinating Center and other study leadership, the CORU maintains software to condense and summarize data from the various grading programs.

Transmission of data is accomplished either by direct computer-to-computer transfer or by sending of a magnetic computer tape. The former system utilizes internal checking procedures to be sure information is not garbled in telecommunication, and the latter includes hard copy of the data encoded on the tape for checking.

All CORU data storage systems have provision for backup in the event of loss of a primary file. These procedures allow rapid and economical regeneration of any files needed, either from disk or tape media.

At the end of the DCCT or when requested, the CORU will provide the Coordinating Center with the originals of all data collection forms completed at the CORU.

14.9 QUALITY CONTROL

The CORU program to monitor and improve the quality of grading has internal and external components.

Internally, the CORU provides feedback periodically to graders in programs that entail duplicate independent gradings. This information consists of a comparison of that grader's initial grades with the final "grades of record" resulting either from agreement of the two original graders or from adjudication by a third, more senior grader. Also, retraining sessions are held as necessary to deal with problematic lesions.

In addition to the feedback mechanism, the CORU compiles data and runs statistics on the reproducibility of grading. This effort includes comparisons between graders, within graders over time, and between results of the system at different times. Some of these analyses entail the masked regrading of a small proportion of the photo sets handled by the system (usually 5%).

Periodically, the CORU coordinator is directed by the Coordinating Center to submit specified photographs to the CORU grading programs for a repeat reading. Insofar as possible, the grading personnel are not allowed to know that these masked specimens are being regraded.

14.10 PROCEDURES FOR HANDLING PHOTOGRAPHS

Upon receipt of a package of photographs from a clinic, the CORU staff check the contents against the enclosed shipping list (DCCT Form 042, Fundus Photograph Mailing List). Identifying information is examined to see if all materials are present and appear correct.

If inconsistencies, omissions, or damage in shipping are noted, contact is made by phone with the originating center. If the problem cannot be rectified in this manner, the package is mailed back to the clinic for resolution.

At this point, the photography forms accompanying the photo sets are separated from them so that the sets can be graded in a masked fashion and so that the information on the forms can be entered into the computer file.

In the case of the preliminary assessment for photographic quality (and, in the case of follow-up sets, for development of treatable retinopathy, or retinopathy requiring more frequent monitoring by the clinic ophthalmologist), the photographs are graded as they are received at the CORU. In the case of the detailed evaluations, either for color photos or for fluorescein angiograms, the photographs are graded in a randomized order specified on a computer-generated reading list.

Once photographs have been graded, they are filed permanently in clinic and subject order in steel filing cabinets. This collection is indexed in a computerized inventory system for easy access and retrieval.

14.11 MASKING OF PHOTOGRAPHS

Before it is mailed from the clinic, each photo set is assigned a predetermined coded accession number obtained from a list generated by the Coordinating Center. This is done so that photo sets can be read in a masked fashion in the CORU, avoiding any possible bias involving subject, clinic or visit.

When each set arrives at the CORU, it is labeled in the following fashion: each individual slide has a pre-printed adhesive-backed label affixed giving the accession number for the set, and each set has a main sheet label containing both the accession number and the actual identifying information. The main sheet label is located so that a clerical assistant can attach an opaque cardboard mask concealing the actual identifying information from the graders.

Once the set has been fully graded, the mask is removed so that the set can be filed in the proper spot in the permanent file. During grading, a temporary file organized by accession number and reading list is utilized.

It is necessary for the CORU coordinator to have access to the actual identifying information. This is essential for effective checking of incoming shipments, and for any communication with the clinics. By reposing the key in the computerized inventory system as well, it is possible for the CORU to check that all of the required photo submissions are received as they are expected for each subject.

14.12 REPORTS

14.12.1 To the Coordinating Center

The CORU is required to report monthly to the Coordinating Center regarding both its own performance and the performance of clinics in the DCCT.

14.12.2 To the Investigators

Endpoint visit photographs will be reviewed by the CORU in a timely fashion and the Principal Investigator will be notified if any of the following are observed: any proliferative retinopathy; severe non-proliferative retinopathy; moderately severe NPDR, if accompanied by progression of at least three steps on the retinopathy scale during the past year or clinically significant macular edema (DCCT Forms 071 and 094, Observation of Proliferative or Severe Nonproliferative Diabetic Retinopathy and Observation of Clinically Significant Macular Edema).

CHAPTER 15

THE CENTRAL BIOCHEMISTRY LABORATORY

15.1 INTRODUCTION

The Central Biochemistry Laboratory (CBL) will actively participate in the trial, providing important information on the subjects in the study and their abilities to control their diabetes. Since this study may last several years, the continuity of laboratory performance is central to the outcome of the trial including daily monitoring of quality control. Nevertheless, it is important to emphasize that the quality of the laboratory and its work depends in a fundamental way upon the quality of the specimens obtained in each of the clinical centers. Thus, prompt processing and preservation of specimens under ideal conditions with secure and speedy delivery to the CBL will help to maintain the quality of laboratory work. Any questions regarding procurement, preservation and delivery of the specimens should be directly addressed to the laboratory.

15.2 PROCUREMENT OF SPECIMENS

15.2.1 The Facility

Blood and urine specimens will be obtained for assays in the local laboratory (for eligibility studies only) and for measurements in the central laboratory (for eligibility, for baseline studies and for follow-up monitoring). Under optimal circumstances, a facility oriented for examination of patients and procurement of specimens should be utilized; e.g., Clinical Research Center or Outpatient Clinic. Extended protocols for C-peptide and renal function testing will require a place for the patients to remain during each period of testing. Supplies for drawing blood and obtaining urine include venipuncture tubes, needles, containers, alcohol swabs, tourniquet, and racks to hold the tubes and containers. Equipment, including a centrifuge to spin the blood specimens, is ideally located adjacent to the patient facility.

15.2.2 Supplies for Blood and Urine Specimens

All containers utilized with each patient for the procurement of blood or urine samples must be labeled with an accession number. The central laboratory and the Coordinating Center have collaborated to produce a matching set of labels and forms, attempting to minimize labeling errors. The set of labels generated by the Coordinating Center contains sufficient copies so that the samples for blood can be drawn into labeled tubes, and all voided specimens can be collected into labeled containers. Prior to obtaining these specimens, appropriately labeled venipuncture containers and urine receptacles should be organized and available. The procedures outlined in subsequent sections will identify the containers needed for each protocol in the study.

15.2.3 Drawing Blood

Prior to drawing blood, it is imperative to recheck the appropriate accession numbers, labels and forms for the patient. Blood is drawn from an antecubital vein or another convenient vein in the arm. The venipuncture site is swabbed with an alcohol wipe and allowed to dry before venipuncture. The tourniquet is applied prior to venipuncture and removed after successful venipuncture. The person drawing the blood should be sufficiently well organized so the tourniquet will be in place no longer than 30 seconds after venipuncture. Vigorous motion of the arm to attempt to improve the ability to locate a vein should be avoided. Care should be taken to minimize formation of hematomas. The needle is introduced into a vein, and the required number of vacuum containers are filled as completely as possible. All vacutainers containing additives must be gently inverted at least four times to mix the blood and the additive. A dry pad is used to apply pressure when removing the needle, since a wet pad might result in fluid being drawn into the vacutainer.

15.2.4 Processing Specimens

Once the appropriate amount of blood is drawn into the correct vacutainer tube as listed for each test (Table 15.1), prompt processing must be done. Glycosylated hemoglobin tubes will remain as whole blood and must be refrigerated immediately at 4 degrees C (i.e., plus or minus 2 degrees C)[1] until sent to the laboratory.

The red-topped tubes should be allowed to clot for at least 20 minutes and are then spun in a centrifuge at room temperature for 10 minutes at 3000 rpm. Separation of serum and cells should be accomplished within 30 minutes after drawing the blood. Separate the serum with a transfer

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[1] The particular refrigerator used should be calibrated to ensure adequacy of holding 4 degrees C plus or minus 2 degrees C using an accurate max-min thermometer.

pipette into labeled containers and place in a rack in a freezer that does not pass through a frost-free cycle. It is important that the specimens, once frozen, are not thawed.

For urine specimens, the voiding(s) during the renal testing protocol must be collected on ice and pooled into one container with the total volume measured and recorded. Aliquots of this specimen will then be frozen and forwarded to the CBL.

15.2.5 Recommended Precautions for Preventing Transmission of Bloodborne Infectious Diseases

The processing of human biological specimens presents significant biohazard safety concerns. The individuals involved should work under the assumption that all biological specimens may be infectious and require scrupulous aseptic handling.

Routes of Infection: Infectious microorganisms may be contracted by several primary routes. They are:

1. Droplet aerosols. These may be formed when liquids are agitated to cause microscopic droplets to leave the surface of the liquid and become airborne. Aerosols may be created by pouring or pipetting liquids, removing tightly fitting caps from test tubes and during centrifuging.

2. Ingestion. This occurs when infectious microorganisms are taken into the mouth and swallowed. Avoid hand to mouth contact, poor hand washing practices, mouth pipetting of biological specimens and placing objects in the mouth such as pencils, etc.

3. Direction Inoculation. Parenteral exposure occurring as a result of a break in the skin barrier or contact with mucous membranes (conjunctiva). Examples are nicks, cuts, scratches, needle sticks, or splashes to the eyes.

Several Ways to Assure Infection Control Protection During Venipuncture are:

1. Gloves are to be worn when drawing blood from suspected AIDS patients and handling blood specimens and blood soiled items.

2. Needles should be considered as potentially infective and be handled with extraordinary care to prevent accidential injuries.

3. Disposable syringes and needles should be placed into puncture-resistant containers located as close as practical to the area in which they were used. To prevent needlestick injuries, needles should not be recapped, purposefully bent, broken, removed from disposable syringes, or otherwise manipulated by hand.

4. Blood spills should be cleaned promptly with a disinfectant solution such as sodium hypochlorite.

Several Ways to Assure Infection Control Protection During Specimen Processing are:

1. All specimens are to be treated as if they are contaminated; that is, a source of hepatitis B virus, AIDS agent, slow virus such as Creutzfeldt-Jacob or other disease producing agents.

2. Protective rubber gloves are to be worn when processing high risk specimens.

3. All specimens must be capped when centrifuged.

4. All specimens are separated/aliquoted with transfer pipettes, not by pouring.

5. Mouth pipetting is to be avoided.

6. Frequent hand washing with an approved antiseptic soap is essential.

7. Work areas should be cleaned with phenolic disinfectant or 1% sodium hypochlorite solution.

8. High risk (blood precautions/isolation) and known hepatitis specimens are to be sent to the laboratories appropriately labeled and contained in their own plastic bags. The mailing lists are not to be in the bag with the specimen. The word "isolation" or "blood precautions" should be noted in the comments section of the mailing list.

9. All potentially contaminated materials should be decontaminated, preferably by autoclaving, before disposal.

10. The use of a profilset must be limited to one patient. Do not interchange these kits among patients.

11. Blood glucose meters can be safely disinfected with 70% alcohol or other suitable cleansing agent. Do not use Betadine. Removable pieces must be dried thoroughly before reassembling the meter. Care must be taken when cleaning around the display window so as not to get cleaning solution inside the instrument.

15.2.6 Status of the Patient

Instructions regarding the patient are listed with each of the protocols. For drawing eligibility and baseline specimens for the C-peptide test and for lipids, the patient will be fasted prior to procurement of the specimen. The protocol of the Lipid Research Clinic Laboratory emphasizes that patients are instructed to take nothing by mouth other than water for at least 12 hours prior to sampling. This will cause difficulty in managing diabetic patients, but standardized specimens require a fasting period of that length. Therefore, as a compromise, before drawing blood, the subject is asked about his food intake during the previous 12-16 hours. Assure that the patient has fasted for at least eight hours. This may reveal a small number of subjects who in fact did not fast. If you determine that the fast was broken, reschedule the collection.

In the four-hour timed urine testing, fasting is not required. Ideally, this procedure should be performed after breakfast and following the patient's morning insulin dose. However, testing anytime of day or night is allowed. In both morning and afternoon testing sessions, the usual snack is allowed. Caffeine is to be avoided immediately prior and during the test period. It is important that the person be in a resting and relaxed state and should have avoided hard exercise one day preceding the renal testing. The test should not be done when the patient has a urinary tract infection or is actually ill. The patient will be asked to drink copious amounts of water during the testing protocol. Any symptomatic hypoglycemia which the patient or anyone else must treat with food is cause to end the collection (see Renal Studies, Section 15.6).

If the reaction occurs prior to the studies, the patient should be without any symptoms for an hour prior to the commencement of the collection. Questions regarding individual circumstances should be referred to the CBL.

15.2.7 Determinations Measured in the Local Laboratory

As designated in Table 6.2, several determinations will be performed as eligibility tests in the local laboratory. These determinations are to assess the overall health of the patient, to exclude a patient with positive pregnancy test, a positive test for hemoglobinopathy or an abnormal TSH. Results of procedures will be recorded on DCCT Forms 004 and 006 and forwarded to the Coordinating Center. If the laboratory is changed during the course of the study, the new laboratory must supply the Coordinating Center the information requested on the Documentation of Local Laboratory Certification (DCCT Form 007).

15.2.8 Determinations to be Performed in the Central Biochemistry Laboratories

For simplicity and convenience, we have organized by category the eligibility and baseline tests to be performed by the central laboratories. Therefore, the number of protocols needed for procurement of laboratory tests has been limited. It is important to emphasize that the C-peptide test must be performed on a separate day from the protocol for renal function testing. Separate days for these tests will require careful scheduling by the clinic (see Table 15.1).

15.3 BLOOD GLUCOSE PROFILES

The directions for procuring specimens for the blood glucose profiles are given in Section 12.3. The patient will be provided with instructions, lancets, alcohol wipes, capillary tubes into which to draw the blood and a set of tubes containing hemolyzing reagent. Promptly following appropriate filling and wiping of the capillary tubes, they will be placed in the hemolyzing reagent and thoroughly mixed. The following points emphasize the technical and organizational aspects of procuring these specimens.

It is very important that the capillary tubes be filled accurately. Small (on the order of one microliter) mistakes by the patient in filling these tubes can cause dramatic differences in the measured glucose levels. Therefore, each clinical center should spend significant time instructing each patient in appropriate procurement of these specimens. All tubes must be free of bubbles and filled completely end to end with all traces of blood removed from the outside. The latter can easily be done with a finger.

The capillaries are placed in the tubes containing hemolyzing reagent (stored in the refrigerator) and appropriately mixed. The mixed tube is placed into the rack in the refrigerator until all specimens in a series are collected.

One or two days prior to the quarterly and annual endpoint clinic visits, the patient should perform the capillary blood glucose profiles.

After all specimens have been collected and stored appropriately in the patient's refrigerator, the entire profile must be delivered to the clinic. The profile can be brought to the clinic by the patient who should be advised to avoid placing the profile in extreme heat (e.g., locked trunks, cars, etc.).

The clinic will store the hemolysates in a -20 degrees C freezer (that does not vary significantly in temperature) and then forward them to the Central Biochemistry Laboratory at the University of Minnesota.

Upon receipt of these profiles, the specimens will be logged into the laboratory, stored, and thawed only on the day the assays are performed.

Results will be reported directly to the Coordinating Center. If the patient misses the scheduled appointment, advise the patient to freeze the profile and to bring it to the make-up visit.

15.3.1 Clinic Preparation of Hemolyzing Reagent for Profile Set

This reagent hemolyzes the patient's red blood cells in the capillary tube and acts as a preservative and diluent for the glucose test to be performed by the CBL. An accurate blood glucose profile of a patient is dependent upon the careful preparation and exact dispensing of the hemolyzing reagent for the profile kits. Directions must be followed explicitly with careful attention to expiration dates. Amounts prepared at any one time will vary with an individual clinic's needs and should not be stored longer than four weeks at refrigerator temperatures or six months frozen.

15.3.1.1 Reagents

1. Hemolyzing Reagent Tablets -- Provided to clinics by manufacturer. Stable up to the expiration date specified when stored at +2 degrees C to +8 degrees C.

2. Reconstituted Hemolyzing Reagent -- Stable for four weeks at +2 degrees C to +25 degrees C. Stable for six months at -20 degrees C.

3. Redistilled water.

15.3.1.2 Equipment

1. Profile set (Profilset) -- Provided to clinics by the Coordinating Center.

2. Dilution tubes -- Ordered through the Coordinating Center and provided to clinics by the CBL. Profilset can be reused.

3. 50 ml volumetric flask or 50 ml graduated cylinder.

4. 50 ml beaker.

5. Class A one ml volumetric pipet or automatic pipetting device capable of delivering 1.0 ml, e.g., Pipetman Pipet, Brinkman Instruments, Inc. Instructions for proper use of these pipettes and accuracy and precision checks may be obtained from the CBL upon request.

15.3.1.3 Procedure

1. Replace the 10 tubes in the profile set with the dilution tubes provided. These tubes will ensure no leakage in transport for the patient and proper storage while frozen for the clinic and for shipping to the CBL.

2. Dissolve one reagent tablet in 50 ml redistilled water.

3. Mix thoroughly.

4. Pipet 1.0 ml of hemolyzing reagent (room temperature) into each of 10 tubes in the glucose profile set.

5. Place filled profile set in refrigerator or freezer until patient use.

6. Before dispensing to patient, properly label all tubes with appropriate labels provided by the Coordinating Center.

15.4 C-PEPTIDE TESTING

The C-peptide test (described in Chapter 12) begins with an eight hour overnight fast for the patient. The C-peptide test is an eligibility procedure as are the creatinine and cholesterol measurements done on the fasting specimen. Blood for pre- and 90-minute post samples is drawn into red-topped tubes (see Table 15.1). The separated serum is divided into two aliquots and frozen. One aliquot is sent frozen to the CBL at the Univesity of Minnesota. The other aliquot is frozen securely in the clinical center; it can be forwarded to the CBL should there be a problem with the first sample.

With respect to the C-peptide analyses done both at pre-dose (fasting as described above) and at 90 minutes following ingestion of the nutrient, the blood samples should be processed rapidly with the serum separated and frozen for later shipment to the CBL. (See Chapter 12 for more details on procedures.)

15.5 CHOLESTEROL/TRIGLYCERIDE/HDL CHOLESTEROL

The eligibility measurement of cholesterol will be done on the fasting serum specimen also used for the C-peptide test (by the CBL). The baseline specimen for measurement of cholesterol, triglycerides, and HDL cholesterol will be drawn and sent to the CBL two weeks prior to randomization.

Again, the lipids must be drawn after minimally an eight hour fast. Draw blood into a 10 ml red-topped serum tube, separate the serum and freeze the separated serum in two aliquots, one of which is shipped to the CBL.

15.6 RENAL STUDIES

15.6.1 Creatinine and Albumin in Serum and Urine

The measurements of creatinine and albumin in serum and urine must be considered together within one protocol used in determining renal function. Measurement of creatinine in serum and urine, appropriately collected over a defined period of time, will allow calculation of the patient's creatinine clearance. Coupling these values with the albumin levels in the same serum and urine specimens will provide a relative index of the urinary excretion of albumin.

One organizational difficulty with this protocol encompasses the needs to determine eligibility with respect to albumin excretion and to utilize the same measurement for baseline values (if the patient is accepted into this study). Since the protocol for this study is complex, the following explanation assumes that one carefully managed collection procedure can be utilized to send specimens to the CBL both for eligibility and for baseline measurement (see Table 15.1).

When all patient conditions are satisfied (see Status of Patient, Section 15.2.6), renal function testing is begun. Blood glucose monitoring may be done before and during the testing to avoid symptomatic hypoglycemic episodes which would be reason to abort the collection.

First ask the patient to void, discard this specimen and record the time of voiding. During the course of the protocol, the patient will be asked to drink 250 ml of water every half hour. After four hours (and sooner if the patient wishes to void during the course of the study) ask the patient to void, measure the volume of urine voided during the course of the study and record the time of voiding at the end of the study. This time and time noted at the beginning of the study can be used to determine the duration of the study. Total urinary output volume should be at least 400 ml during the four hour collection or 100 ml/hour. Make all collections on ice and mix all collected urine.

Record total volume, time, date and patient's height and weight. Transfer 4.5 ml (see side of tube) of well-mixed urine to each of five appropriately labeled containers. Freeze all specimens and retain one frozen aliquot in the clinical center. Send the remaining four aliquots for creatinine and albumin determinations to the CBL. The extra containers will be stored in the CBL at -70 degrees C for possible reprocessing of specimens at a future time.

Any time during the second two hours of the four-hour protocol, draw 10 ml of blood into a red-topped tube and promptly separate the serum. Divide the serum into two appropriately labeled containers and freeze. Send one aliquot to the CBL for determination of creatinine and albumin and retain one aliquot in the clinical center.

If a patient becomes hypoglycemic after the third hour, end the collection by having the patient void and record the time at this point. This collection may be considered valid and sent to the CBL. A recollection may be required if notified by the Coordinating Center.

If the four-hour urine collections are carried out with GFR the detailed instruction given in Chapter 12 should be followed.

15.6.2 GFR

(See Chapter 12)

15.6.3 24-Hour Urine

(See Chapter 12)

15.7 SAVED SPECIMENS

Specimens, both serum and plasma, are to be obtained in the fasting state from all DCCT patients at baseline and at the annual endpoint visit when a blood specimen is drawn for the assay of lipids. The purpose of this collection is to have a central storage of extra serum and plasma so that assays, currently unspecified, may be performed in the future, if necessary. In the following section, specific instructions are given for the collection, manipulation and storage of these specimens.

1. Draw one 10 ml red-topped tube, allow to clot for at least 20 minutes and spin in a centrifuge at room temperature for ten minutes at 3000 rpm. Separate the serum into three 1.8 ml cryotubes (Nunc or Costar) and promptly freeze.

2. Draw 7 ml EDTA (lavender stopper, T204Q, 13 x 100 mm) tube to which 500 U Trasylol (aprotinin) per ml of whole blood has been added:

   a) With a black felt-tip marker (waterproof), measure and mark EDTA tubes with a black line for 7.35 ml of whole blood. Use one tube filled with liquid as a calibrator.

   b) Add 0.35 mls (equivalent to 3500 U) of Trasylol to the EDTA tube. This can be done with a pipette or if using an insulin syringe U-100, add 35 units to the tube. A 20 G disposable hypodermic needle can be inserted through the lavender rubber stopper when adding the Trasylol. Tubes containing Trasylol are kept refrigerated.

   c) Fill chilled tube containing Trasylol to the black line with whole blood (7.0 ml). Mix thoroughly and place on ice immedi
   refrigerated centrifuge at 2000 rpm for ten minutes. The plasma is transferred to three 1.8 ml cryotubes and immediately placed on dry ice where it will freeze in five to ten minutes.

3. All 1.8 ml vials are labeled with the accession number utilized for the lipid profile specimens. Labels for saved specimens are provided.

4. Send the three vials of serum and the three vials of plasma to the Central Biochemistry Laboratory in Minneapolis with the baseline or annual lipid profile specimen. Indicate in the comment column of the mailing list (DCCT Form 058) that these include serum and/or plasma saved specimens.

15.8 STORAGE OF FROZEN SERUM AND URINE SPECIMENS PRIOR TO SHIPMENT TO THE CENTRAL BIOCHEMISTRY LABORATORY

Each clinical center is asked to identify a freezer (minimally -20 degrees C) that can serve for safe storage of serum and urine specimens. Furthermore, the temperature of the freezer should be checked with sufficient frequency to determine whether the temperature varies significantly. Please utilize a freezer that is not an automatic defrost type. These freezers pass through a warm cycle to prevent the build up of frost on the inside. In doing so, this warm cycle may actually thaw the specimens contained therein. It is very important that these specimens not be thawed following initial freezing. The first thawing should occur at the CBL when the specimens are processed.

15.9 SHIPMENT TO THE CENTRAL BIOCHEMISTRY LABORATORY

Concerning the security and integrity of the specimens, shipment to the central laboratory is the most difficult part of the procedure. For serum and urine specimens and the blood glucose profiles, specimens will be sent frozen to the CBL. For glycosylated hemoglobin measurements on whole blood, specimens will be sent on ice and water mixture to the CBL. The Federal Express account number for the shipment to the CBL is 1085-9444-6. Use the following appropriate protocol when shipping to the laboratory.

15.9.1 For Frozen Specimens

Shipment should always be done on Monday or Tuesday of each week (being careful to avoid any weeks in which a holiday may occur). Shipping on Monday or Tuesday avoids problems in transporting the specimens over weekends.

Each clinical center should utilize the following protocol:

1. Using the insulated shipping containers provided for frozen specimens, pack the specimens with at least two and a half to three pounds of dry ice. This amount could be increased during

the warmer months. Groups of specimens should be bound with string or placed in plastic bags. Enclose the completed specimen mailing list and a return shipping label.

2. Complete the appropriate shipping forms for the carrier (Federal Express in the United States and Purolator in Canada) selected to transport the specimen from your location to the CBL.

3. Once the shipment has been forwarded to the shipper, telephone the CBL to state the number of specimens that has been forwarded, including pertinent information regarding your clinic number and the shipper.

4. Upon receipt of the specimen, the CBL will send a return postcard to the clinical center identifying successful receipt of the specimen or problems regarding preservation of the specimens at receipt.

5. Shipping containers and other supplies will be returned to each of the clinical centers by UPS or the U. S. Postal Service. If you are running short of any supplies, please contact the CBL or the Coordinating Center.

15.9.2 For Whole Blood

1. 3.5 ml of the 7.0 ml whole blood taken in EDTA is aliquotted into plastic (polypropylene - NUNC TUBE : 5ml) screw-top tubes (3.5 ml remainder is kept at four degrees C as backup).

2. Proper label is placed on tube. Label will contain specimen accession number.

3. Tubes of whole blood are pre-cooled to 4 degrees C in the refrigerator or placed in a crushed ice and water mixture for 5-10 minutes before placing in quart size thermos bottle just prior to shipping.

4. An open quart size stainless steel thermos is pre-cooled to 4 degrees C for four hours or kept at 4 degrees C until needed.

5. Pack one inch crushed ice in the bottom of the thermos bottle. Eight to 10 tubes may then be placed in the thermos bottle. Then add four ounces cold tap water and fill thermos with fine size crushed ice. DO NOT HARD PACK. Screw on top tightly so it will not leak water into shipping container.

6. Place thermos bottle in the center of polystyrene shipping container.

7. The space around the thermos is packed with reusable brown paper wadding provided by the Laboratory. Close shipping container and

tape with strong tape. Place shipping labels on containers. (Do not throw away previously acquired icepacks.

8. Enclose label for return by standard mail or UPS to your clinical center. Please do not forget this label.

9. Ship by "FEDERAL EXPRESS" (in U.S.A.) or "PUROLATOR" (in Canada) or other carrier with 24-hour overnight express service.

10. Until notified, ship any and all accumulated samples Monday through Thursday. It is important that specimens be shipped as soon as possible after collection. No specimens should be retained in the clinic for more than four days.

SUPPLIES:

1. (1) Plastic screw-top tubes used for blood -- "Cryotubes" Nunc #1086-1 5 cc polypropylene tubes, Vanguard International, Inc., Neptune, New Jersey.

2. (2) Quart size Aladdin's Stanley Thermos #A944C or equivalent.

3. (3) Polystyrene shipping container -- Polyfoam Packers Corp. Model #355.

15.10 SPECIMEN IDENTIFICATION

An accession number is pre-assigned to each specimen, separately for hemoglobin A_{1c}, C-peptide, renal studies 4-hour urine and serum, GFR and 24-hour urine, lipids, and blood glucose profile. Accession numbers will be prepared by the Coordinating Center and sent to each clinic on a yearly basis for randomized patients. Labels for screening potential volunteers will be generated periodically during recruitment.

Each clinic will be provided with a sequence of accession numbers in blocks of 10,000 contiguous numbers. The blocks will be scrambled and assigned to the clinics.

The accession number labels are printed on a continuous roll with enough duplicates of each number for separate aliquots and mailing lists.

Each specimen tube forwarded to the CBL will be labeled only by accession number. 3-M Scotch Tape should be wrapped around the tube, completely covering the accession number label. The appropriate specimen mailing list, which provides the patient identification for each specimen included in a shipment, is included with the shipment and copies are sent to the laboratory and to the Coordinating Center under separate cover.

The Coordinating Center, prior to the start of the study, has assigned a unique accession number to each patient for each and every specimen collected. Therefore, for example, a patient has four different

accession numbers for hemoglobin A_{1c} per year plus additional numbers for external quality control purposes and for interim visits, if they are necessary.

15.10.1 Patient Schedules of Accession Numbers

The schedules provide identification of the patient, visit and specimen (see Figure 15.1). In the upper right-hand corner you will find the patient's identifying information. Visits have been given sequential month numbers. Quarterly visits are referred to as QV and a number which you will use in completing all forms related to that visit. Thus, QV 05 is the fifth quarterly (or follow-up) visit, QV 08 is the eighth quarterly visit (it is also the second annual visit).

Routine management visits (for experimental patients) between quarterly visits will normally be referred to by their month number (e.g., 13 or 14). For descriptive purposes, we have labeled these visits as "a" and "b" following the quarterly visits. For example, visit RM 04a is the first routine management visit following QV 04; RM 04b is the second routine management visit. Target dates are listed for quarterly and routine management visits.

Standard group patients may be seen on an "interim" basis between quarterly visits; these visits are scheduled as needed.

Quality control samples are to be collected if an accession number appears in one of the quality control columns. If the blood glucose profile series is to be quality controlled, the number of the stick (1 through 7) is noted in the patient schedule. This quality control sample will be labeled as BGP-8. Please note under "Comments" that the quality control sample BGP-8 is included when filling out the Blood Glucose Profile Mailing List (DCCT Form 050) to be sent to the Central Biochemistry Laboratory. If the GFR procedure is to be quality controlled, the time period to quality control (Pre, 1, 2, 3 or 4) is noted on the patient schedule. The quality control scheme for the GFR requires that both the blood and urine collection for the specified time be duplicated, labeled as "U-5" and "B-5" and sent to the CBL along with the rest of the samples for the specified patient. For all other samples (HbA_{1c}, lipids, urine, serum and 24-hour urine), a split aliquot will be collected at the designated scheduled visit and will be handled as an entirely separate sample. Refer to the confidential memo to the clinic staff regarding the handling of quality control specimen. Remember: If the renal studies are indicated to be quality controlled, then ALL components (four-hour collection, GFR, 24-hour collection) are quality controlled.

15.10.2 Accession Numbers for Specimens Which Are Retaken

Any time a second specimen of the same accession number is sent to a central laboratory, the accession number should be marked with a preceding "R." Instances in which this might occur (for example):

1. A HbA_{1c} specimen received at the CBL is hemolyzed and a retake is therefore requested.

2. The investigator strongly believes that a HbA_{1c} value reported back by the laboratory is inaccurate because of the patient's clinical presentation. The sample should be redrawn within two weeks of the time the clinic was notified of the result.

3. A specimen sent to the CBL is delayed or lost by the express carrier and the backup or a retake is requested.

In the case that an investigator wants to track a patient very intensively and obtain a HbA_{1c} specimen more often than once per month, an extra specimen may be sent to the CBL. The specimen should be identified by that patient's most recent medical management (not quarterly) accession number, prefixed by the letter "M" for "medical management."

15.10.3 Accession Number Labels

The labels are divided into sections by information that identifies the patient, clinic, visit month, visit type, and target date for each visit. Following this are all the labels you should need for the visit, plus an extra in case some labels are unusable.

The prefixes used indicate the type of sample being collected. H- preceeds all HbA_{1c} accession numbers, CP- and CPT- indicate C-peptide testing, L- all lipid numbers, U- 4-hour urines, and S- 4-hour serum numbers. GFR- indicates ^{125}I-Iothalamate clearance with a letter and number indicating the collection type and time, e.g., U-0 for urine at time 0 or B-4 for serum (blood) at time 4. 24H- indicates the 24-hour urine collection. BGP- indicates the blood glucose profile series with a number used to identify the sample sequence.

All labels containing the word "sample" or "samp" are to be placed on the collection tubes. Likewise, "mailing" and "mail" signify that the label is to be used on the appropriate Forms Mailing List (DCCT Form 043 for C-peptide, DCCT Form 044 for urine and serum, DCCT Form 050 for blood glucose profiles, DCCT Form 055 for HbA_{1c}, DCCT Form 058 for lipids, DCCT Form 100 for GFR specimens, and DCCT Form 101 for 24-hour urine collections). Be sure to put a label on each copy of the no-carbon-required (NCR) forms.

The series of labels used for lipid collections at annual visits contain additional labels to mark saved specimens as "Tras" if they

contain Trasylol or "No Tras" if they do not. You should send these extra six specimens to the CBL with the annual collection of lipids for each patient.

15.11 SPECIMEN MAILING LIST

For each shipment of specimens to the CBL the appropriate mailing list, DCCT Forms 043, 044, 050, 055, 058, 100, 101, etc. should be completed to identify all specimens included in the shipment. Note any abnormalities of collection in the "Notes" section of the appropriate mailing list. For example, if a study is terminated early, that a QC sample is included for BGP or GFR studies, or that the four-hour renal study was performed in conjunction with the GFR test.

15.12 REPORTING RESULTS TO THE DCCT COORDINATING CENTER

During Phase II the transmission of results from the CBL to the Coordinating Center was accomplished by the CBL Reporting Log (DCCT Form 023). The CBL Reporting Log was mailed to the Coordinating Center in a weekly mailing.

In Phase III the results from the CBL were transferred to the Coordinating Center via the telecommunication system (See Chapter 26).

15.13 EXTERNAL QUALITY CONTROL OF THE HBA1C ASSAY

The laboratory at the University of Missouri serves as the backup laboratory (BHL) for the HbA_{1c} assay. In the event that a catastrophe (such as a fire) necessitates closing the CBL for a period of time, the DCCT HbA_{1c} specimens will be sent to BHL for analysis. Split samples, about 5%, are analyzed in both laboratories to document the comparability of the laboratories.

In the following paragraphs, the details of this procedure are outlined:

1. Use the same form as is used for submission of hemoglobin A_{1c} specimens to the CBL (DCCT Form 055, Hemoglobin A_{1c} Mailing List).

2. Using the system of accession numbers designating submission of the quality control specimen to the CBL, divert half of the 10% sample to the BHL.

3. Those clinics whose clinic number is even send the secondary sample or quality control split to Columbia in months that are even. So, for example, clinics 02, 04, 06, 08, 10, 12, etc.,

would send splits to the BHL in months February (2), April (4), June (6), August (8), October (10), and December (12). The even numbered clinics would send the split duplicates for quality control to the CBL in the other months.

4. The clinics whose clinic number is odd will send the split duplicates to the BHL in the odd numbered months January (1), March (3), May (5) July (7), September (9), and November (11). The odd numbered clinics are to send the quality control to the CBL in the even numbered month.

5. So, in summary, the quality control procedures for the laboratory-to-laboratory comparison are:

Clinic Number	Even Numbered Months	Odd Numbered Months
02, 04, 06, 08, 10, 12, 14, 16, 18, 20, 22, 24, 26	BHL	CBL
01, 03, 05, 07, 09, 11, 13, 15, 17, 19, 21, 23, 25, 27, 41	CBL	BHL

6. Use the same Federal Express number that is used to send specimens to the CBL and simply change the address.

Instructions for shipping to the University of Missouri Health Science Center are the same as those instructions that are in effect for the shipment to the CBL, except the address change.

15.13.1 Discarding Locally Saved Specimen for Backup

All frozen specimens (urine, serum, plasma) should be discarded appropriately one year after the date of collection. A year will be sufficient time for the Coordinating Center to detect the loss of data from specimens lost in transit.

All whole blood samples should be discarded after the two weeks.

Table 15.1

Tests Performed By Central Biochemistry Laboratories

Procedure	Tests	Status and Frequency	Special Specimen Requirements
C-Peptide			
Pre-dose Serum (10 ml red-topped tube)	C-peptide cholesterol creatinine glucose	Eligibility	Serum frozen in 2 equal aliquots
90-minutes post--Serum (10 ml red-topped tube)	C-peptide glucose	Eligibility	Serum frozen in 2 equal aliquots
Renal Studies			
Creatinine Clearance and Albumin Excretion			
Serum (10 ml red-topped tube)	Albumin creatinine	Baseline and annually	Serum frozen in 2 equal aliquots
Urine (timed urine collection)	Albumin	Eligibility and annually	Urine frozen in 5x4.5 ml aliquots
Urine (same urine collection)	Creatinine albumin clearance creatinine clearance	Baseline and annually	
24-hour Urine Collection	Sodium urea nitrogen creatinine	Baseline, second, fifth year and termination	Urine frozen in 24.5 ml aliquots
Glomerular Filtraton Rate (GFR)	GFR (Gamma counts)	Baseline, third year and termination	Serum frozen in 6 EXACT 1.8 cc aliquots, remainder of serum frozen in 6 (1.8 cc) vials Urine frozen in 10 EXACT 1.8 cc aliquots

Tests Performed by Central Laboratories (Continued)

Procedure	Tests	Status and Frequency	Special Specimen Requirements
Lipid Profile Serum (10 ml red-topped tube)	Cholesterol triglycerides HDL cholesterol LDL (Calculated)	Baseline and annually	Serum frozen in 2 equal aliquots
Saved Specimen	Unspecified	Baseline and annually	Serum and plasma frozen separately in 6 equal (1.8cc) vials, 3 plasma with Tracylol, 3 serum without Trasylol
Blood Glucose Profile Capillary blood (obtained by patient as per instructions)	Glucose	Baseline and quarterly	(see explanation)
Glycosylated Hemoglobin (HbAlc) Blood (7 ml EDTA tube)	Glycosylated hemoglobin	Eligibility and baseline and quarterly and monthly in experimental patients	whole blood divided into 2-5 ml transport tubes

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FIGURE 15.1

DIABETES CONTROL AND COMPLICATIONS TRIAL

Hemoglobin A1c Reporting Log

Analyses Performed From

__ __|__ __|__ __ TO __ __|__ __|__ __
Month Day Year Month Day Year

COLLECTION DATE			DATE OF ARRIVAL			DATE OF ANALYSIS			ACCESSION NUMBER	CLINIC NUMBER	PATIENT ID NUMBER	PATIENT'S INITIALS			HEMOGLOBIN A1c RESULTS	CODE
Month	Day	Year	Month	Day	Year	Month	Day	Year				F	M	L		
									H-						.	
									H-						.	
									H-						.	
									H-						.	
									H-						.	
									H-						.	
									H-						.	
									H-						.	
									H-						.	
									H-						.	
									H-						.	
									H-						.	
									H-						.	

• CODES: (If more than one code applies, list the most important one first.)

A =Specimen lost in transit - request backup specimen
B =Specimen thawed in transit - request backup specimen
C =Specimen leaked in transit
D =Backup specimen
F =Frozen
HS=Slight hemolysis
H =Visible hemolysis
HM=Marked hemolysis
I =Specimen lost due to laboratory accident - request backup specimen
J =Unsatisfactory determination - request backup specimen
K =Repeat determination requested by CoC
L=Repeat determination on backup specimen request by CoC
M=Specimen improperly collected
N=Quantity not sufficient - request backup specimen
O=Mislabeled specimen - identification questionable
P=Unlabeled specimen - identification questionable
Q=Test cancelled by clinic
R=Test cancelled by CoC
S=No specimen received
T=Arrival T + B C
U=Shipment delay due to carrier
X=Repeat determination by laboratory
Z=A1c did not separate well from A1a and A1b

CHAPTER 16

DIETARY PROCEDURES

16.1 RESEARCH OBJECTIVE

The principal research objective for collecting and processing nutritional data is to obtain information on dietary habits of the study participants so that it may be possible to determine, at the end of the trial, whether there are clinically and statistically significant differences in diet between the two treatment groups.

16.2 SYSTEM FOR THE DIETARY DATA COLLECTION FOR ANALYSIS

In order to correlate dietary factors with clinical and biochemical measures, estimates of individual usual intake rather than measures of group intake are necessary. The diet history, which provides quantitative and qualitative information on the individual's usual intake, was selected as the most appropriate technique for the DCCT.

All aspects of data collection must be standardized. The dietitians will be trained in the diet history methodology so that the dietary information will be collected under a common protocol using standardized food models and procedures. A diet history will be conducted on both the experimental and the standard group patients at baseline, 2, 5 years post randomization and/or study termination. This will allow for comparison of nutrient intake in the two groups at baseline and at intervals during the treatment period and will permit calculation of any changes in individual diets at these intervals.

A description of each facet of the diet history methodology follows.

16.2.1 Training, Certification and Continuing Education of Diet History Interviewers

Since collection of nutritional data is time-consuming and difficult to check for accuracy, it is desirable to incorporate procedures to reduce error in interpretation of participant responses and in documentation, to keep inter-clinic differences in data collection to a minimum, and to accomplish these objectives in a cost effective manner.

In any study involving many centers over a large geographical area, in-depth training is essential to the uniform collection of data in the field. The training of dietitians for the research interview will provide them with the skills to obtain a complete and accurate history of food intake in an objective manner and to record the information in a careful, standardized method. (See Chapter 23 for more information.)

To achieve this standardization of dietary data collection across all clinics, the dietitians will complete a four-phase training procedure.

1. Pre-training phase -- Materials will be mailed to interviewers prior to attendance at a training session held by the Central Nutrition Coding Unit (CNCU). This provides orientation to the system to facilitate optimum use of time at the two-day session.

2. Training session -- This will be a two-day session at which the attendees are given instructions in coding to provide insight into the level of detail required in data collection. A videotape demonstration is used to illustrate examples of appropriate techniques for a research interview and to lead into a practice session for the diet history. Practice histories are taken and critiqued by the dietitians to help develop their skills in eliciting and recording the information. Details on documentation are reviewed and discussed.

3. Standard History -- A standard history will be given to the attendees at the training session which they will transcribe, code and return to the CNCU for checking.

4. Rehearsal phase -- This phase requires that the dietitian collect three diet histories on study-similar subjects and one of these histories should be coded. These practice histories will be submitted to the CNCU for grading and comment prior to conducting any diet history for the DCCT.

   Dietitians will be certified as diet history interviewers upon submitting complete histories and meeting the minimum standard of less than 4% error in documentation.

Dietitians also have the option of becoming certified by mail upon completing the following steps:

1. Review the CNCU codebook for general instructions on a dietary data collection and coding.

2. Transcribe and code the standard history and submit it to the CNCU for checking.

3. Collect three histories from study-similar subjects and code one of these histories. All three histories will be submitted to the CNCU for review and will be returned to the dietitian with comments on both documentation and coding.

Back-up dietitians should be trained in the clinic by the clinic DCCT certified dietitian for data collection. They can be certified by mail as described above.

Continuing education by means of regular communication with the clinic is another facet of maintaining comparability among clinics. An inquiry will be sent for clarification of any faulty or ambiguous documentation. Dietitians are encouraged to call the CNCU if they have procedural questions on the diet history. Continuing education worksheets will be sent to the dietitians bi-monthly to review documentation and coding skills and will be returned to the dietitians with any corrections.

16.2.2 Dietary Forms

1. Forms Completed by Participant

Two forms will be sent to the participants for completion at home with a cover letter giving detailed explanation, instructions and encouragement. These forms will be brought to the dietitian at the clinic visit.

The Food Pattern Questionnaire (DCCT Form 029) is a self-administered document with questions regarding general dietary habits such as meal frequency, use of special diets, meals eaten away from home, discretionary salt use, and use of dietary supplements. Usual intake in terms of frequency of consumption is recorded but not quantified. This document will be used by the dietitian as a cross-check for identification of any inconsistencies or omissions in the diet history.

The other questionnaire sent to the home is the Food Preparation Questionnaire (DCCT Form 030). This is to be completed by the individual responsible for preparation of the food and is needed to ensure complete detail on dietary intake.

The Food Pattern Questionnaire and the Food Preparation Questionnaire are not intended for analysis. Both of these completed forms will be retained in the patient's clinic file.

2. Form Completed by Dietitian

The Diet History Form (DCCT Form 018) is printed on 11 x 17, two-part, no-carbon-required paper and is completed by the dietitian in the interview at the clinic. This form includes header questions relevant to the study and the following guidelines are for scoring reliability of the history:

a) Recalls all meals: Score as 0 if the patient is unable to remember food intake for one or more meals.

b) Not yea-saying: Score as 0 if the patient gives answers to appear compliant.

c) Cross check validates: Compare with the Food Pattern and Food Preparation Questionnaires.

The original of the form will be sent to the CNCU for nutrient calculations and a copy will be retained at each individual center.

16.2.3 Instructions for Recording Information on the Diet History Form

The form should be filled out using ball point pen, pressing heavily enough to imprint the copy clearly. Do not let descriptive comments overlap into the columns to be keyed. Whenever necessary, use additional lines. Erasures cannot be made. To correct errors, line through the error and re-enter the correct information. Record the clinic number, patient identification number and initials. Do not record the name of the participant.

1. Weekday/Saturday/Sunday -- The purpose of these columns is to separate food intake by an individual's usual weekday, Saturday and Sunday intake patterns. More than one column may be checked per line if everything (meal, where prepared, food or beverage, amount, frequency, salt and fat use) is exactly the same for all days checked. If anything differs, a separate line must be used. The complete description need not be repeated; simply record the food item, page and line number of the original citation.

2. Meal Column -- The purpose of this column is to identify food intake by an individual's usual meal and snack pattern.

   Enter a number in the MEAL column only for each new meal/snack. Each time a number is entered in the MEAL column, every food item following the entry is credited to that meal/snack until a new entry into the column is made.

   Use only one meal code per line. If an item is consumed at more than one meal/snack, have the participant approximate the number of times the item is consumed at each meal/snack, or specify one meal/snack when the item is most likely to be consumed.

   If the participant is unable to identify the meal or snack when the food is consumed, the CNCU will average the amounts throughout the day.

3. Prepared Column -- The place where the food was prepared should be identified by recording the appropriate code in this column. The restaurant category includes school and work cafeterias, vending machines and fast food chains. Whenever a 2 is entered, specify

the place where the food was prepared. If a restaurant, specify the name and price range of the establishment. Identify bakery products by price range.

When several foods have been prepared in the same place, the proper code should be recorded in the PREPARED column on the line with the first food prepared at that place, leaving the column blank on subsequent lines.

4. Foods and Beverages Column -- Each food or beverage should be recorded on a separate line in the FOODS and BEVERAGES column. Often, more than one line may be needed to describe an item or its preparation method. Leave sufficient lines for such items which require multiple lines for coding. For example, a pie must be coded on two or more lines: one for the crust, one for the filling, and one for any topping. A glazed doughnut must be coded on two lines: one for the doughnut and one for glaze. Leave one or more blank lines between each meal and snack. Attention to these details will facilitate coding procedures.

When the participant has eaten a mixed dish or recipe item which differs from a standard recipe, the interviewer should attempt to elicit all ingredients used in the recipe. For recipes with four or fewer ingredients, each ingredient and amount consumed should be itemized on a separate line. Longer recipes should be submitted on a Recipe Specification Form. If the participant cannot delineate the ingredients, the interviewer should obtain as much identifying information as possible, i.e., type of fat, kind and cut of meat, etc.

When the participant has eaten a commercial product, the interviewer should obtain brand name and descriptive information about the product. For example, a single brand of margarine may include several margarine products that vary not only by percent of fat (such as regular, diet, or spread types) but also differ by major ingredient oil. Therefore, it is important that you probe not only for the brand but also for the percent fat and the ingredient oil of the margarine.

Also, probe for the amount of each ingredient in mixed dishes such as spaghetti, chow mein, tortillas and tortilla based dishes, macaroni and cheese and whether the preparation was from scratch or a commercial mix.

Brand names and/or descriptive information are necessary for:

cereals	shortenings
process cheeses	oils
crackers	frozen entrees
cookies	non-dairy creamers and toppings
margarines	salad dressings

Record brand name when it implies special processing techniques or ingredients. For example: Estee, S & W or Batter Lite.

Brand names are not necessary for all items. Some which may be excluded are:

breads
dairy products except process cheeses
cold cuts
canned fruits and vegetables
pastas and rices
peanut butter
jam

Use the Documentation Checklist (Figure 16.1) as an aid in recording all necessary information.

5. Amount Column -- Amounts should be documented in household units, e.g., cup, teaspoon, tablespoon, ounce, gram, or dimensions in inches. Ounces used with non-fluid items will be interpreted as a weight measure, not volume. If the participant is unable to recall the amount eaten, the two-dimensional food portion visual may be used to help estimate the amount. Foods which may be described as small, medium (average), or large could be documented as such without reference to the visuals (see those with an asterisk). Other foods which are relatively standard in size may be documented in servings, slices, etc. These include:

bacon	eggs*
bagels	English muffins
bread, commercial slices	fruits*
buns (hamburger, hot dog, etc.)	hot dogs
American cheese slices	processed lunch meats
chicken parts	sweet rolls
cookies, commercial, brand name or type known	tortillas*
	vegetables*
crackers, brand name or type known	shell fish
doughnuts (yeast, cake)	

When using the two-dimensional food portion visual, use Side A to identify the volume of foods and beverages. This side is appropriate for cups, mounds, scoops and wedges of foods. Some examples include:

cake wedges	fruits, cooked or diced, fresh
casseroles	gravy
cottage cheese	pasta and rice
cereals	salads
chips	sauces
condiments	soups
desserts	vegetables, cooked or chopped, raw

Side B of the visual is used to estimate the amount of food when weight is unknown. Side B may also be used to estimate volumes which do not correspond to Side A. Side B figures must have a thickness assigned to them. When using Side B for meats, be sure to indicate whether bone is included. Some examples of foods for which Side B may be used include:

meats (beef, lamb, pork, fish)
cake other than wedge
cheeses
chicken or turkey slices
deli meats
fresh fruits

Four replica models from NASCO are provided to all DCCT clinics. These models may be used to estimate portion size for pork chops, fish fillets, strip steak and sliced roast beef. No other models may be used for this study. Avoid the use of diabetic exchanges.

6. Frequency Column -- This column is used to indicate how often a food or beverage is consumed. Record frequencies by using a whole number or decimal, with the acceptable abbreviation for the time period as shown below. Separate the number and time period by a slash.

D = Day, e.g., once per day	1/D
W = Week, e.g., 3 times per week	3/W
M = Month, e.g., 5 times per month	5/M
Y = Year, e.g., 30 times per year	30/Y

When an item is eaten at a frequency other than daily, weekly or monthly, express the frequency as a multiple of D, W or M as shown below.

e.g., once every other week	1/2W
e.g., twice in three days	2/3D
e.g., five times in two months	5/2M

Record seasonal intake with the correct frequency followed by the name or length of the season in parenthesis. Each season (fall, winter, spring, summer) will be interpreted as three months.

e.g., daily in summers	1/D (summer)
e.g., twice a week for 5 months	2/W (5M)

If it is unclear how a frequency should be recorded, write it out completely under the FOODS and BEVERAGES DESCRIPTION column leaving the FREQUENCY column blank.

7. Fat in Preparation Column -- This column serves as a cue for the interviewer to ask whether fat was added in the preparation of a food item and to elicit information about the fat used. It is also used by the food coder to determine whether or not a

preparation code is required. This column may be left blank for foods not usually prepared with fat such as coffee or milk.

Record "0" (No) in the column if fat was not added to a food that is usually prepared with fat and provide an explanation in the FOODS and BEVERAGES description column.

Record "9" (Unknown) in the column if it is not possible to ascertain whether or not fat was added to a food which may be prepared with or without fat. A "9" should not be recorded in the FAT IN PREP column simply because the kind of fat is unidentifiable.

When a "9" is recorded in the column for an item not prepared with fat in the CNCU Codebook, no preparation fat will be coded. When a "9" is recorded in the column for an item prepared with fat in the CNCU Codebook, a predetermined type and amount of fat will be added.

8. Salt in Preparation Column -- This column serves as a cue for the interviewer to ask whether salt was added in the home preparation of a food item and is used by the food coder to select the correct food code. The column may be left blank.

   Foods which are commercially prepared without salt or are described as low sodium should be documented as such in the FOODS and BEVERAGES DESCRIPTION column. The column should be left blank.

   Foods which are prepared using a salt substitute should have a "0" in the SALT IN PREP column. The use of a salt substitute should be documented under the FOODS and BEVERAGE DESCRIPTION column.

   Foods which are prepared using less salt than the recipe indicates should have a "1" in the SALT IN PREP column with documentation under the FOODS and BEVERAGES DESCRIPTION column specifying the salt reduction.

9. Salt at Table Column -- This column documents self-assessed amounts of salt added to foods at the table. Foods with the column left blank will be assumed to have no salt added at the table. The column does not have to be filled in for foods usually not salted such as break or milk.

16.2.4 Instructions for the Diet History Interview

In the interview for the diet history, the participant is asked to recall the usual intake of foods and beverages for weekdays and weekend days.

The interviewing area should be quiet, attractive, and private. Since the interview is long and could be fatiguing for both dietitian and participant, it is important to have a pleasant, relaxed atmosphere to help provide a climate conducive to the best possible data collection. Also, it should be kept in mind that food intake times are important to the diabetic so it may be necessary to have a snack available. Total interview time can vary depending on the complexity of the meal patterns.

Before beginning the interview, it is important to establish a rapport with the participant in order to diminish any apprehension about the interview. The dietitian should adopt a friendly, interested, non-judgmental attitude. The interview might begin with a brief description of the purpose of the dietary data collection as it relates to the trial. Explain that the participant is an important team member in a large-scale study and that the dietary information gathered is an important component of the trial. The following is a brief example of how the dietitian might begin the interview after the amenities:

"The information you give me will become part of the information collected from a large group of people. At the end of the trial, it will help us to determine whether differences in diet were present between the two treatment groups. I would like you to tell me what you usually have to eat or drink on weekdays and on weekends. We will collect detailed information so that the Central Nutrition Coding Unit in Minneapolis will be able to assign the proper food codes to the items. Foods eaten less often than a couple times a month will not be recorded. We want to record your usual intake. Let us begin with the first thing you usually have to eat or drink when you get up on a weekday."

After this explanation of what you wish the participant to tell you, allow him or her to speak freely. You may be able to help the participant remember his/her usual intake by suggesting that he/she think about usual activities. Probe for usual food intake without emphasizing a specific time period (such as the past year), selecting typical or representative meals or foods. The interview can proceed through the usual weekday and then move on to usual Saturday-Sunday pattern. If there is no change from weekdays, you may simply check the Saturday and Sunday columns, along with the Weekday column. Record frequent variations to the usual pattern using a guideline of approximately two times per month to define frequent variations. Some foods consumed less than twice per month will fit into a broader category of similar foods consumed more than twice per month. To avoid losing information about the entire category, document these foods as described in the FOODS and BEVERAGES DESCRIPTION column guidelines.

Record commonly consumed seasonal variations using a guidelines of approximately two times per week during the season to define commonly

consumed variations. Document seasonal intake as described in the FREQUENCY column guidelines.

To assist the participant's recall, ask about foods usually eaten together. For example:

1. Coffee, tea -- Any additions? Ask kind and amount of whitener, sweetner.

2. Cereals -- Kind and amount of milk added, and sweetner.

3. Eggs -- Any fat used in cooking? Any ham or bacon eaten?

4. Breads/toast -- Any spread?

5. Mixed dishes -- Any sugar, fat, salt, salad dressing?

A complete Documentation Checklist is included in the training packet. This should be studied and integrated into the dietitian's interviewing routine.

When the history is completed, the dietitian will review the information comparing it to the Food Pattern Questionnaire to identify any items which may have been forgotten. The Food Preparation Questionnaire should be used to complete any missing or unknown information on the preparation of items. This final review must be done carefully so that all necessary information is supplied.

16.2.5 Instructions for Reviewing and Mailing Forms

1. Verify that the Patient ID Number, Clinic Number and date are legible.

2. Verify that all header information is completed -- visit number, dietitian ID, other questions. Do not add the name of the participant.

3. Verify that all pages are numbered and that the order of sequence is indicated (e.g., page 1 of 3).

4. Verify by initial and date in the "Review" space of the header that the form has been reviewed using the Documentation Checklist, the Food Pattern Questionnaire, and the Food Preparation Questionnaire.

5. Fill out the Diet History Mailing List (DCCT Form 052) and send one copy with the original pages to the CNCU. Keep the copies in the clinic files. The address of the CNCU is given on the mailing list.

16.2.6 Coding and Calculations

In order to minimize intercoder variability, the coding of records will be done at the CNCU by a staff of coders trained in a standardized manner. Coding will be done on the form used for data collection. The coding is subjected to internal quality control checks.

The coded interview are sent to the Coordinating Center every quarter on computer tape. The nutrients that are sent to the Coordinating Center are listed below:

Nutrient Calculations Record Description

Field	Contents	Format
1-5	Patient's Id	N5
6-13	Visit Date	MM/DD/YY
14-16	Patient's Initials	A3
17-18	Clinic	N2
19	Takes Supplements	N1
20	Reliability	N1
21	Exercise Level	N1
22-23	Visit	N2
24	Window	N1
25-28	Dietician Certification No.	N4
29-32	Clinic Coordinator Cert. No.	N4
33-40	Date Coded	MM/DD/YY
41-42	Coder's ID	N2
43-44	Codebook Edition	N2
Nutrients Including Supplements		
45-53	Calories (kcal)	N9
54-62	Protein (gm)	N9
63-71	Total Fat (gm)	N9
72-80	Total Carbohydrates (gm)	N9
81-89	Alcohol (gm)	N9
90-98	Caffeine (mg)	N9
99-107	Total Vitamin A (IU)	N9
108-116	Retinol (mcg)	N9
117-125	Beta-Carotene (mcg)	N9
126-134	Vitamin D (mcg)	N9
135-143	Tot Alpha Tocoph Equiv (mg)	N9
144-152	Alpha Tocopherol (mg)	N9
153-161	Beta Tocopherol (mg)	N9
162-170	Gamma Tocopherol (mg)	N9
171-179	Delta Gocopherol (mg)	N9
180-188	Thiamin (mg)	N9
189-197	Riboflavin (mg)	N9
198-206	Niacin (mg)	N9
207-215	Folic Acid (mcg)	N9
216-224	Vitamin B6 (mg)	N9
225-233	Vitamin B12 (mcg)	N9
234-242	Vitamin C (mg)	N9

Nutrients Including Supplements (Continued)

243-251	Crude Fiber (gm)	N9
252-260	Dietary Fiber (gm)	N9
261-269	Cholesterol (mg)	N9
270-278	Saturated Fats (gm)	N9
279-287	SFA 4:0 (gm)	N9
288-296	SFA 6:0 (gm)	N9
297-305	SFA 8:0 (gm)	N9
306-314	SFA 10:0 (gm)	N9
315-323	SFA 12:0 (gm)	N9
324-332	SFA 13:0 (gm)	N9
333-341	SFA 14:0 (gm)	N9
342-350	SFA 15:0 (gm)	N9
351-359	SFA 16:0 (gm)	N9
360-368	SFA 17:0 (gm)	N9
369-377	SFA 18:0 (gm)	N9
378-386	SFA 20.0 (gm)	N9
387-395	SFA 22.0 (gm)	N9
396-404	Polyunsaturated Fats (gm)	N9
405-413	PFA 18:2 (gm)	N9
414-422	PFA 18:3 (gm)	N9
423-431	PFA 18:4 (gm)	N9
432-440	PFA 20:4 (gm)	N9
441-449	PFA 20:5 (gm)	N9
450-458	PFA 22:5 (gm)	N9
459-467	PFA 22:6 (gm)	N9
468-479	Monounsaturated Fats (gm)	N9
477-485	MFA 14:1 (gm)	N9
486-494	MFA 16:1 (gm)	N9
495-403	MFA 18:1 (gm)	N9
504-512	MFA 20:1 (gm)	N9
513-521	MFA 22:1 (gm)	N9
522-530	Calcium (mg)	N9
531-539	Phosphorous (mg)	N9
540-548	Sodium (mg)	N9
549-557	Potassium (mg)	N9
558-566	Iron (mg)	N9
567-575	Magnesium (mg)	N9
576-584	Copper (mg)	N9
585-593	Zinc (mg)	N9
594-602	Insol Dietary Fiber (gm)	N9
603-611	Water Soluble Diet. Fiber (gm)	N9
612-620	Pectins (gm)	N9
621-629	Sucrose (gm)	N9
630-638	Starch (gm)	N9

Nutrients Including Supplements (Continued)

639-647	Glucose (gm)	N9
648-656	Fructose (gm)	N9
657-665	Lactose (gm)	N9
666-674	Galactose (gm)	N9
675-683	Selenium (mcg)	N9
684-692	Sodium Added at Table (mg)	N9

Nutrients Excluding Supplements

693-701	Calories (kcal)	N9
702-710	Protein (gm)	N9
711-719	Total Fat (gm)	N9
720-728	Total Carbohydrates (gm)	N9
729-737	Alcohol (gm)	N9
738-746	Caffeine (mg)	N9
747-755	Total Vitamin A (IU)	N9
756-764	Retinol (mcg)	N9
765-773	Beta-Carotene (mcg)	N9
774-782	Vitamin D (mcg)	N9
783-791	Tot Alpha Tocoph Equiv (mg)	N9
792-800	Alpha Tocopherol (mg)	N9
801-809	Beta Tocopherol (mg)	N9
810-818	Gamma Tocopherol (mg)	N9
819-827	Delta Tocopherol (mg)	N9
828-836	Thiamin (mg)	N9
837-845	Riboflavin (mg)	N9
846-854	Niacin (mg)	N9
855-863	Folic Acid (mcg)	N9
864-872	Vitamin B6 (mg)	N9
873-881	Vitamin B12 (mcg)	N9
882-890	Vitamin C (mg)	N9
891-899	Crude Fiber (gm)	N9
900-908	Dietary fiber (gm)	N9
909-917	Cholesterol (mg)	N9
918-926	Saturated Fats (gm)	N9
927-935	SFA 4:0 (gm)	N9
936-944	SFA 6:0 (gm)	N9
945-953	SFA 8:0 (gm)	N9
954-962	SFA 10:0 (gm)	N9
963-971	SFA 12:0 (gm)	N9
972-980	SFA 13:0 (gm)	N9
981-989	SFA 14:0 (gm)	N9
990-998	SFA 15:0 (gm)	N9
999-1007	SFA 16:0 (gm)	N9
1008-1016	SFA 17:0 (gm)	N9
1017-1025	SFA 18:0 (gm)	N9
1026-1034	SFA 20:0 (gm)	N9
1036-1043	SFA 22:0 (gm)	N9

Nutrients Excluding Supplements (Continued)

1044-1052	Polyunsaturated Fats (gm)	N9
1053-1061	PFA 18:2 (gm)	N9
1062-1070	PFA 18:3 (gm)	N9
1071-1079	PFA 18:4 (gm)	N9
1080-1088	PFA 20:4 (gm)	N9
1089-1097	PFA 20:5 (gm)	N9
1098-1106	PFA 22:5 (gm)	N9
1107-1115	PFA 22:6 (gm)	N9
1116-1124	Monounsaturated Fats (gm)	N9
1125-1133	MFA 14:1 (gm)	N9
1134-1142	MFA 16:1 (gm)	N9
1143-1151	MFA 18:1 (gm)	N9
1152-1160	MFA 20:1 (gm)	N9
1161-1169	MFA 22:1 (gm)	N9
1170-1178	Calcium (mg)	N9
1179-1187	Phosphorous (mg)	N9
1188-1196	Sodium (mg)	N9
1197-1205	Potassium (mg)	N9
1206-1214	Iron (mg)	N9
1215-1223	Magnesium (mg)	N9
1224-1232	Copper (mg)	N9
1223-1241	Zinc (mg)	N9
1242-1250	Insol Dietary Fiber (gm)	N9
1251-1259	Water Soluble Diet. Fiber (gm)	N9
1260-1268	Pectins (gm)	N9
1279-1277	Sucrose (gm)	N9
1278-1286	Starch (gm)	N9
1287-1295	Glucose (gm)	N9
1296-1304	Fructose (gm)	N9
1305-1313	Lactose (gm)	N9
1314-1322	Galactose (gm)	N9
1323-1331	Selenium (gm)	N9
1332-1340	Sodium Added at Table (mg)	N9

Food Group	Did You Specify:	Did You Probe for Additions and Amounts of:
Snacks/Candy	Kind, brand	
Soups	Kind; homemade or commercial Ready to serve, Milk (% fat) or cream added Chunky or regular Low sodium	Croutons, crackers, cheese, etc.
Vegetables	Cooked or raw Fresh, frozen or canned Low sodium Salt in preparation	Fat (kind), cheese, sauce, nuts, dip, etc.
Salads	Kind (major vegetables)	Dressing, kind and/or brand Croutons, seeds, etc.
Baked Potato	Skin eaten or not	Butter, sour cream, etc.
French Fries	Frozen, scratch Fat in preparation (kind)	Catsup
Miscellaneous Medications containing nutrients such as sodium and/or caffeine	Type (e.g. analgesics, antacids, decongestants) Brand	
Dietary Supplements	Kind, brand, amount of each nutrient (I.U., mg, gm, mcg) on the Dietary Supplement Information Form Number of tablets	

APPROVED ABBREVIATIONS

Use these and other standard abbreviations when documenting food intake on Dietary Intake Records.

approx – approximate	fl oz – fluid ounce	sat – saturated
avg – average	gm – gram	sl – slice
brd – breaded	gr – ground	sm – small
c – with	hyd – hydrogenated	swt – sweetened
cnd – canned	lg – large	tb – tablespoon
choc – chocolate	mayo – mayonnaise	ts – teaspoon
chpd – chopped	med – medium	TVP – textured vegetable protein
comm – commercial	misc – miscellaneous	unkn – unknown
ckd – cooked	pkg – package	veg – vegetable
crax – cracker	pc – piece	w – with
cp – cup	poly – polyunsaturated	w/o – without
diam – diameter	prep – preparation	
fg – few grains	s – without	

Nutrition Coordinating Center
2829 University Avenue SE
Minneapolis, MN 55414

DOCUMENTATION CHECKLIST

Record portion sizes in the following standard measurements:

Weight in grams or ounces
Volume in fluid ounces, cups, tablespoons or teaspoons
Fraction of the whole (e.g., 1/8 of 9" pie)
Comparison to approved food model
Dimensions for the following shapes:

Shape	Measurement Needed	Example
Sphere	Diameter	Orange
Cylinder or disk	Diameter x thickness	Meat patty
Rectangle or cube	Length x height x width	Lasagne
Wedge	Length x height x width of arc	Pie

Food Group	Did You Specify:	Did You Probe for Additions and Amounts of:
Beverages		
Coffee, Tea	Brewed, instant, decaf, herbal, cereal type (e.g., Postum)	Sweetener, whitener, cream (type)
Cocoa	Mix (brand; regular, sugar-free or low-cal) Milk (% fat)	Marshmallows Whipped topping (dairy or non-dairy)
Beer	Regular, light or low alcohol	
Liquor, Mixed Drinks, Liqueur	Name of mixed drink, liqueur Proportion of ice	Mix (juice, other non-alcoholic beverage) Cherry, olive, etc.
Wine	Dinner or dessert	
Carbonated Beverages	Cola or non-cola, caffeine-free, diet, sodium-free Proportion of ice	
Dairy/Non-Dairy Products		
Milk, Cream, Toppings	% fat, dairy or non-dairy (brand) If non-dairy: powder, liquid or aerosol	Sweetener, cocoa mixes, etc.
Cheese	Natural or processed Kind (Cheddar, Swiss, etc.) If low fat: brand or % fat Low sodium	
Yogurt	% fat, plain or flavored	Fruit, nuts, etc.
Ice Cream, Ice Milk	Flavor Rich or average fat	Topping
Milk Shakes, Malts	Homemade or restaurant Flavor Ice cream or ice milk	
Egg, Egg Substitute	Method of preparation Brand of substitute Milk (% fat) if scrambled Fat in preparation (kind) Salt in preparation	Cheese, vegetables, meat, etc.

Food Group	Did You Specify:	Did You Probe for Additions and Amounts of:
Desserts, Baked Goods		
Puddings, Custards	Kind Mix or scratch Low-cal or regular Milk (% fat) With or without egg	Topping
Cookies	Kind, brand Mix, scratch or commercial Ingredient fat	
Cakes	Kind Mix, scratch or commercial Layer, sheet or cupcake Number of layers Ingredient fat Additional oil, egg Pudding in mix	Frosting, filling, topping
Pies	Kind (filling) Mix, scratch or commercial Single or double crust Ingredient fat for filling and crust	Topping
Gelatin Desserts	Low-cal or regular	Topping, other additions (fruit, etc.)
Fats		
Oil, Shortening	Brand and/or type of fat	
Salad Dressing	Brand, type Ingredient oil, if homemade Creamy or clear Low-cal or low sodium	
Margarine, Butter	Brand and major oil Form (stick, tub, diet, whipped, spread, squeeze) Salt free	
Fruits/Fruit Juices	Fresh, canned or dried Cooked or uncooked Sweetened or unsweetened With or without peel	Fat (kind)
Grain Products		
Bread, Rolls	Kind (white, whole wheat, rye, etc.)	Butter, margarine, other spread
French Toast	Egg or egg substitute Fat in preparation Kind of bread	Butter, margarine, syrup, etc.
Sweet Rolls, Doughnuts	Yeast or cake-type Mix, scratch or commercial Ingredient fat	Frosting, glaze, nuts, preserves
Pancakes, Waffles Biscuits, Muffins	Kind (whole wheat, buckwheat, bran, etc.) Mix, scratch or commercial Ingredient fat	Butter, margarine, syrup, etc.
Cereal, Granola	Kind, brand Ingredient fat for homemade granola	Milk (% fat) Sweetener, fat, fruit, etc.

Food Group	Did You Specify:	Did You Probe for Additions and Amounts of:
Grain Products (Cont.)		
Pasta, Rice	Kind (spaghetti, brown rice, egg noodles, etc.) Salt in preparation	Fat (kind), sauce, cheese, etc.
Crackers	Kind, brand	Spread
Tortilla	Corn or flour Fat used if fried	Fillings
Gravies, Sauces	Mix or scratch Milk (% fat) or water Fat (kind) Salt in preparation	
Meat, Poultry, Fish		
Meat	Kind, cut Trimmed or untrimmed, % fat of hamburger or type of ground beef (e.g., ground chuck) Fat in preparation (kind) Salt in preparation Cooked or raw weight With or without bone	Sauce, gravy, etc.
Meatloaf, Meatballs	Kind, % fat or type of meat (e.g., ground round)	Sauce, gravy, etc.
Poultry	Light or dark meat (or name of part) Prepared with or without skin Skin eaten or not Breaded or battered and fried Fat in preparation (kind) Salt in preparation Cooked or raw weight With or without bone	Sauce, gravy, etc.
Fish	Kind Breaded or battered and fried Fat in preparation (kind) Salt in preparation Cooked or raw weight Fresh or canned If canned, water or oil pack, drained, undrained or rinsed, low sodium	Sauce, etc.
Cold Cuts, Luncheon Meats	Kind, % fat, brand	
Mixed Dishes	Mix, scratch or commercial Fat in preparation (kind) Salt in preparation Meat, kind and % fat Sauce or gravy Milk or cheese (% fat or kind) Pasta or vegetables	Topping (e.g. croutons, crackers, cheese, etc.)
Pizza	Thick or thin crust	Topping
Restaurant Meals	Price range, name of restaurant	
Seasonings/ Condiments	Salt or seasonings (e.g. celery salt, garlic salt, MSG) added in prep or at table	Pickle, relish, catsup, mustard, steak sauce, etc.

Chapter 17

NEUROLOGICAL PROCEDURES

17.1 GENERAL METHODOLOGY

17.1.1 Clinical Assessment History and Physical Examination

The Neurological History and Examination Form (DCCT Form 005) is used for baseline assessment, and for evaluation at five years followup and/or study termination. The neurological examination should be carried out to permit answering certain specific questions. First, is there neurological evidence of a systemic disorder that could jeopardize the patient's ability to participate in the DCCT study? Second, is there clinical evidence of a peripheral nervous system disorder? If so, is it distal symmetrical polyneuropathy, a proximal motor neuropathy, a mononeuropathy or some other disorder that is unlikely to be related to diabetes? Third, if there is evidence of polyneuropathy, what is the extent of the neurologic deficit at the time of examination? Decisions should be based on the history and physical findings, and must be made independent from the results of any neurophysiological testing.

To answer the first question, it is necessary to complete a standard neurological history. The history should include an inquiry into possible exposure to neurotoxic drugs or chemicals, and a family history of neurological disease, weakness, or arthritis and joint deformities. To answer the second and third questions, specific and detailed inquiry should be made about symptoms of sensory, motor and autonomic dysfunction. A list of these is provided on the Neurological History and Examination form (DCCT Form 005).

17.1.2 Autonomic Nervous System Function

Until recently, methods to assess autonomic nervous system (ANS) function that were both quantitative and sensitive had not been established. With the exception of RR-variation, the Valsalva maneuver, and plasma catecholamines, the methods for the assessment of cardiovascular ANS are not well standardized, the responses are highly variable, and most of the tests do not distinguish between impairment of the parasympathetic (PNS) and/or sympathetic nervous (SNS) systems. Evaluation of other (noncardiovascular) organ systems is also frustrated by lack of adequate methodology.

Sinus arrhythmia during quiet respiration has been termed RR-variation. This measurement has been used as an index of cardiac PNS activity since 1973. Factors such as the position of the subject (supine, sitting, or standing) and the rate of respiration have been shown to influence the results of this method. The methods of analysis of the results have also been variable. The standard deviation of the mean RR-interval for a five-minute period during quiet breathing is a commonly used method to determine RR-variation. However, RR-variation determined by the standard deviation of RR-intervals method does have some inherent problems. A slow change (increase or decrease) in the mean RR-interval during the five-minute period may result in a falsely elevated RR-variation. The heart rate also influences the standard deviation. A fast heart rate will produce smaller RR-intervals and for statistical reasons one would expect a smaller standard deviation. Therefore, a new method of analysis based on vector analysis has been developed and has been termed circular mean resultant. This method eliminates the effects of trends in time and greatly attenuates the effect of intrinsic heart rate and ectopic atrial or ventricular contraction.

RR-variation is usually considered an index of PNS activity because previous studies had shown that atropine, but not propranolol, altered RR-variations. However, it has recently been shown that an increase in SNS activity (isoproterenol infusion) will also mimic the responses seen during decreased PNS activity (atropine infusion). Thus, a decrease in RR-variation could either result from an increase in SNS or a decrease in PNS activity to the heart. For this reason, if a patient should happen to have an adrenergic discharge secondary to hypoglycemia (or another well documented cause) within the preceding 24 hours, or if the 3:00 a.m. blood glucose level on the day of the test is less than 50 mg/dl, then the study should not be done but rescheduled to a more appropriate day. Thus, under standardized conditions and with a little foresight, an increase in SNS activity would not be expected, and the RR-variation would represent a reflex arc involving the parasympathetic pathway.

Recent studies have shown that cardiovascular exercise performance is impaired in diabetic patients with mild (only abnormal RR-variation) as well as more severe autonomic neuropathy (postural hypotension) when compared to normal subjects. These abnormalities were observed for both work-matched and maximal-oxygen-uptake-matched cardiovascular leads. Furthermore, other studies have shown that RR-variation correlates to symptoms of neuropathy. Thus, RR-variation has functional significance in terms of cardiovascular function and neurological symptoms.

Postural testing relies upon measuring blood pressure before and after assuming an upright posture and is dependent upon an intact baroreceptor. In order to standardize the test, it should be done after 30 minutes of supine position. Blood pressure should be measured at set times before and after assuming the upright position. This is a qualitative test. If a patient has postural hypotension, i.e. a drop of diastolic blood pressure greater than 10 mm Hg, the subject could have either autonomic insufficiency or volume depletion. The test should

then be repeated on a separate day with the measurement of plasma catecholamines before and after assuming the upright position. If there is a supranormal plasma norepinephrine (NE) response, it is suggestive of volume depletion or cardiac ANS dysfunction. If, on the other hand, there is a normal NE response or totally lacking NE response, the NE response would be considered an inadequate response for the hypotension. This is an indication of a reflex arc involving vascular autonomic insufficiency. Thus, if orthostatic hypotension develops, plasma catecholamines will be measured in a follow-up examination.

The Valsalva test is a cardiovascular reflex test that relies upon evaluation of cardiac responses before (pre-Valsalva), during, and after (post-Valsalva) a standardized increase in intrathoracic pressure (Valsalva maneuver). This is a quantitative test and the following indices will be determined: the Valsalva ratio (the maximum heart rate during the Valsalva maneuver divided by the slowest heart rate after the Valsalva maneuver) and the initial heart rate. The increase in heart rate during the Valsalva period is due to a combination of decreasing the parasympathetic and increasing the sympathetic nervous system activities. The bradycardia after the Valsalva period is due to both an increase in the parasympathetic and a decrease in the sympathetic nervous system activities to the heart. These reflex changes in the cardiac autonomic nervous system activities are the result of how much sympathetic tone has been established in the peripheral vasculature. An abnormally low Valsalva ratio can be due either to decreased cardiac parasympathetic or decreased cardiac or vascular sympathetic tone. Thus, it serves as a general autonomic test rather than as a parasympathetic or sympathetic evaluator. Although not as sensitive as RR-variation, it has been shown to be an index which may be more useful than RR-variation for the more severely involved diabetics.

Vascular ANS activity is altered by a variety of factors such as eating, coffee, smoking, and volume depletion. It therefore is necessary to avoid these factors when evaluating RR-variation, the Valsalva maneuver, and postural testing in diabetics. Furthermore, medicines often taken by diabetics may alter the ANS. Insulin is known to increase plasma NE, increase heart rate, and may decrease arterial blood pressure in patients with neuropathy. Insulin should be withheld until after the studies are completed. Over-the-counter medications may also alter ANS tests. Sodium salicylate has been shown to augment RR-variation and to potentiate plasma NE and epinephrine responses to hypoglycemia in normal man. Since salicylates have also been reported to augment cholinergic responses in several species, it is possible that over-the-counter products such as aspirin (acetylsalicylic acid) may also alter ANS tests. For this reason, aspirin and other over-the-counter medicines (such as antihistamines) must be avoided for at least eight hours before the ANS studies.

Results of the autonomic neuropathy evaluations which are performed at baseline and biannually thereafter, are sent to the Central Autonomic Coding Unit using a copy of the ANS Documentation Sheet (DCCT Form 070) and the ANS Studies Mailing List (DCCT Form 054). At the Coding Unit, the results are recorded on DCCT Form 028, Autonomic Neuropathy Studies, and forwarded to the Coordinating Center for analysis.

17.1.3 Nerve Conduction Studies

Impaired nerve conduction velocity and amplitude correlate with poorly reversible large and small myelinated nerve fiber loss in overt diabetic polyneuropathy, yet limited electrophysiological improvement may occur with metabolic treatment. In patients without overt neuropathy, motor nerve conduction impairment correlates with duration of diabetes. Eng and Gregerson have demonstrated frequent motor nerve conduction impairment in young diabetics as early as 6 months to one year after diagnosis. Accumulating data suggest an additional nerve conduction impairment present in newly-diagnosed diabetics, which reverses acutely with hypolycemic therapy. However, at all stages motor nerve conduction velocity impairment varies from patient to patient and from nerve to nerve, and many long-standing diabetic patients have individual conduction velocities within the normal stage.

Conventional electrophysiological techniques assess conduction in only the largest and most rapidly conducting myelinated nerve fibers. Therefore, subclinical processes involving small myelinated fibers will be reflected poorly by conventional nerve conduction studies. Techniques to measure conduction directly in small myelinated fibers, however, are invasive and painful and are not justified in patients without clinically evident neuropathy. Consequently, contemplated nerve conduction studies provide an important but incomplete picture of subclinical peripheral nerve involvement in diabetes.

Results of these studies which are performed at baseline, 5 years and/or study termination are recorded on DCCT Form 037, Nerve Conduction Studies, which is mailed to the Coordinating Center for analysis.

17.2 CLINICAL ASSESSMENT

The Neurological History and Physical Examination (DCCT Form 005) should be carried out in a quiet, comfortable room such as an outpatient examining room or an EMG suite. The neurologist's standard neurological examination should be performed. Special attention should be paid to the peripheral nervous system.

The recommended method for testing small-diameter sensory fibers is to begin with evaluation of cold perception. A dense metal object such as the weight at the end of a 128 Hz tuning fork serves as a good cold stimulus. The neurologist should begin by asking the patient to compare the temperature of this object as perceived over the dorsum of the foot and the top of the thigh. If the more proximal stimulus is colder, then, starting on the dorsum of the toes, the object is slowly moved proximalward until the level of change to normal is found. Pin prick should be used to verify this level, since patients without neuropathy may report a change in temperature if they are examined in a cool room. The level at which the pin prick feels normal (compared with the upper thigh or face), and not just "sharp", should be recorded. To examine large fiber functions, the ability to detect the direction of the small

upward or downward movements of the great toe should be determined, as well as the ability to perceive a low amplitude 128 Hz vibration at the first metatarsal-phalangeal joint, using the neurologist's personal experience with individuals without neuropathy as a control.

For the most part, strength will be normal in this group of patients. To look for the earliest evidence of distal weakness, the neurologist should test the strength of great toe dorsiflexion (extensor hallucis longus muscle) and the strength of small toe dorsiflexion (extensor digitorum brevis). In addition, one should look for evidence of atrophy of intrinsic foot muscles and evaluate the size of the contracting EHL muscle for atrophy.

Reflexes should be elicited in the neurologist's usual way. In this study, we will be especially interested in the knee and ankle jerks. Reflexes should be graded as ++++ (very brisk with clonus), +++ (brisk), ++ and + (normal), +/- (elicited only with the Jendrassik maneuver) or 0 (cannot be elicited).

Normal mental status is defined as lucid

17.3 AUTONOMIC EVALUATION

17.3.1 Background and Rationale

Somatosensory and autonomic neuropathy are well recognized as common complications of diabetes mellitus. Clinical somatosensory neuropathy is characterized by symptoms of sensory loss, proprioceptive loss, parathesias, gross and fine motor incoordination, and pain, and is thus usually obvious to the patient. Secondary injuries (e.g. neuropathic ulcers) due to this condition are frequent. Symptoms of autonomic neuropathy, on the other hand, may be more insidious in onset and, therefore, somewhat less obvious. For example, bladder dysfunction, postural hypotension, gastric distension, sweating aberrations, and pupillary abnormalities may not even be noticed or may be ignored by the patient. However, autonomic complications may carry greater morbidity than somatosensory neuropathy. The absence of pain during a myocardial infarction has been attributed to autonomic neuropathy in diabetic patients, as has total cardiac denervation resulting in sudden death. The morbidity associated with autonomic neuropathy after clinical diagnosis in diabetics has been reported as high as 50% in three years, and the presence of autonomic neuropathy has been proposed as a prognostic indicator.

The goal of the DCCT is to use standardized and quantitative methods of evaluating the ANS to define whether it can be partially or totally reversed or prevented by glycemic control. The Central Autonomic Nervous System coding Unit has developed their own operation manual entitled ANS Operation Manual.

17.3.2 Equipment 4 Channel Recorder

The necessary equipment for Autonomic Nervous System testing includes the following:

1. Hokanson ECG Monitor
2. Hokanson Respiration Pacer
3. ECG Cord
4. Foot Pedal for Event Marker
5. TEAC R-61 Tape Recorder
6. Power Supply and Power Jack Connector
7. Four BNC Cables
8. ECG Leads
9. Blood Pressure Cuff and Stethoscope
10. Valsalva Apparatus
11. Timing Device (clock or timer)
12. 90 Minute Cassette Tape

Figure 17.1 Contains a list of equipment ordering information.

17.3.3 Equipment Settings and Calibration

The following is a description of the settings and connections of each piece of equipment used in testing. These steps must be followed to complete the set-up of equipment.

A) Hokanson ECG Monitor

-- POWER button: OFF during set-up and subject hook-up.
-- AUDIO switch: UP = ON.
-- GAIN control: DOWN during set-up and hook-up.
-- Plug ECG CABLE into PATIENT CABLE jack.
-- Plug FOOT PEDAL into REMOTE EVENT jack.
-- Plug RESPIRATION PACER into PACER jack.

B) TEAC R-61 Tape Recorder and Power Supply

-- POWER: OFF during set-up.
-- COMP: OFF (always).
-- CAL USE: USE for testing, CAL for calibration.
-- DC AC: AC.
-- VOLTAGE SWITCH: (+1V 0 -1V) to 0.
-- MEMO IN, MEMO OUT: Not used.
-- CHANNEL SELECTOR: Optional. Can be set to any channel to view the activity being recorded on that channel.
-- FM DR: Both switches to FM.
-- DC 9V: Plug in power jack cord, then attach the alligator clamps to the back of the POWER PACK; red wire to screw marked red, black wire to other screw.

C) Calibration of TEAC R-61 Tape Recorder:

The tape recorder must be calibrated during initial set-up of Hokanson ECG Monitor. However, calibration of tape recorder must be checked periodically to insure that settings remain in proper position.

STEPS FOR CALIBRATION

1. Turn tape recorder power on (on tape recorder and on power supply).
2. Set CAL USE switch to CAL.
3. Set DC AC switch to DC.
4. Set VOLTAGE switch to 0 volts (+1 0 -1).
5. Turn Channel Selector to Channel 1.
6. With small screw driver, adjust first INPUT ZERO screw so needle on gauge is at 0% on bottom scale.
7. Repeat step 6 for Channels 2, 3 and 4 using INPUT ZERO screws 2, 3 and 4.
8. Set voltage switch to +1V.
9. Turn Channel Selector to Channel 1.
10. With small screw driver, adjust first INPUT LEVEL screw so needle on gauge is at +20% on bottom scale.
11. Repeat step 10 for Channels 2 and 4 only using 2nd and 4th INPUT LEVEL screws.
12. Turn Channel Selector to Channel 3. Adjust 3rd INPUT LEVEL screw so needle on gauge is at +100% on bottom scale.
13. Return CAL USE switch to USE.
14. Return DC AC switch to AC.
15. Return VOLTAGE switch to 0.

STEPS TO CHECK FOR PROPER CALIBRATION

The tape recorder must be checked monthly for proper calibration and be entered into a log book. Follow these steps:

1. Set CAL USE switch to CAL.
2. Set DC AC switch to DC.
3. Turn Channel Selector to each channel. All channels should read 0% on gauge on bottom scale.
4. Set Voltage switch to +1V.
5. Turn Channel Selector to each Channel. Channels 1, 2 and 4 should read +20% and Channel 3 should read 100%.
6. If tape recorder is not calibrated correctly, repeat calibration procedure.
7. Return all switches to their original position.

D) Connection of BNC Cables

There are four BNC cables necessary for proper connection to the ECG Monitor and the tape recorder. Place a BNC cable to connect each of the outlets described below:

CHANNEL 1 Input on tape Recorder to PACER SYNC connection on module.

CHANNEL 2 Input on tape recorder to EVENT connection on module.

CHANNEL 3 Input on tape recorder to ECG connection on module.

CHANNEL 4 Input on tape recorder to ECG SYN connection on module.

17.3.4 Tape Recorder Channels

The Channel Selector on the tape recorder can be changed from one channel to the next during a study to view the activity being recorded on each channel. If the subject is properly connected, the following will be seen on each channel of the tape recorder:

Channel 1 - This is the channel for the Respiration Pacer. The needle on the gauge of the tape recorder will be resting at the left. When the bottom light of the pacer is lit, the needle on the recorder will jump to the right and back.

Channel 2 - This channel is for the Event marker. The needle rests at the left of the gauge. When the remote event pedal is pushed or the event switch on the monitor is pushed, the needle will jump to the right, then back.

Channel 3 - This channel is for the QRS complex. The needle will rest at the left side of the gauge and with each heartbeat will go to the right and back. Movement on this channel is not as dramatic as the other channels. If the needle is not moving, or does not rest to the left between heartbeats, the ECG leads should be checked for proper connection.

Channel 4 - The needle will start at the left of the gauge and deflect to the right with each heartbeat. It will be a long uniform movement that reaches the left side of the red area of the gauge.

17.3.5 Equipment - 2 Channel Recorder

The necessary equipment for Autonomic Nervous System testing performed with a 2 channel recorder includes the following:

1. Hokanson ECG Monitor
2. Hokanson Respiration Pacer
3. Patient ECG Cable

4. Foot Pedal for Event Marker
5. JVC Stereo Cassette Recorder
6. Two Connecting Cables
7. ECG Electrodes and Lead Wires
8. Valsalva Apparatus
9. Timing Device (Clock or Timer)
10. 90 Minute Cassette Tape

Figure 17.1 contains a list of equipment ordering information.

17.3.6 Equipment Set-up

A. Hokanson ECG Monitor

The following is a description of the settings of the Hokanson ECG Monitor:

Settings:
-POWER button: OFF during set-up and subject hook-up.
-AUDIO switch: UP = ON.
-GAIN control: DOWN during set-up and hook-up
-Plug ECG CABLE into PATIENT CABLE jack.
-Plug FOOT PEDAL into REMOTE EVENT jack.
-Plug RESPIRATION PACER into PACER jack.

B. JVC Stereo Cassette Recorder

-POWER Button: OFF (OUT) for set-up and patient hook-up.
-NR SYSTEM: Dolby B
-TAPE SELECT: Normal
-INPUT LEVEL: Right and Left both set to 2

C. Connection of Hokanson Monitor to JVC Stereo Cassette Recorder

There are two cables necessary for proper connection of the ECG Monitor and the tape recorder. These cables have a BNC connector on one end, and a color coded pin-plug connector on the other. The pin plugs are placed in the TAPE IN plugs on the rear of the JVC recorder and the BNC connectors are placed on the back of the Hokanson ECG Monitor. Place a cable to connect each of the outlets described below:

- EVENT PACER SYNC on ECG Monitor to right side of TAPE IN on tape recorder.

- ECG SYNC on ECG Monitor to left side of TAPE IN on tape recorder.

17.3.7 Assembly of Valsalva Apparatus:

For the Valsalva Maneuver Studies, a special apparatus is needed which measures the pressure of the patient's blowing during the test. The necessary equipment for proper assembly of the apparatus includes the following:

1. Sphygmomanometer
2. Raindrop Medication Nebulizer System with tee tube and mouthpiece
3. Rubber Stopper

The CACU should be notified when assembly of a new apparatus is necessary since relay of information on ordering the necessary equipment on the list is essential.

Once the proper equipment has been acquired, the following steps should be taken to assemble it correctly:

1. Cut the cuff off of the sphygmomanometer leaving only the gauge with pump and a one foot tubing running from one side.
2. Pull out or loosen the small screw below the gauge on the side opposite the tubing.
3. Unscrew the blue top from the nebulizer and pull out the small white plastic tube in the middle. Then screw the blue top back on, leaving the nebulizer clear inside.
4. Remove any tubing the nebulizer has on it already and place the tubing from the sphygmomanometer on the tube coming out the bottom of the nebulizer.
5. Place the tee tube on the top of the nebulizer. On one side of the tee tube, place the rubber stopper in as far as possible. On the other side of the tee tube, the mouthpiece screws in.

17.3.8 Subject Eligibility

Upon arrival for ANS testing the tester must fully complete an ANS Testing Eligibility form (DCCT form 081). This form is mandatory for all baseline diabetics, randomized follow-ups, and normal control patients. No eligibility form is required for patients done in order to certify a new ANS Technician. This form spells out the requirements for eligibility for ANS testing. If the answer to any question in part B of the form is YES, the patient is ineligible for testing that day with no exceptions. The form can be retained in the clinic files, and the patient must be rescheduled for another day.

17.3.9 Electrode Placement

After the proper connections and adjustments have been made on the equipment, the subject can be prepared for testing.

IMPORTANT: Be sure the power switches on the ECG Monitor and the tape recorder are OFF during subject hook-up.

Place the three electrodes as follows:

A - Upper Right Chest (half-way between the clavical and nipple)

B - The V6 Area (on the left side of the body mid axillary line at level of nipple)

C - Lower Right Abdomen

Note: Placement of electrodes may vary among patients. If the suggested placement does not produce a trigger for each heartbeat, try moving the electrodes until a signal is detected.

17.3.10 Connection of Subject to Equipment

-Place wire from electrode A to the red socket on the patient ECG cable.

-Place wire from electrode B to the green socket on the ECG cable.

-Place wire from electrode C to the white socket on the ECG cable.

Note: The patient ECG cable must be connected to the Patient Cable outlet on the ECG Monitor.

17.3.11 Equipment Operation During Study

-After subject is properly connected, turn power switches on ECG Monitor and tape recorder to the ON position. At this point, the row of lights on the Respiration Pacer will oscillate and the bottom two lights on the row of lights on the ECG Monitor will be lit.

-The gain lever is used to adjust the voltage of the ECG signal so that, for each heartbeat, the monitor may generate a standard electrical signal (square wave pulse).

-The Audio switch must remain on. If desired, an earphone can be placed in the jack on the rear of the monitor to silence the audio to all but the tester.

-Event markers can be placed in the study by using either the remote event pedal or the event switch on the monitor. To use the event switch on the monitor, press and release.

17.3.12 Steps for Adjustment of Gain Lever

1. Set the gain lever to the bottom position. The bottom 1-3 lights on the vertical row of lights should be lit. Neither the trigger light nor the audio will be activated at this time. If they are, make sure the subject is connected properly.

2. Slowly push the gain lever up. More of the vertical lights will begin to light. The lever should be raised until the vertical row of lights completely lights or goes to the ninth light for each R-wave of the subject's QRS complex.

17.3.13 RR-Variation Study

The RR-variation study is a six minute test during which the patient breathes at a fixed rate with the aid of the Respiration Pacer. The test is performed with the patient in the supine position the entire six minutes and is immediately followed by the postural study, during which the patient stands for ten minutes.

Before the RR-variation study begins, the tester must fully complete the ANS Testing Eligibility Form (DCCT Form 081), and the patient must rest in the supine position for 30 minutes. During the 30 minutes, the patient will receive instruction on how to perform the test. He/she will be given the Respiration Pacer to be held at a comfortable angle for viewing and told to inhale as the lights are ascending on the Pacer and to exhale as the lights are descending. The Pacer is timed for five breaths per minute and the patient must be told to "pace" themselves with the lighting of the lights. He/she must be informed that the test will last for six minutes and inhaling as the lights go up and exhaling as the lights go down is mandatory for that time period. The patient must understand that he/she must stand after the six minutes to complete the ten minute postural study. The patient will not need to breath with the Respiration Pacer during the postural, but must stand still and have blood pressure measurements at fixed time periods (see Section 17.3.14). After receiving instructions, the patient is allowed to practice a breath before the test begins. The tester must also ready the equipment during the 30 minute rest. This includes checking channel 4 of the tape recorder on the gauge to insure that the needle moves with each heartbeat and watching the lights on the ECG monitor, making sure they are triggering for each heartbeat. As the patient does a practice

breath, the tester must check the trigger lights on the ECG monitor to be sure the equipment is triggering properly through each stage of the breathing process. The gain lever should be adjusted if necessary (see Section on Equipment Operation). A blood pressure cuff must be made handy for the tester to use at the beginning and end of the study. The tape recorder can be preset to record by simultaneously pushing in the record button and pulling over the play button, then pushing the pause button. The footage marker of the tape should be recorded.

When the patient understands the method of the test, he/she will begin the fixed breathing when the lights on the Pacer start ascending. After one full inhale and exhale, the tester will begin recording the study by releasing the pause button and pushing the event marker once. This should happen as the patient begins inhaling. The time must be noted, or a timer set for the tester to know when the end of the six minutes will occur. Then the tester must measure the patient's blood pressure.

Throughout the study, the patient must be watched carefully to insure he/she is always pacing his/her breathing pattern with the Respiration Pacer. The tester must be positioned so he/she can look across the patient's chest and see the Pacer to watch that the rise and fall of the chest cavity matches the rise and fall of lights on the Pacer. Encouragement can be given to the patient to continue complying with the testing methods, and the patient can be told how much longer he/she has before the test is complete.

If at any time during the RR-variation study the patient fails to inhale and exhale properly (i.e., getting the inhaling and exhaling backwards, falling asleep, talking, etc.), the test must be stopped and restarted. A rest period is not required for a restart of the RR-variation study.

At the end of the six minutes, the patient's blood pressure must be taken and the footage marker noted. Then an event marker must be activated signaling the completion of the RR-variation study.

17.3.14 Postural Study

The postural study is a ten-minute test during which the patient stands in place, blood pressures are taken and heartbeats are recorded. The postural test will always immediately follow the RR-variation study without interruption in the recording unless otherwise stated by the CACU.

Upon the completion of the six minute RR-variation study, the Respiration Pacer will be taken from the patient and set aside. The patient must then stand, being careful not to detach the ECG leads or their connectors. The recording must continue through the standing and into the postural study. The tester must listen for the audio signaling a trigger for each heartbeat. If during the process of standing, the

monitor is signaling too many times or not enough, the gain must be adjusted as stated in the Section on Equipment Operation.

The patient's blood pressure should be taken at one, two, three, four, five and ten minutes into the study. These blood pressures should be recorded on the documentation sheet. An event marker must be placed at the end of ten minutes of standing and the footage marker on the tape recorded. Then the tape recorder can be turned off and the postural study is complete.

If, by the request of the CACU, the postural test is being performed without the RR-variation test preceding it, the patient must rest in the supine position for 30 minutes. The tester should start the recording just before the patient begins to stand and record the test for ten minutes taking blood pressures at the beginning and at minutes one, two, three, four, five and ten.

The patient should be watched carefully during the postural test for signs of hypotension. The tester should have help available in case the patient faints. If a drop of more than 10 mmHg in the diastolic blood pressure occurs, AND THE PATIENT IS SHOWING OBVIOUS SIGNS OF POSTURAL HYPOTENSION, the patient must be placed in the supine position immediately. As soon as the patient is comfortable, the test can be stopped simply by turning off the tape recorder. When the patient developes postural hypotension, he/she must be rescheduled for complete ANS testing on a separate day with plasma catecholamine measurements during the RR and postural studies.

17.3.15 Postural Study with Plasma Catecholamines

Revised August 1, 1990

If a patient has a drop of more than 10 mmHg in the diastolic blood pressure during the postural study, the patient must be rescheduled for ANS testing with plasma catecholamines. The testing must be scheduled on another day within the time window of the original visit. When a repeat is necessary, the tester must notify the CBL immediately. There must be more than one tester to assist with the patient on the repeat study day.

During the repeat study, each of the individual tests must be performed as they are on a normal testing day with some additions (Figure 17.3). The Valsalvas must be performed first after a 15 minute rest in the supine position. During this 15 minute rest, the testers must prepare the patient for the drawing of the blood samples. The samples can be drawn either through a heparin lock or a saline I.V. line. When drawing through the heparin lock, no certain gauge is required. However, in regards to the type of needle, steel is preferrable (not intracath). After completion of the two Valsalvas (with a five minute rest between Valsalvas), the patient must rest for 30 minutes. Blood samples must be collected at the beginning of the RR

variation study, at the beginning of the postural (before the patient actually stands), and at two, five and ten minutes into the postural study. A tourniquet can be used as a last resort if the patient's vein collapses during the study.

Special tubes must be used for the blood samples and are provided by the CBL. The following steps must be followed for the collection and processing of the samples:

1. A special tube prepared by Amersham will be supplied by the CBL. This tube contains EGTA and glutathione and must be refrigerated (2-8 C) until used.

2. The patient should remain in the supine position in a non-stimulatory environment for at least 30 minutes prior to blood sampling. The blood sample may be drawn with a syringe. Remove the rubber stopper of an appropriate tube and transfer 2.5-5 cc immediately. Mix the tube gently and thoroughly and place on ice immediately.

3. Centrifuge the specimen at 5 C for ten minutes at 900 g (2000 rpm). Separate plasma from the cells as quickly as possible (within 45 minutes of collection). Aspirate as much plasma as possible but avoid the buffy coat and platelets. Recentrifuge plasma (5 C, ten minutes, 900 g).

4. Transfer to a 5 ml Nunc tube and freeze. Frozen plasma is stable for at least three months when stored in a tightly closed container below -20 C.

5. Label the tube with the patient's initials, identification number, age, date, and time. Include the original of the Catecholamine Specimen Mailing List (DCCT Form 109) with your shipment. A copy of the Form 109 should be sent to the Coordinating Center in your weekly mailing. Specimen must be delivered early in the week on dry ice to:

   DCCT Central Biochemistry Lab
   Attn: L275 Mayo 626-3645
   University of Minnesota Hospital and Clinic
   420 Delaware Street
   Minneapolis, Minnesota 55455-9980

6. Specimens will be sent by CBL to:

   Ada Simon, Ph.D.
   Cardiovascular Division
   Biochemical Research Lab
   University of Minnesota

17.3.15.1 ANS Assessment with Orthostatic Hypotension

Currently, the autonomic nervous system evaluation is performed on DCCT subjects at baseline, every two years and at study end. There already is a well defined protocol for the collection of catecholamines in the case that a patient develops orthostatic hypotension (a drop of more than 10mmHg in the diastolic blood pressure) during the postural phase of the ANS study (17.3.15). It is less clear, however, in describing procedures at subsequent ANS evaluation in regards to ongoing collection of catecholamines in patients with orthostatic hypotension at previous ANS assessment. The purpose of this section is to describe these procedures for catecholamine assessment at subsequent ANS evaluations.

When a DCCT subject initially demonstrates orthostatic hypotension, the test is stopped and rescheduled for another day. The test is then repeated with catecholamines drawn during the postural study (17.3.15).

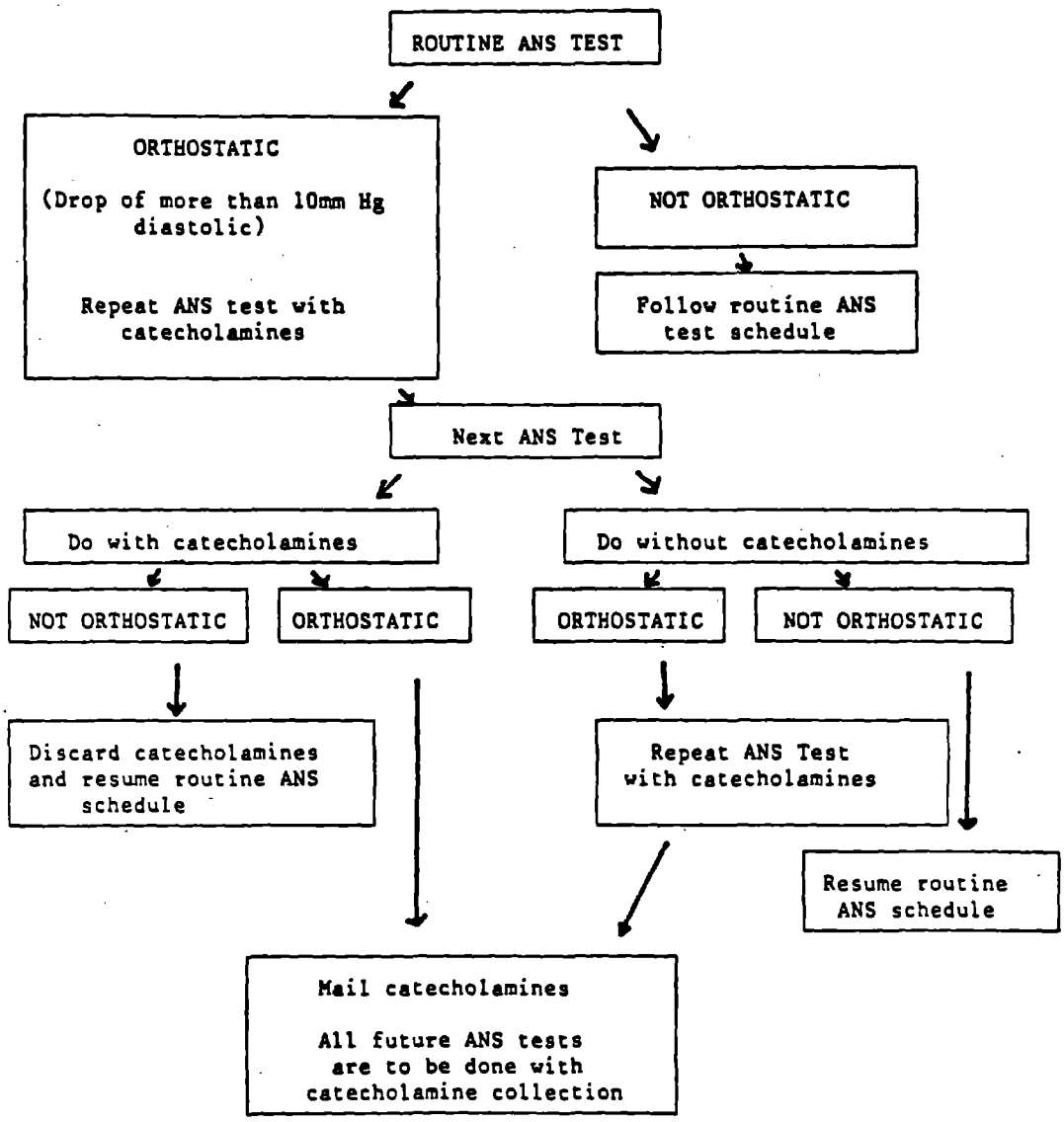
At the next ANS test following the test during which orthostatic hypotension was identified and catecholamine drawn, the clinic will have two options. The first option (1) is to do the procedure outlined in chapter 17.3.15. That is, collect the catecholamine and if the patient does not develop orthostatic hypotension, throw the catecholamine away. The other option (2) is to perform the standard ANS test, without catecholamines, but recognizing that if the patient does become orthostatic, the test will need to be stopped and the patient rescheduled to repeat the test (within that ANS time window), and catecholamines collected.

Option 2 is probably most effective in patients who didn't demonstrate orthostatic hypotension during the postural study where catecholamines were first drawn. In these cases, it may be that another cause could explain the initial orthostasis, i.e., dehydration, anxiety.

Any patient who develops orthostatic hypotension at two regularly scheduled ANS evaluations should automatically have catecholamines drawn at all future ANS tests.

Finally, any patients who are being treated for orthostatic hypotension, either with mineral corticoids or with mechanical means (i.e., pressure stockings) should always have catecholamines drawn at the time of the ANS test. Tests should be done without stockings. Mineral corticoids and other treatments should be noted. The form of treatment can be indicated on DCCT Forms 70 and 81.

ANS ASSESSMENT IN THE CASE OF ORTHOSTATIC HYPOTENSION



17.3.16 Valsalva Maneuver

Following the RR-variation and postural studies, the patient must rest in the supine position for 15 minutes. During this time, the Valsalva maneuver will be explained. The patient will remain in the supine position for two Valsalva studies, and the five minute resting period between the two studies. The first minute of the test the patient will be still and breathe ad libitum. Then the patient will be asked to blow into the mouthpiece of the Valsalva apparatus for 20 seconds, holding the gauge on the Sphygmomanometer at 40 mmHg. After the 20 second blowing period, the patient will again breathe ad libitum for one minute thus concluding the study. The patient is allowed to practice the blowing period before the first Valsalva is actually performed. During the test blowing period, the tester needs to watch the ECG monitor and see if adjustments to the gain are going to be necessary. If so, during the actual study, the tester can adjust the gain as the patient begins blowing so each heartbeat will be properly recognized. Readjustment may also be necessary during the post Valsalva breathing period.

The tester will need the Valsalva apparatus and a timer along with the ANS equipment to conduct the valsalva study. When the patient is ready for the study, the tester will begin recording and note the footage marker of the tape, activate two event markers and start timing the study. Fifty-five seconds into the study, the tester must ask the patient to take a deep breath and begin blowing into the mouthpiece of the Valsalva apparatus. At the time the patient begins blowing, the tester must activate two event markers, time the blowing period, and adjust the gain if necessary. After 20 seconds of blowing, two more event markers must be activated and the patient told to stop blowing. Then one minute of ad libitum breathing should be recorded and two event markers placed at the end of the study.

During the blowing period, the tester must watch the gauge of the sphygmomanometer to ensure that once the pressure reaches 40 mmHg, the patient keeps it there for the remainder of the blowing period. Praise and encouragement should be given to the patient to successfully complete the blowing period. The tester should also listen for the audio sound of the triggering, making sure the heartbeats are properly recognized.

If a patient does not complete the full 20 second blowing period on both Valsalvas, the test should be restarted with a five minute rest period between attempts, until two good Valsalvas are recorded.

On a normal testing day, when both Valsalvas are successfully completed, ANS testing for the patient is then complete (Figure 17.2 for flow sheet of ANS testing).

Revised February 28, 1992

17.3.16.1 Valsalva Manuever in Patients with PDR

Another point of clarification pertains to the question of performing Valsalva manuever in patients who have PDR. You may remember that this question arose about 1 1/2 years ago.

The Planning Committee recommends that all patients who have PDR be excused from this portion of the ANS protocol. The ophthalmologist from each of the clinics was polled about the risks associated with this procedure in patients who have PDR. Fourteen ophthalmologists responded that they would recommend against patients with PDR performing the valsalva maneuver. This is not a local option.

17.3.17 Taping and Documentation

A 90 minute cassette tape must be used to record the studies. These tapes will not be used again but will be kept by the CACU. A medium priced cassette tape works fine. At the beginning of the tape, and in between each of the separate studies, the tape must be advanced at least 20 footage markers. This space between studies must be blank tape. The footage markers for the beginning and end of each study must be recorded on the ANS Documentation Sheet (DCCT Form 070).

One event marker must be placed at the beginning and the end of the RR-variation study and upon completion of the postural. Two quick event markers must be placed at the beginning of each Valsalva, at the beginning and end of the blowing, and at the end of the Valsalva study.

The ANS Documentation Sheet (DCCT Form 070, see Figure 17.4 for an example) must be completed.

If the study is a normal or a certification tape, the patient ID number must not be completed and "normal" or "certification" must be written in the area next to that line. (Normal patients are healthy non-diabetics done properly prepared for control purposes. Certifications are done only for practice and proof of the credibility of a new technician and will be used only for certification purposes. The CACU must be notified for proper instructions when training new technicians.) The follow-up visit number must be correctly included on this sheet. Each tape must also have a label which includes the clinic number, patient's ID number, patient's initials, and the date the studies were done. This label must be directly on the tape not on the case for the tape. Blank labels can be obtained from the CACU.

If, during the course of the studies, the tester encounters any problems, there is space available for comments that will aid the CACU in analyzing the data. If a study is restarted, this must be shown clearly on the documentation sheet.

17.3.18 Mailing

Each ANS recording must be sent to the CACU upon completion of the study. No recording should be kept at the clinic for longer than a week after completion. No more than four studies should be mailed in one container. The tapes and papers must be sent in a padded envelope or box. The catecholamine samples must be sent on dry ice and should be padded for protection. Mail the samples early in the week so the ANS Laboratory can be sure they have arrived and take proper care of them before the weekend.

An RR-Interval ECG Mailing List (DCCT Form 054) must be completed. The Mailing List must have four duplicate copies. The original copy is to be sent in the same container as the tapes. A copy must be mailed to the CACU in a separate envelope. A copy must also be sent to the Coordinating Center and one copy retained in clinic files.

Each study sent must have an ANS Documentation Sheet and an ANS Testing Eligibility Form. A copy of each of these forms must also be retained in the clinic files.

17.4 NERVE CONDUCTION STUDIES

17.4.1 Introduction

Since diabetic patients are subject to a generalized neuropathy, changes of metabolic status theoretically should be reflected equally in all peripheral nerve segments. In the DCCT, the expected changes in nerve conduction may be small and are liable to be obscured by inter-patient and inter-center variability. However, a careful broad screening of several peripheral nerves is time consuming and subject to redundancy and not the least entails the risk of misleading mass significance. Therefore, the following limited protocol has been adopted, covering sensory and motor nerve conduction in one arm and one leg, in order to concentrate the efforts in a carefully conducted study.

17.4.2 General Methodology

17.4.2.1 Patients

Patients should be scheduled one to two hours after a regular meal. Outpatients should be scheduled at least 30 minutes before the actual test in order to accommodate to the temperature of the laboratory.

17.4.2.2 Equipment

The choice of electromyograph or electrodes is not standardized. Any modern equipment is accepted, provided that it includes an averager and that photographic or durable paper recordings are available. The instrument for temperature measurements should include a surface thermistor and should preferably allow continuous monitoring.

17.4.2.3 Examiner

Serial studies on any one patient should be performed under the direct supervision by the same trained electromyographer (M.D.).

17.4.2.4 Nerves

The protocol comprises the following nerve segments:

1. Median nerve. Distal motor latency from wrist to the abductor pollicis brevis muscle. Motor conduction velocity from elbow to wrist. Orthodromic sensory conduction velocity from digit II to wrist. F-wave latency, stimulating at the wrist.

2. Peroneal nerve. Distal motor latency from ankle to the extensor dig. brevis muscle. Motor conduction velocity from capitulum fibulae to ankle. F-wave latency, stimulating at the ankle.

3. Sural nerve. Antidromic sensory conduction velocity, stimulating the nerve about 14 cm. proximal to a recording electrode at the lateral malleolus.

In all follow-up studies, the same nerve segment on the same one side is examined with the same interelectrode distance.

During a ten-year trial, the development of a carpal tunnel syndrome in a diabetic patient is a real possibility. If this is suspected on the basis of an isolated or marked impairment of the distal sensory and/or motor conduction velocity in the median nerve, the following procedure applies:

1. The median nerve protocol is followed and reported, as described, in any event. That is, data must not be left out because of a suspected or proven carpal tunnel syndrome.

2. The report should be accompanied by a comment to the problem.

3. The following electrophysiological observations should be added: The ipsilateral ulnar nerve distal orthodromic sensory conduction velocity from digit V to wrist, and the distal motor

latency from wrist to the hypothenar muscle group, using the same distance as for the distal motor latency in the median nerve.

4. Standard treatment, eventually decompression of the median nerve, should be offered to the patient according to general rules.

17.4.2.5 Stimulation

Surface electrodes are used for stimulation. The cathode will be distal. The anode is placed to approximate the course of the nerve. The optimal location of the electrode is determined by moving the cathode in small steps while stimulating the nerve with submaximal current. The actual recording should be performed with supramaximal stimulus strength, but not higher than 30% above maximum as judged from the amplitude of the evoked response. A minimal number of stimuli should be applied. The site of stimulation is marked accurately with an easily removed marker.

17.4.2.6 Recording

The evoked responses are recorded with surface electrodes. The electrode positions are described below ("Specific Methodology"). For muscle action potential recordings, the "active" electrode is placed so that the potential has a clearly defined negative onset and a maximal amplitude. Only use enough electrode paste to coat the electrode. If the electrode moves during the conduction study, it should be replaced and the entire procedure repeated. To reduce artefacts, the anode may be rotated, the skin dried, excess electrolyte paste removed, bad leads or pin-jacket contacts replaced, the skin under the recording electrode mildly abraded, or recording and stimulating wires kept apart. A ground electrode is placed conveniently between the distal site of stimulation and recording, and it should make an extensive contact with the skin as possible.

The frequency band is inclusive of two 10.000 Hz for muscle potential recordings, and 20 2.000 Hz for sensory potential recordings. The time base should be set to give maximal accuracy in latency measurements, and should be the same for distal and proximal stimulation sites. The potential amplification (gain) should be adjusted to prevent clipping of the peaks, and so that amplitudes are at the least one cm. Sensory action potentials less than five uV in amplitude should be averaged, so that the amplitude is higher than one cm and the baseline less than 10% of the signal amplitude. Preferably, the gain should be the same for distal and proximal stimulation sites. F-waves are recorded with supramaximal stimulation, and the minimal F-wave latency of eight responses is reported and recorded. The gain is adjusted to clearly identify the response. The site of stimulation and recording

and time base and amplification should be clearly indicated on each photographic recording.

17.4.2.7 Temperature Control

Nerve conduction studies in the individual patients should be performed under temperature conditions as similar as possible. If necessary, the extremity should be heated to the temperature of the previous examination. Temperature measurements are performed with surface thermistors throughout. The temperature is recorded before and after the actual nerve conduction study in each nerve, and both values are reported. Note that the nerve conduction velocities should be reported as the actually recorded values without temperature corrections. A centralized temperature correction of data may be considered for the final analysis.

Temperatures are measured at the following sites:

1. Median nerve: On the forearm over the nerve, midway between the wrist and elbow and in the palm between digit II and wrist (distal sensory CV).

2. Peroneal nerve: Over the anterior tibial muscle between knee and ankle.

3. Sural nerve: On the calf midway between the sites of stimulation and recording.

17.4.2.8 Measurements

Motor latencies are measured to the onset of the negative portion of the compound muscle action potential with an accuracy of 0.1 msec. Sensory latencies are measured to the onset of the negative peak of the compound nerve action potential with an accuracy of 0.1 msec. The amplitude of compound muscle action potentials is measured from the baseline to the peak of the negative portion of the potential. The sensory potential amplitude is measured from peak to peak. The accuracy is 0.1 mV and 1 uV for muscle and nerve action potentials, respectively. All measurements of latency and amplitude in a given nerve are made with the same gain and sweep speed. In the sural nerve, absence of a response will mean that no potential could be detected despite stimulation in a series of contiguous steps along the postero-lateral half of the calf, and despite averaging of 32 responses.

Distances will be measured to the nearest mm with a flexible tape, approximating the course of the nerve. The distance of proximal nerve segments is from the centers of the cathode at the proximal and distal site of stimulation. The distance of distal nerve segments is from the center of the distal stimulation cathode to the center of the active recording electrode.

Temperatures are measured to the nearest 0.1 degree C after equilibration of the surface thermistor.

17.4.2.9 Report of Data

Data from nerve conduction studies are reported on DCCT Form 037. All spaces must be filled out at each examination. The form should be accompanied by photographic recordings of the evoked responses, mounted on white paper. All sheets with recordings must be clearly identified with the patient's identification as shown in DCCT Form 037, and each recording should give the name of the nerve, the gain, and sweep speed. In addition, an extra set of recordings should be filed in each laboratory.

Reports and recordings are collected by the clinic coordinator.

17.4.3 Specific Methodology — Electrode Placements

17.4.3.1 Median Nerve -- Motor

1. Stimulating electrodes: Distal -- the cathode is placed two cm proximal to the wrist crease and between the flexor carpi radialis and palmaris longus tendons. The anode is proximal and should be rotated laterally to minimize spread of current to the ulnar nerve. Proximal -- the cathode is on the anterior surface of the upper arm between the biceps tendon and the medial epicondyle of the humerus, immediately over the brachial artery. The anode is proximal and should approximate the course of the nerve.

2. Recording electrodes: The "active" electrode is placed over the abductor pollicis brevis muscle one-third of the distance between the wrist crease and the metacarpel -- phalangeal joint of the thumb. The "inactive" electrode is placed just distal to and on the anterior surface of the metacarpal -- phalangeal joint of the thumb.

3. Ground electrode: A ground electrode is placed conveniently between the distal site of stimulation and the recording electrode.

17.4.3.2 Median Nerve — Sensory

1. Stimulation electrodes: Ring electrodes are wrapped around the index finger (digit II). The cathode is wrapped around the middle of the proximal phalanx of the index finger. The anode is wrapped around the middle of the middle phalanx of the index

finger. Cotton is used to separate the index and middle fingers so that the stimulating electrodes do not touch the middle finger.

2. Recording electrode: The sensory nerve action potential is recorded longitudinally with the same electrode position as used for stimulation of median nerve motor fibers at the wrist.

3. Ground electrode: As in median nerve -- motor.

17.4.3.3 Peroneal Nerve — Motor

1. Stimulation electrodes: Distal -- the cathode is placed on the anterior aspect of the ankle, lateral to the tendon of the anterior tibial muscle and five cm proximal to the lateral malleolus. The anode is proximal along the course of the nerve. Proximal -- the cathode is placed behind the neck of the fibula, just proximal to where the nerve enters the anterior compartment. The anode is proximal, approximating the course of the nerve.

2. Recording electrodes: The "active" electrode is placed over the extensor digitorium brevis muscle one cm distal to its bony origin. The "inactive" electrode is placed over the lateral aspect of the distal end of the fifth metatarsal bone.

3. Ground electrode: A ground electrode is placed conveniently between the distal stimulating electrode and the recording electrode.

17.4.3.4 Sural Nerve — Sensory

1. Stimulation electrodes: The cathode is placed on the calf one to three cm lateral to the midline, and 14 cm proximal to the center of the "active" recording electrode. The anode is proximal and the position adjusted to minimize the stimulus artifact.

2. Recording electrodes: The "active" electrode is placed immediately behind the lateral malleolus. The "inactive" electrode is placed four cm distal to the "active" electrode along the course of the nerve.

3. Ground electrode: A ground electrode is placed between the stimulation and the recording electrodes, just proximal to the "active" recording electrode.

Figure 17.1

INFORMATION ON ORDERING SUPPLIES

9-23-85

ITEM	DESCRIPTION	VENDOR	CATALOG OR MODEL NUMBER	COST	NOTES
ECG Monitor	Specially designed module for ANS testing to use with stereo recorder.	D.E. Hokanson, Inc. 2450 Newport Way, S.E. Issaquah, Washington 98027		$1780.00	
Respiration Pacer	Hand held patient breathing guide.	"		$375.00	
Patient Cable	To connect patient to monitor.	"		$120.00	
Foot Pedal	Used with module to signify events.	"		$30.00	
Tape Recorder	Stereo Cassette Recorder	"		$150.00	
EKG Lead Wires	Connects electrodes to patient cable.	For your local 3M dealer 1-800-323-4087			
Valsalva Apparatus	Used to guage patient blowing during Valsalva Maneuver.	"			
Mouthpieces	For use with Valsalva Apparatus.	National Medical Specialties 1540 South Franklin Road Indianapolis, Indiana 46239 (317) 352-0911	1022	$94.90 per case	500 per case
EKG Electrodes	3M Red Dot Leads	For Your local 3M Dealer Call 1-800-323-4087	2256	approx. $12.00 per bag	25 per bag
Cassette Tapes	Ampex Cassette Tapes	Please see attachment	90 minute tapes	approx. $1.00 ea	

ADDRESSES FOR ORDERING AMPEX TAPES

WEST:

Ampex Corporation (Home Office)
401 Broadway 2-12
Redwood City, Ca. 94063
415-367-4611

500 Rodier Dr.
Glendale, Ca. 91201
213-240-5000

MIDWEST:

719 W. Algonquin Rd.
Arlington Heights, Il. 60005
315-593-6000

SOUTHWEST:

3353 Earhart Dr.
Carrolton, Texas 75006
214-560-1162

SOUTH:

3135 Chestnut Dr. Suite 101
Atlanta, Ga. 30340
404-451-7112

EAST:

10215 Fernwood Rd.
Bethesda, Md. 20817
301-530-8800

5 Pearl Court
Allandale Industrial Parl
Allandale, N.J. 07401
201-825-9600

Figure 17.2

FLOW CHART OF ANS TESTING

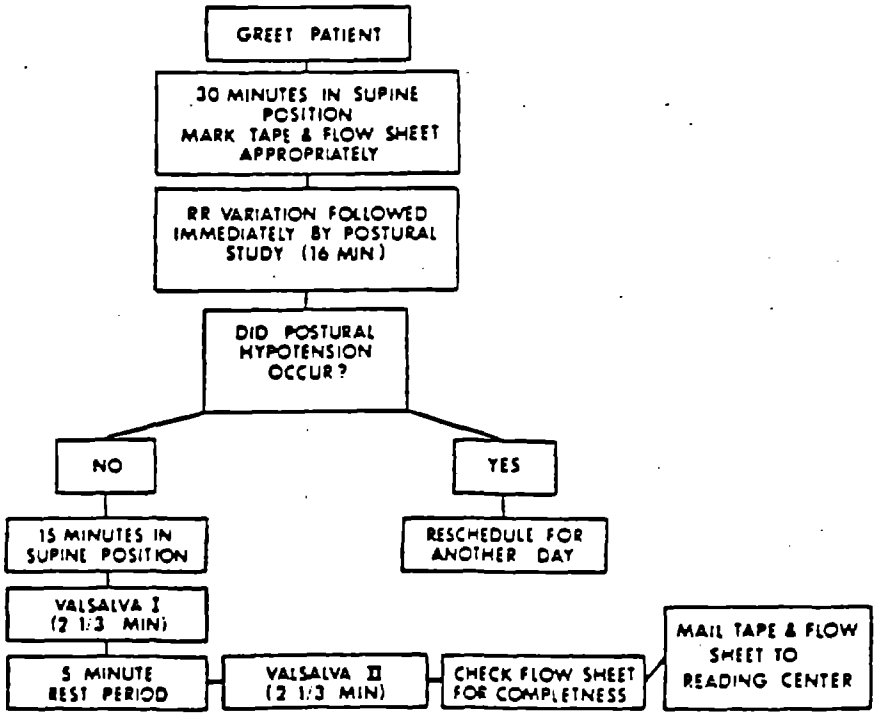


Figure 17.3

FLOWCHART OF REPEAT ANS TESTING WITH PLASMA CATECHOLAMINES

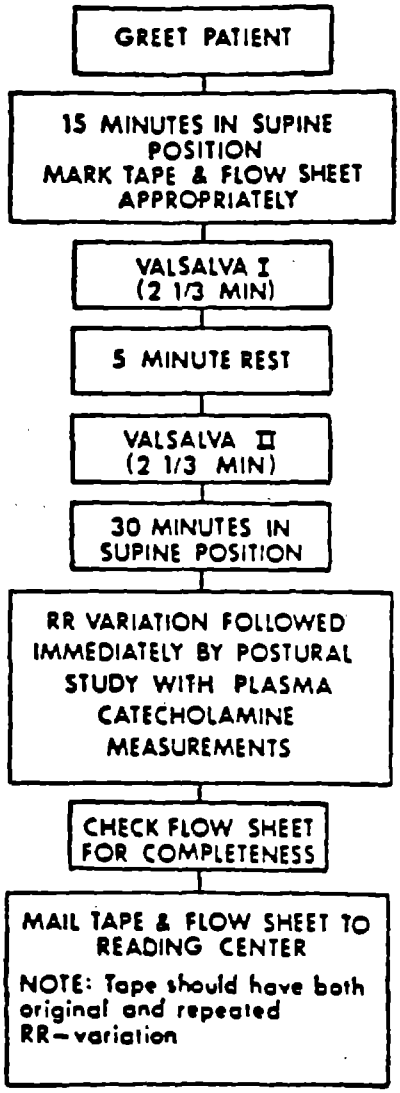


Figure 17.4

DIABETES CONTROL AND COMPLICATIONS TRIAL

4HS Documentation Sheet

Clinic Number

Patient ID Number

Patient's Initials

Date of Studies

Was the visit held within the time window?

Certification number of person performing the studies:

Tape Number:

Study Number:

If a baseline visit, check here:

Otherwise, follow-up visit number:

NOTES: _____

TEST	FOOTAGE MARKER	EVENT MARKER	ACTIVITY/COMMENTS (BLOOD PRESSURE)		
RR	20	1	Begin	118/86	
PO	170	1	Begin	116/84	
			1 min.	118/84	
			2 min.	118/90	
			3 min.	116/90	
			4 min.	116/88	
			5 min.	118/92	
	357	1	10 min.	112/88	END

Patient I. mber

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Date of Studies

Figure 17.4 (Cont.)

TEST	FOOTAGE MARKER	EVENT MARKER	ACTIVITY/COMMENTS (BLOOD PRESSURE)
Valsalva I	377	2	Begin
		2	Begin Blowing Period
		2	End Blowing Period
	405	2	End
Valsalva II	425	2	Begin
		2	Begin Blowing Period
		2	End Blowing Period
	460	2	End

CHAPTER 18

CARDIOVASCULAR PROCEDURES

18.1 ELECTROCARDIOGRAM PROCEDURES

18.1.1 Introduction

Resting electrocardiograms (ECGs) will be obtained during the eligibility screen and at the biannual follow-up visits. In addition, ECGs will be collected to document any myocardial infarction (MI) or other cardiovascular intercurrent events. Operational guidelines and procedures for obtaining and processing ECGs required for this study are discussed in the following sections.

18.1.2 Eligibility ECG

A standard supine 12-lead resting ECG should be obtained on each patient as part of the pre-randomization cardiovascular examination. The purposes of the eligibility ECG are (1) to establish the ECG characteristics of each patient at entry and to exclude any patient with an ECG abnormality; (2) to document the distribution of ECG characteristics among patients in each treatment group; and (3) to provide for each patient an ECG baseline to compare with follow-up ECGs and/or with ECGs obtained in conjunction with any cardiovascular event.

ECGs will be interpreted locally for determination of patient eligibility and the results will be recorded in the appropriate item on DCCT Form 038. ECGs determined to be abnormal on the basis of local reading may be sent via the Coordinating Center to the Central ECG Reading Unit (CERU) for confirmation. All ECGs on eligible patients will be mailed via the Coordinating Center to the CERU for grading using DCCT Form 053. The ECG reading unit will record the results of its grading on DCCT Form 024 and send the form to the Coordinating Center.

The ECG machine that is used to take electrocardiograms should meet the AHA recommendations (Report to Committee on Optimal Electrocardiography, American Journal of Cardiology, March 1978). A single-channel ECG recorder which uses a flat stylus writer (a flat stylus produces a thick baseline during the TR or PR segment and a relatively thin baseline during the inscription of the QRS) is preferred.

One of the following single-channel ECG recorders is preferred:

Hewlitt Packard Model 1500 A or B

Hewlitt Packard Model 1511B
Fukuda Model 501A

Multichannel recorders may be acceptable upon approval of the CERU. The three-channel Fukuda is the preferred multichannel recorder, although others that provide high quality tracings may be used. Provide information on the makes, models, and ages of available ECG equipment, and submit an original and two copies of tracings from all machines that could be made available for the DCCT for evaluation of acceptability by the CERU. It is desirable that a single machine will be used for all evaluations on DCCT subjects.

At least one full minute of ECG tracing should be obtained consisting of five seconds of each of the leads (I, II, III, aVR, aVL, aVF, V1-V6). A stop watch may be used to assure that a full minute of tracing is obtained. A series of one mV calibration pulses should be recorded at the beginning of the ECG recording followed by tracings of leads I, II, III, aVR, aVL, aVF and V1-V6. Tracings must be recorded at a paper speed of 25 mm per second. Leads which must be recorded at one-half standard should be preceded by a half standard calibration pulse and should be marked with the words "1/2 STD".

Comparability of eligibility ECG records with possible subsequent follow-up records requires that uniform procedures for electrode placement and skin preparation are followed. The procedure for standardizing electrode locations is described in Section 18.2.2.

The eligibility ECG tracings should be sent unmounted to the Coordinating Center. A second tracing should be mounted and kept in the patient's file at the clinic. Three eligibility visit ECG labels provided by the Coordinating Center should be completed with the DCCT Clinic Number, Patient ID Number, Patient's Initials, Date of ECG, and the Certification Number of the ECG technician who made the tracing. One completed label should be affixed to the front of an envelope in which the ECG is placed. Two other labels should be inserted in the envelope with the tracings; these labels will be used by the CERU One label will be used on the ECG grading form (DCCT Form 024) and the other label will be affixed at the beginning of the ECG tracing. The ECG strips should be checked for the following details:

1. Each lead should be clearly identified.

2. A standardization strip should be included.

3. There should be no overlap of tracings.

4. The paper speed should be indicated on the ECG if it is other than 25 mm/second.

5. If the sensitivity is other than 1 mV = 1 cm, the grade should be indicated on the ECG.

The ECG strips must be folded accordion style (see Figure 18.1). Beginning with V_6 , make a six-inch fold towards V5 . Fold back six inches away from V4 . The folds do not have to correspond to lead changes. The strip should measure six inches in length once the entire ECG has been folded. The folded strip is inserted in a labeled envelope.

The eligibility ECG will be submitted by the DCCT Coordinating Center to the CERI Unit for grading using the Minnesota Code. The revised Minnesota Code is summaried in Table 18.1.

18.1.3 Follow-up ECGs

Follow-up ECGs will be recorded biannually. Prior to mailing the ECGs to the Coordinating Center, an Endpoint Visit ECG Label provided by the Coordinating Center should be completed with the Clinic Number, Patient ID Number, Patient's Initials, date of the ECG, Follow-up Visit Number, and the certification number of the ECG technician who made the tracing.

18.2 PROCEDURE FOR OBTAINING THE 12-LEAD ELECTROCARDIOGRAM

The procedures for recording the 12-lead resting electrocardiogram are discussed below.

18.2.1 Preparation of the Patient

The participant, stripped to the waist, is instructed to lie on the recording bed with shoulders straight and arms relaxed at the sides. He/she is asked to avoid movements which may cause errors in marking the electrode locations but is encouraged to converse with the technician and/or physician in order to assure a comfortable and relaxed atmosphere. The patient is questioned as to prior experience with electrocardiograms and is informed of the purpose of the ECG recording. The patient may be told that this ECG is for research purposes and as such will not be used by the clinic staff for diagnosis.

18.2.2 Electrode Position Measuring and Marking

A good felt tip pen is used to mark the 12 electrode positions as detailed below. It is important that care be taken to locate and mark the chest electrode positions accurately. The procedure given below must be meticulously followed. Electrode placement is indicated in Figure 18.2.

1.

Electrode V2

a) Locate the sternal angle and second left rib between the index and middle fingers of the right hand.

b) Count down to the fourth rib and identify the fourth intercostal space below it.

c) Locate V2 in the fourth intercostal space at the left of the sternal border.

2. Electrode V1

Locate electrode V1 in the fourth intercostal space at the right sternal border. This should be at the same level as V2 and immediately to the right of the sternum.

3. Anterior 5th Interspace Marker (E Point)

Identify the fifth rib and fifth intercostal space below V2 in the manner previously described. Follow this space to the midsternal line and mark this point. This is the "E" point.

4. Electrode V6

a) Locate the V6 electrode at the same level as the E point in the mid-axillary line. This line identifies the horizontal level for V4-V6 electrodes.

b) Using a metric tape, measure the horizontal distance in centimeters from the E point to V6. The mid-point distance is the V4 electrode location.

c) Using a flexible ruler, measure the distance between V4 and V6. The V5 electrode is placed midway between V4 and V6.

d) In a similar manner, measure the distance between V2 and V4. The mid-point is the location of the V3 electrode.

5. Limb Leads

a) Locate electrode LL on the left leg.

b) Locate electrode RL on the right leg.

c) Locate electrode LA on the left wrist (inside).

d) Locate electrode RA on the right wrist (inside).

18.2.3 Skin Preparation

The following procedure for preparation of the skin before applying electrodes must be followed:

1. If significant baseline drift or irregular deflection occurs, the examiner may, with the patient's consent, remove any excess hair from each electrode site on the chest using an electric shaver or safety razor.

2. At each electrode location in turn, the outer horny layer of the epidermis is removed by gentle dermal abrasion with a piece of 6-0 (220) sandpaper. Only three passes (in the form of an asterisk) at each site using light pressure is required.

If the skin preparation has removed the felt pen marking at any of the electrode sites, these should be accurately re-established by carefully repeating the procedure described in Section 18.2.2. It is important that the electrode sites be marked accurately using the exact technique described previously.

18.2.4 Application of Electrodes

A small amount of electrode jelly is placed on the skin at each prepared site. It is most important that the electrode jelly not be smeared over a wider area than necessary in order to avoid low impedance pathways between electrodes and production of marked distortion of the ECG wave forms.

The limb lead plate electrodes are placed in the appropriate locations. The patient cable is now attached to the appropriate electrodes with the subject in the supine position, hands at the sides, with care not to entangle or pull any of the leads. Calibration pulses followed by the six limb leads are recorded first, followed by the six precordial leads as previously described. If the clinic staff wish to retain a second "original" ECG for the patient's file, it should be recorded at this time.

18.2.5 Fault Detection Procedures

Should problems with noise or drift be encountered, electrodes should be replaced. The following is a guide for determining which electrodes may be faulty. The underlined electrodes are the predominant determinants of the appropriate lead and, therefore, are most likely to be the faulty electrodes for a given lead. After adjustment and/or replacement of suspect electrodes, all leads should be recorded again.

Lead Affected	Possible Faulty Electrode
I	RL, RA, LA
II	RL, RA, LL
III	RL, LA, LL
aVR	RL, RA, LL, LA
aVL	RL, LL, RA, LA
aVF	RL, LL, RA, LA
V1	RL, LL, RA, LA, V1
V2	RL, LL, RA, LA, V2
V3	RL, LL, RA, LA, V3
V4	RL, LL, RA, LA, V4
V5	RL, LL, RA, LA, V5
V6	RL, LL, RA, LA, V6

18.2.6 Self-Evaluation of Technical Performance

A reasonable estimate of the noise level and amount of baseline drift can be obtained by examining the ECG recording and an indication of technical performance level can thereby be obtained. Based on the requirements of the Minnesota Code, acceptable levels of noise and baseline drift have been established as indicated by grades 1 through 5 of the self-evaluation of technical quality performance grade (Figure 18.3A) grade levels given in this table take into account measurement accuracy requirements, the ability of the readers to achieve the required accuracy in the presence of noise and drift, and the level of technical quality expected from the conditions, equipment and the procedures specified for this study.

Baseline drift problems, which are essentially caused by poor electrode-skin interface, should be particularly easy to remedy as should 60 cycle noise. The ECG recordings should be examined for obvious errors such as wave form clipping, missing tracing or excessive noise and drift. The tracings should then be checked for right arm - left arm and other common lead misplacements. Once satisfied that the wave forms are basically correct and no obvious errors are present, the baselines (PR, ST, and TP segments) should be checked for the level of noise (Figure 18.4). No 60 cycle noise should be present, and the baseline should be steady and free of transients. Converting the noise level to peak to peak values, and noting that recording sensitivity is 1 mV per centimeter, the allowable noise level in terms of number of small paper deviations (one small paper deviation = 1 mm or 0.1 mV) are obtained as indicated for each grade level in Figure 18.3. These "eyeball" measurements serve as indications of the noise level performance grade. For instance, baseline fluctuations approaching five small paper deviations (0.5 mV or 5 mm peak to peak) are indicative of unacceptable noise levels. The overall drift criteria may be checked and an indication of the overall drift grade level obtained by searching the record for the maximum and minimum baseline levels (as determined by the PR and TP segments) and measuring the vertical distance between them. This distance must be less than ten small paper deviations (1 mV) to

satisfy the minimum drift criteria. An example of baseline measurement and beat to beat, overall drift and noise is indicated in Figure 18.3B.

The beat-to-beat drift level is determined by searching for the pair of successive QRS complexes and having the largest amplitude differences (vertical distance) between successive PR segments. Average values (numbers of small paper divisions) are given in Figure 18.3. These figures are approximate and serve only to give a general indication of beat-to-beat drift grade level. Certainly, however, a difference of four small paper divisions (0.4 mV) or more indicates an unacceptable record.

Examples of technical problems encountered in the ECG recording are illustrated in 18.5. Remedial actions are as follows:

1. Muscle Tremor

   Muscle tremor causes irregular oscillations (deflections) of low amplitude and varying rapidity, superimposed upon the ECG waveform (Figure 18.5, Part A). Muscle tremor is the involuntary muscle activity of a participant whose state is tense, apprehensive, or uncomfortable. Therefore, a clear explanation of the electrocardiogram test and reassurance are necessary for the participant. The participant is asked if the temperature of the room is too low for him/her and is covered with a blanket if so.

2. Careless Skin Preparation or Electrode Application

   Careless skin preparation or electrode application produces baseline drift, wandering baseline, or irregular or bizarre deflections (Figure 18.5, Parts A, B, and C). Faulty skin-electrode interface is the usual cause of baseline wandering, drift or irregular and bizarre deflection on an ECG tracing. These problems may be avoided by carefully following the prescribed procedure for skin preparation and electrode placement. Similarly, tension on one or more lead wires gives the same effect because it causes interference with proper electrode contact. However, baseline wandering or drift only in the precordial leads (V1 to V6) might be due to the participant's respiratory movements. A faulty connection between an electrode and a lead wire can also be suspected.

3. Sixty-cycle Interference

   Sixty-cycle interference is characterized by perfectly regular fine oscillations occurring at the rate of sixty per second (Figure 18.5, Part E). Electrical equipment of any kind may be the source of AC interference in all or some of the leads. AC interference which appears only in two standard limb leads (i.e., in two of leads I, II, and III) brings suspicion to the extremity which is common to them.

   Lead I is the potential difference between LA and RA.

   Lead II is the potential difference between LL and RA.

Lead III is the potential difference between LL and LA.

Therefore, if only leads II and III show SC interference, the left leg, being the common member, must be at fault. It must, therefore, be checked with regard to:

a) Quality of skin preparation and electrode contact;

b) Secure attachment of the LL cable tip to the electrode;

c) Possible contact to left leg with any metal part of bed or other equipment (or proximity to a wall with hidden wiring);

d) A partially broken cable.

18.3 CLINIC OPTIONS FOR ECG RECORDING

The clinical centers may obtain qualifying visit electrocardiograms for the DCCT by any of three procedures:

Option 1: A properly trained technician may record ECGs in the clinical center. This is the preferred procedure and it is expected that most clinics will follow this option.

Option 2: In some instances, the clinic may find it expedient to have the electrocardiogram recorded in the cardiology laboratory of the local institution. ECGs recorded in this manner should be retrieved by clinical center staff and processed in the usual way. Although it has been specified that ECGs will be sent to the Coordinating Center unmounted, it is recognized that this may be contrary to the established and unchanging practice of the cardiology laboratory. If it is not possible to obtain an unmounted ECG from the cardiology laboratory, a mounted electrocardiogram will be accepted by the Coordinating Center along with the mounted or unmounted rhythm strip. A copy of the ECG should be retained for the clinic files.

Option 3: An internist assigned to the DCCT clinic may record the ECG according to the protocol outlined in this chapter.

18.4 CERTIFICATION PROCEDURES FOR ECG TECHNICIANS AND LABORATORIES

Certification procedures will differ for the three options described in Section 18.3.

Option 1: Technicians charged with responsibility for ECG recording in the clinics should obtain three electrocardiograms according to the specific instructions given in this chapter. The electrocardiograms should be mailed with the appropriate forms to the Coordinating Center in order to obtain certification. If the technician has not had previous

experience as an ECG technician, the technique and tracing should be reviewed by the internist assigned to the clinic for lead placement, elimination of artifact, and appropriate calibration.

Upon receipt of the three electrocardiograms and a Request for Certification for ECG Technician (DCCT Form 067) at the Coordinating Center, the ECGs will be sent to the CERU. Recommendations regarding certification will be returned to the Coordinating Center. If certification is recommended, the ECG technician will be issued a certification number by the Coordinating Center.

Option 2: Tracings recorded by staff of the cardiology laboratory should be obtained under the same circumstances as will be operative for patients in the DCCT. One such tracing should be sent to the Coordinating Center with a letter of explanation of any alterations that have been necessary by virtue of local policy.

Upon receipt at the Coordinating Center, the tracing will be sent to the CERU for review for acceptability for DCCT purposes. If quality and technique are acceptable, certification of the clinic for this task will be recommended to the Coordinating Center and a certification number will be issued for the cardiology laboratory.

Option 3: Principal Investigators who elect to use private internists to obtain ECGs should assure themselves that the internists are interested and available for appropriate periods of time during the patient recruitment. Both the primary internist and a backup internist should be certified for DCCT procedures for ECGs. Each internist to be certified for obtaining ECGs in the DCCT should record tracings for one patient. The ECG will be reviewed by the CERU upon receipt of a Request for Certification for ECG Technician (DCCT Form 067). Certification will be granted or withheld on the basis of this review. If certification is recommended, a certification number will be issued to the internist.

If any problems are observed during review of the ECGs submitted to obtain certification under any of the above options, the CERU will contact the Principal Investigator of the clinical center to resolve the problem.

18.5 PROCEDURES FOR MEASURING BLOOD PRESSURE

18.5.1 Equipment for Measuring Blood Pressure

Sphygmomanometer

1. Bladder and Cuff. The bladder must be the correct width for the patient's arm -- if too narrow, blood pressure will be falsely high; if too wide, falsely low.

   The recommended dimensions for blood pressure cuffs are related to arm circumference (cm) at the midpoint of the arm. This is 50%

of the distance from the acromion to the olecranon. Recommended dimensions are as follows:

Arm Circ (cm)	Cuff Name	Width	Length (cm)
17-26	Small Adult	11	17
24-32	Adult	13	24
32-42	Large Adult	17	32

The cuff should be of the contact closure (Velcro or hook) type.

2. Manometers. A mercury manometer should be used. Care must be taken to avoid loss of mercury. The edge of the mercury meniscus must be kept at zero, with no pressure applied to the cuff, by adding mercury as needed. The column should be vertical for correct reading. Annual servicing is required to check for clogging in air vent or filter and to calibrate.

3. Inflating System, Exhaust Value, Tubing. These must be checked monthly for significant leaks in pressure (greater than one mm Hg/second) and for smooth functioning of the input system and exhaust valves.

4. Stethoscope. Standard variety, in good condition. Sounds generated over the vessels are of low frequency, so the bell head of the stethoscope should be used.

18.5.2 Determination of Blood Pressure

1. The Observer. Prior experience in determining blood pressure is essential. One must be able to hear well and to see well enough to read the manometer. Eyes should be level with the meniscus of the vertically placed mercury column. Inattention, carelessness, or bias may cause errors. An example of bias is "digit preference," a well-documented phenomenon which results in recording blood pressures ending in zero more often than expected by chance. Knowledge of earlier readings and preconceived notions of "normal" blood pressure are other sources of bias to be avoided.

2. The Patient. The patient should be comfortably seated, with the arm slightly flexed, and with the forearm supported at heart level on a smooth surface. Readings representative of ordinary circumstances are sought. Standard conditions are that the patient be in a quiet room at a comfortable temperature, with the arm unconstricted by clothing or other material. The subject is to avoid exertion, exposure to cold, eating, and smoking for at least one half hour before and should be seated for at least five minutes before the measurement of blood pressure.

After determining the sitting blood pressure, the supine and standing blood pressures are also measured in order to check for

postural changes in blood pressure which may result from diabetic neuropathy. Allow the patient to be lying down for at least two minutes before measuring the supine blood pressure, and have him stand for at least two minutes before measuring the standing blood pressure.

Technique

On the baseline and all followup physical examinations, blood pressure is to be taken using the right arm, or the left arm if for some reason the right arm cannot be used.

The deflated cuff is applied with its lower margin two and one-half cm above the antecubital space. The bladder is applied directly over the compressible artery, over the medial surface of the arm. The cuff pressure is raised and lowered so as to give a preliminary palpatory determination of systolic pressure in the radial pulse.

The bell stethoscope is applied to the antecubital space, directly over the previously palpated brachial artery. The stethoscope bell is applied firmly but gently, with no space between the skin and the stethoscope, and with the stethoscope not touching clothing or the blood pressure cuff.

The pressure is raised approximately 30 mm Hg above the point at which the radial pulse disappears. It is then released at a rate of two to three mm Hg/second. As the pressure falls, the Korotkoff sounds become audible. These are:

Phase I: That period marked by the first appearance of faint, clear tapping sounds which gradually increase in intensity.

Phase II: The period during which a murmur or swishing quality is heard.

Phase III: The period during which sounds are crisper and increase in intensity.

Phase IV: The period marked by the distinct, abrupt muffling of sound so that a soft, blowing quality is heard.

Phase V: The point at which sounds disappear.

In some patients, there may be an auscultatory gap in the latter part of Phase I and Phase II. This can lead to underestimation of systolic pressure or overestimation of diastolic pressure. It can be excluded by palpating for disappearance of radial pulse as the cuff pressure is raised.

Systolic Pressure

This is the point at which the initial tapping sound is heard. One should hear at least two consecutive beats as the pressure falls. If the

palpatory pressure is higher, it should be recorded as systolic pressure. Pressures should be read to the nearest two mm Hg mark on the manometer scale. Visual oscillations are not to be used.

Diastolic Pressure

The fifth phase, the point at which sounds disappear, is to be used as the diastolic pressure.

18.5.3 Special Conditions Affecting Blood Pressure Measurement

Arrhythmias

An occasional ventricular contraction will have no effect on blood pressure. However, if they are frequent, or if atrial fibrillation is present, approximate readings must be made. The systolic blood pressure is the average of a series of three readings of the appearance of the first sound. The diastolic pressure is an average of three readings of the fourth and fifth phases. The presence of an irregular rhythm should be recorded on the appropriate item on the form.

Obesity

Falsely high pressures are obtained if standard size bladders are used. Bladders may be narrow and short, and there is excessive loss of cuff pressure through the thick compressible tissues of the obese arm. A proper size cuff is necessary (see above).

TABLE 18.1

ECG Reading Codes

All electrocardiograms collected in the study will be read centrally using the revised Minnesota Code for resting electrocardiograms except that Q/QS patterns, T wave items, S-T junction and segment depression, and S-T segment elevation will be coded separately for three different anatomical sites. These sites are: (1) anterolateral if the findings are in leads I, aVL, or V6; (2) posterior (inferior) for leads II, III, or aVF; and (3) anteroseptal for leads V1 through V5. This modification of the Minnesota Code will make it easier to detect new electrocardiographic changes in the presence of existing findings, particularly when a new pathological event, such as infarction or ischemia, occurs in an area of the myocardium different from that of previous events.

The revised Minnesota Code for resting electrocardiograms is reproduced below. With regard to the modification described above, note that it is possible for an ECG to have 1-1-1 code for each of the three anatomical sites. Thus, if the Q/R amplitude ratios is 1/3 or more and the Q duration is 0.03 sec or more in either of leads I or V6, a code 1-1-1 is recorded for the anterolateral site; if these criteria are met in leads II, a code 1-1-1 is recorded for the posterior site; and if these criteria are met in any of leads V2, V3, V4, V5, a code 1-1-1 is recorded for the anteroseptal site.

1. Q and QS Patterns

(Not to be coded in the presence of codes 6-4-1 or 7-1-1.)

a) Anterolateral site (leads I, aVL, V6)

1-1-1 Q/R amplitude ratio 1/3 or more plus Q duration 0.03 sec or more in either of leads I or V6.

1-1-2 Q duration 0.04 seconds or more in any of leads I, V6.

1-1-3 Q duration 0.04 seconds or more, plus R amplitude of 3.0 mm[1]

1-2-1 Q/R amplitude ratio 1/3 or more plus Q duration at least 0.02 seconds and less than 0.03 seconds in any of leads I, V6.

---

[1] It is assumed throughout this appendix that 1 mm = 0.1 mV.

1-2-2 Q duration at least 0.03 seconds and less than 0.04 seconds in any of leads I, V6.

1-2-3 QS in lead I.

1-2-8 Initial R amplitude decreasing to 2 mm. or less in every beat, absence of codes 3-2, 7-1-1, 7-2-1, or 7-3 between V5 and V6.

1-3-1 Q/R amplitude ratio at least 1/5 and less than 1/3 plus Q duration of at least 0.02 seconds and less than 0.03 seconds in any of leads I, V6.

1-3-3 Q duration at least 0.03 seconds and less than 0.04 seconds, plus R amplitude of 3.0 mm or more in lead aVL.

b) Posterior (inferior) site (leads II, III, aVF)

1-1-1 Q/R amplitude ratio 1/3 or more plus Q duration 0.03 seconds or more in lead II.

1-1-2 Q duration 0.04 seconds or more in lead II.

1-1-4 Q duration 0.05 seconds or more in lead III plus Q wave of at least 1.0 mm amplitude in a majority of beats in aVF.

1-1-5 Q duration 0.05 seconds or more in lead aVF.

1-2-1 Q/R amplitude ratio 1/3 or more plus Q duration at least 0.02 seconds and less than 0.03 in lead II.

1-2-2 Q duration at least 0.03 seconds and less than 0.04 seconds in lead II.

1-2-3 QS pattern in lead II. Not coded in the presence of 7-1-1.

1-2-4 Q duration of at least 0.04 seconds and less than 0.05 seconds in lead III, plus a Q wave of at least 1.0 mm amplitude in the majority of beats in aVF.

1-2-5 Q duration at least 0.04 seconds and less than 0.05 seconds in lead aVF.

1-2-6 Q amplitude of 5.0 mm or more in either of leads III, aVF.

1-3-1 Q/R amplitude ratio at least 1/5 and less than 1/3 plus Q duration of at least 0.02 seconds and less than 0.03 seconds in lead II.

1-3-4 Q duration of at least 0.03 seconds and less than 0.04 seconds in lead III, plus any Q wave of at least 1.0 mm amplitude in a majority of beats in lead aVF.

1-3-5 Q duration of at least 0.03 seconds and less than 0.04 seconds in lead aVF.

1-3-6 QS pattern in each of leads III and aVF. Not coded in the presence of 7-1-1.

c) Anteroseptal site (leads V1, V2, V3, V4, V5)

1-1-1 Q/R amplitude ratio 1/3 or more plus Q duration 0.03 seconds or more in any of leads V2, 3, 4, 5.

1-1-2 Q duration 0.04 seconds or more in any of leads V1, 2, 3, 4, 5.

1-1-6 QS pattern when initial R wave is present in adjacent lead to the right on the chest in any of leads V2, 3, 4, 5, 6. For lead V1, an initial R is considered present when the majority of beats have an initial positive deflection in the QRS of greater than or equal to 0.25 mm. For leads V2-V5, if any beat has an initial R greater than or equal to 0.25 mm it is considered present for all beats in the lead.

1-1-7 QS pattern in all of leads V1-V4 or V1-V5.

1-2-1 Q/R amplitude ratio 1/3 or more, plus Q duration at least 0.02 seconds and less than 0.03 seconds in any of leads V2, 3, 4, 5.

1-2-2 Q duration at least 0.03 seconds and less than 0.04 seconds in any of leads V2, 3, 4, 5.

1-2-7 QS pattern in all of leads V1 through V3. Not coded in the presence of 7-1-1.

1-2-8 Initial R amplitude decreasing to 2.0 mm or less and absence of codes 3-2, 7-2-1, or 7-3 in every beat between any of leads V2 and V3, V3 and V4, and V4 and V5. All beats in the lead immediately to the right must have an initial R greater than 2 mm.

1-3-1 Q/R amplitude ratio at least 1/5 and less than 1/3 plus Q duration of at least 0.02 seconds and less than 0.03 seconds in any of leads V2, 3, 4, 5.

1-3-2 QS pattern in absence of code 3-1 or 7-1-1 in each of leads V1 and V2.

2. <u>High Amplitude R Waves</u>

(Not to be coded in the presence of codes 6-4-1, 7-1-1, 7-2-1, or 7-4.)

3-1 Left: R amplitude greater than 26 mm in either of leads V5 or 6; or R amplitude greater than 20 mm in any of leads I, II, III, aVF; or R amplitude greater than 12 mm in lead aVL.

3-2 Right: R amplitude equal to or greater than 5 mm and R amplitude equal to or greater than S amplitude in the majority of beats in lead V1, when S waves greater than R waves somewhere to the left of V1 on the chest. (Includes code 7-3 which meets the above criteria.)

3-3 Left (optional code when 3-1 is not present): R amplitude greater than 15 mm but less than or equal to 20 mm in lead I, or R amplitude in V5 or 6, plus S amplitude in V1 greater than 35 mm.

3-4 Criteria for 3-1 and 3-2 both present.

3. S-T Junction (J) and Segment Depression

(Not to be coded in the presence of codes 6-4-1, 7-1-1, 7-2-1, or 7-4; codes 4-1, 4-2, and 4-3 require a concomitant T wave code in 5-1, 5-2, 5-3.)

a) Anterolateral site (leads I, aVL, V6)

4-1-1 S-T-J depression 2 mm or more and S-T segment horizontal or downward sloping in any of leads I, aVL, V6.

4-1-2 S-T-J depression at least 1 mm but less than 2 mm, and S-T segment horizontal or downward sloping in any of leads I, aVL, V6.

4-2 S-T-J depression at least 0.5 mm and less than 1 mm and S-T segment horizontal or downward sloping in any of leads I, aVL, V6.

4-3 No S-T-J depression as much as 0.5 mm but S-T segment downward sloping and segment or T wave nadir at least 0.5 mm below P-R baseline in any of leads I, aVL, V6. (4-3 may have an elevated J point.)

4-4 S-T-J depression of 1 mm or more and S-T segment upward sloping or U-shaped in any of leads I, aVL, V6.

b) Posterior (inferior) site (leads II, III, aVF)

4-1-1 S-T-J depression 2 mm or more and S-T segment horizontal or downward sloping in any of leads II or aVF.

4-1-2 S-T-J depression at least 1 mm but less than 2 mm, and S-T segment horizontal or downward sloping any of leads II or aVF.

4-2 S-T-J depression at least 0.5 mm and less than 1 mm and S-T segment horizontal or downward sloping in any of leads II or aVF.

4-3 S-T-J depression as much as 0.5 mm, but S-T segment downward sloping and segment or T wave nadir at least 0.5 mm below P-R baseline in any of lead II. (4-3 may have an elevated J point.)

4-4 S-T-J depression of 1 mm or more and S-T segment upward sloping or U-shaped in lead II.

c) Anteroseptal site (leads V1, 2, 3, 4, 5)

4-1-1 S-T-J depression 2 mm or more and S-T segment horizontal or downward sloping in any of leads V1, 2, 3, 4, 5.

4-1-2 S-T-J depression at least 1 mm but less than 2 mm, and S-T segment horizontal or downward sloping any of leads V1, 2, 3, 4, 5.

4-2 S-T-J depression at least 0.5 mm, and less than 1 mm and S-T segment horizontal or downward sloping in any of leads V1, 2, 3, 4, 5.

4-3 No S-T-J depression as much as 0.5 mm but S-T segment downward sloping and segment or T wave nadir at least 0.5 mm below P-R baseline in any of leads V1, 2, 3, 4, 5. (4-3 may have an elevated J point.)

4-4 S-T-J depression of 1 mm or more and S-T segment upward sloping or U-shaped in any of leads V1, 2, 3, 4, 5.

4. T Wave Items

(Not to be coded in the presence of codes 6-4-1, 7-1-1, 7-2-1, or 7-4.)

a) Anterolateral site (leads I, aVL, V6)

5-1 T amplitude negative, minus 5 mm or more negative in any of leads I, 6, or in lead aVL when R amplitude is 5 mm or more.

5-2 T amplitude negative or diphasic (positive-negative or negative-positive type) with negative phase at least minus 1 mm but not as deep as minus 5 mm in any of leads I, V6, or lead aVL when R amplitude is 5 mm or more.

5-3 T amplitude zero (flat), or negative, or diphasic (negative-positive type only) with less than 1 mm negative phase in any of leads I, V6, or in lead aVL when R amplitude is 5 mm or more.

5-4 Optional code: T amplitude positive and T/R amplitude ratio less than 1/20 in any of leads I, aVL, V6; R wave amplitude must be 10 mm or more.

b) Posterior (inferior) site (leads II, III, aVF)

5-1 T amplitude negative, minus 5 mm or more negative in lead II, or in lead aVF when QRS is mainly upright.

5-2 T amplitude negative or diphasic (positive-negative or negative-positive type) with negative phase at least minus 1 mm but not as deep as minus 5 mm in lead II, or in lead aVF when QRS is mainly upright.

5-3 T amplitude zero (flat), or negative, or diphasic (negative-positive type only) with less than 1 mm negative phase in lead II; not coded in lead aVF.

5-4 Optional code: T amplitude positive and T/R amplitude ratio less than 1/20 in lead II; R wave amplitude must be 10 mm or more.

c) Anteroseptal site (leads V2, V3, V4, V5)

5-1 T amplitude negative, minus 5 mm or more negative in any of leads V2, 3, 4, 5.

5-2 T amplitude negative or diphasic (positive-negative or negative-positive type) with negative phase at least minus 1 mm but not as deep as minus 5 mm in any of leads V2, 3, 4, 5.

5-3 T amplitude zero (flat), or negative, or diphasic (negative-positive type only) with less than 1 mm negative phase in any of leads V3, 4, 5.

5-4 Optional code: T amplitude positive and T/R amplitude ratio less than 1/20 in any of leads V3, 4, 5; R wave amplitude must be 10 mm or more.

5. A-V Conduction Defect

6-1 Complete (third degree) A-V block (permanent or intermittent) in any lead. Atrial and ventricular complexes firing independently and atrial rate faster than ventricular rate, with ventricular rate less than 60.

6-2-1 Mobitz Type II.

6-2-2 Partial (second degree) A-V block in any lead. (2:1 or 3:1 block)

6-2-3 Wenckebach.

6-3 P-R (P-Q) interval 0.22 seconds or more in the majority of beats in any of leads I, II, III, aVL, aVF.

6-4-1 Wolff-Parkinson-White syndrome: Persistent, normal P wave. P-R (P-Q) interval less than or equal to 0.12 seconds, plus QRS duration 0.12 seconds or more, plus R peak duration 0.06 seconds or more, coexisting in the same beat and persistent in the majority of beats in any of leads I, II, aVL, V4, 5, or 6.

6-4-2 WPW-Intermittent, WPW pattern in less than or equal to 50% of beats in appropriate leads.

6-5 Short P-R (P-Q) interval: P-R (P-Q) interval less than 0.12 seconds in all beats in any two leads I, II, III, aVL, aVF.

6-6 Intermittent aberrant ventricular conduction: P-R greater than 0.12 seconds (except in presence of 6-5 or heart beat greater than 100). Bizarre QRS complex greater than 0.12 seconds wide. Normal P wave when most beats are normal sinus rhythm. (Suppressed by 6-4-2.)

6-8 Artificial pacemaker.

6. Ventricular Conduction Defects

7-1-1 Complete left bundle branch block (LBBB) -- suppressed by 6-1, 6-4-1, 6-8, 8-2-1 or 8-2-2. QRS duration greater than or equal to 0.12 seconds in a majority of beats (of the same QRS pattern) in any of leads I, II, III, aVL, aVF, PLUS R peak duration greater than or equal to 0.06 seconds in a majority of beats (of the same QRS pattern) in any of leads I, II, aVL, V5, V6. 7-1-1 suppresses 1-2-3, 1-2-7, 1-2-8, 1-3-2, 1-3-6, all 3, 4, 5, 9-2, 9-4, 9-5 codes. If any other Q wave coexists with the LBBB pattern, code the Q and drop the 7-1-1 code to a 7-4 code.

7-1-2 Intermittent left bundle branch block -- same as 7-1-1 but with presence of normally conducted QRS complexes of different shape to the LBBB pattern.

7-2-1 Complete right bundle branch block (RBBB) -- suppressed by 6-1, 6-4-1, 6-8, 8-2-1 or 8-2-2. QRS duration greater than or equal to 0.12 seconds in a majority of beats (of the same QRS pattern) in any of leads I, II, III, aVL, aVF, PLUS R' greater than R in V1 or V2 OR QRS mainly upright plus R peak duration greater than or equal to 0.06 seconds in V1 or V2 OR S duration greater than R duration in all beats of either leads I or II, 7-2 suppresses 1-2-8, all 2, 3, 4 and 5 codes, 9-2, 9-4, 9-5.

7-2-2 Intermittent right bundle branch block -- same as 7-2-1 but with presence of normally conducted QRS complexes of different shape to the RBBB pattern.

7-3 Incomplete right bundle branch block: QRS duration less than 0.12 seconds in each of leads I, II, III, aVL, aVF, and R prime greater than R in either of leads V1, 2. (To be reported as 3-2 if those criteria are met.) 7-3 suppresses 1-2-8 code.

7-4 Intraventricular block (in absence of 6-4-1, 7-1-1, or 7-2-1): QRS duration 0.12 seconds or more in a majority of beats in any of leads I, II, III, aVL, aVF.

7-5 R-R prime in either of leads V1 or V2 with R prime less than or equal to R.

7-6 Incomplete left bundle branch block: QRS duration at least 0.10 seconds and less than 0.12 seconds in the absence of codable Q or QS waves, in the majority of beats in each of leads I, aVL, and V5 or V6.

7-7 LAH (Left-Anterior Hemiblock). QRS duration less than 0.12 seconds in the majority of beats in any of leads I, II, III, aVL, aVF, plus a Q wave that is greater than or equal to 1/4 mm amplitude and less than 0.03 seconds duration in lead I plus axis less than minus 45 degrees. In presence of 7-2, code 7-8 if axis is less than minus 45 degrees and Q wave in lead I meats the above criteria.

7-8 Combination of 7-7 and 7-2.

7. Arrhythmias

8-1-1 Frequent premature atrial, or nodal beats (10% or more of recorded cycles).

8-1-2 Frequent premature ventricular beats (10% or more of recorded cycles).

8-1-3 Frequent premature atrial and/or junctional beats, and ventricular beats (so that individual frequencies are less than 1 per 10 cycles but combined premature beats are greater than 1 per 10 cycles). Not to be coded in the presence of 8-1-1 or 8-1-2.

8-1-4 Wandering atrial pacemaker.

8-1-5 Presence of 8-1-2 and 8-1-4.

8-2-1 Ventricular fibrillation or ventricular asystole.

8-2-2 Persistent ventricular (idioventricular) rhythm.

8-2-3 Intermittent ventricular tachycardia. Three or more consecutive ventricular premature beats occurring at a rate greater than or equal to 100.

8-2-4 Ventricular parasystole (should not be coded in presence of 8-3-1).

8-3-1 Atrial fibrillation (persistent in all leads).

8-3-2 Atrial flutter (persistent)

8-3-3 Intermittent atrial fibrillation (code if three or more clear-cut, consecutive sinus beats present in any lead).

8-3-4 Intermittent atrial flutter (code if three or more clear-cut, consecutive sinus beats present in any lead).

8-4-1 Persistent supraventricular rhythm. QRS duration less than 0.12 seconds. Absent P waves or presence of abnormal P waves (inverted or flat in aVF). Regular rhythm.

8-4-2 Intermittent supraventricular tachycardia. Three consecutive atrial or junctional premature beats occurring at a rate of greater than or equal to 100.

8-5-1 Sino-atrial arrest. Unexpected absence of P, QRS and T. RR-interval fixed multiple of normal interval plus or minus 10%.

8-5-2 Sino-atrial block. Unexpected absence of P, QRS, and T preceded by progressive shortening of P-P intervals. (R-R interval fixed multiple of normal interval or plus or minus 10%.)

8-6-1 A-V dissociation with ventricular pacemaker without capture. P-R and R-R occur at variable rates with ventricular rate as fast or faster than the atrial rate. Variable P-R intervals. No capture beats.

8-6-2 A-V dissociation with ventricular pacemaker with capture.

8-6-3 A-V dissociation with atrial pacemaker and with no capture beats.

8-6-4 A-V dissociation with atrial pacemaker with capture beats.

8. S-T Segment Elevation

(Not to be coded in the presence of codes 6-4-1, 7-1-1, 7-2-1, or 7-4.)

a) Anterolateral site (leads I, aVL, V6)

9-2 S-T segment maximum elevation of 1 mm or more in any of leads I, aVL, or V6.

b) Posterior (inferior) site (leads II, III, aVF)

9-2 S-T segment maximum elevation of 1 mm or more in any of leads II, III, or aVF.

c) Anteroseptal site (leads V1, 2, 3, 4, 5)

9-2 S-T segment maximum elevation of 1 mm or more in lead V5 or S-T segment maximum elevation of 2 mm or more in any of leads V1, V2, V3, V4.

9. Miscellaneous Items

9-1 Low QRS amplitude: QRS peak-to-peak amplitude less than 5 mm in all beats in each of leads I, II, III, or QRS peak-to-peak amplitude less than 10 mm in all beats in each of leads V1, 2, 3, 4, 5, 6.

9-3 P wave amplitude of 2.5 mm or more in any of leads II, III, aVF on a majority of beats.

9-4-1 QRS transition zone at V3 to the right (on the chest) of lead V3. (Not to be coded in the presence of 6-4-1, 7-1-1, 7-2-1, or 7-4.)

9-4-2 QRS transition zone at lead V4 or to the left of V4 on the chest. (Not to be coded in the presence of codes 6-4-1, 7-1-1, 7-2-1, or 7-4.)

9-5 T wave amplitude greater than 12 mm in any of leads I, II, III, aVL, aVF, V1, 2, 3, 4, 5, 6. (Not to be coded in the presence of 6-4-1, 7-1-1, 7-2-1, or 7-4.)

9-8-1 Technical problems present and interferes with coding.

9-8-2 Technical problems present but ECG codable.

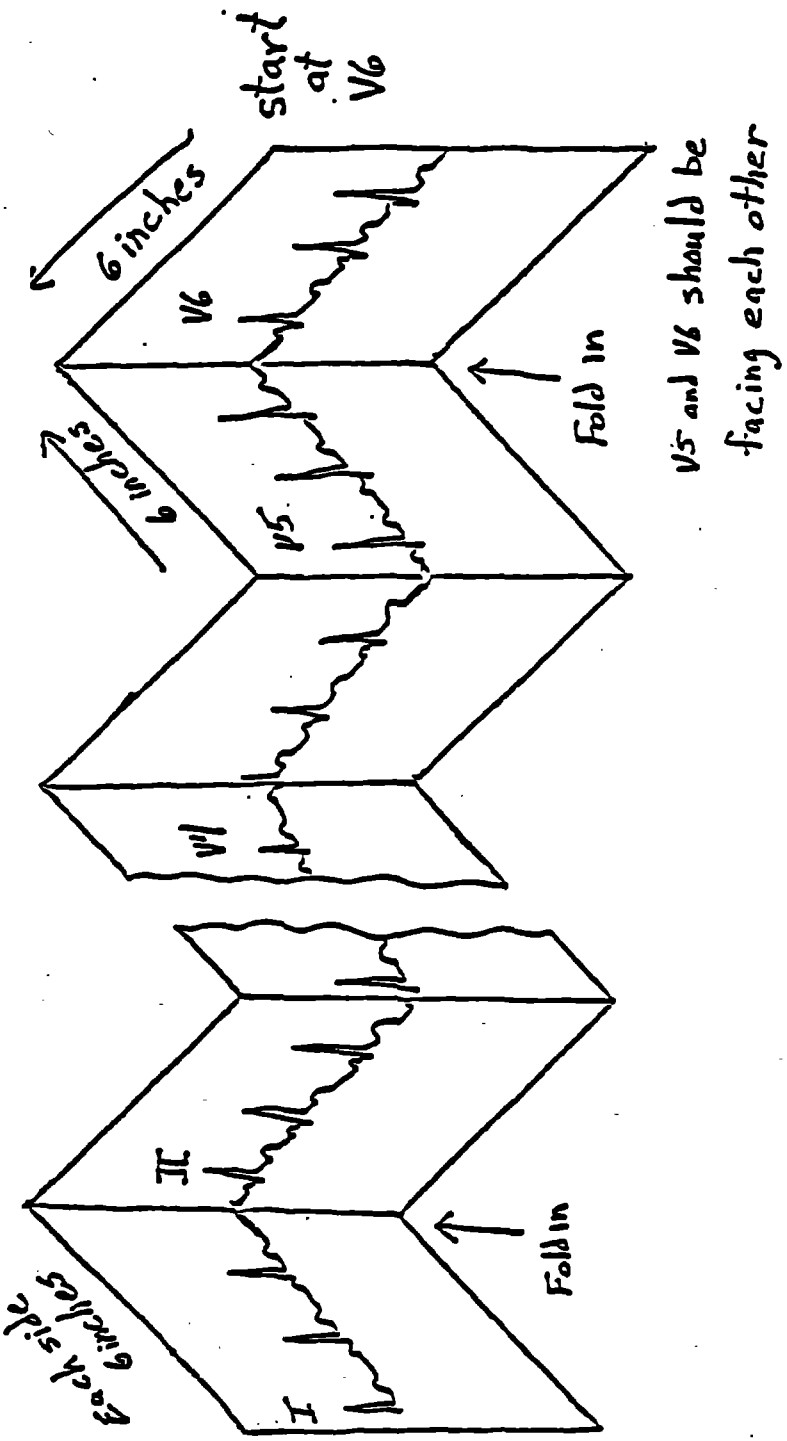


Figure 18.1

PROPER FOLDING OF EGG TRACINGS FOR DCCT

Figure 18.2

CONVENTIONAL PRECORDIAL LEAD ELECTRODE PLACEMENT

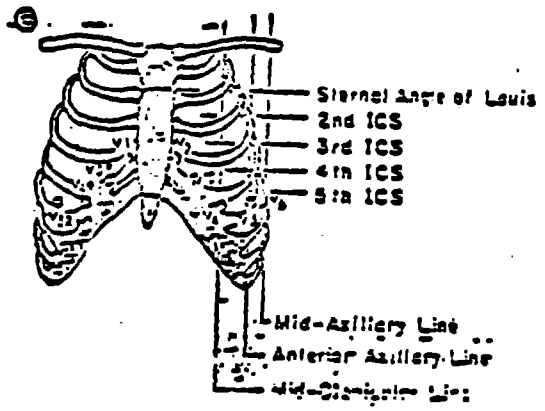
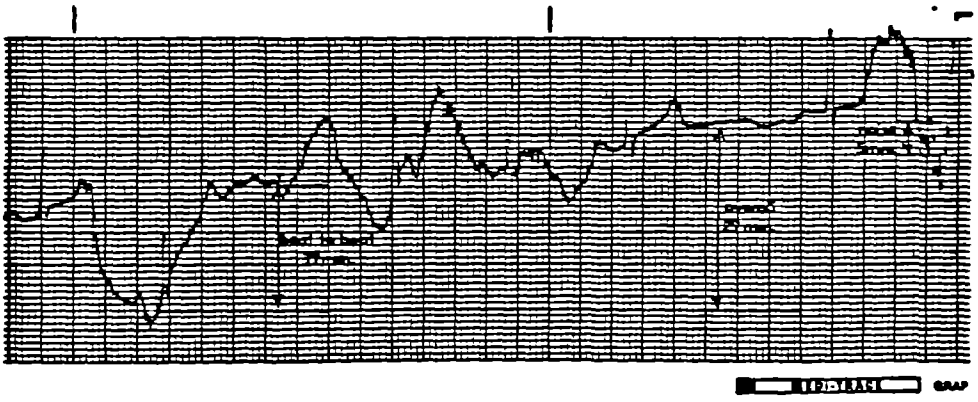


Figure 18.3A

SELF-EVALUATION OF TECHNICAL QUALITY PERFORMANCE GRADE

QUALITY GRADE LEVEL	NOISE (NUMBER OF SMALL PAPER DIVISIONS)	DRIFT OVERALL (NUMBER OF SMALL PAPER DIVISIONS)	DRIFT BEAT-TO-BEAT (NUMBER OF SMALL PAPER DIVISIONS)
1	≤ 1	≤ 7	≤ 1 3/4
2	≤ 2 1/4	≤ 8	≤ 2 1/2
3	≤ 3 1/2	≤ 9	≤ 3
4	≤ 4 1/2	≤ 10	≤ 3 1/2
5	> 4 1/2	> 10	> 3 1/2

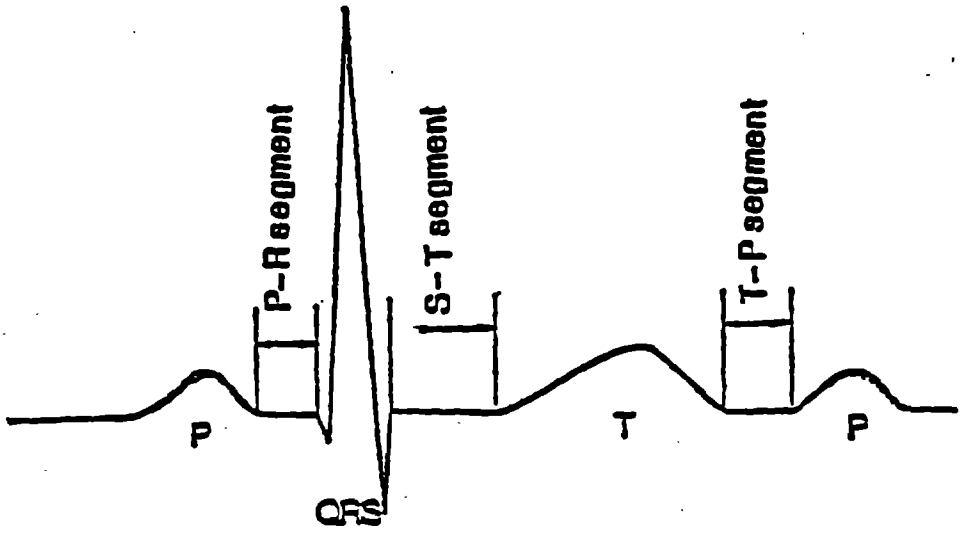
Figure 18.3B



The record is unacceptable in terms of noise, overall drift, and beat-to-beat drift.

Figure 18.4

MEASUREMENT OF NOISE AND DRIFT



A. The baseline level of a waveform is determined by its P-R, S-T, and T-P segments.

Figure 18.5A

Muscle Artifact

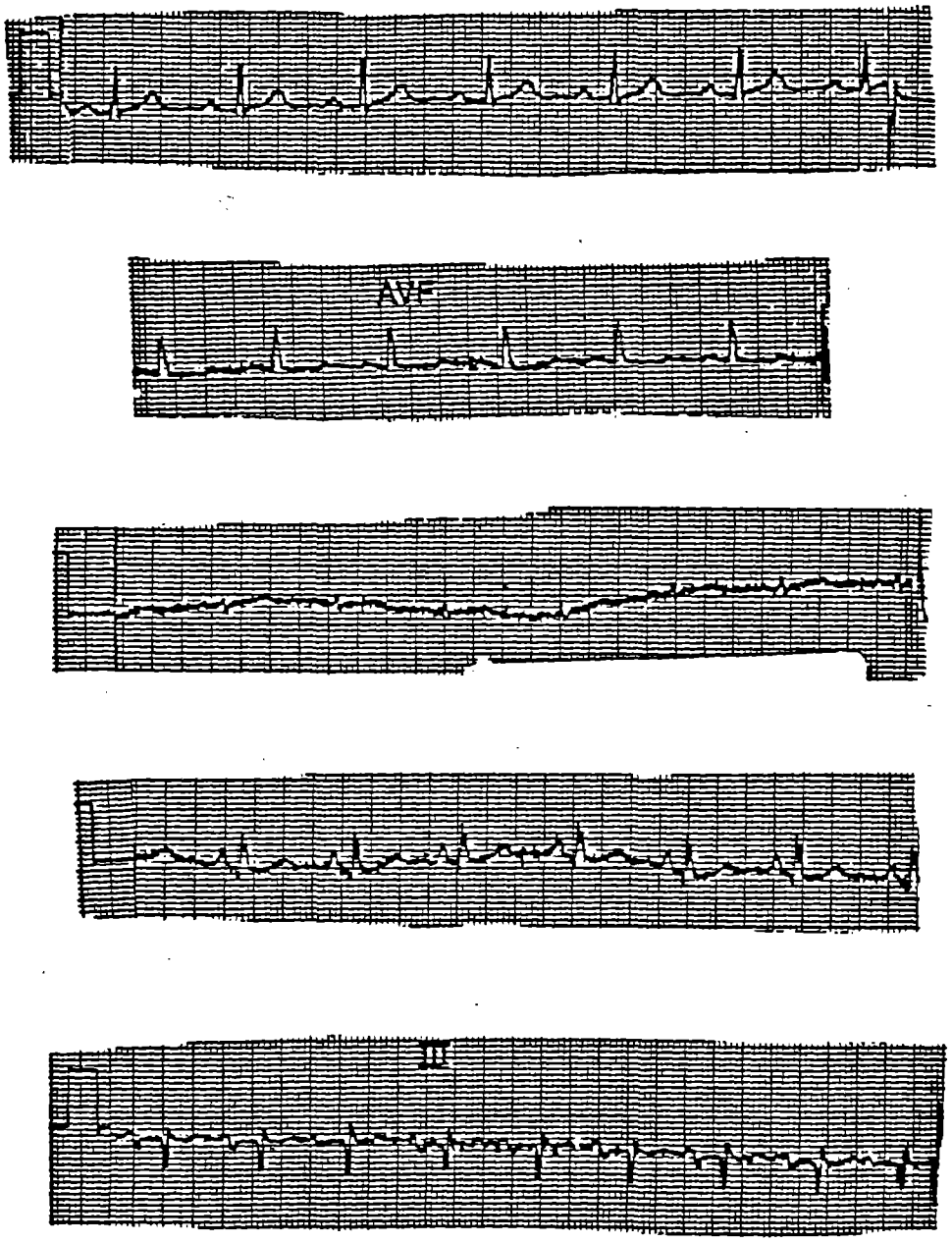
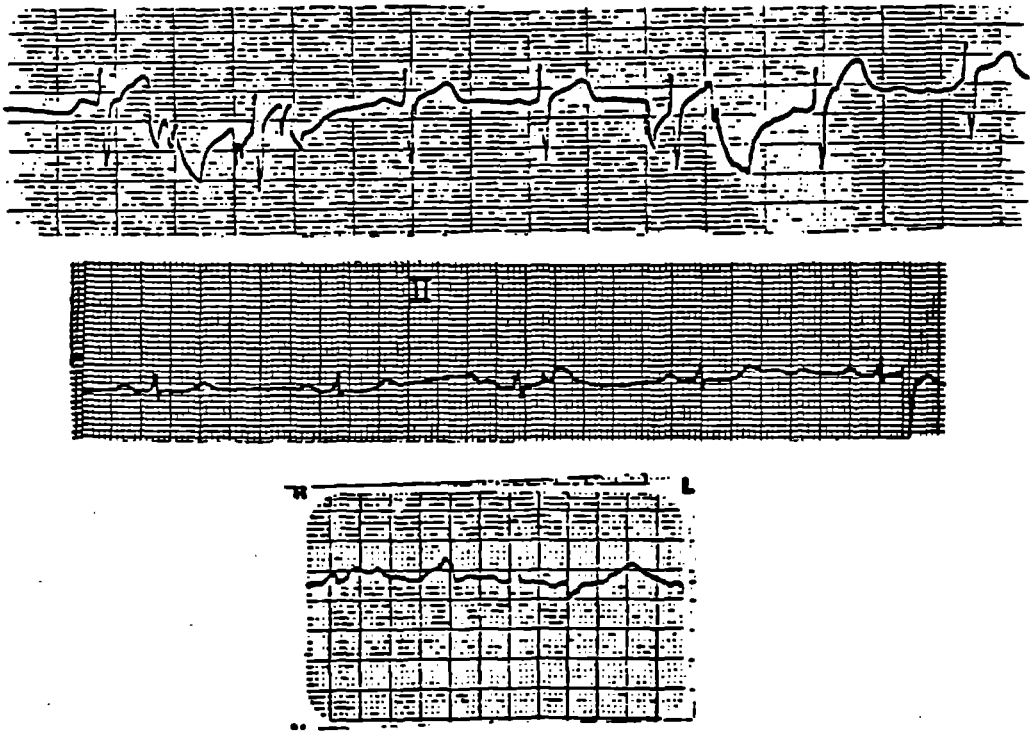


Figure 18.5B

Wandering Baseline



Baseline Drift

Figure 18.5C

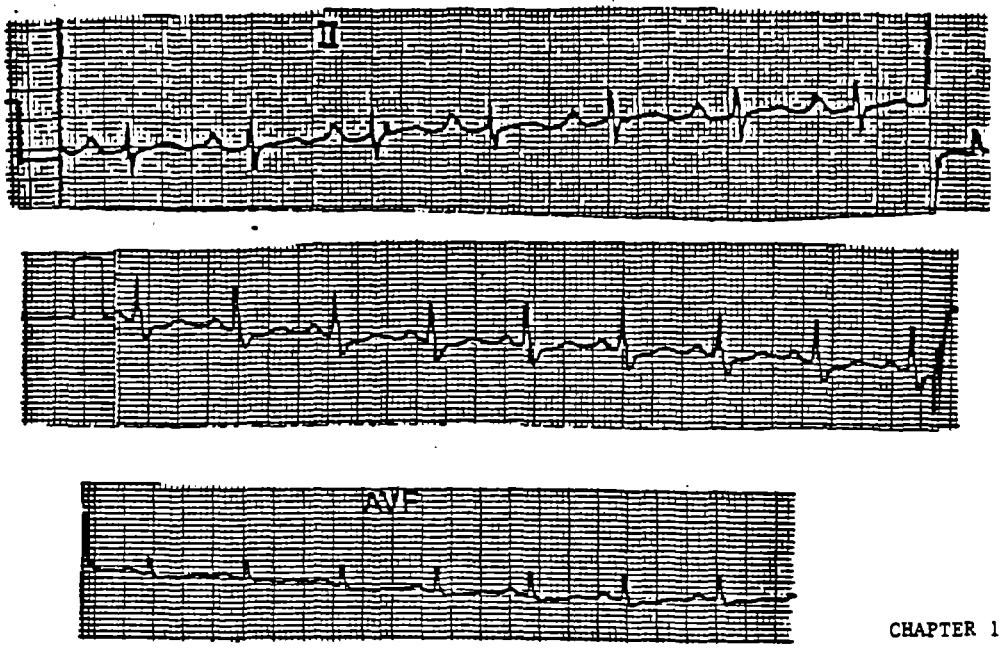


Figure 18.5D

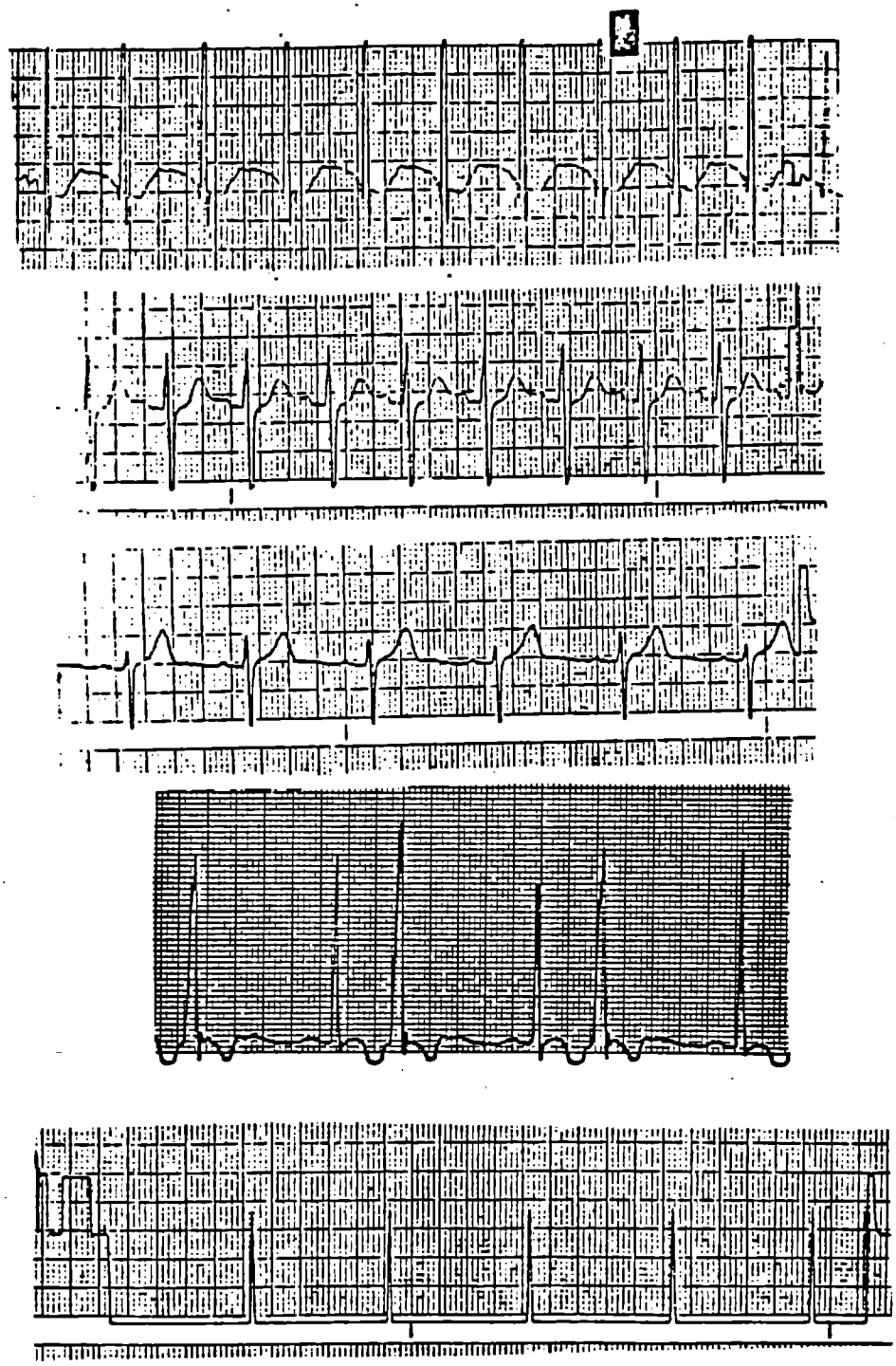
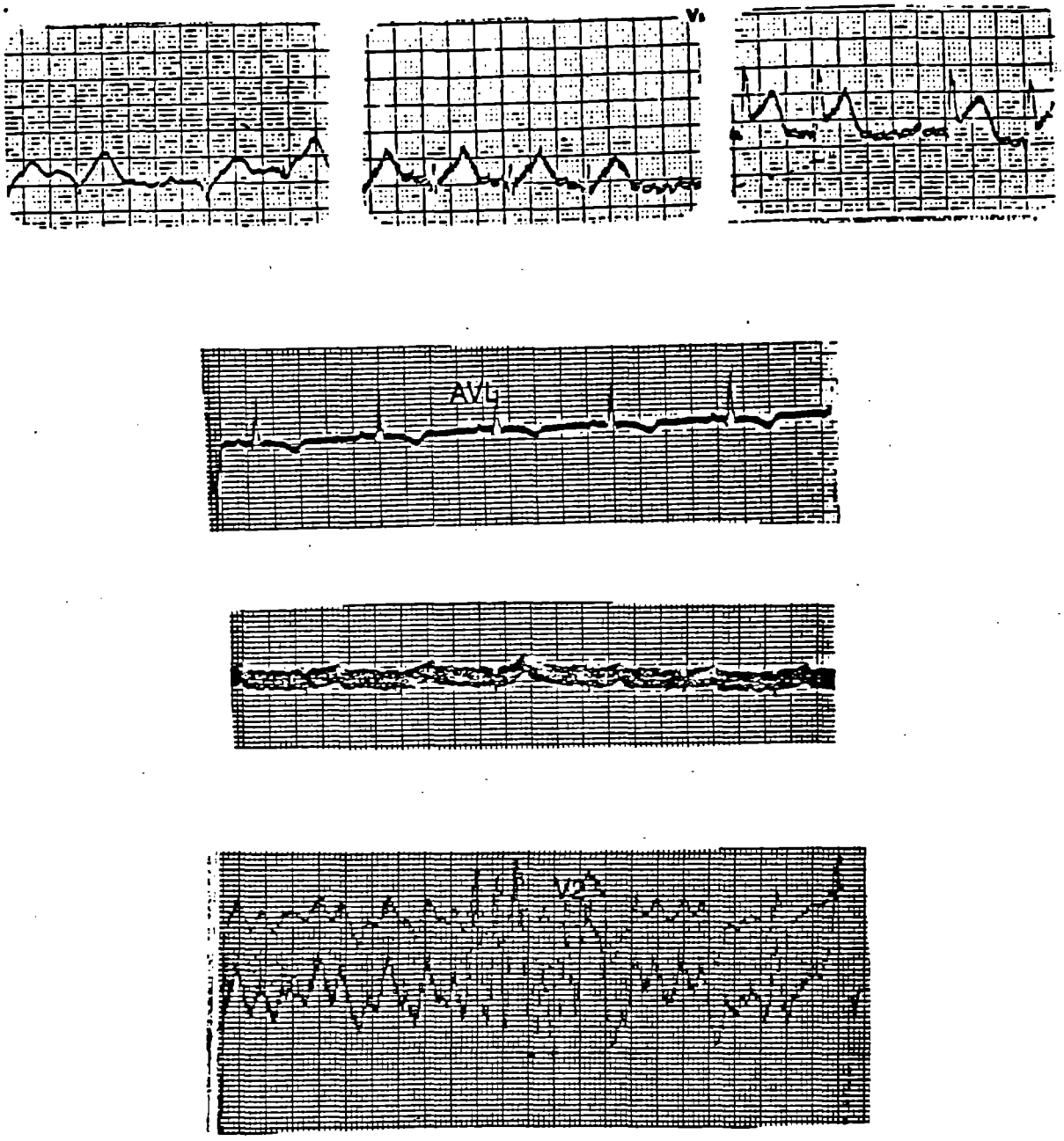


Figure 18.5E

60 Hz Voltage



Chapter 19

PSYCHOLOGICAL PROCEDURES

19.1 NEUROBEHAVIORAL TEST BATTERY

The primary purpose of the neurobehavioral test battery is to determine whether any clinically significant impairment in information-processing ability develops over the course of the DCCT. To that end, a battery of tests which are known to be sensitive to acquired brain damage has been assembled. All have extensive normative data, and are appropriate for subjects between the ages of ten and 65. The complete test battery, to be administered at baseline, two years, five years, seven years and study termination, can be administered in approximately four hours by a certified DCCT technician who has had some previous psychological testing experience. The shortened version of the battery was eliminated from the Protocol effective July 1, 1988.

While the sensitivity of neuropsychological tests to brain damage is high, their specificity, unfortunately, is not. Performance on many tests can be affected by a variety of factors (e.g., personality style; mood; level of motivation) which may or may not be associated with brain damage. In an effort to increase specificity and reduce the probability of making too many false-positive errors, the battery has incorporated a procedure which assesses both quantitative (e.g., time to complete task; number of errors made) and qualitative (e.g., types of errors made) aspects of a particular subject's performance. These qualitative features reflect the sorts of strategies a subject uses in reaching a particular solution, and are much less influenced by non-cognitive factors. Thus the presence of a constellation of these features can be considered to be more strongly pathognomonic of organic brain dysfunction than mere quantitative between-group differences.

The complete test battery samples all areas of cognitive functioning: general intelligence, problem-solving and abstract-reasoning, calculation skills learning and memory, visuoperceptual and visuoconstructional ability, attention and perceptuomotor speed, and manual dexterity. Visual information-processing functions, mnestic skills, and motor control are oversampled because these particular processes have been found to be more readily affected by subtle brain damage than are verbal information-processing functions.

Each neurobehavioral tester is responsible for administering the tests as detailed in the DCCT Neurobehavioral Test Battery Manual of Operations. (This Manual of Operations can be obtained from the coding unit.) Scoring of each protocol will be carried out by the Central

Neurobehavioral Coding Unit, where the neuropsychologist will be masked to the subject's treatment group.

Descriptions of each test in the complete battery are presented in the following section; information on the partial battery follows in Section 19.1.2.

19.1.1 The Complete Battery

1. Measures of General Intelligence

Information. This subtest from the Wechsler Adult Intelligence Scale (WAIS) and Wechsler Intelligence Scale for Children, Revised (WISC-R) evaluates an individual's fund of general knowledge with a series of questions (e.g., "Who invented the electric light?") which can be scored unambiguously. This test correlates highly with Full Scale IQ ($r = .87$) and hence provides an excellent measure of general intelligence. It also tends to be remarkably resistant to acquired brain damage, and thus can be used to estimate premorbid intelligence in brain-damaged individuals. Wechsler's dichotomous scoring system (correct/incorrect) will be used to compute raw scores. Total raw score from this and every other Wechsler subtest will be transformed into an age-corrected scaled score (Mean = 10; S.D. = 3).

Comprehension. This Wechsler subtest contains a series of questions which assess social judgement and practical reasoning (e.g., "Why should people pay taxes?"). This measure of intelligence is less influenced by educational background than are Information and Vocabulary. Each response will be scored according to Wechsler's three point scoring criteria.

Picture Arrangement. This Wechsler subtest consists of a series of cartoon pictures that make up a story. Each set is presented in a scrambled order, and the subject is told to rearrange them so that they tell a story. story. This test examines the ability to think in a sequential fashion and to size up social situations. Both speed and accuracy determine the subject's raw score on this test.

2. Verbal Skills

Vocabulary. On this Wechsler subtest, the subject is asked to define 40 words, ranging in difficulty from "winter" to "travesty." Wechsler's three point scoring criteria will be used. Like Information, this subtest is regarded as an excellent estimate of premorbid intelligence. Also, of all the Wechsler subtests, this is least affected by diffuse brain injury.

Verbal Fluency Test. This test provides a measure of the ability to rapidly produce words beginning with a particular letter of the alphabet (F, A, and S). The response measure is the number of words produced in 60 seconds.

3. Problem-Solving and Abstract-Reasoning

Similarities. In this Wechsler subtest, the subject is presented with pairs of words (e.g., radio/telephone) and asked to tell how they are alike. This test of verbal concept-formation provides a measure of general intelligence which is virtually independent of one's educational experience. It is also sensitive to the effect of brain injury regardless of locus. Each response will be scored according to Wechsler's three-point scoring criteria.

Category Test. This well-known test from the Halstead-Reitan Battery provides a measure of deductive reasoning. On this test, the subject is presented with a series of visual slides (e.g., a slide may show four red circles) and is instructed to guess the principle underlying the series (e.g., "number") by pressing one of four levers. Every response is followed by immediate feedback. Seven different subtests, each with its own underlying principle, are administered. The booklet form, rather than the usual slide projector form, will be used in this trial.)

4. Calculation Skills

Arithmetic. This Wechsler subtest assesses attention, calculation, and problem-solving ability. A series of arithmetic problems are presented orally (e.g., "The price of canned peas is two cans for 31 cents. What is the price of one dozen cans?"), and the subject's task is to solve them -- without pencil and paper -- as rapidly as possible. Wechsler's scoring criteria will be used, with bonus points added to the score if correct responses are made within a set time.

WRAT Arithmetic. This subtest from the Wide Range Achievement Test examines basic calculation skills. The subject is presented with a page of tasks ranging in difficulty from simple addition to finding the square root of a five digit number. The raw score is the number of items answered correctly in ten minutes. These scores can then be transformed into grade ratings, T scores, and percentiles.

5. Learning and Memory Tests

Digit Span. This Wechsler subtest measures attention and immediate memory capacity for orally presented digits. In the first part of the test, the subject repeats strings of digits immediately after their presentation. In the second part, he repeats them in reversed order. A computer program has been

developed which will score the type of error (e.g., serial position order; extralist intrusion).

Symbol-Digit Paired-Associate Learning Test. This test examines the ability to form associations between unrelated stimuli by asking subjects to learn a list composed of seven unfamiliar symbols, each paired with a single digit. During the study phase, each symbol-digit pair will be presented visually for three seconds. Following study of the entire list, the subject is tested by showing the symbol alone as a retrieval cue. Each of the subject's responses is followed immediately by presentation of that particular symbol-digit pair for three seconds. Four such test trials are administered. Number of correct responses made on each trial and type of error (e.g., preseverative) will be recorded. Several recent studies have found this test to be very sensitive to subtle brain dysfunction in children and adults.

Visual Reproductions. This modification of the Visual Reproductions subtest from the Wechsler Memory Scale (WMS) assesses short- and long-term memory for nonverbal information. Four geometric designs are presented for study. Immediately after presentation of each design card, the subject draws the design from memory. Following this, the designs are re-presented for the subject to copy. This copy stage permits the separation of visuoconstructional impairments from visual memory impairments. Following a 30 minute delay, the recall test is re-administered. The standard Wechsler scoring criteria will be supplemented by identification of qualitative features pathognomonic of organic brain dysfunction (e.g., perseverative responses; segmented drawing strategies).

Four Word Short-Term Memory Test. This task provides an estimate of how well a subject can hold small amounts of verbal information in memory for several seconds. On each trial, four unrelated words are read to the subject at the rate of one word per second. This is immediately followed by a three-digit number. As soon as the number is presented, the subject begins counting backwards by threes until the examiner says "stop!" At that point, the subject is asked to recall the words. The purpose of the mental arithmetic task is to prevent the subject from rehearsing the words during the retention interval. Three retention intervals (5, 15, 30 seconds) will be used. Measures include the number of correct responses per trial and type of error made (e.g., perseverations; prior-trial intrusion errors). Fifteen trials will be administered.

Logical Memory. This modification of the Logical Memory subtest from the Wechsler Memory Scale assesses short- and long-term recall of connected discourse. A number of studies have found this to be quite sensitive to mild organic brain dysfunction. The subject is read two brief passages and is asked to recall each one immediately after hearing it, and

again 30 minutes later. Detailed scoring criteria have been established by Russell.

6. Visuoperceptual and Visuoconstructional Tests

Picture Completion. This Wechsler subtest assesses visual recognition, remote memory, and general information by presenting the subject with a series of pictures in which some important part is missing (e.g., no sock on foot). Of all the WAIS/WISC-R Performance tests, this correlates highest with general intelligence, and like Information, is relatively unaffected by brain damage. Raw scores will be computed using Wechsler's dichotomous scoring criteria. In addition, time to respond will be recorded.

Boston Embedded Figures Test. This test examines the ability to locate a specific geometric target embedded in a random line matrix. On each test trial, subjects are presented with a card containing a relatively simple line drawing in the upper portion, and four complex patterns below. Their task is to rapidly identify the pattern containing the target stimulus. Both speed and accuracy of response is recorded.

Block Design. This Wechsler subtest is a test of visuoconstructional ability and of motor speed and manual dexterity. Subjects are required to arrange red and white blocks to correspond to a printed design. Wechsler has established time limits for each of the test problems and gives bonus points for rapid responses. To allow separation of the visuoconstructive component from the speed component, both timed and untimed scores will be computed. In addition to measures of speed and accuracy, qualitative analysis of type of error (e.g., broken configuration; figure/ground reversals; etc.) will be made. This latter measure greatly increases the test's sensitivity and specificity in detecting brain damage.

Object Assembly. This Wechsler subtest is comprised of four cut-up cardboard figures of common objects (e.g., hand). The subject's task is to put together each of these jigsaw-type puzzles as rapidly as possible. This test requires little abstract-reasoning ability and is considered to measure visuospatial organizational ability and motor speed. Raw scores are based on both speed and accuracy of responses.

Tactual Performance Test. On this test, a blindfolded subject attempts to place each of ten wooden geometric forms into its appropriate place on a formboard. This task is first completed with the dominant hand, then repeated with the nondominant hand, and finally with both hands together. Following that, subjects are asked to draw the board from memory. Time for each trial, memory of each shape, and location of each shape are scored. This task is very sensitive to brain damage, both diffuse and lateralized.

7. Attention and Perceptuomotor Speed

Digit Symbol Substitution Test. This subtest from the WAIS consists of an array of nine numbers, each paired with a symbol. Beneath the array is a set of numbers alone, and the subject's task is to write the correct symbol under each of these numbers as rapidly as possible. The raw score is computed by counting the number of correct responses made in 90 seconds. All subjects, regardless of age, will take this test (normative data on children taking this test has now been collected). This is a powerful test of diffuse brain damage because it places a demand on speed, attention, visual scanning and memory. The task has been modified by allowing the subject to complete the entire matrix, and then asking him/her to recall as many of the symbol-digit pairs as possible. In this way a measure of incidental memory efficiency is obtained.

Trailmaking A and B. This is a well-known test of attention and visuo-motor tracking. On Trails A, the subject is presented with a sheet of paper on which circled numbers are randomly arrayed across the page. His task is to connect the numbers in consecutive order as rapidly as possible. In Trails B, the sheet contains both numbers and letters; his task is to rapidly alternate between the two. Response measures include the number of seconds to complete each sequence, and the number of errors (false trails) made. Again, this test is very sensitive to subtle brain dysfunction.

Digit Vigilance Test. This test, developed by Rennick and his associates, requires the subject to visually scan a page of numbers and select a particular target. It is particularly sensitive to diffuse brain damage. Time to complete the task and the number of errors, both of omission and comission, are recorded.

8. Motor Speed and Manual Dexterity

Grooved Pegboard. This is a test of finger dexterity which requires the subject to rapidly place notched pegs into a board of 25 holes. Each hole contains a groove, thus there is only one correct way a given peg will fit into a hole. Response measures include the time to insert 25 pegs, the number of pegs dropped, and the time to remove 25 pegs. Two trials are given: dominant hand and non-dominant hand.

Halstead Finger-Tapping Test. On this test of finger agility, the subject is required to tap a counter with his index finger as rapidly as possible. Five ten second trials are given with each hand, starting with the dominant hand. The scores on each hand must be within five taps of one another; if that is not the case, additional trials are given until that criterion is met. The response measure, computed for each hand, is the average number of taps completed on the five

criterion trials. This test is considered to be sensitive to cortical lesions, and is particularly useful in detecting lateralized lesions.

Star Drawing Test. This test provides quick measures of visuomotor coordination, motor steadiness, and speed. The subject's task is to draw a line as accurately and as rapidly as possible, while staying within a one-quarter inch boundary around a star design. The task is first completed with the dominant, and then the nondominant hand. Time to complete each star, and number of errors made, are the response measures.

9. Summary Measures

   a) WAIS Full Scale IQ

   b) WAIS Verbal IQ

   c) WAIS Performance IQ

10. Impairment Index

   This index is based on those tests which previous studies have found to be particularly sensitive to brain damage in patients with a history of diabetes or other medical disorders.

   a) Symbol-Digit Paired-Associate Learning

   b) Visual Reproductions - Immediate and Delayed

   c) Logical Memory - Delayed

   d) Block Design

   e) Digit-Symbol Substitution

   f) Trailmaking

   g) Digit Vigilance

   h) Category Test

   i) Tactual Performance Test

This set of specimen answer sheets should be copied on the very best quality copying machine available. There is nothing worse than having subjects work on answer sheets (e.g., for Trail Making) covered with all sorts of extraneous lines, dots, etc.

The subject's blood glucose levels are measured at the beginning and end of the session to ensure that low blood glucose is not affecting the subject's performance. The testing session should be delayed if the measured blood glucose is less than 55 mg/dl.

A formal quality control monitoring procedure will be implemented to insure that errors in administering the neurobehavioral tests or recording test scores will be minimal. To that end, each protocol will be rated on a 3-point scale (1=satisfactory; 2=acceptable but with minor problems; 3=unacceptable). Unacceptable tests will include instances where a test was not administered because of examiner error, or the wrong test was administered, or the scores that were reported are uninterpretable and cannot be salvaged. Whenever a minor or major problem is detected, you will receive a memo from us detailing the problems; these ratings will also be sent to the Coordinating Center so that quality control statistics can be maintained.

The neurobehavioralists are to use the "Clinical Rating" forms (last two pages in each protocol) to record any observations you have on your subject's current level of functioning. If you notice any motivational changes, changes in mood, or motor, or medical disabilities that could affect the interpretation of the neurobehavioral test results, please note them on these pages.

On the other hand, the neurobehavioralists are to refrain from discussing the actual test results with other members of the DCCT treatment team. There is serious concern that such anecdotal information might somehow bias or otherwise affect the patient's treatment. While it is permissible to describe your behavioral observations (e.g., "so and so seems very poorly motivated; or was uncooperative; or was depressed; or reported that they were having trouble with their new job; etc."), it is not permissible to make statements which make reference to the subject's tests performance (e.g., "so and so was terrible on a number of tests this morning, but I think it is because they were not very motivated; or so and so seems to be performing worse this year than last year").

There are other requests:

1. Please fill out a DCCT Form 013, Neurohavioral Studies Demographic Questionnaire, on each patient.

2. Please do not send test batteries to the coding unit by Federal Express (or a similar courier service) unless you have been instructed to do so. The cost of those special services is astronomical.

3. In binding protocols for mailing, please use clips or elastic bands; do not staple protocols together.

See the DCCT Neurobehavioral Test Battery Manual of Operations for more information on administering these tests.

19.2 QUALITY OF LIFE ASSESSMENTS

19.2.1 Introduction

The Quality of Life Questionnaire (DCCT Form 036) is a questionnaire designed to assess objectively and subjectively the impact of diabetes upon the individual and his/her total living situation. It therefore includes questions which focus on life satisfaction, frequency of activities, and worries, and takes about 10 minutes to complete.

Some parts of the form apply to all subjects; others to only some groups such as adolescents or adults, but all subjects complete the same form.

19.2.2 Procedures

1. The Quality of Life Questionnaire is given prerandomization, and at each annual followup visit. This questionnaire should be administered at the same session as the Symptom Checklist-90-R (DCCT Form 035). It should be given so that the subject always fills it out before the SCL-90-R. Remember, DCCT Form 036 precedes DCCT Form 035.

2. The person administering the questionnaire should explain, using the following, why it and the SCL-90-R are being given. "We are asking you to answer these questions to broaden our understanding of diabetes and this study in particular. They provide one way for you to have an input into the evaluation of the outcome of the DCCT. Thus, we are very interested in your viewpoints on each of the questions."

3. The first time the Quality of Life Assessment is given, the individual administering it should read the instructions to the patient. The questions are designed to minimize confusion. A patient's confusion may center around the "rightness" or "wrongness" of answers. Patients should be reassured that there are no correct answers to these questions, but individual opinions only. They should feel free to approximate a best answer if they are not sure how to choose between specific alternatives. If patients refuse to answer any or all parts of the questionnaire, try encouraging them by (1) asking for their reasons and (2) reviewing the reasons (or asking them to fill out the forms). If they still refuse, do not push further. Please return the forms with any explanation and notify the Principal Investigator at your site as refusal may be part of an overall negative reaction to the study. Outright refusal will be very rare. These forms or ones like them have been widely used in many other studies.

4. When the Questionnaire is finished, the administrator should review it to make sure all items have been filled out.

5. When complete, this form should be returned to the Coordinating Center for scoring.

6. The data from the scored instrument, when stored on the patient's data file, will include total scores, as well as individual item scores.

7. Data from the Quality of Life Assessment will be analyzed to assess the impact of the study on individual patients. This data may be useful for understanding differential rates of specific problems in individual centers.

19.2.3 Methodology

The Instrument

A useful measure for supplementing th DQOL is the SF-36 (Ware & Sherbourne, 1992). The SF-36 is ideal for supplementing the DQOL because the scale has been validated (Ware & Sherbourne, 1992), shown reliable and precise (McHorney C, Ware J, Rogers, et al., 1992), and administered by over 75 health care institutions (Hudson, 1992) in over 10,000 patients (InterStudy OMS Update, 1991). Moreover, a recent study reported that measuring quality of life with the SF-36 is practical in an ambulatory diabetes clinic setting and can provide new information that can be useful to physicians in managing the care provided to their patients with diabetes (Nerenz, Repasky, Whitehouse, et al., 1992).

Administering the Instrument

The SF-36 is self-administered and is made up of 36 questions that require about seven minutes for the respondent to complete. Thus, administering the SF-36 will not require any appreciable effort by the clinic team to collect the data. The SF-36 should be administered at the end of the trial but before the DCCT participants are informed of the results.

Patients should be asked to fill out the questionnaire after completing the DQOL. Specifically, a member of the DCCT clinic team (e.g., the research assistant) will ask the DCCT to fill out the SF-36 along with the DQOL during the clinic visit. The research assistant will inform the patient that the questionnaire is self-explanatory and that there are no right nor wrong answers. The questionnaire should be returned to the Coordinating Center along with the DQOL for scoring and data entry.

19.3 SYMPTOM CHECKLIST-90R

19.3.1 Introduction

The SCL-90-R is a 90-item psychological symptom rating scale which takes approximately 15 minutes to answer and is filled out by each patient in the trial.

19.3.2 Procedures

1. The SCL-90-R will be given immediately after the Quality of Life measure during the prerandomization phase and at annual followup visits.

2. The administration of the SCL-90-R should follow the administration of the Quality of Life Questionnaire (please see Section 19.2).

3. The SCL-90-R contains detailed instructions for the patient. The patient is asked to describe how much discomfort he/she is experiencing currently and in the past seven days. The instructions should be read to the subject on the first administration and then the subject will be asked if there are any questions. Typical questions include:

   a) "What if I am not sure about the best answer?" The administrator should tell the subject that there are no right or wrong answers, but to please pick the one that fits best.

   b) "I am not sure that I remember." Again, the technician can suggest selecting the answer he/she thinks fits best.

   c) If the patient refuses outright, please refer to the approach outlined above for the Quality of Life assessment.

4. Though the patient may ask for help in providing answers, in no situation should the administrator suggest possible answers. The administrator can emphasize, if the patient seems perplexed, that there are no right answers, just a best opinion.

5. When the patient has finished the SCL-90-R, the technician should quickly review it to make sure that each item has been filled out. If items have been left blank, ask the patient to fill in the blank items.

6. The SCL-90-R should be forwarded to the Coordinating Center when completed.

7. Data from the SCL-90-R will be scored at the Coordinating Center and the computer file data will include (a) a total score; (b) standardized subscale scores; (c) multiple-choice answers to each of the 90 items. The scoring is performed by a computer program that was written following the scoring instruction for the SCL-90-R in SCL-90-R Administration, Scoring and Procedures Manual by Leonard R. Derogatis, Ph.D. All scores are transformed to standard T-score (Mean=50, SD=10) from the gender-age appropriate norm.

8. If more than 20% of the 90 items are missing or if more than 40% of the items are missing from any one subscale, then the score is considered unreliable for the entire test or the dimension, respectively.

CHAPTER 20

COMPLIANCE

20.1 GENERAL PRINCIPLES OF ADHERENCE

20.1.1 Definitions and Synonyms

Adherence suggests yielding to the wish, request or command of another. Terms such as compliance, obedience, cooperation, collaboration, concordance, agreement, etc. have been used in lieu of adherence. For our purposes, adherence will be used to express the extent to which the participant's behavior, in terms of taking medications, following diets, making observations, keeping records, keeping appointments and making changes in life style coincides with the regimens and schedules of the DCCT Protocol.

20.1.2 Need to Monitor Adherence

The participant's non-adherence with medication and other treatment regimens has been recognized as a major problem in the delivery of health care. Sackett and Snow (1979) stated that the gap between the regimen prescribed by the clinician and that adhered to by the participant is often distressingly wide and that the clinician is often the last to know about non-adherence. Studies such as that by Svarstad (1976) found that when a physician monitors the participant's degree of committment to therapeutic regimens, the participant was much more likely to adhere, was more accurate in reporting, less inhibited in expressing complaints, and more likely to admit to having problems in conforming to a regimen. A number of the factors which influence adherence both in the setting of general medical care and in the specific context of clinical trials have been identified. This knowledge can be used to improve the level of adherence. The requirements made of the participant in a clinical trial often exceed, both in range and complexity, those made of a participant in the ordinary delivery of medical care. This Chapter will set out general guidelines to be used in addressing the issue of adherence, but it is anticipated that these guidelines will be developed and refined as experience in the application of the general principles of adherence to the specific regimens and Protocol of the DCCT is acquired.

20.1.3 Determinants of Adherence

The many factors which have been found to influence adherence can be divided into the following four general categories:

1. The regimen that the participant is being ask to follow.
2. The environment in which care is provided.
3. The characteristics and behavior of the professional staff providing the care.
4. The characteristics of the participant as they affect his/her ability to follow the regimen.

The general relationship of each of these categories to adherence is outlined before considering its specific application to diabetics and the Protocol of the DCCT.

20.1.3.1 The Regimen

In general, adherence is inversely related to the complexity of the medical regimen and the extent of the required behavior changes. The long-term regimens that are required for the management of chronic disease, especially asymptomatic disease, present special problems of adherence which are best approached by adapting the regimen, as much as possible, to the habits of the individual participant.

20.1.3.2 The Environment

The nature of the physical surroundings in which medical care is provided has an important bearing on the attitude of the participant towards the care and indirectly on his/her adherence to the prescribed regimen. If the participant finds the environment in which care is delivered congenial, he/she will be more likely to keep appointments. The general attractiveness and accessibility of the facility, including public transport, parking and the provision of maps, signs and directions will raise the probability that appointments are kept. The use of telephone and/or mailed appointment reminders is probably a key factor in maximizing appointment keeping. Waiting times should be minimized and schedules should be flexible enough to allow appointments at times which are convenient for the participant. As appointments are made, the use of specific appointments rather than block scheduling improves appointment keep rates.

20.1.3.3 The Provider

The general term "provider" includes all the staff with whom the participant comes into contact. While it may be necessary for the participant to see individuals of several disciplines at a given visit, e.g., physician, nurse, and nutritionist, it is desirable that the participant be seen by the same individual of each discipline at each visit. Continuity of care has emerged as one of the important determinants of adherence in addition to the more obvious qualities of warmth, empathy, and interest in the provider(s). That the staff communicate well with one another and are fully coordinated is a necessary prerequisite to their caring for the participant in such a way as to maximize adherence. It is also important that the provider have the necessary skills to instruct the participant on how to carry out the regimen so that the participant's ability to understand, remember, and carry out the program of care are maximized.

20.1.3.4 The Participant

Early research into adherence was based on the postulate that the "nonadherer" was a person with a particular set of personality characteristics that dictated his/her adherence behavior. However, it has become clear that there is no such set of personality characteristics and that adherence is a function of the treatment regimen itself, the behavior of the provider, and such participant-related characteristics as his/her knowledge of the regimen, social support, and skills in managing the regimen rather than of a particular parsonality type. This concept provides a much more optimistic view of adherence as a behavior which can, in principle, be developed under appropriate circumstances by all individuals who are appropriately educated to carry out the prescribed regimen.

20.2 THE DCCT REGIMEN

Participants in the DCCT are expected to follow the clinical prescriptions and requested behaviors shown in Table 20.1.

The therapeutic regimen for diabetes, especially IDDM, is complex even in its less sophisticated forms such as that prescribed to the standard group. As is clear from Chapter 9, the regimen for the experimental group is complex and therefore makes great demands on both the participant and the provider to obtain any given degree of adherence. All efforts should be made to minimize difficulties. Both the standard and experimental group's regimens should be made to fit the participant's daily routine. Inconveniences should be minimized. The use of behavioral prompts or cues, such as a call, reminder cards, alarm signals, reinforcements, and problem solving strategies, can be of help in assisting the participants to plan and to carry out their program of treatment. Additionally, ongoing adherence monitoring, counseling, and

followup will be useful in preventing or remediating problems as well as on maintaining adherence.

20.3 THE DCCT ENVIRONMENT

The DCCT clinic itself should provide both the participant and the staff members with a positive experience. We know that environments do affect attitudes and behaviors. Crowded, noisy rooms with uncomfortable chairs and sterile walls to stare at are likely to make us irritable and uncomfortable -- anxious to avoid that place. No participant should leave the study or develop negative attitudes toward the study because of environmental conditions which could have been avoided.

20.3.1 Clinic from the Participant's Perspective

1. Accessibility -- Because of the relatively large number of part-time clinical staff involved and because of the need for ancillary services such as fundus photography, it is likely that most DCCT clinics will be located in a large medical complex even though the location of the complex within the city may not be optimal for transportation, parking and safety. For these reasons, it is especially important to ensure that convenient parking (preferably free) is available, maps are provided, and that readily visible directional and identifying signs are posted on clinic days. Consideration should be given to assisting participants with transportation if they do not have their own transportation or are disabled for any reason. Volunteer services can sometimes help with transportation.

2. Reception, waiting and office facilities -- The general atmosphere should be pleasant and relaxing with special attention to the following:

   a) low noise levels or soft background music;

   b) suitable light for reading without strong glare;

   c) areas that are clean and orderly with attractive wall decorations;

   d) current reading material, including newspapers and magazines to appeal to participants of different ages and backgrounds;

   e) attractively displayed information on the DCCT, current newsletters, and newsletters of other clinics;

   f) a clinic bulletin board;

g) comfortable furniture arranged for quiet reading and easy conversation;

h) offices providing privacy and comfort for the participant;

i) the opportunity for suggestions to improve the clinic environment.

3. Scheduling system and waiting time -- Minimize waiting time by efficient scheduling and clinical center promptness. The participant can be actively engaged in completing forms, answering questionnaires or reviewing procedures with a member of the staff when waiting is unavoidable. Do not, however, create an atmosphere of tension and be willing to spend time with the participant who enjoys a leisurely visit. Movement from office to office should be well coordinated with suitable waiting areas if necessary. The reason for any delay should be explained.

   The scheduling system should be flexible enough to allow appointments which will not cause the participant to lose pay or miss school. This may necessitate operating the clinic on weekends, in the early morning, and in the evening.

   The participant should receive an appointment card for the next visit before leaving the clinic. It should include the date, day, time, expected duration, clinic phone number, the name of the person to contact to change the appointment, and instructions for any necessary preparation such as fasting. An appointment reminder should be mailed one week before the scheduled visit, with periodic checks on the receipt of these reminders. For participants who tend to forget visits, it may be useful to make a telephone call on the day before or morning of a scheduled visit. Visit "window sheets" should be available to the individual making appointments, and these should be checked each week with the list of completed appointments. Participants who have missed a visit should be telephoned as soon as possible to reschedule the visit.

   Tea, coffee, juice, and non-caloric drinks should be available at all visits. A snack or light breakfast should be provided in a suitable place after procedures that require fasting. It is important to ensure that the composition of the meal is consistent with diet prescriptions and the occasion often provides an opportunity for teaching.

20.3.2 Clinic from the Staff's Perspective

The environment should also be pleasant for the staff. Staff attitudes will be transmitted to the participants who will in turn be affected by their attitude to and participation in the program. Comfortable office space should enhance the conduct of the job. In particular, appropriately private and sound-proof rooms should be available for history taking, physical examinations and counseling.

The clinic should be designed to maximize communication among staff members who should also be encouraged to make suggestions for improvements.

20.4 ROLE OF DCCT STAFF

All participants should be called by name and made to feel that they are important and that their committment to the study is a valuable and indispensable contribution. Positive comments, expression of appreciation and praise for successful areas of participation should be given as frequently as possible. Only the participant who becomes totally inactive in the study lacks any success in adherence.

The organizational structure should be clearly delineated and understood by each staff member. Job tasks should be stimulating and rewarding to those performing them. Staff meetings should be held regularly and all staff members should be encouraged to participate in face to face discussion, including periodic review of staff working conditions.

Consistency is the key to successful communication with participants. All staff should convey the same information, instructions and attitudes to participants. The participant confronted with two opposing messages is unlikely to be a good adherer or to have much trust in the clinic staff. Supportive cohesive staff activities should be fostered and periodic recognition of the team effort in the conduct of the study should be made.

Over and above these general considerations, staff have the following four specific responsibilities toward participant adherence throughout the trial:

1. To educate all participants so that they are aware of exactly what is expected of them;

2. To identify participants having difficulties in one or more areas;

3. To intervene with participants who are having difficulties and bring them to their maximal level of adherence;

4. To maintain adherence in those areas where the participant in having success.

20.4.1 Education

Most participants express interest in educational programs. Educational programs can serve as motivating and reinforcing events for participants. In order to maintain interest and adherence, an educational program should be designed to include the following topics:

1. Periodic review of study progress
2. Yearly reeducation of participants and staff about DCCT study goals and protocol
3. Periodic general programs on diabetes, its control and complications
4. Routine skills assessment and retraining

A variety of methods should be utilized for educating participants, including:

1. Newsletters
2. Educational materials on clinic bulletin boards
3. Relevant reading materials in waiting rooms
4. Periodic educational audio-visual programs in the clinic
5. Individual and group instruction.

20.4.2 Identification of Problems

Each participant's chart should have a clearly visible display of that participant's adherence over time to the following required behavior:

1. Insulin administration -- how well does the participant follow prescribed treatment? Daily self reports should be collected to provide documentation.
2. Glucose testing -- again, daily self reports should be collected.
3. Visit attendance -- missed, rescheduled and out-of-window visits and the reasons for them should be recorded together with follow-up actions.
4. Diet adherence -- an assessment of adherence in specific areas as well as specific goals and problem areas should be recorded

Weekly chart conferences should be held to review all participants with particular attention to identifying any adherence problems.

20.4.3 Intervention

The scheduling of each visit should include time for adherence counseling. It is valuable to hold a conference of all staff members who will interact with a participant at a given visit to agree on a strategy for dealing with any adherence problems which that participant is experiencing.

20.4.4 Maintenance

This program should provide continuous support and encouragement to each participant in all the areas in which he/she is adhering to the requirements of the study. The following procedures are recommended:

1. Tailor the assigned regimen to the participant's lifestyle and daily habits.

2. Maintain frequent contacts with the participant and whenever appropriate with his family and social supports.

3. Provide adequate feedback about present health status at each visit.

4. Consider participant's ideas and choices in selecting alternatives to minimize any source of difficulties.

5. Involve participant in activities at the center to sustain interest as a participating member of the team.

6. Have periodic group meetings with participants in each treatment group for the sharing of experiences and providing on-going education.

7. Provide recognition for successful completion of tasks or certain aspects of them.

20.5 THE DCCT PARTICIPANT

The subjects who volunteer for the DCCT will have a range of characteristics that will affect her/his ability to follow the regimens. Those characteristics that are closely related to compliance will be determine only at the conclusion of the trial.

20.6 ASSESSMENT OF ADHERENCE

20.6.1 Pre-randomization Assessment

To assist in the assessment of adherence, three structured interview forms have been developed. These are the Availability, Adherence and Expectation Interview (DCCT Form 047), Family Understanding and Expectation Interview (DCCT Form 048), and Request Behaviors Confidence Questionnaire (DCCT Form 049). These forms are designed to guide the research team in assessing each subject and are NOT to be used for automatic exclusion or inclusion. These forms only elicit the most basic information related to the participant's availability and expected adherence in this study. The Principal Investigator or other members of the research team may ask supplemental and more detailed questions should they deem it necessary. Detailed instructions for administration are included within each form.

In general, the questionnaires are designed for administration by the nurse clinician or behavioral scientist who are both experienced in participant interviewing. The questionnaire should be presented in a relaxed, non-threatening manner. It should also be stressed to the participant that the purpose of the interview is not for exclusion or inclusion. Subjects should be instructed that the purpose of the interviews is to:

1. Have a better understanding of what their past diabetes care has been and what problems they may have had with that treatment.

2. To understand what they expect from the study.

3. To understand what the family expects from the study.

4. To determine any scheduling or other logistical problems that need to be considered prior to the subject's participation.

In general, these interviews should be approached as being educational in nature and providing the research team an opportunity to interact with the subject to correct any misconceptions, and to anticipate any possible adherence/scheduling problems.

20.6.1.1 Availability, Adherence and Expectation Interview (DCCT Form 047)

This interview form should be administered after the slide tape show and after the subject has had the opportunity to read the Participant Information Handbook. Basically, this form is composed of three parts, e.g., an availability section, a past adherence section, and an expectation section. As stated, the basic purpose is to anticipate any problem areas such as scheduling or logistic problems, specific factors which have in the past interferred with adherence, and to elicit any unrealistic expectations. Except for the question in Section D, question

2 (i.e., "Would you be willing to accept being randomly assigned to either of the treatment groups?"), none of the questions are meant to lead to automatic exclusion. Instead, the purpose is to elicit information that can be used in the educational component of the protocol so that the participants can overcome possible barriers to adherence.

20.6.1.2 Family Understanding and Expectation Interview (DCCT Form 048)

This interview is designed to elicit information from the family similar to that elicited from the subject in DCCT Form 047. The basic purpose is to ensure that family members understand the protocol and to ensure that they do not have any unrealistic expectations regarding the study. The adherence literature suggests that one important component of adherence is appropriate family and social support. Considering the complexities of the DCCT trial, it is extremely important to involve the family early in this process. As in DCCT Form 047, this interview is seen as being educational in nature and allowing the research team an opportunity to understand family's perception of the protocol and to correct any of their misconceptions.

20.6.1.3 Request Behaviors Confidence Questionnaire (DCCT Form 049)

The questionnaire is designed to allow the participant to (1) state his/her confidence in the ability to perform what is required, and (2) state his/her prediction of how adherent they will be.

This form is derived from the self-efficacy concept of social learning theory and from the person-as-predictor model from the adherence literature. Self-efficacy, that is a person's confidence and perceived ability to perform certain tasks, has been found to be a reliable predictor of behavior in a number of areas not related to diabetes. Although the concept has not been applied specifically in diabetes, we feel that this form can be both of assistance to the research team and used in the educational process to increase the participant's feelings of confidence and perceived abilities.

This form is designed to be used on two occasions: once in conjunction with DCCT Form 047, after the subject has reviewed the slide and tape presentation and has read the Participant Volunteer Handbook. The second administration should follow the completion of the pre-randomization behavioral task when the participant has had an opportunity to experience and participate in a number of activities associated with this protocol. It is not expected that the subject will be 100% confident prior to randomization. Areas which are rated quite low in confidence will be those in which extensive education will be necessary to increase the participant's feelings of confidence.

20.6.1.4 Evaluation (Pre-Randomization) Behavioral Tasks

Prior to a review of the final consent forms, all potentially eligible volunteers will carry out a set of behavioral tasks which approximate tasks required of one or both treatment groups during the course of the DCCT. The tasks which are described in detail in this chapter should be performed by each participant undergoing evaluation and should not be altered, but may be repeated if necessary. Deviations are not accepted without the appropriate revisions by the Eligibility Committee and the approval of the Steering Committee. The purpose of these tasks is twofold: (1) to familiarize the potential volunteer with selected DCCT required behaviors so that a more fully informed decision can be made about participation, and (2) to provide DCCT center staff with an evaluation of the potential volunteer's ability to learn and willingly carry out certain of the DCCT required behaviors. These behavioral tasks include an in-clinic demonstration of the following skills:

1. Ability to draw up accurately a specified amount of sterile water in an insulin syringe.

2. Ability to mix long and short acting insulin.

3. Ability to color match and interpret accurately a urine test for glucose.

4. Ability to perform calculations which would be necessary to adjust insulin doses in accordance with the protocol for the Experimental Treatment Group.

5. Ability to state the symptoms and treatment of mild, moderate, and severe hypoglycemia.

6. Ability to state at least three possible causes of ketoacidosis.

7. Ability to state warning symptoms and management of ketoacidosis.

8. Ability to follow the required protocol for capillary blood collection.

20.6.1.5 Instructions for Administration and Evaluation of Behavioral Tasks Performed During Clinic Visits

The purpose of the in-clinic behavioral tasks is three-fold:

1. To obtain a gross estimate of the volunteer's skill level in his/her management regimen prior to randomization.

2. To obtain a gross estimate of how easily the volunteer learns in the case where skills are not acceptable.

3. To determine whether the volunteer can safely carry out the at-home behavioral tasks.

Conduct of skills assessment:

1. Materials required:

   a) 0.5cc syringe

   b) 1.0cc syringe

   c) one bottle saline labeled "regular insulin"

   d) one bottle saline labeled "NPH insulin"

   e) clinitest tablets with result chart

   f) diastiks with result chart

   g) testape with result chart

   h) watch with second hand

   i) dropper

   j) test tube

   k) glass container

   l) medicine cups or other containers for water

   m) urine specimen cups

   n) access to running water

   o) alcohol wipes

   p) copy of questions: actions for hypoglycemia, actions for ketoacidosis, causes of ketoacidosis

   q) copy of hypo/hyperglycemia symptom match question

   r) copy of in-clinic behavioral tasks evaluation form (DCCT Form 056)

2. Procedure:

   Ask the volunteer to perform each task listed in question B.1. of DCCT Form 056. The volunteer should select the correct materials and carry out the skill without prompting. The clinician rates that performance on the same form in the column labeled Trial 1. If the volunteer made errors, the clinician offers corrective instruction, asks the volunteer to repeat the

task, and rates performance in the column labeled Trial 2. The specific instruction given is noted also under the column headed "Specify Instruction or Prompt."

Continue by asking the volunteer to perform Tasks 6 through 9 and rate them on the evaluation form after the tasks are done.

The tasks are rated on the following five point scale, which is further defined for each task (1 through 9) on the following pages:

1 - excellent; perfect performance

2 - good; minor error

3 - fair; two minor errors or one more serious error

4 - poor; three or four errors

5 - very poor; five or more errors and/or incorrect dose

TASK 1. Draw up nine units of insulin in a 0.5cc syringe

1 = Rolls the bottle to insure mixing,
cleanses the top of the bottle,
injects nine units of air,
pulls the plunger down to nine units,
checks for air bubbles and if present, eliminates them,
withdraws exactly nine units of insulin.

2 = Omits cleansing the bottle or rolling the bottle.

3 = Omits two of the following:
cleansing the bottle,
rolling the bottle,
injecting air,
or omits injecting air alone.

4 = Omits three of the following:
cleansing the bottle,
exactly nine units air,
injecting air,
or omits checking for air bubbles
before drawing up NPH insulin alone.

4 = Omits three of the following:
cleansing the bottle,
rolling the bottle,
inject nine units of air.

5 = Error at each step or
withdraws more/less than nine units plus or minus one.

TASK 2. Draw 16 units of insulin in 1.0cc syringe. The rating is exactly as for Task 1, except 16 units should be substituted for nine units.

TASK 3. Draw 14 units of NPH and mix with six units regular insulin.

1 = Rolls both bottles of insulin,
cleanse the top of both bottles,
injects 14 units of air in bottle of NPH insulin,
removes needle from NPH bottle,
draws up 6 units of air and injects this into the regular insulin bottle,
slowly inverts the bottle and withdraws 6 units of regular insulin,
removes needle from regular bottle,
inverts the NPH bottle, inserts the needle, and slowly withdraws 14 units of NPH,
checks that total insulin is 20 units.

2 = Omits cleansing or rolling one or both bottles.

3 = Omits both cleansing and rolling bottles or
omits injecting air in one or both bottles.

4 = Omits cleansing, rolling, and injecting air in one or both bottles or
does not check for air bubbles before drawing up the NPH insulin.

5 = Omits cleansing, rolling, and injecting air in one or both bottles as well as omits checking for air bubbles or withdraws more/less than:
14 units plus or minus one unit NPH insulin, or
six units plus or minus one unit regular insulin, or
20 units plus or minus one unit total insulin.

TASK 4. Perform urine glucose test. (The volunteer should perform the test which he/she usually uses.)

(i) Clinitest:

1 = Places ten drops of water in tube,
places correct drops of urine in tube (2;5) -- holding the dropper vertically so that the drop falls directly to the bottom,
rinses dropper,
withdraws one clinitest tablet without touching it (uses bottle cap or forceps) places tablet in the tube,
puts cap back on the bottle,
holds tube still by the top while it boils,
waits 15 seconds after boiling stops,
compares tube with color chart.

2 = Did not put water in first or
did not rinse dropper after putting urine in or
did not put cap back on clinitest bottle.

3 = Omitted two of the above (2) or
did not hold the dropper vertically.

4 = Omitted three of the above (2,3) or
agitated the tube during boiling.

5 = Used the incorrect number of drops of water or
used the incorrect number of drops of urine or
used the incorrect time (e.g., 15 seconds plus or minus two seconds) or
used more than one clinitest tablet or
read the result incorrectly.

(ii) Diastix:

1 = Removes strip from container without touching,
replaces cap on the container,
dips strip in urine for two seconds,
removes strip,
waits 30 seconds by a second hand -- holding strip in hand,
reads results on paper side of tape -- using proper color chart.

2 = Does not replace cap immediately.

3 = Leaves strip in the urine more than two plus or minus two seconds or
lays the strip down while waiting.

4 = Two or more of the above (2,3) errors or
touched the strip while removing it.

5 = Used incorrect timing (e.g., 30 seconds plus or minus two seconds) or
read the results incorrectly.

(iii) Testape:

1 = Pulls off approximately one and a half inches of tape and cuts off on the bottle,
returns reagent to glass container,
holds tape at the end not using for dipping,
dips approximately one-quarter inch into urine for two seconds,
pulls tape out of urine,
waits 60 seconds by a second hand -- holding the tape in the hand,
reads the test correctly -- using the end with last darkest color,
if one-half percent or higher, waits 60 seconds and re-reads.

2 = Omits returning reagent to the glass container.

3 = Leaves the strip in the urine for more/less than two plus or
minus two seconds or laid the strip down.

4 = Touched the reagent end of the strip.

5 = Used incorrect timing (e.g., more or less than 60 plus or minus two seconds or read the results in more than one category or did not read result correctly.

TASK 5. Collection of capillary blood specimen. (Please refer to instructions in Chapter 12.)

1 = Carries out every step in the protocol accurately.

2 = Omits handwashing and/or uses the first drop of blood

3 = Omits preparation of the autoclix and/or does not hold the tube horizontally

4 = Omits warming the tube prior to sample collection or omits handwashing and/or uses the first drop of blood and also does not prepare the autoclix and/or does not hold the tube horizontally.

5 = Omits any step in the preparation of the sample or does not check for air bubbles or does not fill the tube end to end or does not mark the time sample is taken

TASK 6. The volunteer should be able to match the following symptoms with hypo- or hyperglycemia: increased thirst, shakiness, waking up to urinate, increased urination, sweating, blurred vision.

TASK 7. J. J. is a 15 year old person with IDDM playing baseball at 4:00 p.m. While in the outfield, he developed shakiness, sweating and palpitations. What should J. J. do?

TASK 8. The volunteer should be able to state at least two common causes of ketoacidosis.

TASK 9. The volunteer should be able to answer accurately the following question: A. K., a 20 year old person with IDDM, developed the flu and reportedly has a dry mouth, feels very thirsty and has developed nausea and vomiting. What are the first two things he/she should do to determine if he/she is in ketoacidosis?

TASK 10. The volunteer should be able to solve the following problems:

1. A.B. is on 45 units of NPH insulin a day, with the dose divided so that one-third is given at night and two-thirds in the morning. How many units of insulin does A.B. take in the morning? In the evening? (Answer: morning 30; night 15)

2. C.D. takes NPH insulin which peaks for him in eight hours. If the insulin was usually taken at 7:00 a.m., at what time would it peak? (Answer: 3:00 p.m.)

The Tasks 6 to 10 should be evaluated as noted on the in-clinic behavioral tasks form (DCCT Form 056). That is, the number correctly matched should be noted for item 6; the responses noted on the form for items 7 to 9 should be checked as "Yes" or "No" and any other responses noted on the form; and item 10 should be marked "correct" or "incorrect." DCCT Form 056 is returned to the Coordinating Center as indicated on the form.

20.6.1.6 Evaluation of Behavioral Tasks Performed at Home

The purpose of carrying out behavioral tasks at home is to obtain additional information whether the participant is adequately performing these tasks at home independently of immediate supervision. The following skills are required to be done at home using DCCT Form 061:

1. Record date home behavioral tasks started.

2. Urine tests for glucose four times daily for 14 days; record date and time of early morning and first and second voided urines, time and quantity of water ingested between these voids, as well as the time and result of each of the four tests in a daily record supplied by the DCCT.

3. Capillary blood collection by finger stick will be done four times during the 14 day home behavioral tasks. They will be collected as follows:

   a) Four pre-prandial collections for two consecutive days.

   b) One 3:00 a.m. and seven pre- and post-prandial collections on day 7 of home behavioral tasks.

   c) One 3:00 a.m. and seven pre- and post-prandial collections on day 14 of home behavioral tasks.
   All of the capillary blood collections will be returned to the clinic. The capillary blood collections will be used in evaluating adherence to the required tasks. (Procedures for drawing, preserving and transporting blood are described in Chapters 12 and 15.) Record date and time every time blood is drawn, as well as the number of the tube in a daily record supplied by the DCCT Form 061.

4. Record daily the type and dosage of insulin administered as well as the date and time of each administration in a daily record supplied by the DCCT Form 061.

5. List for three consecutive days on DCCT Form 062 (to include one weekend day) all foods eaten. Record the brand name, the amount and how the food was prepared. Also record the time of day the food was consumed.

6. Record daily on DCCT Form 061, for 11 days, type of meal and time food was consumed.

7. Specify physical activity in the exercise section of the daily record (DCCT Form 061) specifying the time, type of activity and duration.

The Behavioral Task Log, DCCT Form 061, was devised to record urine tests, insulin administration, physical activity, mealtimes and capillary blood collections. If any of these activities are omitted, the explanation of why should be given in the column "Comments."

The performance of these home behavioral tasks should be reviewed and recorded on a performance evaluation form (DCCT Form 057). This form should be reviewed prior to the decision to randomize the volunteer for the following:

1. Specific areas the participant may need added attention in terms of eduction.

2. Specific areas the participant may need added attention in terms of adherence.

To complete DCCT Form 057, please enter the number of times that the performance of the tasks was required and the percent of times which the tasks were performed as indicated in the form. Performance of tasks will vary between tasks, e.g., pre-prandial capillary blood collections should be drawn on four days while the 3:00 a.m. capillary blood collection should be drawn on two days. Please write in any comments about missed tests and the quality of completeness of the log as requested in item 8.

20.6.2 Post-Randomization Assessment

Monitoring of wide and individual center performance with regard to participant adherence will include:

1. Completion of self-monitoring records.

2. Glucose testing, blood and urine - daily (including 3:00 A.M. for experimental group) and profile-sets completes.

3. Insulin administration.

4. Dietary adherence, total calories, meal/snack frequency.

5. Visit attendance, quarterly both groups and monthly experimental group.

6. Correspondence between self-reported glucose testing and HbA1C; between self-reported glucose testing and profil-sets.

Assessment will be made at quarterly followup visits (Form 021) and annual followup visits (Form 003)

20.7 REFERENCES

1. Sackett, DL and Snow, JC. The magnitude of compliance and noncompliance. Compliance in Health Care, pp 11-22, The Johns Hopkins University Press, Baltimore, MD, 1979.

2. Svarstad, BL. Physician-patient communication and patient conformity with medical advice. The Growth of Bureaucratic Medicine, pp 220-238, Mechanic D (ed), Wiley, New York, 1976.

Table 20.1

DCCT Participant Request Behaviors

Behavior	Standard Care	Experimental Care
Visit attendance	every 3 months	every month
	additional visits as needed	additional visits as needed
Insulin administration	1-2 times daily	3-4 times daily or use insulin pump
Home glucose monitoring	3-4 times daily urine OR once a day blood	4-7 times daily blood; weekly 3:00 a.m. blood
Capillary blood profiles	7 times daily, every 3 months,	7 times daily every 3 months,
Home acetone monitoring	as needed	as needed
Study diet: 45-55% CHO less than or equal to 25% simple CHO 30-35% FAT 12% PRO less than or equal to 300 mg CHOL 0.8-1.0 P/S RATIO encouraged fiber moderation ethanol	specific meal plan individualized	specific meal plan individualized
Attain/maintain desirable weight	90-120% of ideal	90-120% of ideal

CHAPTER 21

COMPLETION AND MAILING OF FORMS

The DCCT forms have been constructed to serve the following functions:

1. to allow the evaluation of the eligibility of a patient candidate;
2. to provide the data required for a thorough statistical evaluation of the baseline comparability of the two treatment groups and the endpoint data;
3. to allow the followup and monitoring of a randomized patient in a thorough format that is standard for all clinical centers;
4. to document that certain study procedures have been followed either by the clinic staff or by the patient;
5. to request certification of new clinic staff;
6. to collect data for ancillary studies.

This chapter will describe the various types of study forms, how to complete them, and how to distribute them to their proper destination.

21.1 THE VARIOUS TYPES OF FORMS

Although there are a large number of forms (Table 21.1), many of these are used only once per patient (such as during eligibility evaluation) or are designed for a special purpose and rarely need to be completed.

The forms used by the Central Units for reporting results to the Coordinating Center are not used in the clinic. There are a large number of forms of this type (Table 21.2).

The forms used to inventory specimens or other materials mailed to the Central Units are also used to create an audit trail for the Coordinating Center for tracking any missing material. These administrative forms are listed in Table 21.3. These "mailing lists" are typically printed on multi-part NCR (no-carbon-required) paper. The instructions on the form, as well as Table 21.3, indicate the use of each of the copies.

Another special type of form is that which is used by a clinical center to request that the certification process be initiated for a new clinic staff member (Table 21.4). Chapter 23 of this Manual describes certification procedures.

There are a number of special-purpose forms which the clinic will rarely need to complete (Table 21.5). Some of these are used on an as-required basis to notify the Coordinating Center and the study review groups of intercurrent events affecting patient health, missed follow-up visits, transfer of a patient to another clinical center, and so on. Another special-use form is that used for ordering clinic supplies (DCCT Form 068).

Several forms are used by only the patients and the clinical centers and are not to be sent to the Coordinating Center (Table 21.6). Of particular note is DCCT Form 012, Personal Information on Study Volunteer, which collects information that may be used to locate a randomized patient who loses contact with the study.

Because of the stringent eligibility criteria for this trial, a number of forms have been developed especially for screening purposes (Table 21.7). Much of the information on these data forms is also used to characterize the baseline status of the randomized volunteers. Some of these forms are also completed during followup.

Table 21.8 lists forms which are used exclusively during followup of an enrolled patient. (Note: DCCT Form 021 is only partially completed pre-randomization. It is primarily intended as a follow-up instrument.)

21.2 FORMS SUPPLIES

Prior to the start of the study, the Coordinating Center will ship an initial supply of DCCT forms to each clinic for use during the first few months of the study. Prototypes of the first and second Informed Consent forms (DCCT Forms 031 and 032) will be supplied by the Coordinating Center. Informed consent forms and additions to the other informed consent documents for clinic use should be printed locally to reflect any changes requested by that institution's IRB (see Chapters 3 and 7).

The initial supply will consist of simple copies of each form. Whenever a form is completed, the appropriate number of xerox copies should then be made by the clinical center. This will allow the Coordinating Center to rapidly and inexpensively modify any deficiencies encountered during the early use of the forms. After final revisions, the forms will be printed on NCR (no-carbon-required) paper, which will automatically yield the appropriate number of copies when each form is completed.

The Coordinating Center will develop a system of inventory control which will require the collaboration of the clinics. The Trial Coordinator should maintain an inventory of all forms in stock. By imprinting the forms with incrementing inventory control numbers, the Coordinating Center will also monitor form consumption by the study units.

The inventory control numbers of data forms will be monitored as completed study forms are submitted to the Coordinating Center for entry into the computer files. Each unit's supplies of study forms will be reviewed periodically by the Coordinating Center.

Other consumable materials, such as the Research Volunteer's Information Handbook and the Manual of Diabetes Tests, Terms and Special Procedures, also will be imprinted with an incrementing inventory control number. When the supplies are distributed from the Coordinating Center, an inventory control "reorder" card will be inserted within the supply prior to the last 20% of the materials. As the supply is consumed, when the "reorder" card is reached it will be mailed to the Coordinating Center and the supply will be replenished.

As a further check, each unit will periodically be requested to complete a statement of the inventory control numbers of the next material (e.g. form, handbook, etc.) to be used. These statements will be reviewed by the Coordinating Center to ensure that there have been no breakdowns in inventory control procedures, thus ensuring that each unit is continually supplied with all needed study materials.

21.3 FORM, PATIENT AND VISIT IDENTIFYING INFORMATION

21.3.1 Form Number and Version Number

Because the development of the DCCT forms was a process occurring concurrently with the evolution of the Protocol and Manual of Operations, the forms are not numbered in a systematic fashion. As a form is created for a particular need, the next available number is assigned to the form.

The number for each form consists of an integer and a decimal. The integer indicates the form and the decimal indicates the version of the form. For example, from Table 21.1, DCCT Form number 001.6 indicates that this is the form entitled "Initial Clinic Visit" and that it is the sixth version. The date on the upper right corner of the form indicates when this version was adopted.

21.3.2 Identifying Information

Before a patient arrives for a scheduled visit, all forms required for that visit should be assembled with that patient's folder and the I.D. section should be filled out. On all forms, the following identifying information will be employed.

1. Clinic Number
2. Patient ID Number
3. Patient's Initials

4. Date of Visit

5. Follow-up Visit Number

21.3.3 Collaborating Clinic Number

Each of the 27 DCCT clinical centers is assigned a Clinic Number which is used on every study form. These Clinic Numbers are:

01	Case Western Reserve University
02	Children's Hospital of Philadelphia
03	Cornell University
04	Henry Ford Hospital
41*	University of Michigan
05	Joslin Diabetes Center, Inc.
06	Massachusetts General Hospital
07	Mayo Foundation
08	Medical University of South Carolina
09	International Diabetes Center
10	University of Iowa
11	University of Minnesota
12	University of Missouri at Columbia
13	University of Pittsburgh
14	University of Tennessee
15	University of Texas
16	University of Toronto
17	University of Washington
18	University of Western Ontario
19	Vanderbilt University
20	Washington University
21	Yale University
22	Albert Einstein College of Medicine
23	Northwestern University
24	University of California, San Diego
25	University of Maryland
26	University of New Mexico
27	University of South Florida

*Satellite clinic to Henry Ford Hospital.

21.3.4 Patient Identification Number

A permanent DCCT identification number (ID No.) is assigned to each patient who appears at a clinical center for one or more of the evaluation examinations. The patient identification numbers are assigned in order on DCCT Form 001, Initial Clinic Visit. The five-digit patient identification number consists of two digits which designate the clinical center in which the patient is first screened for eligibility and a

three-digit code to identify the patient. At the start of screening, a patient is assigned the next available fivedigit code for that clinic. Once a number has been assigned to a particular patient it remains associated with this patient even if he/she later transfers to another clinical center. If a patient is ineligible or excluded on the basis of the results of the screening exams, refer to Table 6.5 for a list of screening exams that may be retested during the four-month evaluation period (retakes). Some patients who are excluded may be restarted six months later. If a patient is restarted, a new identification number is assigned.

Issuance of a patient identification number does not imply that the patient is enrolled in the DCCT. Entry into the study takes place when the patient is randomized.

21.3.5 Patient's Initials

The patient's initials, comprising the patient's first, middle and last initials, constitutes a second patient identifier. If the patient has no middle name or initial, an "X" is used as the middle initial. The initials identifier, once determined, is never changed, although the patient may change his/her name during the course of the study. If a patient who was ineligible is restarted with a new identification number and his/her initials have changed, however, the new initials may be used.

21.3.6 Examination Date or Date of Visit

Some examination procedures may require more than one day to complete. The date an examination is begun is regarded as the examination date. A number of procedures may be associated with each examination. An examination is not regarded as complete until all procedures have been completed.

21.3.7 Follow-up Visit Number

The follow-up visit number is the number of quarters (three month time period) post randomization. This number is sequentially numbered from 0 for baseline, 1 for first three month visit, 4 for first annual visit, 8 for second annual visit, through 40 for tenth annual visit.

0 = Baseline	4 = 12 months	8 = 24 months
1 = 3 months	.	.
2 = 6 months	.	.
3 = 9 months	7 = 21 months	40 = 120 months

21.3.8 Patient Schedules

After a patient is randomized, the Coordinating Center will generate a schedule of target dates and windows for all regularly scheduled follow-up visits for that patient (Figure 21.1). This schedule will indicate all the forms to be completed at each visit. Besides this schedule of routine visits, the clinic will also receive a list of the forms mailing date of every week and Study Week Number in order to identify the week of followup during which a form is completed and mailed (Figure 21.2, DCCT Mailing Schedule of Forms).

21.4 COMPLETING FORMS

Each form has been prepared such that all instructions required for properly completing the form are self-contained. Forms should be filled out carefully using a ballpoint pen with black ink. (A ballpoint pen is needed because many forms are printed on multi-part paper. Black ink is preferred because experience has shown that it is clearest on microfiched copies.) Changes should be made carefully and neatly with special attention paid to the second, third and/or fourth copies. Extra notations should not be made if there is no space designated for them. If you find that there are inadequacies in a form, please notify the Coordinating Center so that revisions can be considered.

Sometimes an item on a form requires a written response rather than a simple check of a box or an entry of a number. In these cases, the clinic staff should print the answer clearly, avoiding the use of abbreviations, especially abbreviations of medical terms.

Before the patient leaves the clinic, at the conclusion of the visit, the Trial Coordinator should review each of the required forms for accuracy and completeness. The Trial Coordinator should also ensure that all tests and procedures required for that visit have been conducted and the appropriate forms completed (see Chapter 6).

Each form should bear the signature and typed or printed name of the individual who completed the form, or the person with primary responsibilitiy, if more than one person completed it.

21.5 BATCHING AND MAILING

Forms should be mailed on Thursday of each week to the Coordinating Center. A weekly batch of forms, therefore, will comprise all forms completed since the last mailing.

21.5.1 Copying and Inventorying Forms

Each Thursday afternoon, all forms completed during the preceding week should be collected and sorted by Form Number and by Patient I.D. Number within Form Number. A copy of the Clinic Forms Inventory (DCCT Form 040), which requires specification of the Form Number, date and Patient ID number, should be completed. The batch of forms are then photocopied and the copies are compared against the just completed Forms Inventory. The clinic's copies of the forms may then be re-sorted by Patient ID number and filed in the clinic's medical record for each patient.

Forms and the Clinic Forms Inventory are organized by Form Number in order to facilitate processing at the Coordinating Center, where the forms must be batched and keyed by Form Number.

When photocopying forms, be sure to use one-sided copying only. One-sided copies are required by the data entry and microfiching procedures used by the Coordinating Center.

21.5.2 Batching Forms

The Coordinating Center's copies of the forms (which are always the originals) will then be batched for mailing to the Coordinating Center. A copy of the Clinic Forms Inventory and the Forms Mailing List should be included with the batch. During followup, all forms within a weekly batch should first be sorted by number, i.e., all forms of a given type should be together in the batch. The Trial Coordinator will then inventory the batch of forms by completing the the Forms Mailing List (DCCT Form 041). On this form, the number of each type of form included in the batch is listed. The entries on the mailing list should correspond to the total number of entries on the Clinic Forms Inventory.

21.5.3 Mailing Forms

The forms are then placed in one or more envelopes and mailed to this address:

DCCT Coordinating Center--Forms
The Biostatistics Center
6110 Executive Boulevard, Suite 750
Rockville, MD 20852

When more than one envelope is required to mail a batch, the date of mailing should be written on each envelope, and each should then be numbered at the bottom as 1 of x, 2 of x, etc., where x is the total number of envelopes included in that mailing.

Another copy of the Forms Mailing List is then placed in a separate envelope for mailing to the Coordinating Center. This is done as a

security measure; it helps insure that the Coordinating Center will become aware of a missing batch of forms. The batch, Clinic Forms Inventory, and Forms Mailing List should then be mailed with first-class postage on Thursday afternoon so that the forms will arrive at the Coordinating Center the following Monday.

Copies of the Notification Forms, (DCCT Forms 007, 025, 026, 042, 043, 044, 055) should be sent to the Coordinating Center and central laboratories or reading units with specimens, photographs, etc.

There will be some weeks in which no forms have been completed. In this event, the clinic should complete the Forms Mailing List and check the box indicating that no forms are being sent. This form alone should then be mailed to the Coordinating Center.

21.6 RECEIPT OF FORMS

When forms arrive at the Coordinating Center, the Data Control Clerk will open the mail and reassemble the batch if multiple mailing envelopes were used. Forms should arrive at the Coordinating Center by the Monday following the Thursday mailing. If a complete batch has not been received by the next Thursday, a trace will be initiated. The clinical center will also be contacted so that copies of any missing forms may be mailed with the next week's batch.

When the batch is reassembled, the Clerk will count the number of forms received and compare the counts with those given on the Mailing List and the Inventory. If there are any discrepancies noted, the clinical center is called immediately.

21.7 EDITING DATA ON FORMS

Each form is edited by a separate edit program which searches for missing data, inconsistencies, and values that are out of range. An error notice is printed which lists all the errors detected for a given form. An example of an error notice printing from the DCCT is presented in Figure 21.3. These notices are mailed back to the originating clinic for recording the correct information. The error notice is a "turn-around" document on which the corrections to the error notices are written and the document returned to the Coordinating Center.

An edit message should be returned to the Coordinating Center within two weeks, even if the data in question are correct.

An edit message consists of a table showing the form number, the Clinic Number, the Patient ID and initials, the date the form was completed and the study week it was mailed, and the certification number of the clinic staff member who completed the form. Below this information is listed one or more error notices. Each error notice lists

the form Item Number and an abbreviated description of the item. The Variable Name for the datum in question (as used in the Coordinating Center's edit and analysis programs) is printed next to the value of the variable. A message describing the reason for questioning the value is printed. A line labeled "new value" is provided for entering a response to the message. The possible responses include:

1. entering a new value;

2. entering the word "missing" if the correct datum cannot be retrieved;

3. entering the word "okay" if the original value is correct;

4. entering another explanation.

The edit program also prints a table of control totals for forms edited in that batch to compare with the data entry control totals. In addition, tables containing the number of forms edited and the number of errors per form are printed by form type and clinic. These edit summary tables can be used to monitor clinic performance.

There will be occasions when the clinic staff will realize they have made an error in completing a form, yet the nature of the error may be such that an edit program may not detect it. To make an unsolicited correction to a form, the clinic should:

1. make a copy of page 1 of the form and the page(s) to be updated;

2. write "correction" in red ink on page 1;

3. indicate all needed changes in red ink;

4. send the pages to the Coordinating Center. Corrections may be sent with the regular weekly mailing but should be clearly separate from it and from any edit messages generated by the Coordinating Center's edit programs.

Table 21.1

December 3, 1987
SCR/form/b

LISTING OF DCCT FORMS

Form	Code	Name	Date of Latest Version
001.6	E/N	Initial Clinic Visit	03/26/87
002.4	E/N	Baseline Medical History and Physical Examination	03/26/87
003.2	F/N	Annual Medical History and Physical Examination	11/19/86
004.4	E/F	Locally-Performed Blood Count and Chemistry	12/01/86
005.1	B/F	Neurological History and Examination (completed by neurologist)	05/25/83
006.4	E/F	Locally-Performed Urinalysis and Urine Culture	12/01/86
007.1	S	Documentation of Local Laboratory Certification	08/03/82
008.2	E	Baseline Ophthalmic Examination and Ocular History (completed by ophthalmologist & visual acuity examiner)	08/23/83
009.2	E	Preliminary Grading Form (Central Ophthalmologic Reading Unit use)	12/18/86
010.3	B/F	Neurobehavioral Assessment (Complete Battery) (Central Neurobehavioral Coding Unit use)	03/26/87
011.2	B	Randomization Report	09/01/83
012.1	B/F/*	Personal Information on Study Volunteer	06/14/83
013.2	B/F	Neurobehavioral Studies Demographic Questionnaire	03/26/87
014.2	S	Notification of Missed Clinic Visit	10/29/86
015.1	S	Notification of Death	04/11/83
016.2	S	Application for Transfer to Inactive Status	10/29/86
017.1	S	Bradburn Scale	07/20/84
018.2	B/F/N	Diet History (completed by dietitian)	(no date)
020.4	S/N	Notification of Intercurrent Event	03/26/87
021.6	B/F/N	Quarterly Visit	03/26/87
022.2	S	Notification of Deviation from Assigned Treatment	10/29/86
023.3	E/B/F	Central Biochemistry Laboratory Results (Central Biochemistry Laboratory use)	06/16/87
		SECTION A (C-peptide)	06/16/87
		SECTION B (Renal Studies)	06/16/87
		SECTION C (Lipid Studies)	06/16/87
		SECTION D (Blood Glucose Profile)	06/16/87
		SECTION E,R (Elevated Cholestrol, Repeats)	06/16/87
		SECTION F (24-Hour Urine Studies)	Paradox
		SECTION G (Glomerular Filtration Rate)	Paradox
024.1	B/F	Resting Electrocardiogram Grading Form (Central Electrocardiogram Reading Unit use)	06/01/83
025.2	E/F	Fundus Photography (completed by ophthalmic photographer)	07/18/85
026.2	B/F	Fluorescein Angiography (completed by ophthalmic photographer)	07/18/85
027.1	F	Endpoint Visit Ophthalmic Examination (completed by ophthalmologist & visual acuity examiner)	08/02/84
028.5	B/F	Autonomic Neuropathy Studies (Central Autonomic Coding Unit use)	05/21/86

Form	Code	Name	Date of Latest Version
029.1	*B/F	Food Pattern Questionnaire (dietitian's local use)	06/83
030.1	*B/F	Food Preparation Questionnaire (dietitian's local use)	06/83
031.3	E	First Informed Consent (Prototype)	12/02/86
032.3	B	Second Informed Consent (Prototype)	02/06/87
033.1	E/F	Detailed Color Grading Form (Central Ophthalmologic Reading Unit use)	(no date)
034.2	B/F	Detailed Fluorescein Grading Form (Central Ophthalmologic Reading Unit use)	06/10/87
035.1	B/F	Symptom Checklist-90-R (SCL-90-R)	(no date)
036.1	B/F	Quality of Life Questionnaire	03/21/83
037.2	B/F	Nerve Conduction Studies (completed by electromyographer)	08/31/83
038.2	E	Eligibility and Exclusion Checklist	02/11/85
039.2	S	Notification of Patient Transfer	03/07/86
040.2	A/N	Clinic Forms Inventory	07/18/85
041.3	A/N	Forms Mailing List	11/13/84
042.2	A/N	Fundus Photograph Mailing List	07/18/85
043.3	A/N	C-Peptide Specimen Mailing List	07/18/85
044.2	A/N	Renal Studies Specimen Mailing List	07/18/85
045.2	E	Volunteer Understanding Questionnaire (Version A)	02/12/85
046.2	E	Volunteer Understanding Questionnaire (Version B)	02/12/85
047.1	E	Availability, Adherence and Expectation Interview	03/21/83
048.1	E	Family Understanding and Expectation Interview	03/21/83
049.2	E	Request Behaviors Confidence Questionnaire	07/18/85
050.2	A/N	Blood Glucose Profile Specimen Mailing List	07/18/85
051.3	A/N	Neurobehavioral Assessment Mailing List	03/26/87
052.2	A/N	Diet History Mailing List	07/18/85
053.2	A/N	Resting Electrocardiogram Mailing List	07/18/85
054.2	A/N	Autonomic Neuropathy Studies Mailing List	07/18/85
055.1	A/N	Hemoglobin Alc Mailing List	03/10/83
056.1	E	Clinic Evaluation of Volunteer's Performance on Behavioral Tasks I (Clinic)	08/03/83
057.3	E	Clinic Evaluation of Volunteer's Performance on Behavioral Tasks II (Home)	07/18/85
058.2	A/N	Lipid Specimen Mailing List	07/18/85
059.1	S	Certification of Visual Acuity Examiner	03/21/83
060.1	*E	Screening Log	04/12/83
061.1	*E	Daily Behavioral Tasks Log	08/03/83
062.1	*E	Three-Day Food Record	05/31/83
063.1	*F	Daily Diabetes Monitoring Record--Standard Treatment	07/20/83
064.1	*F	Daily Diabetes Monitoring Record--Multiple Daily Injection Users	07/20/83
065.1	*F	Daily Diabetes Monitoring Record--Pump Users	07/20/83
066.4	E/B/F	Hemoglobin Alc Reporting Log (Central Biochemistry and Back-up Laboratory use)	03/26/87
067.2	S	Request for Certification of ECG Technician	01/27/86
068.6	S	Supplies Order Form	08/01/86

Form	Code	Name	Date of Latest Version
069.2	E/B/F	Hemoglobin Alc Performance Characteristics (Central Biochemistry and Back-up Laboratory Use)	06/16/87
070.1	B/F	ANS Documentation Sheet	10/31/83
071.4	S	Observation of Proliferative or Nonproliferative Diabetic Retinopathy (Central Ophthalmologic Reading Unit use)	08/07/85
076.1	S	Request for Ophthalmic Committee Consultation	07/11/84
077.1	S	Psychosocial Adjustment to Illness Scale SR	(no date)
078.1	F	Documentation of Interim Contact with a Standard Group Patient	09/17/84
079.2	F	Neurobehavioral Assessment (Partial Battery) (Central Neurobehavioral Coding Unit use)	03/26/87
080.1	S	Next of Kin Interview	(awaiting approval)
081.1	B/F	ANS Testing Eligibility	10/19/84
082.1	S	Patient/Family Group Report	12/11/84
083.2	S	Notification of Hypoglycemic Intercurrent Event	03/26/87
084.1	S	Request for Certification of Neurobehavioral Technician	06/06/85
085.1	S	Final Notification of Death	(awaiting approval)
086.1	S	Deceased Experimental Patient's Form	(awaiting approval)
087.1	S	Procedures for Mechanical Inspection of Insulin Infusion Devices and Blood Glucose Meters	(awaiting approval)
088.2	B/F	Neurobehavioral Consensus Rating (Central Neurobehavioral Coding Unit use)	03/06/87
089.1	S	Request for Certification of Autonomic Nervous System Technician	03/07/86
090.1	S	Request for Certification of Nerve Conduction Technician	03/07/86
091.2	S	Request for Certification of Dietitian	03/26/87
092.2	S	Further Details of Hypoglycemic Event	03/26/87
093.1	S	Random Day Questionnaire	05/06/86
094.1	S	Observation of Clinically Significant Macular Edema (Central Ophthalmologic Reading Unit use)	02/24/86
095.1	S	Diet Behavior Questionnaire	03/25/86
096.1	S/A	Special Forms Mailing	07/29/86
097.1	B/F	GFR Worksheets	04/23/87
098.1	B	I-125 Iothalamate Renal Function Study (Addendum Consent Form) (Prototype)	12/02/86
099.2	F	Neurobehavioral Assessments (Partial Battery at Visit 12) (Central Neurobehavioral Coding Unit use)	03/26/87
100.1	A/N	GFR Specimen Mailing List	04/23/87
101.2	A/N	24-Hour Urine Specimen Mailing List	09/15/87

A = administrative (i.e., used to mail materials to central study units)
B = used in baseline assessment
E = used in eligibility screen
F = used in followup
N = printed on NCR paper
S = special-purpose; rarely needs to be completed; notifies Coordinating Center of special events or used in an ancillary study.
* = local use only; do not mail to Coordinating Center

Table 21.2

Forms Used by Central Units Only

CENTRAL OPHTHALMOLOGIC READING UNIT:

009	Preliminary Grading Form
033	Detailed Color Grading Form
034	Detailed Fluorescein Grading Form
071	Observation of Proliferative or Nonproliferative Diabetic Retinopathy
094	Observation of Clinically Significant Macular Edema

CENTRAL BIOCHEMISTRY LABORATORY:

023	Central Biochemistry Laboratory Results
066	Hemoglobin Alc Reporting Log
069	Hemoglobin Alc Performance Characteristics

CENTRAL ELECTROCARDIOGRAM READING UNIT

024	Resting Electrocardiogram Grading Form

CENTRAL AUTONOMIC CODING UNIT:

028	Autonomic Neuropathy Studies

CENTRAL NEUROBEHAVIORAL CODING UNIT:

010	Neurobehavioral Assessment (Complete Battery)
079	Neurobehavioral Assessment (Partial Battery)
088	Neurobehavioral Consensus Rating
099	Neurobehavioral Assessment (Partial Battery at Visit 12)

Table 21.3

Use of DCCT Mailing Lists

040.2	Clinic Forms Inventory
041.3	Forms Mailing List
042.2	Fundus Photograph Mailing List
043.3	C-Peptide Specimen Mailing List
044.2	Renal Studies Specimen Mailing List
050.2	Blood Glucose Profile Specimen Mailing List
051.3	Neurobehavioral Assessment Mailing List
052.2	Diet History Mailing List
053.2	Resting Electrocardiogram Mailing List
054.2	Autonomic Neuropathy Studies Mailing List
055.1	Hemoglobin Alc Mailing List
058.2	Lipid Specimen Mailing List
096.1	Special Forms Mailing
100.1	GFR Mailing List
101.1	24-Hour Urine Mailing List

Table 21.4

Forms Used to Request Certification
of a Clinic Staff Member

059	Certification of Visual Acuity Examiner
067	Request for Certification of ECG Technician
084	Request for Certification of Neurobehavioral Technician
089	Request for Certification of Autonomic Nervous System Technician
090	Request for Certification of Nerve Conduction Technician
091	Request for Certification of Dietitian

Table 21.5

Special-Purpose Forms

014	Notification of Missed Clinic Visit
015	Notification of Death
016	Request for Transfer to Inactive Status
020	Notification of Intercurrent Event
022	Notification of Deviation from Assigned Treatment
039	Notification of Patient Transfer
068	Supplies Order Form
076	Request for Ophthalmic Committee Consultation
080	Next of Kin Interview
083	Notification of Hypoglycemic Intercurrent Event
085	Final Notification of Death
086	Deceased Experimental Patient's Form
087	Procedures for Mechanical Inspection of Insulin Infusion Devices and Blood Glucose Meters
092	Further Details of Hypoglycemic Event

Table 21.6

Forms for Local Clinic Use Only

012	Personal Information on Study Volunteer
029	Food Pattern Questionnaire
030	Food Preparation Questionnaire
061	Daily Behavioral Tasks Log
062	Three-Day Food Record
063	Daily Diabetes Monitoring Record--Standard Treatment
064	Daily Diabetes Monitoring Record--Multiple Daily Injections Users
065	Daily Diabetes Monitoring Record--Pump User

Table 21.7

Forms Used to Document the Voluneer's Eligibility, Consent and Baseline Status

COMPLETED BY THE INTERNIST/PEDIATRICIAN OR NURSE:

001 Initial Clinic Visit
002 Baseline Medical History and Physical Examination
004 Locally-Performed Blood Count and Chemistry*
006 Locally-Performed Urinalysis and Urine Culture*

COMPLETED BY OPHTHALMOLOGIST OR PHOTOGRAPHER:

008 Baseline Ophthalmic Examination and Ocular History
025 Fundus Photography*
026 Fluorescein Angiography*

COMPLETED BY NEUROLOGIST OR NERVE CONDUCTION TECHNICIAN:

005 Neurologic History and Physical Examination*
027 Nerve Conduction Studies*

COMPLETED BY THE PSYCHOLOGIST OR PSYCHOLOGIC TECHNICIAN:

013 Neurobehavioral Studies Demographic Questionnaire*

COMPLETED BY THE AUTONOMIC NEUROPATHY TECHNICIAN:

070 ANS Documentation Sheet*
081 ANS Testing Eligibility*

COMPLETED BY THE DIETITIAN:

018 Diet History*

FORMS RELATED TO THE PATIENT'S MENTAL HEALTH AND PERCEIVED QUALITY OF LIFE:

035 Symptom Checklist-90-R*
036 Quality of Life Questionnaire*

FORMS EVALUATING THE PATIENT'S ABILITY AND WILLINGNESS TO FOLLOW STUDY REGIMENS:

047 Availability, Adherence and Expectation Interview
048 Family Understanding and Expectation Interview
049 Request Behaviors Confidence Questionnaire
056 Clinic Evaluation of Volunteer's Performance on Behavioral Tasks I (Clinic)
057 Clinic Evaluation of Volunteer's Performance on Behavioral Tasks II (Home)

Table 21.7 (Continued)

FORMS DOCUMENTING THE PATIENT'S INFORMED CONSENT:

031	Informed Consent #1
032	Informed Consent #2
038	Eligibility and Exclusion Checklist
045	Volunteer Understanding Questionnaire (Version A)
046	Volunteer Understanding Questionnaire (Version B)

FORMS DOCUMENTING THE COMPLETING OF ALL BASELINE PROCEDURES AND ENROLLMENT OF THE VOLUNTEER:

011	Randomization Report
021	Quarterly Visit*

*This form is also completed during followup.

Table 21.8

Forms Used by Clinic During Patient Followup

COMPLETED PRE-RANDOMIZATION AND QUARTERLY, BUT NOT AT ANNUAL VISIT:

021 Quarterly Clinic Visit

COMPLETED ANNUALLY:

003 Annual Medical History and Physical Examination
027 Endpoint Visit Ophthalmic Examination

Figure 21.1

DCCT -- SCHEDULE FOR RANDOMIZED PATIENTS
VISIT WINDOWS AND PARTIAL LIST OF FORMS TO BE COMPLETED

* * S A M P L E * *

Schedule Prepared on 11/16/87 at CoC

PATIENT: 99999
INITIALS: XXX
CLINIC: 99
GROUP: EXPERIMENTAL

MONTH #	VISIT #--TYPE	TARGET DATE	TIME WINDOW FOR VISIT	FORMS TO BE COMPLETED
				003 004 005 006 012 018 021 025 027 035 036 037 070
25	MONTHLY	06/28/87	06/12/87 TO 07/14/87	HbA1c Only
26	MONTHLY	07/28/87	07/12/87 TO 08/13/87	HbA1c Only
27	09--QUARTER	08/28/87	08/12/87 TO 09/13/87	—
28	MONTHLY	09/28/87	09/12/87 TO 10/14/87	HbA1c Only
29	MONTHLY	10/28/87	10/12/87 TO 11/13/87	HbA1c Only
30	10--QUARTER	11/28/87	11/12/87 TO 12/14/87	— —
31	MONTHLY	12/28/87	12/12/87 TO 01/13/88	HbA1c Only
32	MONTHLY	01/28/88	01/12/88 TO 02/13/88	HbA1c Only
33	11--QUARTER	02/28/88	02/12/88 TO 03/15/88	—
34	MONTHLY	03/28/88	03/12/88 TO 04/13/88	HbA1c Only
35	MONTHLY	04/28/88	04/12/88 TO 05/14/88	HbA1c Only
36	12-3/ANNUAL	05/28/88	05/07/88 TO 06/18/88	— — — — — — — — — —
				Also at This Annual Visit : Neurobehavior Short Battery, GFR

NOTE: Laboratory specimen schedules are provided separately.
NOTE : Use Mailing Forms Where Appropriate

Figure 21.2

DCCT Mailing Schedule of Forms

WEEK #	MAILING DATE	WEEK #	MAILING DATE	WEEK #	MAILING DATE
142	01/02/86	189	11/27/86	235	10/15/87
143	01/09/86	190	12/04/86	236	10/22/87
144	01/16/86	191	12/11/86	237	10/29/87
145	01/23/86	192	12/18/86	238	11/05/87
146	01/30/86	193	12/25/86	239	11/12/87
147	02/06/86	194	01/01/87	240	11/19/87
148	02/13/86	195	01/08/87	241	11/26/87
149	02/20/86	196	01/15/87	242	12/03/87
150	02/27/86	197	01/22/87	243	12/10/87
151	03/06/86	198	01/29/87	244	12/17/87
152	03/13/86	199	02/05/87	245	12/24/87
153	03/20/86	200	02/12/87	246	12/31/87
154	03/27/86	201	02/19/87	247	01/07/88
155	04/03/86	202	02/26/87	248	01/14/88
156	04/10/86	203	03/05/87	249	01/21/88
157	04/17/86	204	03/12/87	250	01/28/88
158	04/24/86	205	03/19/87	251	02/04/88
159	05/01/86	206	03/26/87	252	02/11/88
160	05/08/86	207	04/02/87	253	02/18/88
161	05/15/86	208	04/09/87	254	02/25/88
162	05/22/86	209	04/16/87	255	03/03/88
163	05/29/86	210	04/23/87	256	03/10/88
164	06/05/86	211	04/30/87	257	03/17/88
165	06/12/86	212	05/07/87	258	03/24/88
166	06/19/86	213	05/14/87	259	03/31/88
167	06/26/86	214	05/21/87	260	04/07/88
168	07/03/86	215	05/28/87	261	04/14/88
169	07/10/86	216	06/04/87	262	04/21/88
170	07/17/86	217	06/11/87	263	04/28/88
171	07/24/86	218	06/18/87	264	05/05/88
172	07/31/86	219	06/25/87	265	05/12/88
173	08/07/86	220	07/02/87	266	05/19/88
174	08/14/86	221	07/09/87	267	05/26/88
175	08/21/86	222	07/16/87	268	06/02/88
176	08/28/86	223	07/23/87	269	06/09/88
177	09/04/86	224	07/30/87	270	06/16/88
178	09/11/86	225	08/06/87	271	06/23/88
179	09/18/86	226	08/13/87	272	06/30/88
180	09/25/86	227	08/20/87	273	07/07/88
181	10/02/86	228	08/27/87	274	07/14/88
182	10/09/86	229	09/03/87	275	07/21/88
183	10/16/86	230	09/10/87	276	07/28/88
184	10/23/86	231	09/17/87	277	08/04/88
185	10/30/86	232	09/24/87	278	08/11/88
186	11/06/86	233	10/01/87	279	08/18/88
187	11/13/86	234	10/08/87	280	08/25/88
188	11/20/86				

Figure 21.3

Example of an Error Notice Printing from the DCCT

DCCT CLINIC NUMBER= 33 CERTIFICATION NO.=33-21 PATIENT ID= 33033

FORM= 001.5 WEEK NO= 171 FORM DATE= 07/09/86 INITIALS= ABC

ITEM	VARIABLE	OLD VALUE	NEW VALUE
C.4.B	OADXTIME=	0	_____
YEARS WITH DX OF IDDM			GENERATES THE FOLLOWING MESSAGES(S)
C.4.E	OADX1YR =	.	_____
DIAGNOSED LESS THAN 1 YR AGO			MISSING
C.6.B	OAPREGN2=	4	_____
PLANS PREGNANCY			OUT OF RANGE
C.4.C	OABGNINS=	1376	_____
MONTH/YEAR BEGAN USING INSULIN			INVALID MONTH ON INSULIN DATE

CHAPTER 22

SUPPLIES AND INVENTORY

Many medical supplies and patient care products used in this trial are either fully donated by manufacturers or are available for bulk purchase by the DCCT. Patient-care products and other DCCT supplies should be channeled through the Coordinating Center. The Coordinating Center functions as liasion between clinical centers, central units, and vendors.

The Coordinating Center provides continual monitoring of study materials to ensure initial distribution and subsequent replenishment of supplies to each study component. A computerized inventory is maintained of study documents, manuals, forms, recruitment and adherence aids, labels, directories, and medical or patient-care supplies donated or discounted for trial use. Privately-owned equipment is also inventoried at the Coordinating Center, at vendor request.

The Coordinating Center acts as the ordering agent for patient-care products and equipment supplied directly by vendors as well as for study administrative and adherence materials supplied by the Coordinating Center should be made on DCCT Form 068, Supplies Order Form. Products listed DCCT Form 068 have been donated by various manufacturers. Because there may be a limitation on the quantity of specific items donated, brand names may change during the course of the trial. Efforts will be made to ensure consistent quality of items. The Supplies Order Form will be updated periodically to reflect newly donated items or items no longer donated to the study. Clinics will be notified of such changes, and will be asked to use the newest version of the form. Examples of items not donated will be found on Table 22.1. These items may be purchased by the clinics.

When placing an order, anticipate future needs and order enough to cover a 3-month period. Orders should be places six weeks in advance of need, but certainly no later than the time the stock quantity is half used. From the date of your order, allow a 6-week interval for the goods to arrive. This interval allows for possible manufacturer's back orders and transit time, although Canadian clinics might have a greater delay because of Customs. Even though the Coordinating Center maintains a stock of supplies and can usually fill, package and ship material to the clinics within a week of receiving an order, that 6-week interval allow and should be maintained.

While most supplies are shipped to the Coordinating Center in bulk, warehoused temporarily, repackaged and shipped to the clinics by the Coordinating Center, a few donated items continue to be shipped by the

vendors directly to the clinics. Some supplies are purchased at a discounted price (not donated) and shipped by the vendor directly to the clinics. Bills covering these discounted items accompany these shipments and must be paid by the clinics.

Packing slips are provided with each shipment from the Coordinating Center. Packing slips should also accompany shipments from vendors, but if one is not available, make a note on a slip of paper of what arrived and when it arrived. Packing slips are a very important part of the supplies monitoring system and must be returned to the Coordinating Center as soon as possible after receipt of goods.

Discrepancies between packing slips and actual goods received should be reported to the Coordinating Center immediately. Damaged goods should also be reported to the Coordinating Center with serial numbers or lot numbers for identification.

Insulin is ordered through the Coordinating Center. Insulin from Eli Lilly is stored at the Coordinating Center in bulk under refrigeration and is dispersed by the Coordinating Center. The other insulin vendors ship directly to the clinics from their warehouses via instructions from the Coordination Center. Watch expiration dates to avoid wasting insulin.

Equipment items in need of repair should be reported to the Coordinating Center. In addition, clinics should contact the vendor's service representative using the 800 number. Service personnel at that time will authorize return of the instrument and instruct the clinic as necessary in that return. If a new instrument is issued in lieu of repair, the new serial number (as well as the old one) must be reported to the Coordinating Center for inventory purposes.

Coordinators should retain copies of their supply orders and compare incoming supplies with them to ensure proper stock quantities. After the requisite 6-week wait, report discrepancies and/or unfilled back orders to the Coordinating Center.

Serial number of all instruments, whether DCCT furnished or privately owned and DCCT used, should be on file at the Coordinating Center. Reporting lost, stolen, broken or replaced instrument numbers is vital to the system.

Return any disposable supply, equipment or insulin you know will not be used at your clinic. Someone will need it.

Table 22.1

Examples of items that are not donated for trial use and that must be ordered to perform eligibility/baseline testing. (This list is not exhaustive and may be shortened if donations occur later.)

Renal function test:	24-hour urine jugs Timers
Urine testing:	Routine urine containers Urine culture kits
Local bloods:	Purple top tubes (CBC, diff., retic.,hematocrit, sickle cell, HGB electrophoresis could use Hgb Alc tubes) Tiger top tubes (T4, TSH, preg) Red top tubes (SMAC--could use C-peptide tubes) Test tube racks
All blood tests:	Band-aids Cotton balls Iodine prep Pipettes Pipette bulbs
C-peptides:	Sustacal
EKG testing:	Lead gel EKG paper
Eye exams:	Plastic sleeves for eye photos (4 per patient) Film
ANS testing:	Grey top tubes (FBS prior to exam) EKG leads 90-minute tapes
Other:	Thermometer for freezer and refrigerator

CHAPTER 23

CERTIFICATION PROCEDURES

23.1 INTRODUCTION

In multicenter clinical trials, it is essential that procedures be standardized within each center and among the participating clinical centers to assure that findings from all centers are comparable and, therefore, can be pooled. Training sessions are one way to ensure standardization of procedures. At the initiation of Phase II, the entire study group attended an orientation session. As new clinics were acquired in Phase III, another orientation session was held. Individuals performing the procedures for acquiring the multiple outcome measurements need to be trained, tested and certified as competent. Periodic retraining and certification are useful in long-term studies because people forget and there is personnel turnover. In the following sections, the steps necessary for certification of a clinic and new personnel are given.

For purposes of certification, forms should be clearly marked "FOR CERTIFICATION" in red, and patients should be identified by initials and patient I.D. number XX000 (XX = clinic number).

23.2 INITIAL CERTIFICATION OF A DCCT CLINICAL CENTER

The DCCT certification process has two levels. Level 1 is the certification of staff and procedures necessary to begin recruiting patients. Level 2 includes the certification of staff and procedures necessary to perform baseline studies prior to randomizing and treating patients. Fulfillment of the criteria established for certification is documented by the Coordinating Center (see Figures 23.1 23.2, Level 1 and Level 2 Certifications).

23.2.1 Level 1 Certification Requirements

The Level 1 certification requirements include:

1. Directory:

   Sending names, mailing addresses and direct phone numbers of DCCT staff members to the Coordinating Center.

2. Forms Completion:

Pretesting DCCT Forms 001, 002, 040 and 041 on two IDDM patients who are not eligible for the DCCT. DCCT Forms 040 and 041 should be marked in red ink "FOR CERTIFICATION" at the top of the form and mailed to the Coordinating Center forms mailing address.

3. Certification of the Fundus Photographer:

Certification of ophthalmic photographers by the Central Ophthalmic Reading Unit (CORU) requires:

a) Sending photographs to the CORU of two patients (four eyes) taken and mounted as described in Chapter 13 of the Manual of Operations.

b) Sending two fluorescein angiograms to the CORU taken as described in Chapter 13 of the Manual of Operations.

The photography protocol is quite demanding and can be a time consuming process; therefore, it should be started as soon as possible. Contact the CORU if you have any questions regarding the protocol before you begin.

4. Certification of the Visual Acuity Examiner:

No training or special material or funding was available for non-ophthalmologists to be certified as visual acuity examiners. If, however, an ophthalmologist wished a non-ophthalmologist to be certified, he/she is responsible for the training of that individual and for the examinations done by that person. The certification process for visual acuity is as follows:

a) The visual acuity examiner who wishes to be certified should complete the refraction and acuity sections of DCCT Form 008 the Baseline Ophthalmic Examination and Ocular History Form, on two non-DCCT patients, after careful review of the Manual of Operations. These should be sent to the Coordinating Center with a DCCT Form 059, Certification of Visual Acuity Examiner.

b) Dr. Kassoff, or his designated certification examiner, will contact the applicant to review the Manual of Operations procedures and report certification status to the Coordinating Center. The Coordinating Center will then notify the clinical center of certification.

5. Informed Consent Forms:

Copies of local informed consent forms corresponding to the prototype Informed Consent #1 and Informed Consent #2 must be mailed to the Coordinating Center.

6. Shipping Frozen Specimens to the CBL:

Specimens from non-DCCT patients shipped to the Central Biochemistry Laboratory (CBL) at the University of Minnesota (see Chapter 15). Each clinic should attempt to ship by Federal Express, or your preferred overnight carrier, ONE INSULATED SHIPPING CONTAINER, a styrofoam container large enough to contain two and a half to three pounds of dry ice, with five 5 ml tubes of frozen serum. This process is to identify those clinics which may have difficulty shipping specimens to the CBL. Each clinic needs to ship only one such container unless directed to ship another by the CBL or the Coordinating Center. The Coordinating Center will notify those clinics which have fulfilled this certification requirement.

7. Shipping HbA_{1c} Specimens to the CBL:

HbAlc specimens (fresh whole blood) from non-DCCT patients shipped to the CBL. Each clinic should ship by Federal Express overnight delivery, an appropriate container with the thermos holding five 5 ml Nunc Tubes or equivalent tubes containing 3.5 ml whole blood obtained in EDTA. Enclose a shipping label for return by mail to your clinical center. On your clinic letterhead, indicate the time and date shipping container was sealed. Also include the name and phone number of the Principal Investigator, and name and phone number of the person performing the shipment. This process will allow the laboratory to evaluate the adequacy of the shipping procedures. The Coordinating Center will notify those clinics that have fulfilled this certification requirement.

8. Certification of the ECG Technician:

Technicians charged with responsibility for ECG recording in the DCCT clinics must submit three 12 standard lead electrocardiograms and a Request for Certification of ECG Technician form, DCCT Form 067 to the Coordinating Center. Technicians on staff of the cardiology laboratory and internists, however, need submit only one 12 standard lead ECG and DCCT Form 067. The ECG's will be sent to the Central ECG Reading Unit (CERU) for review. All recommendations regarding certification will be returned to the Coordinating Center and forwarded to the clinic.

23.2.2 Level 2 Certification Requirements

The next stage in certification involves training and certifying personnel to perform baseline studies which are required by the DCCT Protocol. The requirements for Level 2 certification consist of the training of staff to perform the following baseline studies: neurobehavioral, neurological (ANS testing and nerve conduction studies), and diet histories.

1. Certification of the Neurobehavioralist:

Certification of the neurobehavioralist will require training by either a currently certified neurobehavioralist or the Central Neurobehavioral Coding Unit (CNBCU). Usually, a practice protocol will be completed by the neurobehavioralist and reviewed by Dr. Ryan for his comments before a second protocol is completed. Call Dr. Ryan's office to either review procedures with him before completing a practice protocol or to set up a training session with CNBCU personnel. Also, use DCCT Form 084 to request certification. This form and practice protocol should be sent directly to Dr. Ryan's office and a copy of the DCCT Form 084 (only) to the Coordinating Center. Dr. Ryan will forward a copy of DCCT Form 084 to the Coordinating Center and the clinic will be notified when certification is complete.

2. Certification for Neurological Tests:

a) Nerve Conduction -- DCCT Form 037, Nerve Conduction Studies, and EMG tracings on two subjects are sent to Dr. Kamp-Nielsen at the University of Pittsburgh with DCCT Form 090, Request for Certification of Nerve Conduction Technician. Send a copy of the DCCT Form 090 to the Coordinating Center. Procedures in Chapter 17 of the Manual of Operations should be followed.

b) ANS -- Persons becoming certified for autonomic nervous system testing must be trained either by a certified ANS tester or a staff member of the Central Autonomic Coding Unit (CACU). Costs for travel associated with training are the responsibility of the clinic.

Procedures for Certification: Produce two ANS practice tapes and send them to the CACU with DCCT Form 089, Request for Certification of Autonomic Nervous System Technician. Send a copy of DCCT Form 089 to the Coordinating Center. The tapes need not be on fasting or on diabetic patients. The CACU will notify the Coordinating Center of certification status and the Coordinating Center will forward the information to the clinic.

3. Certification of the Dietitian:

Following the training session and review of the CNBCU codebook, three diet histories should be performed on non-DCCT IDDM patients. These are to be submitted to the NCC for grading using DCCT Form 091, Request for Certification of Dietitian. CNBCU recommendations regarding certification will be forwarded to the Coordinating Center.

A dietitian may be trained to perform the dietary assessment in one of two ways:

a) In his/her own clinic by a DCCT certified dietitian using a training packet provided by the Central Nutrition Coding Unit

(CNBCU). All individuals who serve as back-up to the dietitian must be trained on site by the certified dietitian.

b) At the CNBCU in Minnesota (1-2 day session). The cost of training sessions at the CNBCU must be borne by the clinic.

23.3 CERTIFICATION OF NEW PERSONNEL AT A CERTIFIED CLINICAL CENTER

The DCCT is designed to last through the 1980's and into the 1990's. It is a certainty that new personnel will assume key positions in each and every clinic. Ideally, the training of new personnel should be performed by the individual who is being replaced. If the local training is not possible because of non-overlapping of staff, there are contingency plans for training at the central units, but the costs associated with such training will be from clinical center budgets and not the Coordinating Center's budget. Any costs associated with review for certification, such as for the dietitians, will be paid by the Coordinating Center, however.

The new personnel should follow the appropriate procedures for certification described in the previous sections.

23.4 CERTIFICATION NUMBERS

The Coordinating Center issues unique numbers to each of the clinical center staff. These numbers are a mean of keeping track of turnover in clinic staff. We will wish to describe the stability of the clinics at the conclusion of the study. In the interim, on a random basis, the Coordinating Center will cross-check the issued number with the name of the person completing the form. This process will provide some assurance that the proper individuals are collecting the appropriate data.

Figure 23.1

Level 1 Certification Requirements

DCCT CLINICAL CENTERS	1	2	3	4	5	6	7	8	CERTIFICATION DATE

LEGEND:

1 = Sending staff names, etc. to CoC for the directory
2 = Pretesting forms
3 = Provisional certification of photographers
4 = Certification of visual acuity technician
5 = Copies of local versions of Informed Consent Forms #1 and #2 sent to CoC
6 = Frozen specimens shipped to CBL
7 = HbAlc specimens shipped to CBL
8 = Certification of ECG technician

Figure 23.2

Level 2 Certification Requirements

DCCT CLINICAL CENTERS	1	2	3	4	CERTIFICATION DATE

LEGEND:

1 = Certification of neurobehavioralist
2 = Certification of nurse/clinician to perform ANS testing
3 = Certification of nerve conduction technician
4 = Certification of dietitian to complete diet history forms

Chapter 24

POLICY AND GUIDELINES FOR PATIENT TRANSFERS

24.1 INTRODUCTION

The ultimate goal of the policies and guidelines that follow is to keep patients participating in the study. The prime considerations in transferring medical management of the patient are the safety and welfare of the patient. These guidelines are intended to establish uniform policies throughout the study group and to encourage open communications and a sense of teamwork among the clinics.

These policies and guidelines pertain to: (1) permanent and temporary relocations of DCCT patients to the geographic locale of another DCCT center, (2) permanent and temporary relocations of DCCT patients to a geographic area not served by a DCCT center, and (3) establishment and utilization of a centrally maintained resource directory to provide information that may be useful in identifying non-DCCT resources to assist in management and follow up of DCCT patients when they cannot be seen in a DCCT center.

24.2 INTRODUCTION

Patients who change residence during a long term, multicenter clinical trial pose numerous potential problems. These include loss of the patient to the study, decreased adherence to the protocol, increased costs and increased workload for the DCCT treatment team in maintaining contact with the volunteer and sustaining his/her interest in participating in the DCCT.

Each time a DCCT patient moves from a clinic, a whole set of individual circumstances is set into motion. Each situation is unique and needs to be considered in a most sensitive manner. Taking the time to fully inform the patient of information pertinent to the situation will promote the patient's willingness to remain in the study.

Patient relocations may be either permanent or temporary. A PERMANENT move is defined as a relocation with the intention of establishing a permanent change of residence. A TEMPORARY move is defined as a change of address without the intention of establishing a permanent residence, e.g., someone who is assigned to work temporarily in a new area.

The Clinic Monitoring Group will routinely review transfer activities and report to the Eligibility/Adherence Committee at their regular meetings. In addition, the Clinic Monitoring Group will act as arbitrator in any disagreements pertaining to transfers between clinics.

24.3 PATIENT MOVES THAT ARE NEAR ANOTHER DCCT CENTER

"Near" is operationally defined by each clinic. It is considered to be the clinic's area of reference that is close enough for a patient to travel to the clinic without requiring undue time, trouble an hardship, or significant expense.

Relocations should not be viewed as an opportunity to pass off a problem patient to another clinic or to avoid the hassle of managing a patient long distance.

24.3.1 Permanent Move

A patient who makes a permanent move to a locale near another DCCT center should be officially transferred to the new center. It is s recommended to immediately transfer such patients to the closer DCCT center. Experience has shown the "cold turkey" approach to be successful.

If the transfer occurs before randomization, credit for recruitment of DCCT volunteers will be given to the clinic who first shows the slide presentation. Credit for randomization will be given to the clinic who actually randomizes the subject. It is expected that over the course of the trial most clinics will both receive and transfer research volunteers within the established centers. The five-digit subject identification number assigned when volunteers are entered into the screening process (Initial Clinic Visit, DCCT Form 001) will remain with the patient for the duration of the study.

The procedures outlined below should be followed:

1. Transferring Clinic

   a. Transfer of a DCCT patient should be initiated by the current DCCT treatment team with the consent of the patient. The patient should be provided with information about the transfer clinic including names, addresses, phone numbers of key team members. The potential for differences in treatment styles and DCCT clinic modes of operation should be discussed with the patient.

   b. The receiving clinic should be contacted at the earliest possible opportunity to inform them of the need to transfer a subject to their clinic and in sufficient time to allow

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new locale. The principal investigator, or another physician who may be more familiar with the patient, should call the receiving P.I. as soon as possible to discuss the transfer. The clinic coordinator should contact the new clinic coordinator to discuss the transfer.

c. A summary of the patient's DCCT history is to be written by the DCCT physician who has had primary responsibility for the patient and be sent to the receiving clinic along with all pertinent medical records, accession numbers, DCCT files (including nutrition summary) as soon as possible.

d. Form 39 is to be filed with the Coordinating Center in advance of the move.

2. Receiving Clinic

a. A DCCT clinic is expected to accept all transfer patients from other DCCT clinics. The receiving clinic should expect to be contacted by staff of the transferring clinic in sufficient time to allow opportunity for questions of the transferring DCCT team and for planning prior to the patient's arrival in the new locale.

b. As soon as possible a welcome letter should be sent to the transferring patient explaining clinic hours and method of operation, including information about the staff who will be assigned to the patient.

c. If the patient is doing well on the present regimen, caution should be exercised in making changes until the patient becomes familiar with the new clinic and new treatment team. Abrupt changes in regimen can be disruptive to the transition and can be made gradually after a new relationship has been established.

d. If difficulties arise, the transferring clinic should be contacted for consultation and advice.

3. Former Clinic's Role

a. Relinquish the position of management team and defer to the new clinic if the patient contacts you for purposes of treatment advice. Recognize and accept that management and operational styles are likely to differ between clinics and that confusion will result if patients are given conflicting advice by two clinics. Criticism (either implied or specific) of the new clinic or its methods only serves to undermine the patient's confidence in the study.

b. Maintaining social contact through greeting cards, local newsletters, etc., is recommended and can serve to reassure the patient that he has not been abandoned.

c. If the patient communicates concerns regarding the new clinic, tactfully transmit this information to the receiving clinic and assist, as possible, in helping the patient and the new clinic in resolving the issues.

24.2.2 Temporary Move

A relocation that is not permanent does not require official transfer of the patient; rather the "home" clinic is requesting the temporary assistance of another clinic in the follow-up of a DCCT patient.

1. Home Clinic Responsibilities

a. As soon as the intention to temporarily relocate is made known to the clinic by the patient, the principal investigator and the trial coordinator of the geographically closest DCCT clinic should be contacted, individually, to discuss the need for their assistance.

b. After arrangements to receive the patient have been made with the assisting clinic, a plan for follow-up should be discussed first with the new clinic and then with the patient. Open communications between the patient and both centers should be fostered.

c. Well in advance of the patient's first visit to the assisting clinic, a written summary of the patient's pertinent medical history and current regimen should be prepared by the patient's primary DCCT physician and the trial coordinator and be sent to the assisting clinic along with necessary mailing labels and other study-required materials.

d. Reimbursement for travel expenses to the assisting clinic is the responsibility of the home clinic.

e. Form 39 is to be filed with the Coordinating Center in advance of the move.

2. Assisting Clinic's Role

a. It is expected that each clinic will provide all assistance required to maintain follow-up of DCCT subjects who will temporarily reside near another DCCT clinic. An expanded team approach involving both clinics is advantageous in making treatment decisions.

b. The assisting clinic will assume temporary responsibility for management of the patient, obtaining and shipping blood samples, and performing follow-up exams as needed and as mutually arranged between clinics. Clinics do not reimburse one another for performance of procedures.

c. Feedback to the home clinic should be provided after each patient visit and whenever concerns arise.

24.3 PATIENT MOVES TO NON-DCCT AREAS

While any patient move can be disruptive to maintaining DCCT participation, additional difficulties arise when logistic and financial aspects of a patient relocation make it impractical to transfer a subject to another DCCT clinic for direct management and follow-up. Furthermore, procedures to be utilized in handling moves to non-DCCT areas may not always be clear cut and, while immediate transfer of the patient to the closest DCCT clinic might appear to be the simplest approach, this may not always be advisable. Long distance treatment management is still long distance whether it be 300 miles or 3000 miles from a DCCT clinic. Overall, the needs of both the patient and the study may be better served by extending the arm of the home treatment team to include a local physician and by utilizing other non-DCCT resources for periodic outcome assessments.

In these situations, responsibility for patient management remains with the home clinic. The home clinic must make every attempt to help the patient locate a physician who will not only provide appropriate medical care, but who can also be enlisted to work with the DCCT clinic to maintain the patient on his/her assigned treatment regimen. A gradual transition from the home clinic to the local physician may be indicated and may require development of ad hoc solutions appropriate for the particular situation.

The home clinic must set up procedures for maintaining contact with the patient and for obtaining at least minimal endpoint ascertainment. For example, arrangements might be made for monthly blood draws to be obtained locally for experimental patients which are shipped by the lab or the patient to the DCCT CBL. Arrangements might be made to send profilsets directly to the patient and for the patient to return them to the clinic or CBL via overnight carrier. These arrangements, along with weekly phone calls from the home clinic, are sometimes adequate in conjunction with quarterly visits with a local physician and periodic follow-up visits at a DCCT clinic.

While long-distance management is less than ideal, it is possible with routine phone contact, close cooperation

between the DCCT clinic and the non-DCCT health care providers, and proper motivation and attitude on the part of the patient.

All patient moves to non-DCCT areas, whether permanent or temporary, must be reported to the Coordinating Center on Form 39. In addition, Form 105 (Resource Registry) should be completed and submitted to the Coordinating Center for entry in the DCCT Resource Registry in order to provide information for use by other clinics needing to locate resources to assist in management of DCCT subjects (see Section III).

A patient who makes a permanent move to a non-DCCT area and who has not been officially transferred to another DCCT clinic remains in the home clinic's census of patients as long as he/she remains active in the study by continuing to in any DCCT follow-up assessments such as yearly eye photos. Costs associated with management of patients utilizing non-DCCT facilities or with assistance in follow-up provided by another DCCT clinic are the responsibility of the home clinic. Patients attending a new institution must sign the institution's release of information form. This form should be copied and sent to the Coordinating Center as well as kept on file at the home clinic.

24.3.1 Permanent Move

The procedures outlined below should be followed.

1. Finding a Local Physician

a. With the patient's permission, the home clinic should assist the patient in finding a local physician. (See 24.4. Resource Registry" for suggestions regarding how to find a local physician or certified photographer). In particular, physicians with interests in clinical research or associated with an NIH General Clinical Research Center (GCRC) should be sought.

b. The Principal Investigator (or patient's primary physician) should phone the local practitioner to request assistance in carrying out the DCCT treatment plan. The DCCT, its objectives, and needs should be carefully explained and written information should be provided including relevant parts of the Protocol and Manual of Operations. A plan for co-management of the patient should be worked out.

c. The DCCT resources that can be made available to the physician for his management of the patient should be explained with frank discussion of the costs that will have

to be borne by the patient and those that can be borne by the study (see below). Since the physician is being asked to participate in a research study, the possibility of seeing the patient at reduced or no charge should be explored. The DCCT resources that can be made available are consultation, endpoint ascertainment, HbA1c determinations and supplies such as insulin, syringes, etc. Once again, an expanded team approach involving the local clinic and the DCCT home clinic is advantageous.

d. Local physicians who agree to participate with the DCCT clinic should be told that their role will be acknowledged in all major study publications in which they will be listed by name as a "Collaborating Physician."

e. After agreement is obtained from a local physician, the DCCT home clinic must compile information from the patient's medical and study records (as described above for a permanent move to a DCCT clinic) and send it to the local treatment team. (See current MOO Chapter 24).

f. The Trial Coordinator needs to contact appropriate nursing, laboratory, and dietician staff in the local clinic to set up procedures for shipment of samples to DCCT central units and to explain the patient's regimen (including the DCCT Protocol) to local support staff. Written information should be provided, including relevant parts of the Manual of Operations, Protocol, and Trial Coordinator's Handbook.

g. Set up a system for contacting patient at required intervals. It is recommended to maintain social contact also by sending clinic newsletters, greeting cards, etc.

h. File Form 39 and Form 105 (Resource Registry) with the Coordinating Center.

2. Locating Other Non-DCCT Resources

a. In addition to issues related to medical management, it may be possible to arrange for endpoint assessments such as fundus photos to be performed in non-DCCT centers having photographers who have been certified by the DCCT CORU for other studies. A list of these resources is maintained in the DCCT Resource Directory (see below).

b. File Form 105 (Resource Registry) anytime non-DCCT resources are identified for use by a DCCT patient.

3. Quarterly and Annual Visits

a. As a general rule, patients from both treatment groups should be seen at least yearly at a DCCT clinic and, if feasible, it is highly desirable that fundus photos be obtained every six months. If the DCCT will be providing travel expenses, it is preferable that the DCCT clinic that can be accessed in the most cost-efficient manner be utilized for yearly visits regardless of whether or not it is the patient's home clinic.

b. DCCT quarterly exams (Form 21) without eye photos can be completed by a non-DCCT physician if there has been proper training in advance by the home clinic.

c. Eye photos may be performed in non-DCCT locations that have CORU-certified photographers and which are convenient for the patient to access. A list of such facilities will be maintained in the DCCT Resource Directory and arrangements will have to be made with the facility on a case-by-case basis.

d. While responsibility for patient management remains with the home clinic, endpoint assessments may need to be performed by a different DCCT center. The home clinic coordinator needs to consult with the assisting clinic to discuss this and develop follow-up plans, to open the lines of communication, and to foster a spirit of cooperation as described previously for assisting with temporary moves to another DCCT area.

e. A transfer to the assisting clinic may occur if the patient requests such or agrees to such a transfer at the request of the DCCT.

f. The assisting clinic is expected to provide care and to accept subsequent transfer of any DCCT patient.

g. A transfer should be considered if a patient has missed visits due to distance traveled and can more easily get to another DCCT center.

h. Until such official transfer occurs, the financial and treatment/follow-up responsibilities lie with the home clinic.

4. Responsibility for Medical Care Costs at Non-DCCT Facilities

a. It must be made clear to patients and providers that the DCCT cannot promise to pay the costs of follow-up care by non-DCCT personnel on a long-term basis once they move away from an area that can be served by a DCCT clinic. The patient should understand that he/she may be responsible for costs of office visits and laboratory

procedures required for diabetes care at non-DCCT facilities. While efforts should be made to locate physicians who will see DCCT patients at minimal or no charge, this cannot be guaranteed. Obtaining courtesy care from local practitioners has been possible in some cases; others have found that courtesy care can sometimes lack the commitment needed to enhance patient adherence.

b. Nominal reimbursement to practitioners for quarterly visits performed for the DCCT (i.e., completion of Form 21) and/or for collection of specimens or performance of procedures specifically needed for the DCCT (such as HbA1c or fundus photos) may be appropriate and should be considered if deemed essential to securing the cooperation of the non-DCCT practitioners.

5. Reimbursement for Patient Travel

a. If necessary to maintain continued participation in the trial and if costs are within reason, funds for expenses associated with once yearly transportation to a DCCT clinic for outcome assessment may be provided. When the costs of transportation of a given patient to any DCCT clinic are great, costs may be shared with the patient depending on his/her personal resources.

b. If the costs of travel are modest, patients may be reimbursed for travel expenses associated with obtaining fundus photos every six months.

c. Reimbursement for patient travel is the responsibility of the clinic to which the patient is officially assigned. The clinic's decision to offer reimbursement and the extent of that reimbursement is dependent upon individual circumstances and need. In order to minimize travel costs, patients should be encouraged to have follow-up exams completed at the clinic that can be accessed with the least cost. Alternatively, patients may elect to return to their home clinic if they pay for their own travel or are willing to pay the difference in travel costs that can be provided by the DCCT.

24.3.2 Temporary Move to a Non-DCCT Area

The procedures outlined below should be followed.

1. As described above, assist patient in finding a local practitioner who will assist the home clinic in maintaining the subject on his/her assigned treatment regimen.

24.4 DCCT RESOURCE REGISTRY

24.4.1 Purpose

A database will be maintained by the Coordinating Center consisting of information on potential resources for obtaining outside help in providing follow-up of DCCT patients who have relocated to areas not served by DCCT clinics. This registry will contain information on practitioners who may be available to provide health care for DCCT patients as well as on non-DCCT (but CORU-certified) facilities that might be utilized to obtain fundus photographs on DCCT volunteers.

The database on health care providers will be based primarily on information provided by staff of the DCCT clinics based on their knowledge of, or experience in, a geographic area. As new information is made available to the Coordinating Center, it will be incorporated. Information also will be provided by cataloging persons who have made known it to a member of the study group that they are interested in helping with the DCCT. In addition, the cooperation of Program Directors of NIH General Clinical Research Centers will be sought through official channels and those with the capability and expressed desire to be of assistance will be listed.

A list of certified fundus photographers will be compiled from information obtained through the DCCT CORU of photographers who have been certified by them for other eye studies. This list will be updated by the Coordinating Center periodically based on new information provided by the CORU.

24.4.2 Function

The DCCT Resource Registry can only provide information on possibilities for obtaining assistance that will need to be explored further by each clinic for each patient. All of these possibilities will require individual research by the clinic staff. The Registry is but a first step in trying to identify a local facility; it is not a list of readily available physicians or facilities who are contracted or obligated to see DCCT patients.

24.4.3 Using the Resource Registry

1. The Coordinating Center database will be accessed using the DCCT Hewlett Packard computers.

2. The Resource Registry will provide information indexed by geographic area. It should be consulted as soon as the clinic is informed of a patient's intention to relocate to an area not served by a DCCT clinic. In particular, consultation should be initiated with those clinics listed as having patients who have transferred to the same or nearby locales to obtain specific information on their experiences.

3. If there is no information on a needed area, contact the clinics located nearest the area for information and recommendations on health care providers.

4. In particular, explore the possibility of the patient being followed by a physician with access to a GCRC.

CHAPTER 25

PROCEDURES TO BE FOLLOWED IN THE EVENT OF A DEATH OF A DCCT VOLUNTEER

Given the number of volunteers enrolled, the expected duration of the DCCT, and the mortality associated with insulin-dependent diabetes mellitus, it is possible that one or more of these volunteers may die during the course of the trial. In order for the Morbidity/Mortality Classification Committee to appropriately assign a cause of death, timely and accurate information regarding the clinical course and events occurring immediately before and after each death will need to be carefully collected and documented. The information being requested is in addition to the information mandated for the various intercurrent events that are described in Chapter 10 and may become causes of death. The circumstances surrounding each death will be unique and it is impossible to anticipate all of them. What follows is a description of basic procedures that should be followed along with some suggested special procedures which may or may not be appropriate in a given case.

These procedures are directed primarily at providing information that will assist in determining causes of deaths that are unattended and/or occur outside of a hospital setting and in identifying events that may have been associated with or precipitated such death. Many of these procedures, however, would be equally appropriate for unexpected attended deaths occurring in the hospital (e.g., those due to myocardial infarction, stroke, DKA) and professional judgement will need to be exercised in deciding whether or not basic and special procedures are indicated.

25.1 GENERAL PROCEDURES

It is important that every reasonable effort be made to obtain permission to have an autopsy performed within constraints dictated by humanitarian considerations and the religious beliefs of the family. The information gained from the autopsy, as well as from blood or urine samples obtained immediately preceding death, will be invaluable in helping to specify the immediate, underlying and contributory causes of death. If possible, the autopsy should be performed at the DCCT institution.

Under certain circumstances, an autopsy is required by law. These circumstances vary from one jurisdiction to another; the responsible physician will need to determine the conditions that mandate autopsy in his or her area. If an autopsy is to be done, it should be performed as

soon after the death as possible. Prompt communication with the medical examiner or pathologist must be established. Relevant clinical information must be transmitted to the medical examiner or pathologist including the fact that the deceased was a volunteer in the DCCT; the significance of that association should be explained. There are several procedures which will be asked for, and the person performing the autopsy should be aware of these and their relevance to the volunteer's participation in the DCCT. A DCCT information sheet is available for the pathologist (Figure 25.1).

Immediately upon learning of the death of a DCCT volunteer, the Principal Investigator or other DCCT physician is to notify a member of the DCCT Executive Committee by telephone. After working hours, on weekends, and during holidays the Steering Committee Chairman should be notified at his home (615-322-2197). If he is unavailable, contact either of the other members of the Executive Committee (Patricia Cleary at 703-241-1650 or 301-867-7381 or Carolyn Siebert at 301-963-9336). DCCT Form 015, Notification of Death, is to be completed within 24 hours of the volunteer's death or discovery of death and sent to the Coordinating Center. Copies of the autopsy report, laboratory reports and death certificate are to be sent to the Coordinating Center as soon as they are available.

Family members, friends, hospital staff, or others who may have attended the death or precipitating events, as well as those who had last contact with the deceased, should be interviewed as soon as possible after the death. These interviews may take place over the phone. The information should be transmitted in written narrative form to the Coordinating Center. The interview should obtain any information on medical problems, psychosocial problems, and diabetes management in the past 24 hours, 72 hours and previous ten days. A checklist of possible problems follows:

	Problems occurred within the previous		
	<24 hours	<72 hours	<10 days
Medical			
Hypoglycemia			
Symptoms of ketosis/ketoacidosis			
Other illness or symptom			
No illness or symptom			
Psychosocial			
Clinical symptoms of depression			
Marital discord			
Job disruption			
Substance involvement			
Other			

If an autopsy is to be performed, the information gathered from these interviews should be shared with the medical examiner or pathologist with the object of making the determination of the death as accurate as possible. It is important to determine if the victim received intravenous fluids (especially glucose solutions) or glucagon injections during resuscitative measures as these can affect post-mortem body fluid glucose concentrations measured subsequently.

25.2 SPECIAL PROCEDURES

In many cases, determining the immediate, underlying, and contributory causes of death will be straightforward; in other cases, particularly in unattended, sudden, or accident-related deaths, the cause(s) may be obscure. There are several causes of death that could be related to insulin therapy for IDDM. The following is a list of causes of death which have been associated with insulin therapy and which should be in the differential diagnosis of the the medical examiner or pathologist:

1. Hypoglycemia
2. Diabetic ketoacidosis
3. Hyperosmolar coma (without acidosis)
4. Hypokalemia
5. Toxic shock syndrome
6. Bacterial endocarditis
7. Myocardial infarction
8. Accidents (automobile, drowning, falls, etc.)
9. Renal failure
10. Cerebrovascular accidents
11. Suicides

Other causes of death related to diabetes and insulin therapy may come to light and should be considered when determining the cause of death of a DCCT volunteer. These causes may require other special procedures to be performed to substantiate their presence. Professional judgement will need to be exercised to determine when such procedures are indicated.

The procedures listed below should be performed by the local pathologist or medical examiner on all patients who die while enrolled in the DCCT (-- patients who die during screening prior to randomization may undergo these procedures but it is not imperative --) on samples drawn as soon after death as possible.

1. Vitreous humor glucose
2. Vitreous humor acetone
3. Blood glucose (glucose oxidase method)
4. Blood acetone
5. Urine glucose
6. Urine acetone
7. Toxicology screen (alcohol, barbiturates, etc.)
8. Serum potassium
9. Insulin level

Cases in which the death was unattended and the body undiscovered for several days present special problems. Sample-taking has to be with the approval of the medical examiner and has to be coordinated with his needs. The effects of tissue and body fluid decomposition on sample-taking and analysis has to be taken into consideration.

In addition to the procedures performed locally, split aliquot specimens are to be sent to the DCCT Central Biochemistry Laboratory (CBL) for additional procedures. Procedures for shipping these frozen samples can be obtained from the CBL.

The best source for blood is a peripheral vein. Urine samples can be obtained with a uretheral catheter by percutaneous bladder aspiration. It is extremely important that the time of death and the time that the sample is obtained are accurately recorded. Body temperature obtained by rectal thermometer at the time the samples are obtained may be helpful for interpreting results when the exact time of death is not known.

Additional tests which may prove helpful in identifying the correct cause of death include:

1. Vitreous humor lactate
2. Cerebrospinal fluid glucose
3. Blood cultures
4. Heart valve cultures
5. Skin culture at infusion site (if suspicious of cutaneous infection)

Again, the time of death and time the samples are obtained must be accurately recorded.

Blood and urine samples obtained prior to death may also provide valuable information. If analyses were performed on blood drawn or urine collected immediately (i.e., within one hour) BEFORE the death, these values should be reported along with the time before death at which they had been drawn or collected. It is very important to ascertain whether any such samples are available for further analysis. Also, it is important to report any special procedures or medication that may influence these samples.

25.3 SPECIAL PROCEDURES FOR AUTOMATED INSULIN DELIVERY SYSTEM

25.3.1 Non-Medical Legal Case

In non-medical legal cases in which the subject was using an insulin infusion device (e.g., at or shortly before the time of death, the Principal Investigator or other appropriate DCCT personnel should promptly inspect the device paying special attention to the following points:

1. Note presence of alarms, if any.
2. Is the pump running?
3. Note the readings of all displays.
4. The insulin reservoir should be checked and the volume of insulin remaining noted.
5. The infusion line and needle should be inspected for obvious clogging.
6. The patency of the needle and infusion line should be tested with water or saline.
7. The infusion site should be inspected for signs of inflammation and infection.
8. The insulin should be saved for analysis of estimation of concentration.

25.3.2 Medical Legal Cases

The Principal Investigator must remember that the medical examiner is lawfully responsible for the evaluation of evidence such as insulin pumps, infusion lines and needles. The examination of such items by the Principal Investigator can be carried out only with the knowledge and approval of the medical examiner.

25.3.3 Disposition of the Insulin Delivery System

It is very important that an infusion device not be handled by unauthorized persons since an engineering inspection may be subsequently required. In non-medical legal cases, the Principal Investigator is to place the device in the possession of an official of the hospital for safekeeping until instructions for the disposition of the device are received from NIDDK. The NIDDK is to be notified by phone immediately of the death of any patient using an insulin pump regardless of whether a malfunction is suspected. The manufacturer, in turn, will be notified of the event by the NIDDK. In medical legal cases, the medical examiner is legally responsible for the safekeeping of evidence. Obviously, in such cases, close communication and cooperation among the Principal Investigator and other involved DCCT physicians, the medical examiner, NIDDK officials, and representatives of manufacturers are vital. Equally important, all concerned should display a high regard for the feelings of the family of the deceased.

If a malfunction in the insulin delivery system is suspected, or if warranted by other circumstances related to the death, the NIDDK will, with the approval of the medical examiner in medical legal cases, obtain the device and convene an ad hoc committee of experts to carefully examine it. This committee will comprise a representative chosen by the manufacturer, an independent expert selected by the NIDDK, a representative of the Office of Medical Devices of the Food and Drug Administration, a member of the Morbidity/Mortality Classification Committee, and others as deemed necessary or appropriate. A report of the findings will be submitted to the NIDDK. Subsequent actions will be determined on the basis of these findings.

Figure 25.1

Information for the Local Pathologist and/or Medical Examiner

The Diabetes Control and Complications Trial (DCCT) is a NIH-sponsored clinical trial involving 27 institutions throughout the United States of America and Canada and approximately 1400 highly selected volunteers with insulin-dependent diabetes mellitus (IDDM). The DCCT will test whether therapies that enable alteration of metabolic control can change the natural history of early vascular complication in persons with IDDM compared to conventional treatment approach. Study subjects have been randomly assigned to either a standard group (receiving conventional treatment) or an experimental group (receiving intensive treatment). The Trial is expected to conclude in 1993; diabetic retinopathy, carefully assessed with retinal photography performed periodically throughout the study, is the principal study endpoint.

Given the duration of the study, the large number of volunteers enrolled, and the mortality associated with IDDM, it is expected that one or more study subjects will die during the study. If such an event does occur, it will be most important to determine accurately the cause(s) of death. It may be that the immediate, underlying, and contributory causes of death will be readily determined. On the other hand, if the death is unattended, sudden or accident-related, the causes may be obscure. There are several causes of death that could be directly or indirectly related to insulin therapy and that should be in the differential diagnosis of the pathologist or medical examiner. Some of these are diabetic ketoacidosis, hypoglycemia, non-ketotic hyperosmolar coma, hypo- or hyperkalemia, accidents (automobiles, falls, drownings, etc.), and suicide.

To enhance the likelihood of arriving at definitive post mortem diagnoses, the pathology or medical examiner is urged to:

1. Consult with the DCCT attending physician regarding the clinical events prior to death;

2. Commence the autopsy as promptly as possible; and,

3. Carry out special procedures when indicated.

The latter include (1) blood glucose, acetone, lactate, pH and potassium; (2) urine glucose and acetone; (3) vitreous humor glucose, acetone and ptassium; (4) serum and urine toxicology screen for alcohol and drugs; (5) serum insulin level. Aliquots of these biological fluids should be provided to the DCCT attending physician who will, in turn, ship them to the DCCT CBL for analysis.

The investigators of the DCCT, realizing that these requests represent added work for the pathologist or medical examiner, are grateful for this extra effort. If deaths do occur during the course of the study, careful documentation as to their cause will contribute to the credibility of the study.

CHAPTER 26

DCCT OPERATIONS AND TELECOMMUNICATIONS SYSTEM

During the autumn of 1986, in response to the growing number of DCCT clinical centers, volunteers being screened and randomized, and the enormous amount of data processed at the Central Biochemistry Laboratory (CBL) and Coordinating Center, the Coordinating Center selected hardware and software to develop a system for transferring data and mail among the various study centers through a network of microcomputers. While other multicenter clinical trials have implemented systems for data entry at clinical centers and transfer of these data to a data coordinating center over telephone lines, the major DCCT need was for an electronic mail system linking the various study centers. Using this network, the Coordinating Center sends eligibility reports, HbA_{1c} results, threshold alerts, procedural memos and other correspondence to the centers. At the same time, each center can send mail to any other center on the network. The network provides speed and accuracy in disseminating important information while eliminating personnel time and other costs involved in duplicating written materials and addressing, postaging and mailing envelopes. The network also cuts down on the amount of time personnel need to spend on the telephone to report results, clarify data and request information. Finally, the system ensures that each center has received its messages by documenting the successful transmission of the electronic mail files.

In addition to these communications, the CBL uses the network to rapidly transfer analyses of biochemistry data to the Coordinating Center. The Coordinating Center developed data entry programs for use at the CBL. When specimens arrive at the CBL, staff log the information from the specimen mailing list into a microcomputer database using a data entry screen which follows the format of the particular mailing list. There is a separate database for each type of specimen (HbAlc , blood glucose profile, renal, lipid, C-peptide, GFR and 24-hour urine). After a batch of specimens has been analyzed, the records in the database are modified to add the results. This is done using a second data entry screen which follows the format of the particular laboratory results log. The completed records are then exported into a data file suitable for transmission to the Coordinating Center. At the Coordinating Center, the data files are uploaded to the mainframe computer and are added to the study database.

The DCCT telecommunications system was installed in February 1987 at the following offices:

DCCT Coordinating Center
Central Biochemistry Laboratory
Clinical Centers (including satellite)
NIDDK
Chairman of the Steering Committee

Currently, there is one hub in this system, the Coordinating Center, and all communications must pass through the hub to reach other locations. This was necessary because the Coordinating Center personnel could not possibly be available to provide assistance to other centers experimenting with the software and hardware while the system was still under development.

In addition to regular, unattended, overnight transmissions, the system can be used under special circumstances for "Special Delivery" communications during the day by appointment with the Coordinating Center.

There were several considerations involved in designing the current operating and telecommunications system. Paramount among these was to maximize the ease of learning and use of the system by clinical center staff. To this end, the following measures were taken:

1. All centers in the network were provided with identical hardware configurations -- computer, printer and modem. All computers were Hewlett-Packard Vectra microcomputers with 20 megabyte hard disks, one 120K and one 360K floppy drive, 640K RAM and internal 1200 baud modems. The printers selected were NEC P6 24-pin dot matrix printers.

2. All centers were provided with the same word processing software, Microsoft Word. MS Word is a popular and powerful word processor with excellent documentation and technical support from the manufacturer.

3. A total operating system was developed to allow a user to create, edit, rename, mail, receive and delete files without learning anything about DOS commands and directories. All instructions needed to operate the system are contained in a short manual prepared by the Coordinating Center.

4. A sophisticated telecommunications system was created. While crude transfer of a file from one computer to another over telephone lines is simple enough, for the DCCT it was desired to automate the process to minimize user effort. A user selects files to be mailed by choosing a menu option corresponding to the file number and a second option corresponding to the destination of the mail. The system then copies the file to be mailed, renames it as needed, marks it for transmission, and delivers it overnight to the addressee.

Each of the network offices has a copy of the "DCCT Operations and Telecommunications System Operations Manual" which explains in detail how the system is organized and used. As updates to the system occur, the offices will be provided floppy diskettes containing the new software and instructions on how to install the software onto the hard disks of their microcomputers. The manual will also be revised as needed.

Chapter 27

MORBIDITY AND MORTALITY CLASSIFICATION COMMITTEE PROCEDURES

27.1 INTRODUCTION

In a study such as the DCCT, the patient's treatment group is known and there is a risk that the reporting of mortality and morbidity may be influenced by that knowledge. In other studies where the treatment group is unknown, this type of bias is not so influential but there remains a need for rules for classification of certain events. The Morbidity/Mortality Classification Committee (M&M) is an independent committee established by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to review and classify all deaths and major intercurrent events that occur among patients randomized into the DCCT. The major intercurrent events include: major accidents (accidents requiring hospitalization), myocardial infarction, cerebrovascular accident with persistent neurological deficit, non-traumatic amputation, loss of vision, renal insufficiency, neuropathy, and other events as requested. These events were selected because the causal or contributing role of diabetes may be direct or indirect; therefore the data are difficult to interpret.

The objective of these reviews is to: determine the primary and contributing causes of death; validate the basis for diagnosis of important morbid events; and evaluate the likelihood that the event is attributable to diabetes and in the case of major accidents, comment on the role of hypoglycemia. The classifications by this committee will be the bases for counting outcomes for final statistical analyses. The decisions of the Committee are final.

In order to ensure professional and unbiased attributions of these study outcomes that may be diabetes related, the M&M Committee comprises 3 physicians who otherwise are uninvolved in the DCCT. These individuals were selected on the basis of their knowledge of diabetes and for previous experience in clinical trials. The study will rule out a contributing role of diabetes in these events only with the concurrence of the M&M Committee.

27.2 ASCERTAINMENT OF EVENTS

The clinics are required to notify a member of the Executive Committee immediately when they learn of the death of a DCCT patient. A member of the Coordinating Center (CoC) is notified as soon as possible of all major accidents and deaths (Figure 27.1, Information to Report Category 1 Intercurrent Events).

As every death is unique, it is not always possible to collect comparable data on each case. However, the DCCT uses a standard approach to acquire data from a variety of sources. This ensures that standard information is obtained as quickly as possible. Deaths are subsequently detailed on Form 15, Notification of Death, and nonfatal intercurrent events are reported on Form 20, Notification of Intercurrent Event. The Morbidity and Mortality Review, Instruction for Clinics (Section 27.3) provides detailed directions regarding what materials should be provided to the Coordinating Center for a thorough review.

Procedures to be Followed in the Event of a Death of a DCCT Volunteer (MOO Chapter 25) are reviewed with the Principal Investigator as appropriate. The information requested is in addition to that mandated for an intercurrent event. The procedures are directed primarily at providing information that will assist in determining causes of unattended or unexpected deaths.

27.3 INSTRUCTIONS FOR CLINICS

For each event that the committee will review, the clinic needs to provide copies of all information that was used to arrive at the local determination (or diagnosis). This includes the complete medical and hospital records; laboratory reports; ECG tracings; summaries of interviews with patients, relatives, or witnesses to an event; and additional information such as police reports. If the complete hospital record is unavailable, the minimal records necessary for review are: ER reports, laboratory reports with dates and times noted, discharge summaries and, if available, admission notes. Additionally, in some situations a narrative describing the process followed in arriving at the local determination should be submitted. For example, the narrative could explain any missing data and how the final local determination was made in light of the missing information.

For fatal events, death certificates and medical examiner's reports should be obtained and provided.

The second task of ascertaining the role of diabetes and/or hypoglycemia in the event is more difficult. Of particular importance is any information that may allow the committee to rule out, with reasonable assurance, any role of diabetes or hypoglycemia. For example, in the case of an accident for which it is suspected that the

patient may have lost consciousness, information indicating that loss of consciousness may have been due to alcohol or drug abuse might be useful in ruling out hypoglycemia as contributing to the accident.

With the exceptions noted below, events to be reviewed by the M&M Committee will be reported on DCCT Form 20, Notification of Intercurrent Event. The materials required for the M&M Committee to review each type of event are indicated on the Morbidity and Mortality Transmittal Form, which is prepared by the Coordinating Center for transmittal to the M&M Committee with the supporting documentation. When an event occurs the coordinating center will request the clinic to provide the appropriate information, specific for each type of event, as follows.

27.3.1 Deaths and Major Accidents

In the case of a death or major accident, the clinic should submit a narrative written history of hypoglycemia. Information on any deviation from patient's usual pattern of insulin administration and eating habits in the 36 hours preceding the incident should be obtained from patient records and interviews with family members, friends or other witnesses. A general psychological profile should be included: e.g., is the patient accident prone, responsible, depressed, etc. The treatment group assignment should not be mentioned in the clinic report. If mention cannot be avoided, it would be useful if discussion of treatment group could be segregated into one separate paragraph.

Death Procedures specified in Chapter 25 of the Manual of Operations should be reviewed at the time the clinic learns of the death of a DCCT volunteer. Form 15, Notification of Death, should be submitted for each event as soon as possible. It is extremely important that the clinic submit copies of all sources of information used to complete the form. This includes medical and hospital records and those items requested in question 8 for Form 15: death certificate, autopsy report and interviews.

In the case of deaths not medically attended, essential information can often only be obtained from interviews with third parties. Accordingly, if unavailable from other sources, the clinic should make strenous efforts to interview persons likely to have knowledge of events preceding the death and/or witnesses to the event which lead to the death.

If a police report was filed, a copy should be obtained and submitted. The police report may contain interviews with witnesses and hence relieve the clinic staff of the need to conduct separate interviews.

If the clinic believes it prudent to also interview a family member, that interview should be submitted. The interview with a family member should include as a minimum whether the patient had any medical or psychosocial problems within ten days of death and the extent of his/her

compliance with the assigned study treatment within three days of death. A summary of each interview should be submitted.

Finally, the clinic should report in a written narrative whether it believes diabetes contributed to a death by natural causes or whether hypoglycemia contributed to an accidental death, and why.

Major Accident. For purposes of M&M review, major accident has been defined as an event which requires overnight admission to a hospital, or results in the death, of a DCCT patient. In addition to Form 20, the clinic should submit a copy of the ambulance, emergency room and hospital records concerning the admission for the accident. Also, the clinic should report in a written narrative whether it believes hypoglycemia contributed to the accident. The clinic decision reported in the narrative might be based on a police report or an interview with the patient, a relative, and/or a witness to the accident. Police reports and interview summaries should be submitted when available. Forms 83 should be submitted when applicable.

27.3.2 Other Intercurrent Events

This group of events will be submitted for M&M review only when the clinic believes the event should be classified as unrelated to diabetes or when the clinic believes the relationship of the event to diabetes is unclear. In such cases, the clinic should submit a narrative detailing the reasons for ruling out diabetes or for questioning the relationship of the event to diabetes. Copies of a ll relevant supporting evidence in addition to the required study forms should be provided. In the absence of such review by the M&M it will be assumed for purposes of data analysis that all occurrences of these events are related to the concomitant presence of diabetes and they will be so tabulated in reporting final results of the study.

Neuropathy. Neuropathy is reported on DCCT Form 5, Section D. The Coordinating Center will periodically review all Forms 5, and any neuropathy reported as other than diabetic symmetrical sensory-motor neuropathy will be transmitted to the M&M Committee for review. All such events should be accompanied by a narrative explaining why the clinic believes the neuropathy is not due to diabetes.

Cerebrovascular Accident (CVA). All CVAs are reported on Form 20. Diagnosis of CVA requires a complete workup; this will include either a CT scan or another imaging examination. The clinic should submit copies of the hospital record of the admission for the CVA. In addition, it is necessary to assess all patients who experience a CVA 12 months post-event to determine whether there is persistent neurological deficit. This determination is to be made on the basis of clinical examination of the patient by the DCCT neurologist. Form 5 should be used to document the presence of a neurological deficit at the 12 months follow-up of the event.

Myocardial Infarction. In addition to Form 20, the clinic should submit photocopies of all ECG tracings, enzyme reports, and hospital records.

Amputation. The hospital record for all admissions involving an amputation should be submitted for committee review.

Loss of vision. For all cases of loss of vision, the committee will review the relevant Form 20, the corresponding Form 27, and the Form 27 from the annual visit following its occurrence. Vision must be documented to be less than 20/200 in either or both eyes, at both time points, to meet the study definition.

Renal Insufficiency. The clinic is notified by the CoC when a patient has passed the threshold for serum creatinine. Form 20 should be submitted when a local serum creatinine confirms the elevated value.

Other. Any event identified by a clinic or the coordinating center for which there is uncertainty as to its relevance to the DCCT, or of the role of diabetes in the event, may be submitted to the M&M for review. Accordingly, the information needs for such events will have to be specified on a case-by-case basis.

27.4 REVIEW PREPARATION

The CoC reviews reports of death and intercurrent events for consistency with study definitions and completeness of supporting documentation. When the CoC is satisfied that a reportable event is as fully documented as possible, the supporting documentation is edited so that the subject's treatment group assignment is masked to the extent possible. Patient's name, address, social security number, telephone number, the same for relatives, and any reference to treatment group are edited from the documentation. Descriptions of insulin therapy and glucose testing are masked if they will result in treatment group identification. Any additional information, such as history of hypoglycemia, will be included in the patient file if necessary.

A Form 103, Morbidity and Mortality Transmittal, and 104, Morbidity and Mortality Review, is prepared by the CoC for each case review. The documents are masked, prepared and reviewed by the study Scientific Officer in advance of mailing to the M&M Committee. (Figures 27.2 and 27.3).

27.5 ACTUAL REVIEW

Periodically the CoC sends a set of cases for review to the M&M Committee members. The reviewers have the option of 1) completing the review; 2) requesting additional information about the event; 3) requesting information that was edited to mask treatment assignment; or 4) requesting review by a subspecialist. If a subspecialist review is requested, it will be obtained and provided to all reviewers. Requests for additional information will be passed on to the clinical centers and, if available, will also be provided to all reviewers. Responses are returned to the CoC.

In some circumstances, a reviewer may request information about treatment group, or insulin and glucose testing data that could disclose treatment group. In these cases, the study Scientific Officer will be consulted. Information will be released to the reviewers only after approval by the study Scientific Officer. If any member requests unmasking, the case will go before the entire committee for adjudication.

When all reviews have been received, the CoC tabulates the results to determine whether there is agreement. If two reviewers agree in their conclusions the review will be judged complete. If there is disagreement among all three committee members, the event is adjudicated by discussion at a meeting of the committee. The CoC prepares a summary of these classifications and comments by Committee members to be used during the adjudication meeting. All deaths are discussed during an adjudication meeting.

During the adjudication meeting there is an effort to reach consensus classification of each event; agreement among two of the members will be the basis for consensus. Additional information may be requested by the reviewers in which case discussion may be tabled for final decision at a later time. The results of the reviews are tabulated by the CoC and reported to the Data, Safety and Quality Review Group. The Data Safety and Quality Review Group is informed of those events that require unmasking.

27.5.1 Assessment of the Role of Diabetes in Deaths

The assessment of the role of diabetes in DCCT deaths is based on the following guidelines.

Diabetes or diabetes related events/complications are considered to be underlying or contributory when they contribute significantly to the death. The role of diabetes is evaluated after considering all ways in which diabetes may contribute to the death, independently of the specific cause of death.

The ways in which the role of diabetes may relate to death include:

1) as principal cause of death (e.g., DKA),
2) as a risk factor (major contributing cause) for another related disease process (e.g. MI),
3) as a complicating factor impeding the recovery of another condition (minor contributing cause e.g., complicating the recovery from an unrelated accident), or
4) diabetes played no role.

Members of the committee are asked to base their classification on a reasonable amount of certainty (95%). (See Form 104)

It is important to note that diabetes may relate to a death in more than one way, e.g. as a risk factor for MI and as a factor complicating recovery from MI. It is possible for apparent contradictions to arise between the assessment of cause of death and the role of diabetes. For example: diabetes may have been related to an accident through probable hypoglycemia. Hypoglycemia may not be thought important enough to be listed as a contributing cause of death but nonetheless be ranked as having a minor role in the death through this link. Diabetes might also have a role in death by complicating recovery from accidental injuries.

In summary, the two components of mortality review, assigning in order of importance the causes of death and quantifying the role of diabetes, are considered independent but related activities.

It is likely that some, but not all, deaths will be preceded by a reportable intercurrent event. For example, a patient may experience an accident, be hospitalized for two weeks, and then die. Such a situation will count as both an intercurrent event (accident) and a death and hence will be classified twice. It is conceivable that the committee may decide that diabetes played no role in the occurrence of the accident, but did in the death. All accidental deaths will be reviewed by the committee as both an accident and a death.

27.5.2 Assessment of the Role of Hypoglycemia in Major Accidents

Members of the M&M Committee are asked to consider ways in which hypoglycemia may have contributed to the major accident, and evaluate whether it is related as the principal cause, the probable cause, a possible cause or played no role. They assess the role of hypoglycemia based on their reasonable amount of certainty (95%) (See Form 104)

27.5.3 Assessment of the Role of Diabetes in Neuropathy

Committee members consider the nature of events that the clinics report to be "other than, or in addition to, diabetic symmetrical sensory-motor neuropathy", and evaluate whether this classification is correct.

It is recognized that carpal tunnel syndrome can present some of the same symptoms as diabetic symmetrical sensory-motor neuropathy (DSSMN) and that diabetics carry an increased risk of the disorder. If reported, it is recognized by the committee as an "other" neuropathy, separate from DSSMN.

27.5.4 Assessment of the Role of Diabetes in Other Events

Committee members consider ways in which diabetes may have contributed to events other than major accidents and evaluate whether it might be related as a major contributing cause (e.g. a risk factor) or as a minor contributing cause (e.g. a complicating factor). They assess whether they can rule out with reasonable certainty (95%) that diabetes is a contributing cause.

For MI, Cerebrovascular Accident, Amputation, Loss of Vision and Renal Insufficiency the committee is asked to rule out with reasonable certainty whether an acute metabolic disturbance of diabetes precipitated the event.

Figure 27.1

INFORMATION TO REPORT CATEGORY 1 INTERCURRENT EVENTS

Clinic _____ Patient Age____

Clinic Person Calling _____ Gender _____

Patient I.D. #_____ Date of Call_____ Treatment Group ____

Coordinating Center Person Receiving Call _____

I. NATURE OF EVENT

{ } Major event requiring hospitalization
{ } Major event not requiring hospitalization
{ } Catastrophic hypoglycemia
{ } Suspected catastrohpic hypoglycemia
{ } Death

II. DETAILS OF EVENT

1. Date of event _____ Time of event _____

2. Date Clinic learned of event _____

3. Brief Description_____

_____

_____

4. Diagnosis_____

	YES	NO
5. Did the patient require ER/Paramedic assistance?	{ }	{ }
If so, what treatment? _____		
6. Was the patient hospitalized overnight?	{ }	{ }
7. Who was with the patient at the time of the event? _____		
8. Any injuries to other persons? (If yes, complete Part IV)	{ }	{ }
9. Were other authorities involved/notified? (police, paramedics, fire, etc.?)	{ }	{ }
10. Are copies of accident reports/certificate available/obtained?	{ }	{ }
11. Are copies of death certificate available/obtained?	{ }	{ }
12. If this was a motor vehicle accident: a) Was the patient driving? If not, who was driving? _____	{ }	{ }
b) Was patient restrained or unrestrained? (seatbelts)	{ }	{ }
c) If motorcycle or ATV vehicle, was patient wearing a helmet?	{ }	{ }

d) Who appears to be responsible for the event? (Patient or other involved) _____

_____

e) What appears to be responsible for the event? (Weather, speeding, ETOH or drugs, hypoglycemia, etc.) _____

_____

13. Were there witnesses? YES { } NO { }
Names/Addresses/Phone Numbers, etc):

_____

_____

_____

III. RELATIONSHIP TO HYPOGLYCEMIA:

1. GLUCOSE INFORMATION

{ } Available
{ } Done, not available
{ } Not done

a) At the time of event:
Value _____
Who measured it _____
Measured by { } Visual { } Meter { } Lab

b) Before event:
Value _____
Who measured it _____
Measured by { } Visual { } Meter { } Lab
Amount of time prior to event that glucose was measured: _____

c) After event:
Value _____
Who measured it _____
Measured by { } Visual { } Meter { } Lab
Amount of time after event that glucose was measured: _____

2. Were there symptoms of hypoglycemia? YES { } NO { }
{ } Recognized by patient { } Recognized by other person

3. Does this patient normally have symptoms associated with hypoglycemia? { } { }

4. Was someone with the patient at time of the event? { } { }
Were they capable of recognizing hypoglycemia? { } { }
Did they take appropriate action? { } { }
What did they do? _____

_____

	YES	NO
5. Is this a pump patient?	[ ]	[ ]
If so, was it collected and/or checked by DCCT Staff?	{ }	{ }

What appeared to be wrong with the pump? _____

_____

IV. DETAILS OF TREATMENT:

Patient: Injuries _____
Diagnosis _____
Prognosis _____
Where is the patient now? _____
Name/address/phone# of treatment facility _____
_____

Other Injured People: #1 Name:
Overnight hospitalization { } { }
Injuries _____
Diagnosis _____
Prognosis _____
Where is the patient now? _____
Name/address/phone# of treatment facility _____
_____

Other Injured People: #2 Name:
Overnight hospitalization { } { }
Injuries _____
Diagnosis _____
Prognosis _____
Where is the patient now? _____
Name/address/phone# of treatment facility _____
_____

IF OTHERS WERE INVOLVED, PLEASE ATTACH A SEPARATE SHEET.

PAPERWORK/ADMINISTRATIVE DETAILS:	N/A	YES	DATE COMPLETED	NO	UNABLE TO OBTAIN
Coordinating Center called	___	___	_____	___	_____
Medical release forms obtained	___	___	_____	___	_____
Patient	___	___	_____	___	_____
Injured party #1	___	___	_____	___	_____
Injured party #2	___	___	_____	___	_____
Medical records obtained	___	___	_____	___	_____
Patient	___	___	_____	___	_____
Injured party #1	___	___	_____	___	_____
Injured party #2	___	___	_____	___	_____
Medical Examiner's report	___	___	_____	___	_____
Death certificate obtained	___	___	_____	___	_____
Patient	___	___	_____	___	_____
Injured party #1	___	___	_____	___	_____
Injured party #2	___	___	_____	___	_____
Summary of legal proceedings	___	___	_____	___	_____
Accident report obtained	___	___	_____	___	_____
Form 15 sent to Morb.& Mort. Comm. (Notification of Death)	___	___	_____	___	_____
Form 85 sent to Morb. & Mort. Comm. (Final Notification of Death)	___	___	_____	___	_____
Form 86 sent to Morb. & Mort. Comm. (Deceased Experimental Patient Form)	___	___	_____	___	_____
Form 87 sent to _____ (Procedures for Mechanical Inspection of Insulin Infusion Devices and Blood Glucose Meters)	___	___	_____	___	_____
Form 20 sent to Morb. & Mort. Comm.	___	___	_____	___	_____
Form 83 sent to Morb. & Mort. Comm.	___	___	_____	___	_____
Form 92 sent to Morb. & Mort. Comm.	___	___	_____	___	_____

Figure 27.2

DCCT Form 103.2
October 28, 1991
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DIABETES CONTROL AND COMPLICATIONS TRIAL

Morbidity and Mortality Transmittal Form

This checklist is completed by Coordinating Center staff in preparing materials for the Morbidity and Mortality Classification Committee to review.

A. IDENTIFYING INFORMATION

1. Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. Event Date: __ __/__ __/__ __ (Month / Day / Year)
5. Event to be Classified:

Death	(1)	Neuropathy	(6)
Major Accident	(2)	Loss of Vision	(7)
Myocardial Infarction	(3)	Renal Insufficiency	(8)
Cerebrovascular Accident	(4)	Other	(9)
Amputation	(5)		

B. MATERIALS DOCUMENTING THE EVENT

1. All Deaths	Not Applicable	Date Received Month / Day /Year
Intercurrent Event (DCCT Form 020)	_____	__ __/__ __/__ __
Notification of Death (DCCT From 015)	_____	__ __/__ __/__ __
Clinic report on role of diabetes	_____	__ __/__ __/__ __
Clinic history of Hypoglycemia	_____	__ __/__ __/__ __
Clinic psychological profile	_____	__ __/__ __/__ __
Medical and/or hospital records	_____	__ __/__ __/__ __
Death certificate	_____	__ __/__ __/__ __
Medical examiner's report (Autopsy)	_____	__ __/__ __/__ __
Interviews with family members	_____	__ __/__ __/__ __
Other _____	_____	__ __/__ __/__ __

Patient ID _____

DCCT Form 103.2
Page 2 of 3

	Not Applicable	Date Received Month / Day / Year
2. Major Accident or Traumatic Death		
Intercurrent Event (DCCT Form 020)	____	__ __/__ __/__ __
Hypoglycemic Event (DCCT Form 083)	____	__ __/__ __/__ __
Clinic summary of event (explanation of missing items if necessary)	____	__ __/__ __/__ __
Clinic report on role of hypoglycemia	____	__ __/__ __/__ __
Clinic history of hypoglycemia	____	__ __/__ __/__ __
Clinic psychological profile	____	__ __/__ __/__ __
Summary of legal proceedings	____	__ __/__ __/__ __
Summary of interviews: witnesses, patient	____	__ __/__ __/__ __
Emergency room record	____	__ __/__ __/__ __
Hospital record	____	__ __/__ __/__ __
Discharge Summary	____	__ __/__ __/__ __
Police report	____	__ __/__ __/__ __
Other _____	____	__ __/__ __/__ __
3. Myocardial Infarction		
Intercurrent Event (DCCT From 020)	____	__ __/__ __/__ __
Clinic report on role of diabetes	____	__ __/__ __/__ __
Hospital record	____	__ __/__ __/__ __
ECG tracings	____	__ __/__ __/__ __
Enzyme reports	____	__ __/__ __/__ __
4. Cerebrovascular Accident		
Intercurrent Event (DCCT Form 020)	____	__ __/__ __/__ __
Clinic report on role of diabetes	____	__ __/__ __/__ __
Hospital record	____	__ __/__ __/__ __
CAT scan report (or other imaging)	____	__ __/__ __/__ __
Neurological Examination (DCCT Form 005) {12 months after event}	____	__ __/__ __/__ __

Patient ID _____

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		Not Applicable	Date Received Month / Day / Year
5. Amputation			
Intercurrent Event (DCCT Form 020)		____	__ __/__ __/__ __
Clinic report on role of diabetes		____	__ __/__ __/__ __
Hospital record		____	__ __/__ __/__ __
6. Neuropathy			
Neurological History and Examination (DCCT Form 005)		____	__ __/__ __/__ __
Clinic report on role of diabetes		____	__ __/__ __/__ __
7. Loss of Vision			
Intercurrent Event (DCCT Form 020)		____	__ __/__ __/__ __
Endpoint Visit Ophthalmic Examination (DCCT Form 027) (< 20/200)	1st	____	__ __/__ __/__ __
	2nd	____	__ __/__ __/__ __
Clinic report on role of diabetes		____	__ __/__ __/__ __
8. Renal Insufficiency			
Intercurrent Event (DCCT Form 020)		____	__ __/__ __/__ __
Renal data summary		____	__ __/__ __/__ __
Clinic report on role of diabetes		____	__ __/__ __/__ __
9. Other			
See Attached.			

C. COORDINATING CENTER CERTIFICATION

1. Materials complete

_____ Signature _____ Date

2. Treatment group masked

_____ Signature _____ Date

3. Final review

_____ Signature _____ Date

Figure 27.3

DCCT Form 104.5
March 12, 1993
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DIABETES CONTROL AND COMPLICATIONS TRIAL

Morbidity and Mortality Review Form

This form is to be completed by a member of the Morbidity and Mortality Classification Committee following his review of materials submitted to classify an intercurrent event. The completed form should be returned to the Coordinating Center along with the materials reviewed.

A. IDENTIFYING INFORMATION (filled in by CoC)

1. Clinic Number: __ __

2. Patient I.D. Number: __ __ __ __ __

3. Patient's Initials: __ __ __

4. Event Date: __ __/__ __/__ __
   Month Day Year

5. Initials of Reviewer: __ __ __

6. Event to be Classified:

Death	(1)	Neuropathy	(6)
Major Accident	(2)	Loss of Vision	(7)
Myocardial Infarction	(3)	Renal Insufficiency	(8)
Cerebrovascular Accident	(4)	Other	(9)
Amputation	(5)		

B. RESULTS OF REVIEW (fill in appropriate section)

1. **Cause of Death**

What, in your judgement, is the underlying cause of death: (e.g. acute myocardial infarction, diabetic nephropathy, diabetic ketoacidosis, cancer):

_____

Please list, in order of importance, all other conditions that contributed to the death: _____

_____

_____

Patient ID _____

Assess the role of diabetes in this death. Are you reasonably certain (95%) that:

___ Diabetes is the principal cause (e.g., diabetic ketoacidosis)

___ Diabetes is a major contributing cause (e.g, myocardial infarction)

___ Diabetes is a minor contributing cause (e.g., kidney failure following exposure to a nephrotoxic agent)

___ Diabetes played no role (e.g, lung cancer)

Explain how you believe diabetes played a role in this death:

_____

_____

_____

2. Major Accident

Assess the role of hypoglycemia on this event. Are you reasonably certain (95%) that:

___ Hypoglycemia is the principal cause

___ Hypoglycemia is the probable cause

___ Hypoglycemia is a possible cause

___ Hypoglycemia played no role

If you believe diabetes played a role in causing this accident other than through hypoglycemia, please explain:

_____

_____

_____

3. Myocardial Infarction, Cerebrovascular Accident, Amputation, Loss of Vision or Renal Insufficiency

It is acknowledged that diabetes plays at least a contributory role as a risk factor in these morbidities.

Can you rule out with reasonable certainty (95%) that an acute metabolic disturbance of diabetes precipitated this event?

___ Yes ___ No If no, explain: _____

_____

Patient ID _____

4. Neuropathy

Do you agree this event can be classified as: "other than, or in addition to, diabetic symmetrical sensory-motor neuropathy"?

___ Yes

___ No

If no, please explain: _____

_____

C. CERTIFICATION OF REVIEW

1. If additional documentation is required, please specify:

_____

_____

2. If the opinion of a specialist is requested, please specify the question to be posed and the requisite specialty: _____

_____

_____

_____Signature

_____Date

Chapter 28

BODY COMPOSITION

28.1 INTRODUCTION

Weight gain associated with intensified therapy in the DCCT remains a significant problem. It is believed that insulin therapy may promote weight gain (or make weight loss more difficult) by three distinct mechanisms: by the anabolic effects of insulin itself, by causing mild hypoglycemia and stimulating appetite, and by decreasing the "wasting" of calories (as sugar) in the urine seen in poorly controlled diabetes.

It is generally assumed that this weight gain is a result of excessive accumulation of body fat. An alternative hypothesis is that at least some of this extra weight is due to increases in two other body compartments also regulated in part by insulin: body water and body protein. Insulin has been shown to have a direct effect on the distal tubule of the renal medulla to increase sodium reabsorption. Thus, hyperinsulinemia can cause retention of salt and thus water. Similarly, insulin is also anabolic for protein, and therefore chronic hyperinsulinemia might promote accretion of muscle protein. Thus, comparing body composition in the experimental versus the standard group in the DCCT offers an opportunity to better understand the nature of the weight gained in association with intensified insulin therapy.

Finally, the advent of newer methods of body composition analysis will greatly simplify this task. Bioelectrical impedance analysis (BIA), for example, has been demonstrated to quantify lean body mass (LBM), body fat (BF), and total body water (TBW) in a reliable and accurate fashion as compared to deuterium-isotope dilution (Kushner & Schoeller, 1986) and densitometry by hydrostatic weighing (Lukaski et al, 1986). It is based on the conduction of an applied electrical current and the fact that the body contains intra- and extra-cellular fluids that behave as electrical conductors and cell membranes that act as electrical condensers.

28.2 MEASURES TO BE EMPLOYED

28.2.1 Height, Weight, Body Mass Index (BMI)

Height and weight give reasonable estimates of relative body fatness. However, they cannot separate fat from lean. Problems can arise when lean tissues are present in unusually small or large amounts. The NHANES 1982 Workshop on BW, Health and Longevity recommended the reporting of RBW (Relative Body Weight) or BMI (Body Mass Index).

28.2.2 Waist-to-hip ratio (WHR)

The pattern of distribution of adipose tissue through the body has metabolic consequences and may be a more important factor than total adipose tissue mass. Thus, a person with fat located predominantly in the abdominal region may be at greater risk of hypertension, heart disease and DM than another individual with a greater amount of adipose tissue that is located predominantly in the gluteal-thigh area. (Kisselbah AH et al. Relation of body fat distribution to metabolic complication of obesity. J. Clin End Metab: 54:254-260, 1982).

28.2.3 Bioelectrical Impedance Analysis

To measure body composition (fat-free mass and body fatness) an inexpensive and fairly accurate method is Tetrapolar Bioelectric Body Impedance Analysis (BIA) which estimates the total body water and the fat free mass.

28.3 TIMING

The BIA will be done on each DCCT patient and can be done at any visit. Height, weight and hip and waist circumferences will be obtained at the visit. If these body composition assessments are done at the annual visit, the following sequence of events must be used:

1) lipid blood specimens are drawn after overnight fast;
2) a light meal is consumed;
3) a two hour delay is necessary for the body to reequilibrate;
4) the BIA performed;
5) water loading may commence for the four hour renal collection.

28.4 MEASURING AND RECORDING GUIDELINES

All measurement should be taken to the nearest unit as allowed on the Body Composition Form (114.1) After each measurement is taken, its value is recorded in the appropriate space. If a recorder is present, the recorder should repeat the value that was called aloud by the examiner.

All measurements will be done twice. If the two measures differ by more than the recommended amount, two additional measures are taken and recorded. NOTE: A set of measurements is taken and then repeated. Do not take the same measure twice in a row.

Recommended limits for difference between measures are:

Weight:	Within 200 grams
Stature:	Within 1.0 cm
Waist Circumference:	Within 0.5 cm
Hip Circumference:	Within 0.5 cm
BIA Reactance	Within 1 ohm
BIA Resistance	Within 2 ohms

28.5 WEIGHT

To minimize variability in the weight measurement, patients should be requested to wear lightweight clothing and to remove shoes before the weight is taken. Other steps to consider to reduce variability are: 1) Ask the patient to empty his/her bladder (for non-GFR Visits) before weight is taken; 2) Schedule monthly appointments, as feasible, at approximately the same time of day; and 3) Encourage the patient to eat relatively the same volume of food at meals that precede an appointment. (For example, the patient should not skip breakfast--unless a fasting blood must be drawn--before one appointment, and then eat a large breakfast before the next appointment.)

Ask the patient to stand in the center of the scale and not to touch or support themselves on anything. The patient should stand so that his/her weight is equally distributed on both feet. Two measures will be taken. The patient should step off the scale between measurements and the scale should be reset to zero. Repeated measurements should agree within 200 grams. If they do not, two more measures should be taken and recorded. Check the scale at "0" to be sure it balances each morning. The scale should be left with the weights at zero when not in use.

28.6 STATURE

Ask the patient to stand with his/her back against the stadiometer, with the heels together, and both heels touching or a minimal distance from the wall (no greater than the depth of the stadiometer). The back (scapula) and buttocks should also be in contact with the board (See Figure 1).

Occasionally it will be impossible to position the patient's heels, buttocks, scapula, and the back of the head in one vertical plane against the board and still have him/her stand naturally and comfortably. His/her back may be arched due to the large size of the buttocks. If this occurs, move the patient forward and have only the buttocks and heels in contact with the board.

Be sure that in this position the patient maintains erect posture, that is, no slouching. Heels should be together and the medial borders of the feet at an angle of about 45 degrees, with the weight equally distributed and the head in the "Frankfort Horizontal Plane". This requires the subject to look straight ahead. A line running from the opening of the ear to the corner of the eye should be parallel to the floor. The movable headboard is brought down firmly on top of the head. It may be necessary, upon occasion, to remove or alter the hairdress of some of the patients. This may be necessary for the headboard to maintain a right angle and to make contact with the top of the scalp.

Have the patient inhale deeply, again not altering position by, for example, raising the heels off the floor. Stature is measured just before the patient exhales. The measurement is recorded to the nearest millimeter and agreement between measurements must be within 1.0 cm.

28.7 CIRCUMFERENCE MEASUREMENTS

Measurement of hip and waist circumferences will require two individuals. The measurements will be recorded on DCCT Form 114 (Body Composition). Two different waist references are to be used in the DCCT to provide maximum comparability to data published by other trials. All requested data should be provided, even for extremely obese individuals.

Insulin can cause both atrophy and hypertrophy of fat. Lipoatrophy is reported to be the more common of the two and is usually seen in children and young women. The areas affected show circumscribed depressions from the deep dermal and subcutaneous loss of fat. Insulin hypertrophy is less common and clinically resembles lipomas. It may be important for the analysis of the waist-to-hip ratio to know the extent of the prevalence of these two conditions. The assessment of the presence of lipohypertrophy or lipoatrophy affecting these measurements will be made most appropriately by a nurse or physician that has some experience with these conditions.

28.7.1 Natural Waist

The subject wears little clothing so that the tape may be correctly positioned. The measurements should not be made over clothing. If clothing must be worn, subjects should undress to light underwear and wear only a cloth or paper smock during the measurement. The subject stands erect with the abdomen relaxed, the arms at the sides and the feet together. The measurer faces the subject and places an inelastic tape around the subject, in a horizontal plane, at the level of the natural waist, which is the narrowest part of the torso, as seen from the rear. An assistant is needed to help position the tape in a horizontal plane. In some obese subjects, it may be difficult to identify a waist narrowing. In such cases, the smallest horizontal circumference should be measured in the area between the ribs and iliac crest. The measurement should be taken at the end of a normal expiration, without the tape compressing the skin. It is recorded to the nearest 0.5 cm. If patients are measured with a gown, it should be pulled tight so that landmarks are obvious.

28.7.2 Iliac Crest Waist

The patient is in a standing position. The patient is asked to hold up his/her gown. The examiner stands behind the patient and palpates the hip area for the right iliac crest. The examiner marks a horizontal line at the high point of the iliac crest and then crosses the line to indicate the midaxillary line of the body. The pants and underclothing of the patient must be lowered slightly for the examiner to palpate directly on the hip area for the iliac crest. The examiner then stands on the patient's right side and places the measuring tape around the trunk in a horizontal plane at the level marked on the right side of the trunk. The recorder walks around the patient to make sure that the tape is parallel to the floor and that the tape is snug, but does not compress the skin. The measurement is made at minimal respiration to the nearest 0.5 cm. If patients are measured with a gown, it should be pulled tight so that landmarks are obvious.

28.7.3 Buttocks (Hip) Circumference

The subject should wear only nonrestrictive briefs or underwear, or light smock over underwear. The subject stands erect with arms at the sides and feet together. The measurer squats at the side of the subject so that the level of maximum extension of the buttocks can be seen. An inelastic tape is placed around the buttocks in a horizontal plane at this level without compressing the skin. An assistant is needed to help position the tape on the opposite side of the subject's body. The zero end of the tape should be below the measurement value. The tape is in contact with the skin but does not indent the soft tissues. The

measurement is recorded to the nearest 0.5 cm. If patients are measured with a gown, it should be pulled tight so that landmarks are obvious.

28.8 BIOELECTRICAL IMPEDANCE ANALYSIS

28.8.1 Equipment

1. Impedance plethysmograph/monitor (RJL model 101)
2. Biological emulator: 1
3. Stainless steel rod electrodes: 4 (diameter: 1/8th inch; length: 8 inches)
4. Velcro straps: 4: (no metal clip or buckle; (2) length 24 inches; (2) length 30 inches
5. Velcro closures: 4
6. Adhesive electrodes: 4 (RJL resting ECG electrodes ONLY - available through CoC)
7. ECG gel/cream (Medi-Trace Conductivity Gel brand ONLY - available through CoC)
8. Non-conductive table with pad
9. Body weight scale
10. Stadiometer
11. Non-elastic tape measure

28.8.2 Instructions to Patients

All participants whose percent fat free mass will be assessed via BIA should receive the following instructions regarding the guidelines for body composition testing:

1. Refrain from ingestion of alcohol or alcohol-containing beverages for 24 hours before scheduled testing.

2. Participants should continue to participate in their usual activities before testing. However, strenuous exercise, such as exercise classes or physical training, should be avoided during the 24 hours preceding scheduled testing. Individuals who engage in physical labor as part of their usual employment should be tested, if possible, before participating in these activities.

3. For patients regularly taking prescribed medication, the duration between taking the medication and testing should remain constant for repeated tests.

4. If possible, a light meal should be consumed about 2 hours before testing. Patients should not abstain from food and water before testing.

5. Caffeine-containing beverages should be avoided for 2 hours before testing.

6. If there is sweat accumulated on the skin, or the patient has a fever, the testing should be rescheduled.

7. The patient should be tested with this protocol prior to commencing the water loading if done on the day that a 4-hour renal collection is scheduled.

8. If a woman is pregnant the study should be postponed until after delivery.

28.8.3 Testing Protocol

1. On each testing date, before the first patient is measured, the biological emulator is measured and the measurements are recorded on the data sheet. If readings are not within the tolerance listed (2 ohms for resistance and 3 ohms for reactance) the test should be rescheduled.

2. Standing height and body weight are measured and recorded for each patient.

   Hip and waist (natural and iliac) circumferences should be measured and recorded.

3. Patient is informed about how the measurements will be performed and then is asked to remove shoes and socks and clothing covering the knees and elbow. No jewelry other than rings should be worn. Insulin pumps may remain in place but should be laid away from electrodes.

4. Patient is positioned supine on the testing table. Patient should not be leaning to one side or overhang the table in any direction.

5. Adhesive, current-inducing spot electrodes are placed medially at the distal metacarpals of each hand and the distal metatarsals of each foot. The electrodes are taken from the package, cut in half longitudinally and then attached with the tab placed laterally.

6. The ECG conductive cream is applied in an even distribution along two thirds of the length of one rod electrode.

7. The patient is asked to abduct one arm from the torso and to extend the arm. The rod electrode is then placed horizontally along the natural fold of the elbow joint. Approximately one inch of the rod should extend from the medial aspect of the elbow joint; a larger extension of the rod should be present on the lateral aspect of the elbow joint. The electrode should be slowly moved (twisted) into this position to insure complete and proper contact of the ECG

cream with the skin. The electrode is held in place with a Velcro strap. (See Figures 2 and 3).

8. The portion of the electrode between the elbow and the torso is placed into the sewn loop on one end of the strap. The strap is then placed behind the elbow, wrapped over the lateral extension of the electrode then returned to the loop attachment where a Velcro closure is used to secure the strap snugly in place.

9. Another rod electrode is prepared and positioned at the contralateral elbow in the same fashion as described.

10. After the electrodes have been positioned on both arms, ask the patient to extend each elbow and to position each arm with the palm of the hand on the table. Extend the thumb of each hand and allow the thumb to touch the lateral aspect of the adjacent thigh. Flex the thumb so it returns adjacent to the fingers. During the impedance measurements, the thumb should not touch the thigh nor should the electrode touch the torso.

11. Prepare another rod electrode as described in #6. The patient is asked to flex one knee up from the table. The electrode is placed behind the knee along the natural fold in the popliteal fossa. Extend about one inch of electrode medially. Attach the Velcro strap similarly as described in #8. (See Figures 4 and 5).

12. Repeat the rod electrode placement for the contralateral knee.

13. Ask the patient to extend both knees, relax and lie quietly. The legs should be separated with no skin contact between them. The rod electrodes placed at the knees should not touch.

14. Identify the two pairs of electrode leads exiting from the impedance plethysmograph. With one pair of electrode leads, attach the alligator clip with the black connector to the adhesive electrode on one foot and the clip with the red connector to the lateral projection of the rod electrode at the knee of the same leg. (See Figure 6).

15. With the other pair of electrode leads, attach the clip with the black connector to the adhesive electrode on one hand then attach the clip with the red connector to the lateral projection of the rod electrode at the elbow of the same arm.

16. Before the impedance data are collected, ask the patient to relax and lie quietly, not to move his/her head to watch, or move arms or legs. <u>IT IS IMPORTANT</u> that the patient lie level and still. Determine the resistance (R) and reactance (Xc) values by moving the switch on the impedance monitor, then record the values on the data sheet for this electrode placement.

17. Repeat this electrode attachment process until measurements have bee made and recorded with electrodes placed on the right arm and

right leg, left arm and left leg, right arm and left leg, and left arm and right leg.

18. Remove each electrode and wipe off the ECG cream with a tissue.

19. The rod electrodes should be wiped off with alcohol pads after each use. These electrodes are reusable.

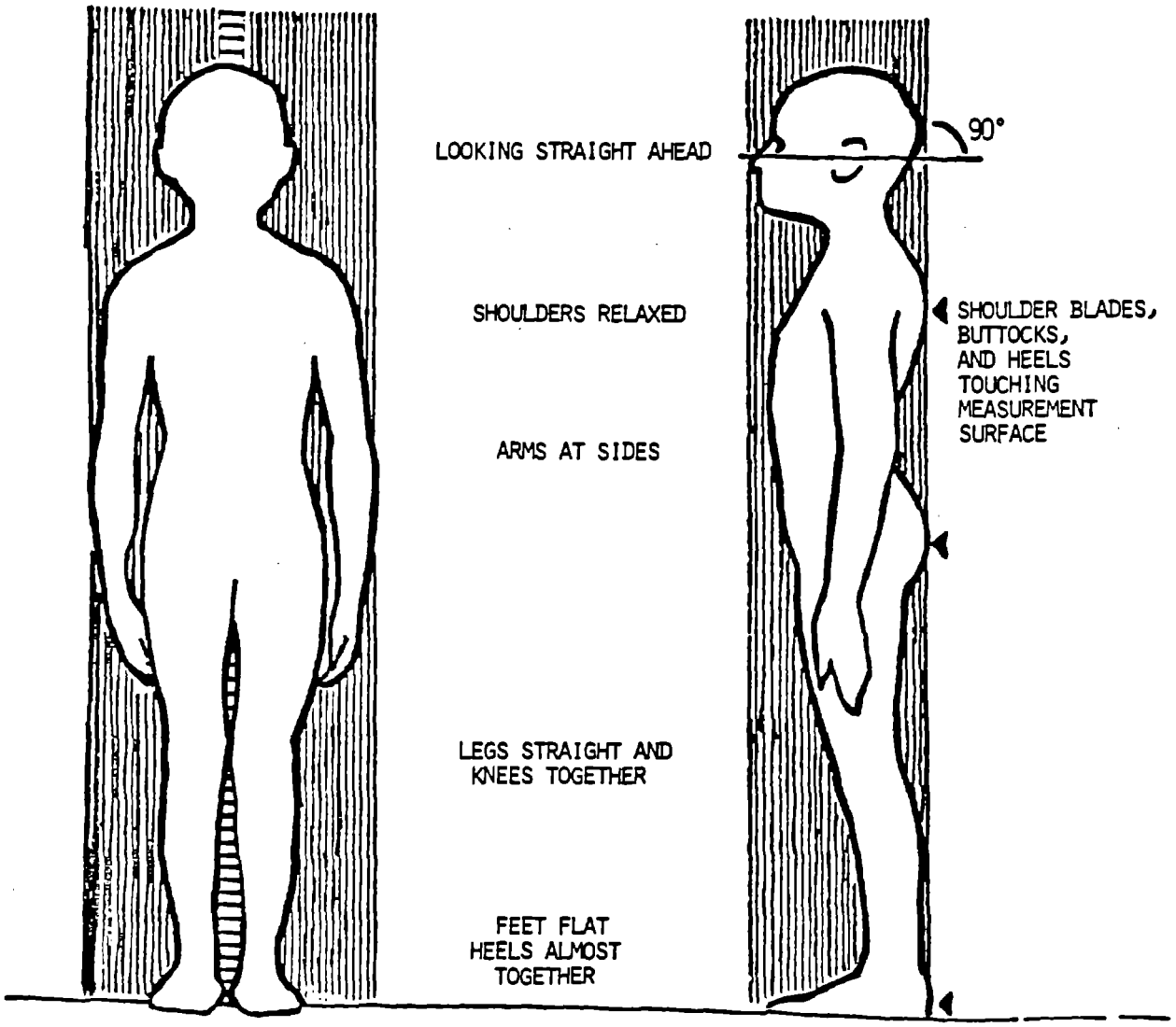
28.9 CERTIFICATION

The Body Composition protocol is designed to be performed by DCCT dietitians who have been trained and certified in the procedures. It is recognized that this is a completely different data collection activity than the usual DCCT dietary data collection. Clinical center personnel need to be certified in the measurement of hip and waist circumferences and in the use of the BIA machines.

Each dietitian who will perform the procedures on DCCT patients must submit a completed Body Composition Measurements (DCCT Form 114) - Certification Version form to the Coordinating Center for evaluation and approval. All information requested on the form should be provided including first and second measurements of all circumferences and BIA data. Third and fourth measurements should be made if initial reproducibility criteria are not met. Values obtained for the emulator are also reported to the CoC. Once all measurements meet the predefined criteria, the CoC will send written notification to the Trial Coordinator and the certified personnel and measurements on DCCT patients may begin.

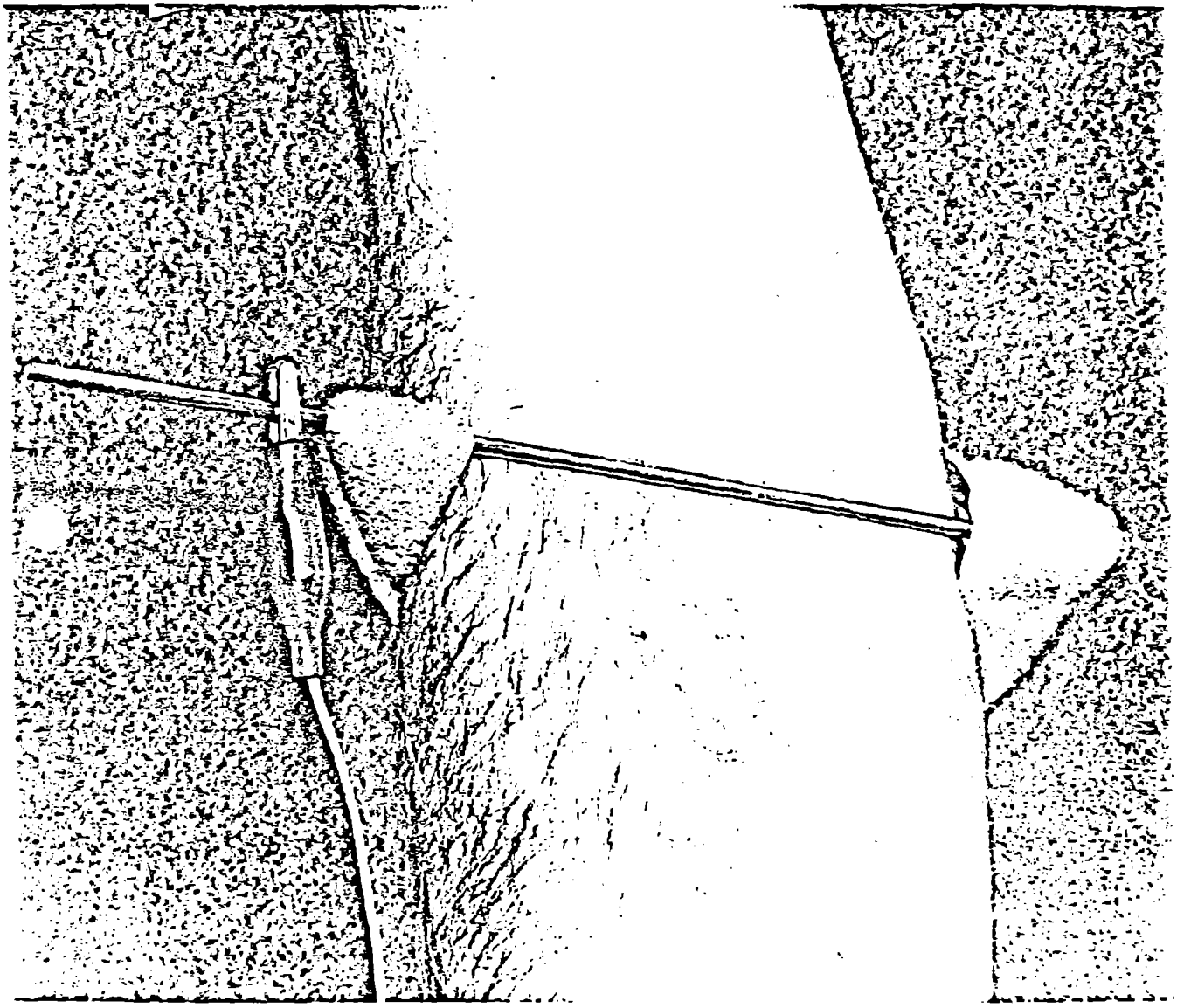
FIGURE 1

POSITION FOR STANDING HEIGHT



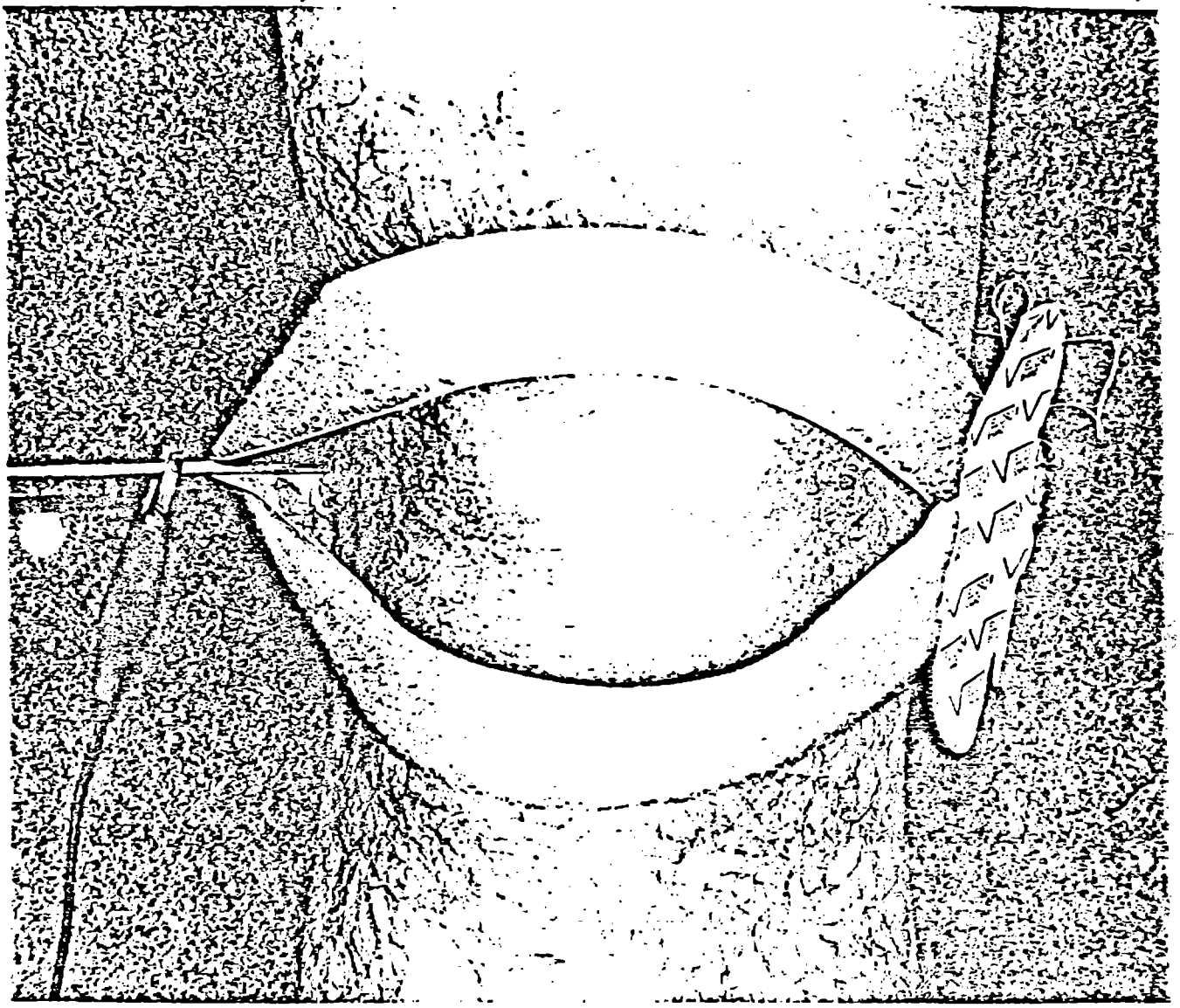
FROM: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY III
BODY MEASUREMENTS (ANTHROPOMETRY). OCTOBER 1988

(RIGHT ARM) FIGURE 2 (TOP)



(RIGHT ARM) FIGURE 3

(RIGHT LEG) FIGURE 4 (TOP)



(RIGHT LEG) FIGURE 5

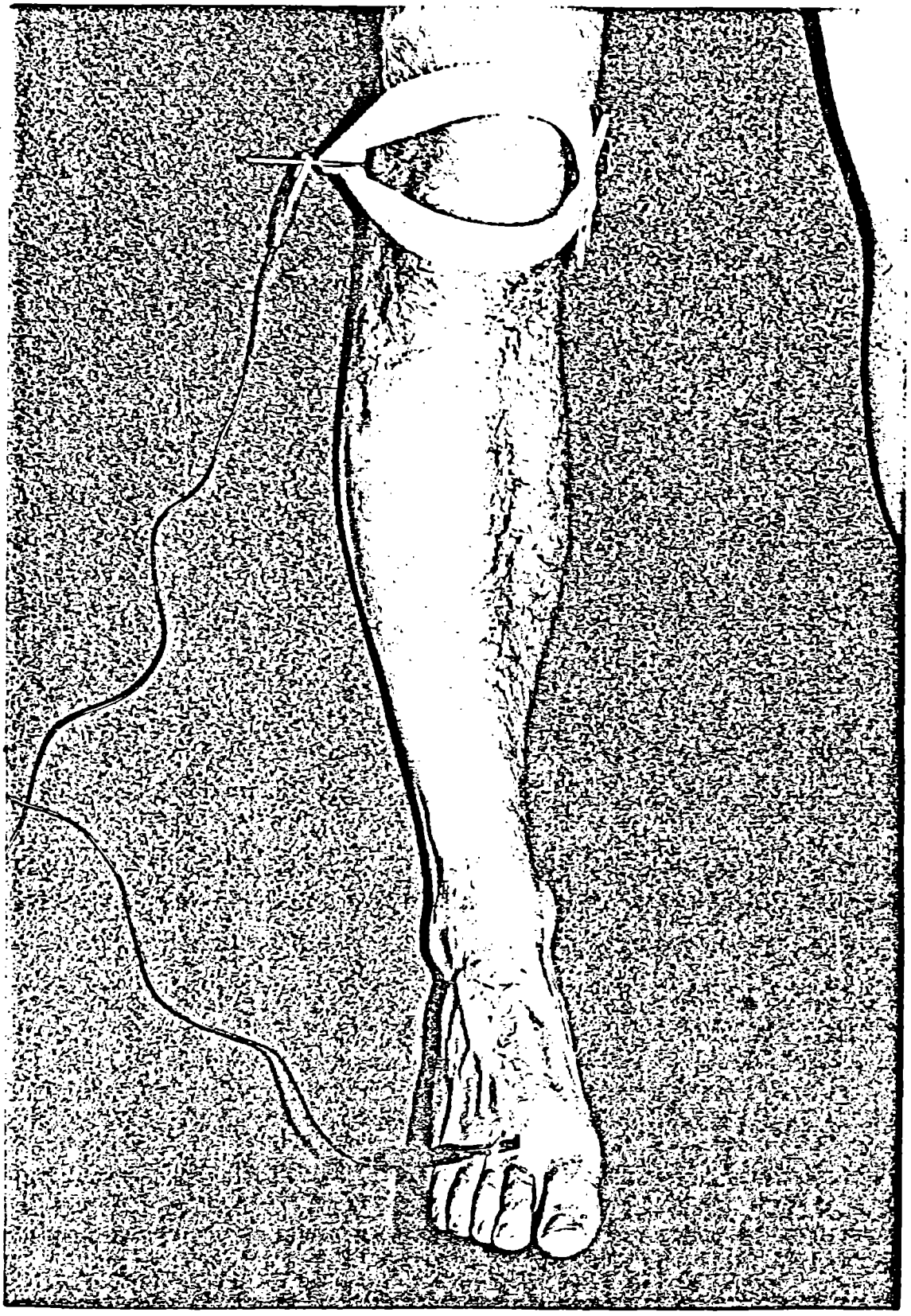
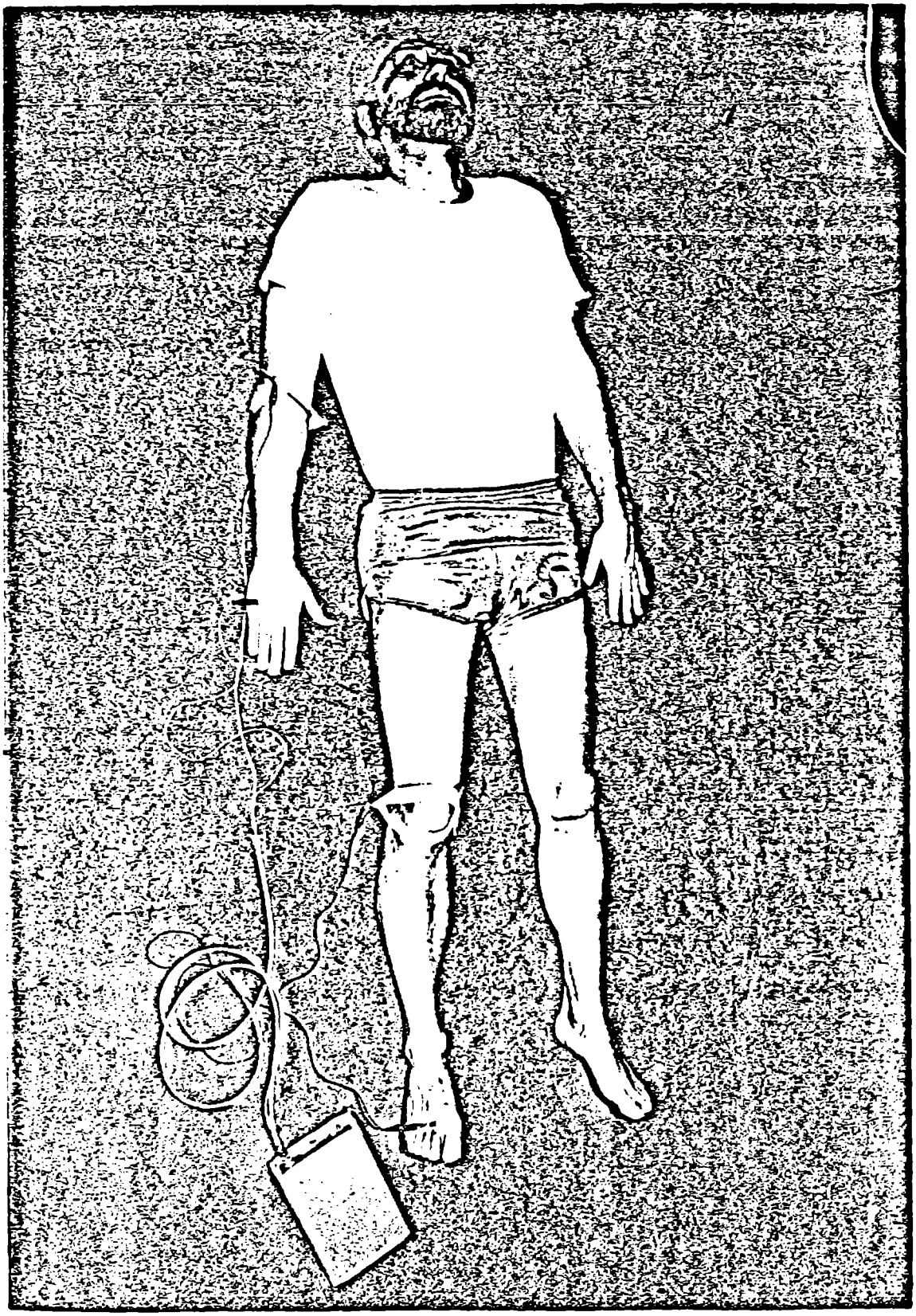


FIGURE 6



Appendix A

DCCT FORMS

DIABETES CONTROL AND COMPLICATIONS TRIAL

Initial Clinic Visit

This form is to be completed whenever a potential patient first visits the DCCT clinic. The form serves several purposes:

1) It records the patient's name, address and telephone number.
2) Individuals who are obviously ineligible to participate in the study can be informed of this fact straight-away, so that they need not be further evaluated.
3) A record will be kept of the number of people who visited your clinic, how they heard about the study, and why various individuals were found ineligible. This information will be useful in planning future recruitment efforts.

In completing this form, you may check a box marked "HOLD" which indicates a condition has been found which makes the subject temporarily ineligible for the study. In this case, you should continue the interview to see if there are any further reasons why the subject cannot participate. If a box with "STOP" is checked, a condition has been found which causes the patient to be permanently ineligible to participate. But again, continue the interview. We are interested in collecting information on all interviewees.

When you have finished asking all of the screening questions, you should look over the responses to see if any STOP boxes were checked. If so, you should explain to the subject why he/she will not be eligible for the DCCT. If no STOP boxes were checked, but one or more HOLD boxes were, you should explain to the subject why he/she is temporarily ineligible for the study.

Everyone who visits a DCCT clinic is assigned a Patient ID Number. The five-digit Patient ID Number is simply the two-digit DCCT Clinic Number followed by a three-digit accession number. (Thus, for example, the first patient visiting Clinic 15 will have ID Number 15001. The second patient visiting this clinic will have ID Number 15002 even if the first patient had been found ineligible and will not be participating.) When a patient is transferred from one DCCT clinic to another, the patient retains his original ID Number. This screening form is not to be used for transferred patients; Form 039, Notification of Clinic Transfer, should have been completed by the Clinic Coordinator at the patient's previous clinic.

Each interviewee is assigned another identifier in addition to the Patient ID Number. This second identifier comprises the patient's first, middle and last initials. If the patient has no middle name or initial, an "X" is used as the middle initial. The initials identifier, once determined, is never changed, although the patient may change his/her name during the course of the study.

In the event that the patient is being rescreened, i.e., was screened once before and was found ineligible at that time, the Patient's ID Number must be changed and his/her initials may be changed.

Send the originals (white copies) of pages 2 and 3 of this form to the DCCT Coordinating Center in the weekly forms mailing. Keep page 1 and the yellow copies of pages 2 and 3 in the clinic files.

A. SUBJECT'S NAME, ADDRESS AND TELEPHONE NUMBER

1. Subject's name: Mr. / Ms. / Mrs. / Miss _____ (First Name) _____ (Middle Initial) _____ (Last Name)

2. Subject's address: _____ (Number and Street)

_____ (City) _____ (State or Province) _____ (Zip Code)

3. Subject's home phone number: _____ (Area Code and Number)

Patient ID _____

B. PATIENT IDENTIFICATION

1. Enter the Clinic Number: __ __

2. Enter the Patient ID Number: (If patient is being restarted, use next available ID) __ __ __ __ __

3. Enter the Patient's Initials: (First, Middle or "X", Last) __ __ __

4. Enter today's date: __ __ Month __ __ Day __ __ Year

C. SCREENING QUESTIONS

1. How did the subject learn of the Diabetes Control and Complications Trial? (CHECK ALL THAT APPLY; SPECIFY ON THE LINE PROVIDED)

a) Local chapter of American Diabetes Association (1)

b) Local chapter of Juvenile Diabetes Foundation (1)

c) Advertisement in newspaper (1)

d) Advertisement in magazine/journal (1)

e) Article in newspaper or journal (1)

f) Radio or television announcement (1)

g) Poster at health care center (1)

h) Referred by private physician (1)

i) Contacted by DCCT clinic personnel (1)

j) Other source: (1)

Specify: _____

2. Was the subject referred to your clinical center via the interactive telephone technology (i.e., screened by the 800 number)? No (1) Yes (2)

3. What is the subject's gender? Male (1) Female (2)

4a) When was the subject born? __ __|__ __|__ __ Month Day Year

b) What is the subject's age? __ __ Years

c) If 40 years old or older, check here: STOP (1)

d) If less than 13 years old, check here: HOLD (1)

5a) Has the subject been diagnosed as having insulin-dependent diabetes? No STOP (1) Yes (2)

b) If YES, how long ago did the subject begin using insulin? (IF LESS THAN ONE YEAR, ENTER 00) __ __ Years

c) Month and year began using insulin __ __ Month __ __ Year

d) If more than 15 years ago, check here: STOP (1)

e) If less than one year ago, check here: HOLD (1)

6. Does the subject plan a permanent move outside of North America? No (1) Yes STOP (2)

7. Answer this question if the patient is female.

a) Is the subject pregnant? No (1) Yes HOLD (2)

b) Does the patient plan or desire to become pregnant within the next two years? No (1) Yes STOP (2)

c) When is the baby due?
__ __|__ __|__ __

8. Has the subject ever used an insulin infusion pump for more than four weeks at a time for a reason other than to manage an illness or to determine optimal blood glucose control? (For a female subject who used the insulin pump during pregnancy or while planning a pregnancy, and who will have been using only one or two insulin injections per day for at least one year by the time of randomization, answer NO.) No (1) Yes STOP (2)

Patient ID ________________

9. Has the subject ever used three or more injections of insulin per day for more than four weeks at a time for a reason other than to manage an illness or determine optimal blood glucose control? (For a female subject who used three or more insulin injections per day during pregnancy or while planning a pregnancy, and who will have been using only one or two insulin injections per day for at least one year by the time of randomization, answer NO.) — No (1) / Yes STOP (2)

10. Has the subject's eyes ever received laser treatment (photocoagulation)? — No (1) / Yes STOP (2)

11. During the past year, has the subject had any chronic disease requiring, for more than a total of four months, a prescription medication which is listed as an excluding medication in Table 8.6 of the Manual of Operations? — No (1) / Yes STOP (2)

12. Ask the subject to list any medical problems which he/she has other than diabetes. Does the subject report a history of a medical condition which makes him/her ineligible? (See Table 8.4 of the Manual of Operations) — No (1) / Yes STOP (2)

If YES, specify medical condition:

____

D. PREVIOUS SCREENING

1. Is the patient a "restart," i.e., was the patient previously screened for eligibility? — No (1) / Yes (2)

> 2a) Previous ID Number: _ _ _ _ _
>
> b) Previous initials: _ _ _
>
> 3. Reason for not being enrolled:
>
> ______________________________

E. CONCLUSION OF SCREENING QUESTIONS

1. Is the subject potentially eligible and willing to participate at this time? — No (1) / Yes (2)

> SKIP QUESTIONS 2 and 3

2. The exclusion decision to not participate is considered:

Permanent (1)

Temporary (2)

3. Specify the reason for ineligibility if a STOP or HOLD box has been checked. (CHECK ALL THAT APPLY. IF ITEM (f) IS CHECKED, BRIEFLY STATE THE REASON, USING ONE BOX FOR EACH LETTER.)

a) Moving away (1)

b) Time commitment too great for patient or family or other incompatible with lifestyle (1)

c) Patient or family refuses randomization or strongly prefers one treatment group (1)

d) Lack of interest of patient or family (1)

e) Lack of support from family (1)

f) Other (1)

|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

Type or print name of person completing this form:

____

Certification Number (if any)

_ _ - _ _

DIABETES CONTROL AND COMPLICATIONS TRIAL
Baseline Medical History and Physical Examination

The Baseline Medical History and Physical Examination should be one of the first eligibility evaluations that a potential patient undergoes. Prior to completing this form, the Initial Clinic Visit Form (DCCT Form 001) should have been completed to exclude patients who are obviously ineligible.

In completing this form, you may check a box marked "STOP." This indicates that a condition has been found which makes the patient permanently ineligible for the study. If you check a STOP box in Sections A-C of this form, continue to complete these three Sections. If a STOP box is checked in any other Section of the form, you may stop completing the form at that point, but complete Section L.

If a box marked "HOLD" is checked, the patient is temporarily ineligible for the study. One should continue to complete the form to see if the patient is otherwise eligible, but the patient cannot be randomized until or unless the HOLD condition is removed.

If the patient is judged ineligible on the basis of a finding during the baseline history and physical, the reason(s) for exclusion must be noted on the Eligibility and Exclusion Checklist (DCCT Form 038).

The original of this form should be send to the Coordinating Center in the weekly forms mailing. Retain a copy in the clinic files.

A. IDENTIFYING INFORMATION

1. Clinic Number — —
2. Patient ID Number — — — — —
3. Patient's Initials — — —
4. Date of Visit — — / — — / — —
   Month / Day / Year

B. DEMOGRAPHIC AND GENERAL INFORMATION

1a) Birthdate: — — / — — / — —
   Month / Day / Year

b) Is the patient less than 13 years of age?	No (1)	Yes HOLD (2)
c) Is the patient 40 years of age or older?	(1)	STOP (2)

2. Sex:
   - Male (1)
   - Female (2)

3. *Predominant* Race/Ethnicity: (CHECK ONLY ONE. SEE CHAPTER 6 OF THE MANUAL OF OPERATIONS)
   - White, not of Hispanic Origin (1)
   - Black, not of Hispanic Origin (2)
   - Hispanic (3)
   - Asian or Pacific Islander (4)
   - American Indian or Alaskan Native (5)

4a) Marital status of patient: (CHECK ONLY ONE)
   - Never married (1)
   - Married or remarried (2)
   - Separated (3)
   - Divorced (4)
   - Widowed (5)

b) If married, how many times? —

c) If married, remarried, separated, divorced, or widowed, how many years since marital status changed? — — . —

5. Occupation of patient and household providers: (CHECK ONLY ONE BOX FOR EACH PERSON DESCRIBED. SEE CHAPTER 6 OF THE MANUAL OF OPERATIONS. IF THE PATIENT IS MARRIED, INDICATE THE OCCUPATION OF HIS/HER SPOUSE. IF NOT MARRIED AND IF LIVING WITH PARENT(S), INDICATE OCCUPATION(S) OF PARENT(S). IF LIVING WITH GUARDIAN OR FRIEND WHO PROVIDES ECONOMIC SUPPORT TO THE PATIENT'S HOUSEHOLD, INDICATE OCCUPATION OF GUARDIAN/FRIEND. ALWAYS INDICATE OCCUPATION OF PATIENT. IF ANY OF THESE ARE RETIRED OR CURRENTLY UNEMPLOYED, CHECK CATEGORY CORRESPONDING TO THE TYPE OF OCCUPATION WHICH THE INDIVIDUAL DID OR COULD DO; ALSO CHECK THE CORRESPONDING BOX MARKED "UNEMPLOYED OR RETIRED.")

	Patient	Spouse	Mother	Father	Guardian/ Friend
a) Professional, technical, or similar worker	(1)	(1)	(1)	(1)	(1)
Manager, official, or proprietor	(2)	(2)	(2)	(2)	(2)
Craftsman, foreman, or similar worker	(3)	(3)	(3)	(3)	(3)
Clerical or similar worker	(4)	(4)	(4)	(4)	(4)
Sales worker	(5)	(5)	(5)	(5)	(5)
Operative or similar worker	(6)	(6)	(6)	(6)	(6)
Service worker	(7)	(7)	(7)	(7)	(7)
Laborer	(8)	(8)	(8)	(8)	(8)
Farmer	(9)	(9)	(9)	(9)	(9)
Homemaker	(10)	(10)	(10)	(10)	(10)
Student	(11)	(11)	(11)	(11)	(11)
Other or unknown	(12)	(12)	(12)	(12)	(12)
b) Unemployed or retired	(1)	(1)	(1)	(1)	(1)

6. Education of patient and household providers: (CHECK HIGHEST COMPLETED BY EACH PERSON FOR WHOM OCCUPATION IN GIVEN IN QUESTION 5)

	Patient	Spouse	Mother	Father	Guardian/ Friend
Graduate school	(1)	(1)	(1)	(1)	(1)
College graduate	(2)	(2)	(2)	(2)	(2)
Some college or trade school	(3)	(3)	(3)	(3)	(3)
Secondary school graduate	(4)	(4)	(4)	(4)	(4)
Some secondary school	(5)	(5)	(5)	(5)	(5)
Elementary school	(6)	(6)	(6)	(6)	(6)
None	(7)	(7)	(7)	(7)	(7)
Unknown	(8)	(8)	(8)	(8)	(8)

Patient ID _____

		No	Yes
7a)	Is the patient currently a student?	(1)	(2)
b)	If YES, note current level in school:		
	If in elementary or secondary school, grade:		__ __
	If in trade school, year:		__
	If in college, year:		__
	If in graduate school, year:		__
8.	Is the patient currently participating in another medical study which may interfere with his/her participation in the DCCT?	(1)	(2) HOLD
9.	Does the patient have a spouse, child, parent, sibling or household member participating in the DCCT in any capacity?	(1)	(2) STOP
10.	Has the patient been treated for hypertension at any time within the past two years?	(1)	(2) HOLD
11a)	Is the patient currently taking any prescribed medication?	(1)	(2)
b)	Has the patient required any prescribed medication for more than a total of four months during the past year?	(1)	(2)
c)	If YES to either 11a or 11b, are any of these medications listed as excluding ones in Chapter 8 of the Manual of Operations?	(1)	(2) STOP

If YES, specify all excluding medications:

_____

_____

_____

If NO, specify all non-excluding medications:

_____

_____

_____

C. DIABETES HISTORY

1a) Date patient first uninterruptedly began using insulin (use best estimate): __ __ / __ __ (Month / Year)

If unknown, give range: __ __ - __ __ years ago

		No	Yes
b)	At the time of randomization, will the patient have been using insulin uninterruptedly for less than one year?	(1)	(2) HOLD
c)	At the time of randomization, will the patient have been using insulin uninterruptedly for more than 15 years?	(1)	(2) STOP

2. Conditions, symptoms and circumstances present at onset: (ANSWER EACH)

	Absent	Present	Unknown
a) Ketonuria	(1)	(2)	(3)
b) Suspected ketoacidosis	(1)	(2)	(3)
c) Documented ketoacidosis	(1)	(2)	(3)
d) Other, specify:	(1)	(2)	(3)

_____

_____

		No	Yes
3.	Has the patient ever used oral hypoglycemics?	(1)	(2)

If YES, list by date those used and dose:

_____

_____

_____

Patient ID _____

4. Has the patient ever received treatment for diabetes with three or more daily injections of insulin or with an insulin infusion pump (except for periods of less than four weeks to manage an intercurrent illness or to determine optimal blood glucose control or for a period at least one year ago for management of a pregnancy)? No (1) Yes STOP (2)

5. Number of episodes of DKA requiring hospitalization in past YEAR: __ __

6. Is the number of episodes of DKA in Question 5 greater than two? No (1) Yes STOP (2)

7. Number of hospitalizations for hypoglycemia in past YEAR: (Hospitalization implies overnight admission to the hospital; an emergency ward visit that did not result in hospitalization does not apply.) __ __

   If any, give specific reasons:

   _____

   _____

   _____

8. How many times during the past YEAR did the patient experience hypoglycemia of such severity that the patient

   a) lost consciousness without seizure __ __

   b) lost consciousness with seizure __ __

9. How many times during the past YEAR did the patient experience hypoglycemia of such severity that the patient required professional medical assistance, including placement of an IV or an intravenous injection of glucose? __ __

10. How many times during the past YEAR did the patient experience hypoglycemia of such severity as to require the assistance of another person, such as for the administration of parenteral glucagon, but not require any of the assistance described above? __ __

11. How many times during the past YEAR did the patient experience hypoglycemia of such severity as to require the assistance of another person but did not require any of the help described above? __ __

12. How many times during the past MONTH did the patient experience hypoglycemia which was mild enough for the patient to treat himself/herself? __ __

13. What is the total number of times *EVER* that the patient has lost consciousness due to hypoglycemia? (ESTIMATE) __ __

14. Has the patient experienced more than two hypoglycemic seizures and/or coma during the past two years? No (1) Yes STOP (2)

15. Does the patient have a history of recurrent hypoglycemic episodes resulting in cerebral impairment (e.g., coma, severe confusion, seizure) before the development of warning symptoms of hypoglycemia (e.g., excessive sweating, tremors, etc.)? No (1) Yes STOP (2)

Patient ID _____

D. ROUTINE DIABETES CARE

1. Routine Insulin Therapy

a) Indicate types of insulin used: (CHECK ALL THAT APPLY)

Conventional beef/pork	(1)
Highly purified beef	(1)
Highly purified pork	(1)
Human	(1)
Other; specify: _____	(1)

b) Specify average dose in units: (IF ZERO, ENTER 00)

AM:	Long-acting or Ultralente	__ __
	NPH or lente	__ __
	Regular or Semi-lente	__ __
PM:	Long-acting or Ultralente	__ __
	NPH or lente	__ __
	Regular or Semi-lente	__ __

2. Routine Diet

a) Indicate type of diet followed: (THE TYPE OF DIET ACTUALLY FOLLOWED, WHICH MAY OR MAY NOT BE THE SAME AS THAT PRESCRIBED)

Unrestrcted (free)	(1)
Avoid sweets	(2)
Exchange or point system	(3)
Grams, carbohydrate or caloric	(4)
Other; specify: _____	(5)

	No	Yes
b) Does the patient's current diet include a daily caloric prescription?	(1)	(2)

c) If YES to b), enter caloric prescription: __ __ __ __

3. Glucose Monitoring

a) On the average, how many times per week does the patient monitor his/her urine for glucose? (IF ZERO, WRITE 00) __ __

b) On the average, how many times per week does the patient monitor his/her blood for glucose? (IF ZERO, WRITE 00) __ __

	No	Yes
c) Does the patient adjust his/her insulin dose based on the results of self blood glucose monitoring?	(1)	(2)

4. Diabetes Care

a) During the past YEAR, how many routine, scheduled PHYSICIAN contacts did the patient have for diabetes care? __ __

b) During the past YEAR, how many routine, scheduled NURSE contacts did the patient have for diabetes care? __ __

c) During the past YEAR, how many routine, scheduled DIETITIAN contacts did the patient have for diabetes care? __ __

d) Setting of diabetes care: (CHECK ONLY ONE)

Family practitioner	(1)
Pediatrician	(2)
Diabetologist	(3)
Internist	(4)
Other; specify: _____	(5)

Patient ID _____

E. GENERAL MEDICAL HISTORY

1a) Does the patient have any allergies to medications? No (1) Yes (2)

If YES, list:

_____

_____

_____

b) Does the patient have any allery to fluorescein? No (1) Yes (2) Unknown (3)

2. On the average, how many aspirin-containing tablets or other prostaglandin inhibitors does the patient use each month? (IF NONE, ENTER 000) ___

3. Does the patient have a history of drug, alcohol or substance abuse during the past five years? No (1) Yes STOP (2)

4. Does the patient have a history of an endocrine disorder (other than diabetes, corrected primary hypothyroidism, or functional menstrual disorders)? No (1) Yes STOP (2)

Specify: _____

_____

_____

5. Does the patient have any non-diabetic condition that potentially limits life expectancy or that will interfere with participation in the study? No (1) Yes STOP (2)

Patient ID _____

F. SMOKING HISTORY

1. Has the patient ever smoked cigarettes or cigarillos daily? No (1) Yes (2)

   If NO, skip to Question 8.

2. Does the patient now smoke cigarettes or cigarillos? No (1) Yes (2)

   If NO, skip to Question 4.

3. On the average, how many cigarettes or cigarillos a day does the patient now smoke?

   Cigarettes or cigarillos per day: __ __

4a) How long has it been since the patient quit smoking cigarettes or cigarillos?
   __ __ Years __ __ Months

   b) If the patient has never quit, check here: (1)

5. At what age did the patient first become a daily cigarette or cigarillo smoker? __ __ Years of age

6. For how many months (or years) altogether has the patient quit smoking cigarettes and cigarillos since he/she first started?
   __ __ Years __ __ Months

7. On the average, how many cigarettes or cigarillos a day did the patient smoke during the period in his/her life when he/she was smoking the heaviest?

   Cigarettes or cigarillos per day: __ __

8. Has the patient ever smoked pipes or cigars daily? No (1) Yes (2)

   If NO, go to Section G.

9. Does the patient now smoke pipes or cigars? No (1) Yes (2)

   If NO, skip to Question 11.

10. On the average, how many pipefuls or cigars a week does the patient now smoke?

    Pipefuls or cigars per week: __ __ __

11a) How long has it been since the patient last quit smoking pipes or cigars?
   __ __ Years __ __ Months

   b) If the patient has never quit, check here: (1)

12. At what age did the patient first become a daily pipe or cigar smoker? __ __ Years of age

13. For how many months (or years) altogether has the patient quit smoking pipes and cigars since he/she first started?
   __ __ Years __ __ Months

14. On the average, how many pipefuls or cigars a week did the patient smoke during the period in his/her life when he/she smoked the heaviest?

    Pipefuls and cigars per week: __ __ __

Patient ID _____

G. DRINKING HISTORY

1. Has the patient ever consumed an average of at least one alcoholic beverage per week for a period of one year or more? No (1) Yes (2)

   If NO, go to Section H.

2. During the past year, has the patient consumed an average of at least one alcoholic beverage per week? No (1) Yes (2)

   If NO, go to Question 8.

3. How many 12-oz. bottles of beer (excluding "light" beer) did the patient consume during the past seven days? (IF THE PAST SEVEN DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) (A) Bottles

4. How many 12-oz. bottles of "light" beer did the patient consume during the past seven days? (IF THE PAST SEVEN DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) (B) Bottles

5. How many 4-oz. glasses of wine did the patient consume during the past seven days? (IF THE PAST SEVEN DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) (C) Glasses

6. How many 1 1/2-oz. shots of straight hard liquor and 1 1/2-oz. mixed drinks did the patient consume during the past seven days? (IF THE PAST SEVEN DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) (D) Drinks

7. Does the total amount of alcohol consumed by the patient in the past seven days (OR IN A TYPICAL WEEK) exceed 560 grams? No (1) Yes HOLD (2)

   Use this table if necessary:

	AMOUNT	X	GRAMS	
(A)	___	X	13 =	_____
(B)	___	X	10 =	_____
(C)	___	X	12 =	_____
(D)	___	X	15 =	_____

   TOTAL GRAMS OF ALCOHOL PER WEEK _____

8. Has the patient had periods where his/her alcohol consumption was greater than it is now? No (1) Yes (2)

   If NO, go to Section H.

NOTE: Questions 9 through 14 refer to the period in the patient's life when his/her weekly alcohol consumption was the heaviest. Ask the patient to consider this period.

9. On the average during this period of heaviest alcohol consumption, how many 12-oz. bottles of beer (excluding "light" beer) did the patient consume per week? (E) Bottles

10. On the average during this period, how many 12-oz. bottles of "light" beer did the patient consume per week? (F) Bottles

11. On the average during this period, how many 4-oz. glasses of wine did the patient consume per week? (G) Glasses

12. On the average during this period, how many 1 1/2-oz. shots of straight hard liquor or 1 1/2-oz. mixed drinks did the patient consume per week? (H) Drinks

13. Did the average amount of alcohol consumed by the patient during this period exceed 560 grams per week? No (1) Yes (2)

    Use this table if necessary:

	AMOUNT	X	GRAMS	
(E)	___	X	13 =	_____
(F)	___	X	10 =	_____
(G)	___	X	12 =	_____
(H)	___	X	15 =	_____

    TOTAL GRAMS OF ALCOHOL PER WEEK _____

14. If Question 13 is answered YES,
    (i) did this period of heaviest alcohol consumption last for more than five years? No (1) Yes (2)

    (ii) did this period last for at least one month and end less than five years ago? No (1) Yes STOP (2)

H. EXERCISE AND ACTIVITY

1. Which of the following best describes the patient's level of activity on the job, at school or, for homemakers, in homemaking?

   Sedentary (such as office work with occasional inter-office walking, etc.; e.g. secretary) (1)

   Moderate Activity (requires considerable, but not constant, lifting, walking, bending, pulling, etc.; e.g., homemaker with family and without domestic assistance; policeman; student taking physical education course) (2)

   Strenuous Activity (requires almost constant lifting, bending, pulling, scrubbing, etc.; e.g., furniture mover; heavy domestic work) (3)

2. During the past seven days, how many hours and minutes did the patient spend in the following types of leisure time activities? (IF THE PAST SEVEN DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.)

   Light Activity
   (Examples: billiards; bowling; ballroom dancing; golf with power cart; non-competitive volleyball.) Hours Minutes

   Moderate Activity
   (This level is marked by modest increases in heart rate and breathing. Most healthy individuals find these activities comfortable and can continue them for a few hours without undue fatigue. Examples: leisure cycling (5.5 mph); frisbee playing; horseback riding; sailing; table tennis; croquet; golf without power cart.) Hours Minutes

   Hard Activity
   (When exercising at this intensity most people will have noticeable increases in breathing and will likely perspire. Most untrained people could not exercise at this intensity without taking frequent rest periods. Examples: cycling (9.4 mph); half-court basketball; water skiing; downhill skiing; karate or judo; doubles tennis; roller skating; gymnastics.) Hours Minutes

   Very Hard Activity
   (Includes strenuous sports involving a lot of movement or running. Only a well-trained individual can perform at this intensity for extended periods of time. Examples: racing cycling; football; full-court basketball; rapid marching; squash; continuous, moderate to fast swimming; rope jumping; cross-country skiing; cross-country running; singles tennis; field hockey.) Hours Minutes

I. FAMILY MEDICAL HISTORY

1. Number of persons living in the patient's household: (INCLUDE THE PATIENT) __ __

2. Diabetic history of patient's blood-related parents:

	DIABETIC? No	Yes	Unknown	IF DIABETIC, TREATED WITH INSULIN? No	Yes	Unknown	IF DIABETIC, ENTER ESTIMATED AGE AT ONSET. IF AGE AT ONSET WAS LESS THAN 1 YEAR, ENTER 01. IF UNKNOWN, ENTER 00.
Father:	(1)	(2)	(3)	(1)	(2)	(3)	__ __
Mother:	(1)	(2)	(3)	(1)	(2)	(3)	__ __

3. Diabetic history of patient's blood-related siblings:

a) How many siblings does/did the patient have? __ __

If none, enter 00 and go to Question 4. If unknown (such as if adopted), enter 99 and go to Question 4.

b) How many of these are/were known to be diabetic? __ __

If none, enter 00. If unknown, enter 99.
If any, complete the following for these diabetic siblings:

	TREATED WITH INSULIN? No	Yes	Unknown	ESTIMATED AGE AT ONSET. IF UNKNOWN, ENTER 00. IF LESS THAN ONE YEAR, ENTER 01.
Oldest diabetic sibling:	(1)	(2)	(3)	__ __
2nd oldest:	(1)	(2)	(3)	__ __
3rd oldest:	(1)	(2)	(3)	__ __

4. Diabetic history of patient's blood-related children:

a) How many children does/did the patient have? __ __

If none, enter 00 and go to Question 5.

b) How many of these are/were known to be diabetic? __ __

If none, enter 00.
If any, complete the following for these diabetic children:

	TREATED WITH INSULIN? No	Yes	Unknown	ESTIMATED AGE AT ONSET. IF UNKNOWN, ENTER 00. IF LESS THAN ONE YEAR, ENTER 01.
Oldest diabetic child:	(1)	(2)	(3)	__ __
2nd oldest:	(1)	(2)	(3)	__ __
3rd oldest:	(1)	(2)	(3)	__ __

5. If a parent or sibling is deceased, specify relation to patient and relative's cause of death and age at death:

_____

6. Is there a family history of diseases of the following types? (Consider parents, grandparents, siblings, children)

	Parents			Grandparents			Siblings				Children			
	Yes	No	Un-known	Yes	No	Un-known	Yes	No	Un-known	Not Applic-able	Yes	No	Un-known	Not Applic-able
a) Hypertension	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
b) Myocardial infarction	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
(i) If YES, before age 40?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
(ii) If YES to (i), in a diabetic person?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
c) Autoimmune endocrine disease	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
d) Serious eye disease or blindness	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
If YES, due to diabetes?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
e) Renal disease	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
If YES, due to diabetes?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
f) Psychiatric disorders	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
g) Neurologic disease	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
If YES, due to diabetes?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
h) Hyperlipidemia	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)

J. REVIEW OF SYSTEMS

The Review of Systems covers many of the exclusion criteria listed in Chapter 8 of the Manual of Operations. Other exclusion criteria exist, and the clinician should question the patient concerning all the exclusion criteria. In addition, for each of the following categories, the question is asked whether the Principal Investigator chooses to exercise his/her right to exclude the patient because the patient has a medical condition which may significantly interfere with the patient's participation in the DCCT, but is not listed as an exclusion criterion in the Protocol or Manual or is not listed below as a STOP condition.

1. SKIN

a) Does the patient have a history of any of the following?	No	Yes
Eruptive xanthoma	(1)	(2)
Xanthelasma	(1)	(2)
Necrobiosis	(1)	(2)
Shin spot (diabetic dermopathy)	(1)	(2)
b) Other significant skin condition?	(1)	(2)

If YES, specify: _____

_____

c) Will the patient be excluded on the basis of a skin condition?	No	Yes STOP
	(1)	(2)

2. MUSCULOSKELETAL

a) Does the patient have a history of any of the following?	No	Yes
Arthritis	(1)	(2)
Muscle pain or weakness	(1)	(2)
b) Other significant musculoskeletal condition?	(1)	(2)

If YES, specify: _____

_____

c) Will the patient be excluded on the basis of a musculoskeletal condition?	No	Yes STOP
	(1)	(2)

3. EXTREMITIES

a) Does the patient have a history of any of the following?	No	Yes STOP
Gangrene	(1)	(2)
Amputation	(1)	(2)
Ulcers	(1)	(2)
Cellulitis	(1)	(2)
Charcot joints	(1)	(2)
b) Other significant conditions of the extremities?	(1)	(2)

If YES, specify: _____

_____

c) Will the patient be excluded on the basis of a condition of the extremities (other than the listed STOPs)?	No	Yes STOP
	(1)	(2)

4. EYES

a) Does the patient have a history of any of the following?	No	Yes
Severe myopia	(1)	(2)

IF YES, CONSIDER PERFORMING THE OPHTHALMIC EXAMINATION EARLY IN THE ELIGIBILITY SCREENING PROGRAM

	No	Yes
Abnormal color vision	(1)	(2)

IF YES, NOTE THAT THIS MAY INTERFERE WITH THE PATIENT'S USE OF THE GLUCOSE-INDICATING STRIPS.

	No	Yes STOP
Photocoagulation	(1)	(2)
Aphakia (cataract extraction)	(1)	(2)
Glaucoma requiring medication	(1)	(2)

Patient ID _____

4. EYES (Continued)

	No	Yes
b) Other significant eye pathology?	(1)	(2)

If YES, specify: _____

_____

	No	Yes
c) Will the patient be excluded on the basis of an eye pathology (other than the listed STOPs)?	(1)	STOP (2)

5. EARS, NOSE, MOUTH AND NECK

	No	Yes
a) Does the patient have a history of any significant pathology of the ears, nose, mouth or neck?	(1)	(2)

If YES, specify: _____

_____

	No	Yes
b) Will the patient be excluded on the basis of an ear, nose, mouth or neck pathology?	(1)	STOP (2)

6. RESPIRATORY

	No	Yes
a) Does the patient have a history of any significant respiratory pathology?	(1)	(2)

If YES, specify: _____

_____

	No	Yes
b) Will the patient be excluded on the basis of a respiratory pathology?	(1)	STOP (2)

7. CARDIOVASCULAR

a) Does the patient have a history of any of the following?

	No	Yes
Hypertension, treated, but not within past 2 years	(1)	(2)
Hypertension, untreated	(1)	(2)

7. CARDIOVASCULAR (Continued)

ALERT: A patient may be excluded on the basis of a high blood pressure. See Section G: Physical Examination.

	No	Yes
Hypertension, treated within past 2 years	(1)	HOLD (2)
Angina	(1)	STOP (2)
Congestive heart failure	(1)	STOP (2)
Myocardial infarction	(1)	STOP (2)
Coronary heart disease	(1)	STOP (2)
Peripheral vascular disease	(1)	STOP (2)
Arrhythmia requiring treatment	(1)	STOP (2)
Transient ischemic attacks	(1)	STOP (2)
Atherothrombotic brain infarction	(1)	STOP (2)
Palpitations or other arrhythmia not requiring medication	(1)	(2)
Heart murmur	(1)	(2)
Intermittent claudication	(1)	STOP (2)
Treatment for hyperlipidemia not due to IDDM	(1)	STOP (2)

	No	Yes
b) Other significant cardiovascular condition?	(1)	(2)

If YES, specify: _____

_____

	No	Yes
c) Will the patient be excluded on the basis of a cardiovascular condition (other than the listed STOPs)?	(1)	STOP (2)

Patient ID _____

8. GASTROINTESTINAL

a) Does the patient have a history of any of the following?

	No	Yes
Liver disease, jaundice	(1)	(2)
If YES, is it a chronic condition?	(1)	STOP (2)
Pancreatitis	(1)	(2)
If YES, is it a chronic condition?	(1)	STOP (2)

b) Other significant gastrointestinal condition? (1) (2)

If YES, specify: _____

_____

c) Will the patient be excluded on the basis of a gastrointestinal condition (other than the listed STOPs)? No (1) Yes STOP (2)

9. GENITOURINARY

Note that the patient may be excluded depending on the severity of any pre-existing nondiabetic kidney disease.

a) Does the patient have a history of any of the following?

	No	Yes
Diseases of the upper urinary tract (e.g., kidney calculi, renal congenital abnormalities, pyelonephritis, etc.)	(1)	(2)

If YES, (i) specify: _____

_____

(ii) has this been a chronic problem requiring treatment?	No (1)	Yes (2)

(iii) how has this been documented?

_____

_____

9. GENITOURINARY (Continued)

Diseases of the lower urinary tract (e.g., cystitis, gonorrhea, congenital abnormalities, etc.)	No (1)	Yes (2)

If YES, (i) specify: _____

_____

(ii) has this been a chronic problem requiring treatment?	(1)	(2)
Family history of urinary tract diseases (e.g., Alport's, polycystic kidney, etc.)	(1)	(2)

If YES, specify: _____

_____

Diseases of the genital tract (e.g., absence of one testicle, testicular atrophy (mumps), venereal diseases, etc.)	(1)	(2)

If YES, specify: _____

_____

Kidney or bladder infection requiring antibiotics	(1)	(2)

If YES, specify numbers of infections ever:

Kidney __ __

Bladder __ __

Both or Uncertain __ __

b) Will the patient be excluded on the basis of a genitourinary condition? No (1) Yes STOP (2)

Patient ID _____

10. NEUROLOGIC

a) Does the patient have a history of any of the following?

	No	Yes	Not Applicable
Severe symptomatic peripheral neuropathy	(1)	(2)	
Seizures	(1)	(2)	
Impotence (psychogenic, endocrine, other)	(1)	(2)	(3)

If YES, specify: _____

_____

b) Is the patient currently using autonomic nervous system drugs? No (1) Yes STOP (2)

If YES, list: _____

_____

c) In the past year, has the patient ever experienced dizziness, lightheadedness or loss of consciousness upon standing up (not due to hypoglycemia)? No (1) Yes (2)

d) In the past year, has the patient ever taken medication for dizziness, lightheadedness or loss of consciousness upon standing up (not due to hypoglycemia)? No (1) Yes STOP (2)

If YES, list medication taken and use duration:

_____

_____

e) Other significant neurologic condition? No (1) Yes (2)

If YES, specify: _____

_____

f) Will the patient be excluded on the basis of a neurologic condition (other than the listed STOPs)? No (1) Yes (2)

11. PSYCHIATRIC

a) Does the patient have a history of any of the following?

Nervousness or anxiety	(1)	(2)
Unreasonable fears	(1)	(2)
Eating disturbance	(1)	(2)
Affective disorder	(1)	(2)
Suicide attempt	(1)	(2)
Criminal conduct	(1)	(2)
Psychiatric hospitalization or outpatient psychiatric treatment which included the use of tranquilizers such as phenothiazines	(1)	(2)

b) Other significant psychiatric condition? (1) (2)

If YES, specify: _____

_____

c) Will the patient be excluded on the basis of a psychiatric condition? No (1) Yes STOP (2)

Patient ID _____

12. FEMALE/REPRODUCTIVE
(SKIP TO QUESTION 13 IF THE PATIENT IS MALE)

a) Does the patient have a history of any of the following?

	No	Yes
Nodules in breast	(1)	(2)
Breast cancer	(1)	(2) STOP
Breast discharge	(1)	(2)
Irregular menses	(1)	(2)
Dysmenorrhea	(1)	(2)
Vaginitis	(1)	(2)

b) Other significant gynecologic condition? (1) (2)

If YES, specify: _____

_____

c) If not menstruating within last three months, check here: (1)

If menstruating, enter date of start of last menstrual period:

__ __ Month __ __ Day __ __ Year

d) Number of pregnancies: __ __

e) Number of live births: __ __

f) Has the patient ever used oral contraceptives? No (1) Yes (2)

If YES, (i) specify type of drug and use duration:

_____

_____

(ii) Is the patient currently using oral contraceptives? No (1) Yes (2)

g) Does the patient use any other form of birth control? No (1) Yes (2)

If YES, specify: _____

_____

h) Will the patient be excluded on the basis of a gynecologic condition (other than the listed STOP)? No (1) Yes (2) STOP

13. OTHER

a) Does the patient have a history of any of the following?

Hypothyroidism No (1) Yes (2)

If YES, was it treated? (1) (2)

Connective tissue disease (polyarteritis, SLE, scleroderma, rheumatoid arthritis) No (1) Yes (2) STOP

If YES, specify: _____

_____

Blood diseases (monoclonal gammopathy, multiple myeloma, pernicious anemia, sickle cell anemia) No (1) Yes (2) STOP

Gastric surgery (phloroplasty, vagotomy, Billroth I/II) (1) (2)

If YES, specify: _____

_____

b) Does the patient have a history of any medical condition other than those listed above for which he/she will be excluded? No (1) Yes (2) STOP

If YES, specify: _____

_____

Patient ID _____

K. PHYSICAL EXAMINATION

1. Date of physical examination __ __ / __ __ / __ __ (Month / Day / Year)

2. VITAL SIGNS

a) Sitting Blood Pressure: (RIGHT ARM AT LEVEL OF HEART. SEE CHAPTER 18 OF MANUAL OF OPERATIONS.)

Systolic (mm Hg) ___

Diastolic (mm Hg) ___

b) Is the systolic blood pressure and/or the diastolic blood pressure greater than the upper limits in Chapter 8 of the Manual of Operations for a patient of this age and sex? No (1) Yes (2)

IF YES, THE PATIENT MUST RETURN ANOTHER DAY FOR A SECOND DETERMINATION OF SITTING BLOOD PRESSURE. COMPLETE THE INFORMATION IN THE BOX BELOW AT THAT TIME, AND THEN MAIL THIS FORM TO THE COORDINATING CENTER.

c) Date of second sitting blood pressure determination: __ __ / __ __ / __ __ (Month / Day / Year)

d) Sitting Blood Pressure:

Systolic (mm Hg) ___

Diastolic (mm Hg) ___

e) Is the systolic blood pressure and/or the diastolic blood pressure greater than the upper limits given in Chapter 8 of the Manual of Operations for a patient of this age and sex? No (1) Yes STOP (2)

f) Supine Blood Pressure:

Systolic (mm Hg) ___

Diastolic (mm Hg) ___

g) Standing Blood Pressure

Systolic (mm Hg) ___

Diastolic (mm Hg) ___

h) Pulse (bpm) ___

i) Height (cm) ___ . __
(To convert inches to centimeters, multiply by 2.54.)

2. VITAL SIGNS (Continued)

j) Body frame size — Small (1) Medium (2) Large (3)

k) Weight (kg) __ __ __ . __
(To convert pounds to kilograms, multiply by 0.454.)

l) Is the patient at greater than 130% ideal body weight? (SEE TABLE 8.3 OF MANUAL OF OPERATIONS) No (1) Yes HOLD (2)

m) FOR ADOLESCENTS: If available, enter patient's

Height (cm) 12 months ago ___ . __

Height (cm) 24 months ago ___ . __

Weight (kg) 12 months ago ___ . __

Weight (kg) 24 months ago ___ . __

n) FOR ADOLESCENTS: Is the patient known to have failed to maintain normal growth and development during the past two years for any reason? No (1) Yes STOP (2)

3. GENERAL EXAMINATION

a) Examine the patient for abnormalities of the following sites.

	Normal	Abnormal	Not Done
Ears, Nose and Throat	(1)	(2)	
Thyroid	(1)	(2)	
Lungs	(1)	(2)	
Breasts	(1)	(2)	
Abdomen (including organomegaly)	(1)	(2)	
Lymphatic system	(1)	(2)	
Rectum	(1)	(2)	(3)
Pelvis	(1)	(2)	(3)
Genitalia	(1)	(2)	

b) Is the patient at or beyond Tanner Stage II? No HOLD (1) Yes (2)

c) FOR ADOLESCENTS, SPECIFY DEVELOPMENT:

Pubic Hair: Tanner Stage (1-5) ___

Breasts (FEMALES): Tanner Stage (1-5) ___

Patient ID _____

4. EYE EXAMINATION

a) Examine the patient for the following ocular abnormalities.

	RIGHT EYE		LEFT EYE	
Neovascularization or other eye condition that would characterize the eye as P2 or worse. (IF PRESENT, MUST BE CONFIRMED THROUGH FUNDUS PHOTOGRAPHY.)	Absent (1)	Present (2)	Absent (1)	Present (2)
Cataract	(1)	(2)	(1)	(2)
Other fundoscopic abnormality:	(1)	(2)	(1)	(2)

If PRESENT, specify: _____

	No	Yes STOP
b) Based on this ocular examination, will the patient be excluded?	(1)	(2)

5. CARDIOVASCULAR EXAMINATION

a) Examine the patient for the following cardiac abnormalities.

Rhythm	Regular (1)	Irregular (2)
Venous Pressure	Normal (1)	Abnormal (2)
Cardiomegaly	Absent (1)	Present (2)
S3 Gallop	(1)	(2)
S4 Gallop	(1)	(2)
Systolic Ejection Murmur	(1)	(2)
Diastolic Murmur	(1)	(2)
Other Murmur:	(1)	(2)

If PRESENT, specify: _____

Rub	(1)	(2)
Other Cardiac Abnormality:	(1)	(2)

If PRESENT, specify: _____

5. CARDIOVASCULAR EXAMINATION (Continued)

	No	Yes STOP
b) Based on this examination, the history, and the sitting, supine and standing blood pressures, do you believe that the patient has significant cardiovascular disease that should make him/her ineligible for the study?	(1)	(2)

6. PERIPHERAL PULSE EXAMINATION

a) Indicate the grade of the peripheral pulses using the following scale for the right and left pulse.

	RIGHT SIDE			LEFT SIDE		
	Normal	Diminished	Absent	Normal	Diminished	Absent
Carotid	(1)	(2)	(3)	(1)	(2)	(3)
Brachial	(1)	(2)	(3)	(1)	(2)	(3)
Radial	(1)	(2)	(3)	(1)	(2)	(3)
Femoral	(1)	(2)	(3)	(1)	(2)	(3)
Popliteal	(1)	(2)	(3)	(1)	(2)	(3)
Posterior Tibial	(1)	(2)	(3)	(1)	(2)	(3)
Dorsalis Pedis	(1)	(2)	(3)	(1)	(2)	(3)

b) Indicate the presence or absence of bruits.

	RIGHT		LEFT	
	Absent	Present	Absent	Present
Femoral	(1)	(2)	(1)	(2)
Carotid	(1)	(2)	(1)	(2)
Other:	(1)	(2)	(1)	(2)

If PRESENT, specify: _____

	No	Yes
c) Based on these questions and the history, is there evidence of clinically significant peripheral vascular disease?	(1)	(2)

Patient ID _____

7. NEUROLOGIC EXAMINATION

In your opinion, does the patient have significant neuropathy or neurologic disease requiring treatment?

Definitely	(1)	STOP
Questionable	(2)	Consider performing neurologic evaluations early in screening
No	(3)	

8. EXTREMITIES AND SKIN EXAMINATIONS

	RIGHT SIDE Absent	RIGHT SIDE Present	LEFT SIDE Absent	LEFT SIDE Present
Ulceration	(1)	(2)	(1)	(2)
Skin discoloration	(1)	(2)	(1)	(2)
Gangrene	(1)	(2)	(1)	(2)
Charcot joint	(1)	(2)	(1)	(2)
Deformity:	(1)	(2)	(1)	(2)
If PRESENT, specify: _____				
_____				
Lipoatrophy	(1)	(2)	(1)	(2)
Lipohypertrophy	(1)	(2)	(1)	(2)
Any abnormality of the extremities or skin that makes the patient ineligible:	(1)	STOP (2)	(1)	STOP (2)
If PRESENT, specify: _____				
_____				

L. CONCLUSION OF VISIT

1. Was the patient judged ineligible for any reason at this visit?	No (1)	Yes (2)
If YES, specify type of exclusion:		
Temporary	HOLD (1)	
Permanent	STOP (2)	
2. If the patient has been only temporarily excluded, will he/she be reevaluated?	No (1)	Yes (2)

IF THE PATIENT WAS DEEMED INELIGIBLE (PERMANENTLY OR TEMPORARILY), THE ELIGIBILITY AND EXCLUSION CHECKLIST (DCCT FORM 038) MUST INDICATE THE REASON(S) FOR INELIGIBILITY.

Certification Number (if any)

Type or print name of person completing history: _____ __ __ - __ __

Type or print name of person completing physical: _____ __ __ - __ __

*Signature of person reviewing form for completeness: _____

*The form must be reviewed by someone other than the persons who completed the history and physical.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Annual Medical History and Physical Examination

This form is to be completed at each of the annual follow-up clinic visits. At the time of the annual visit, data will be collected on this form to document modifications of therapy and to update information on the status of patients on deviations from assigned treatment and transfers to inactive status.

Unless otherwise indicated, questions on this form refer to the patient's experience since the last completed quarterly clinic visit (i.e., approximately the last 90 days).

If in completing this evaluation it is found that the patient has experienced an intercurrent event, complete the Notification of Intercurrent Event (DCCT Form 020) and, if applicable, the Notification of Hypoglycemic Intercurrent Event (DCCT Form 083).

Send the original of this form to the Coordinating Center in the weekly forms mailing, retaining a copy in the clinic's files.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date of Visit __Month __Day __Year
5. Was it necessary to reschedule the patient for this visit for any reason? No (1) Yes (2)

   How many times? __ __
6. What is the follow-up visit number? __ __
7. Enter the date of the LAST COMPLETED quarterly visit. Unless otherwise specified, all questions on this form refer to the patient's experience since this date.

   __Month __Day __Year

B. DEMOGRAPHIC AND GENERAL INFORMATION

1. Birthdate __Month __Day __Year
2. Gender Male (1) Female (2)

3a) Marital status of patient: (CHECK ONLY ONE)

- Never married (1)
- Married or remarried (2)
- Separated (3)
- Divorced (4)
- Widowed (5)

b) If married, how many times? ___

c) If married, remarried, separated, divorced or widowed, when did marital status change? __Month __Year

4. Occupation of patient and household providers:

(CHECK ONLY ONE BOX FOR EACH PERSON DESCRIBED. SEE CHAPTER 6 OF THE MANUAL OF OPERATIONS. IF THE PATIENT IS MARRIED, INDICATE THE OCCUPATION OF HIS/HER SPOUSE. IF NOT MARRIED AND IF LIVING WITH PARENT(S), INDICATE OCCUPATION(S) OF PARENT(S). IF LIVING WITH GUARDIAN OR FRIEND WHO PROVIDES ECONOMIC SUPPORT TO THE PATIENT'S HOUSEHOLD, INDICATE OCCUPATION OF GUARDIAN/FRIEND. ALWAYS INDICATE OCCUPATION OF PATIENT. IF ANY OF THESE ARE RETIRED OR CURRENTLY UNEMPLOYED, CHECK CATEGORY CORRESPONDING TO THE TYPE OF OCCUPATION WHICH THE INDIVIDUAL DID OR COULD DO; ALSO CHECK THE CORRESPONDING BOX MARKED "UNEMPLOYED OR RETIRED.")

	Patient	Spouse	Mother	Father	Guardian/ Friend
a) Professional, technical or similar worker	(01)	(01)	(01)	(01)	(01)
Manager, offical, or proprietor	(02)	(02)	(02)	(02)	(02)
Craftsman, foreman, or similar worker	(03)	(03)	(03)	(03)	(03)
Clerical or similar worker	(04)	(04)	(04)	(04)	(04)
Sales Worker	(05)	(05)	(05)	(05)	(05)
Operative or similar worker	(06)	(06)	(06)	(06)	(06)
Service worker	(07)	(07)	(07)	(07)	(07)
Laborer	(08)	(08)	(08)	(08)	(08)
Farmer	(09)	(09)	(09)	(09)	(09)
Homemaker	(10)	(10)	(10)	(10)	(10)
Student	(11)	(11)	(11)	(11)	(11)
Other or unknown	(12)	(12)	(12)	(12)	(12)
b) Unemployed or retired	(1)	(1)	(1)	(1)	(1)
c) Check here if the answer to either (a) or (b) above represents a change in the occupation category during the past year	(1)	(1)	(1)	(1)	(1)

( )

5. Education of patient and household providers. (CHECK HIGHEST LEVEL COMPLETED BY EACH PERSON FOR WHOM OCCUPATION IS GIVEN IN QUESTION B.4.)

	Patient	Spouse	Mother	Father	Guardian/ Friend
Graduate School	(1)	(1)	(1)	(1)	(1)
College graduate	(2)	(2)	(2)	(2)	(2)
Some college or trade school	(3)	(3)	(3)	(3)	(3)
Secondary school graduate	(4)	(4)	(4)	(4)	(4)
Some secondary school	(5)	(5)	(5)	(5)	(5)
Elementary school	(6)	(6)	(6)	(6)	(6)
None	(7)	(7)	(7)	(7)	(7)
Unknown	(8)	(8)	(8)	(8)	(8)

6. Has the patient been a full-time or part-time student during the past year? No (1) Yes (2)

Proceed to Section C. _____

7. Note current level in school:

a) If in elementary orsecondary school, grade: __ __

b) If in trade school, year: __

c) If in college, year: __

d) If in graduate school, year: __

8. Has the patient ceased attending school during the past year for ANY reason other than graduation (e.g., dropped out, expelled, moved to a new city, could no longer afford school)? No (1) Yes (2)

If YES, explain: _____

_____

_____

C. SMOKING STATUS

1. During the past 12 months, has the patient ever smoked cigarettes or cigarillos? No (1) Yes (2)

Proceed to Question C.5 _____

2. Does the patient currently smoke cigarettes or cigarillos? No (1) Yes (2)

Proceed to Question C.4 _____

3. How long has it been since the patient quit smoking cigarettes or cigarillos? months __ __

4. During the period in the past 12 months when the patient smoked cigarettes or cigarillos, on the average, how many cigarettes and cigarillos a day did he/she smoke? __ __ cigarettes or cigarillos per day

5. During the past 12 months, has the patient ever smoked pipes or cigars? No (1) Yes (2)

Proceed to Section D

6. Does the patient currently smoke pipes or cigars? No (1) Yes (2)

Proceed to Question C.8

7. How long has it been since the patient quit smoking pipes and cigars? months __ __

8. During the period in the past 12 months when the patient smoked pipes or cigars, on the average, how many pipefuls and cigars per week did the patient smoke? __ __ __ pipefuls or cigars per week

D. DRINKING STATUS

1. During the past 12 months, has the patient consumed an average of at least one alcoholic beverage per week? No (1) Yes (2)

Proceed to Section E

2. How many 12-ounce bottles of beer (excluding "light" beer) did the patient consume during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL CHARACTERIZE A TYPICAL WEEK.) (A) __ __ Bottles

3. How many 12-ounce bottles of "light" beer did the patient consume during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) (B) __ __ Bottles

4. How many 4-ounce glasses of wine did the patient consume during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) (C) __ __ Glasses

5. How many 1 1/2-ounce shots of straight hard liquor and 1 1/2-ounce mixed drinks did the patient consume during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) (D) __ __

6. Does the total amount of alcohol consumed by the patient in the past 7 days (OR IN A TYPICAL WEEK) exceed 560 grams? No (1) Yes (2)

Use this table if necessary:

Amount X Grams

(A) _____ X 13 = _____

(B) _____ X 10 = _____

(C) _____ X 12 = _____

(D) _____ X 15 = _____

TOTAL GRAMS OF ALCOHOL _____

E. EXERCISE AND ACTIVITY

1. Which of the following best describes the patient's level of activity on the job, at school or, for homemakers, in homemaking?

Sedentary (such as office work with occasional inter-office walking, etc.; e.g., secretary) (1)

Moderate activity (requires considerable, but not constant, lifting, walking, bending, pulling, etc.; e.g., homemaker with family and without domestic assistance, policeman, student taking physical education course) (2)

Strenuous activity (requires almost constant lifting, bending, pulling, scrubbing, etc.; e.g., furniture mover, heavy domestic work) (3)

2. During the past seven days, how many hours and minutes did the patient spend in the following types of leisure time activities? (IF THE PAST SEVEN DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.)

Light activity (Examples: billiards, bowling, ballroom dancing, golf with power cart, non-competitive volleyball)	__ __ Hours	__ __ Minutes
Moderate activity (This level is marked by modest increases in heart rate and breathing. Most healthy individuals find these activities comfortable and can continue them for a few hours without undue fatigue. Examples: leisure cycling (5.5 mph), frisbee playing, horseback riding, sailing, table tennis, croquet, golf without power cart)	__ __ Hours	__ __ Minutes
Hard activity (When exercising at this intensity, most people will likely perspire. Most untrained people could not exercise at this intensity without taking frequent rest periods. Examples: cycling (9.4 mph), half-court basketball, water skiing, downhill skiing, karate or judo, doubles tennis, roller skating, gymnastics)	__ __ Hours	__ __ Minutes
Very hard activity (Includes strenuous sports involving a lot of movement or running. Only a well-trained individual can perform at this intensity for extended periods of time. Examples: racing cycling, football, full-court basketball, rapid marching, squash, continuous, moderate to fast swimming, rope jumping, cross country running, singles tennis, field hockey)	__ __ Hours	__ __ Minutes

F. DIABETES MANAGEMENT

Answer Section F for all patients *except* where specified. Do not complete this section at the randomization visit. When completing this section, refer to the previous day's insulin dosage only. However, if in your judgement the previous day's dosage was atypical of the patient's regimen, use another recent day that you would consider typical.

1. Specify types of insulins used by this patient: (CHECK ALL THOSE THAT APPLY)

Human regular	(1)	Pork Regular	(1)
Human Semilente	(1)	Pork Semilente	(1)
Human NPH	(1)	Pork NPH	(1)
Human Lente	(1)	Pork Lente	(1)
Human Ultralente	(1)	Pork 70/30	(1)
Human 70/30	(1)		

Beef/pork Regular	(1)
Beef/pork Semilente	(1)
Beef/pork NPH	(1)
Beef/pork Lente	(1)
Beef/pork Ultralente	(1)

2. To what group was this patient randomized?

Standard (1) Experimental (2)

Patient ID _____

3. a) What insulin regimen is currently being used by this patient?

insulin infusion pump (1)
three or more daily injections (2)
one or two daily injections (3)
other: (4)
(describe the regimen in Question Number 6)

b) Is this the regimen prescribed by the DCCT clinic? No (1) Yes (2)

4. Please summarize this patient's usual insulin regimen here. (Refer to the previous day's insulin dosage only. However, if the previous day's dosage was atypical, use the most recent day that you would consider typical. Round off to the nearest whole unit.)

Total number of units per day: __ __ __

Number of Units Used	Breakfast	Lunch	Supper	Bedtime	Other
Regular	__ __	__ __	__ __	__ __	__ __
Semilente	__ __	__ __	__ __	__ __	__ __
NPH	__ __	__ __	__ __	__ __	__ __
Lente	__ __	__ __	__ __	__ __	__ __
Ultralente	__ __	__ __	__ __	__ __	__ __
70/30	__ __	__ __	__ __	__ __	__ __

NOTE: When filling out this table, consider all insulin given between breakfast and lunch as part of the lunch dose. All insulin between lunch and supper is part of the supper dose. All insulin between supper and bedtime snack is part of the snack dose. If a patient gives a prescribed mealtime dose which happened to be zero on the day recorded, record "0" in the appropriate space. If no dose was prescribed for a given time of day, leave the space blank. If a patient is on a pump, do not record basal here. Meal insulin only refers to bolus doses. Capture basal in number 5 following.

5. If the insulin regimen used by this patient on a typical day cannot accurately be recorded on the table (question 4) please leave the table blank and describe the regimen here:

Answer if #4 is blank:	No	Yes
I am describing the insulin regimen here:	(1)	(2)

If yes, specify:

_____

_____

6. COMPLETE ONLY FOR PATIENTS USING AN INSULIN INFUSION PUMP

Total number of UNITS BASAL insulin infused per day: __ __

Total number of different BASAL RATES used per day: __ __

Has the patient had any technical problems with the insulin infusion pump?

No (1) Yes (2)

If YES, specify: _____

_____

7. COMPLETE THIS QUESTION ONLY FOR PATIENTS CURRENTLY ON ONE OR TWO DAILY INJECTIONS:

a) Have you prescribed a change in the insulin regimen or dose since the last visit?

No (1) Yes (2)

If YES, please indicate the reason.

	No	Yes
Symptomatic polyuria/polydipsia/nocturia	(1)	(2)
Unacceptable degree of hypoglycemia	(1)	(2)
Recurrrent ketonuria	(1)	(2)
Hemoglobin A1c above the action limit	(1)	(2)
Pregnancy	(1)	(2)
Other:	(1)	(2)

Specify _____

b) How is this patient monitoring his/her diabetes?

	No	Yes	Uncertain
Self blood glucose monitoring	(1)	(2)	(3)
Urine glucose monitoring	(1)	(2)	(3)

8. COMPLETE THIS QUESTION FOR PATIENTS IN BOTH GROUPS:

Do you suspect that this patient's reported glucose (urine and/or blood) monitoring results are inaccurate or fictitious?

No (1)	Yes (2)	Not Sure (3)

Explain: _____

_____

G. DEVIATIONS FROM ASSIGNED TREATMENT

1. Since the last visit, has the patient been on a "deviation from treatment" (as defined in Section 12.5 of the Protocol) at any time? No (1) Yes (2)

   a. If yes, is the patient currently on deviation from treatment? No (1) Yes (2)

      (i) If NO, enter date of termination of deviation: __ __ Month __ __ Day __ __ Year

      (ii) If this is a new (started since last QV) deviation: enter date of DCCT Form 022, Notification of Deviation from Assigned Treatment: __ __ Month __ __ Day __ __ Year

H. TRANSFER TO INACTIVE STATUS

1. Since the last visit, has the patient been on inactive status at any time? (as defined in Section 12.7 of the Protocol) No (1) Yes (2)

   a. If yes, is the patient currently on transfer to inactive status? No (1) Yes (2)

      (i) If NO, enter date of return to active status: __ __ Month __ __ Day __ __ Year

      (ii) If this is a new transfer to inactive status, enter date of DCCT Form 016, Application for Transfer to Inactive Status: __ __ Month __ __ Day __ __ Year

I. MODIFICATIONS OF FOLLOW-UP SCHEDULE FOR ENDPOINT ASSESSMENT

(See Manual of Operations Chapter 11)

1. Since the last visit, has the patient been on a modified follow-up schedule at any time? No (1) Yes (2)

   If YES, indicate which assessments:

   _____

   _____

2. Is the patient currently on a modified follow-up schedule? No (1) Yes (2)

J. MODIFICATIONS OF THERAPY FOR PATIENTS RANDOMIZED TO THE STANDARD GROUP ONLY

1. Since the last visit, has the patient been on a modified therapy at any time? No (1) Yes (2)

   Proceed to Question K.1 _____|

   a) Since the last visit, has this patient used glucose monitoring at greater frequency than specified in the Protocol (urine testing 4x/day or self blood glucose monitoring once per day) at your direction? No (1) Yes (2)

      IF YES, record frequency: SBGM __/day

      UGM __/day

Patient ID _____

b) Since the last visit has this patient used more than two injections of insulin per day or used an insulin pump to achieve first or second priority standard treatment group goals at your direction at any time?

(NOTE: PERMISSION OF THE TREATMENT COMMITTEE IS REQUIRED PRIOR TO INSTITUTING THIS MODIFICATION OF THERAPY)

No (1) Yes (2)

Proceed to question d) _____|

If this modification was started since the last visit:

(i) Enter date permission was received from the Treatment Committee to institute the regimen in this patient __ __ Month __ __ Day __ __ Year

(ii) Enter date that new regimen was started __ __ Month __ __ Day __ __ Year

c) Is the patient currently using more than two injections per day or an insulin pump to achieve first or second priority treatment goals for the standard treatment group? No (1) Yes (2)

If NO, enter date of return to one or two injections of insulin per day __ __ Month __ __ Day __ __ Year

If this patient is using more than two injections per day or an insulin pump for reasons other than instructed by you to achieve first and second priority goal for the Standard Group, this represents a deviation from assigned treatment, and should be recorded in Section G and on Form 022.

d) Other modification; specify: No (1) Yes (2)

_____

_____

FOR PATIENTS RANDOMIZED TO THE EXPERIMENTAL GROUP ONLY

2. Since the last visit, has the patient been on a modified treatment protocol? No (1) Yes (2)

Proceed to Question K.1 _____|

a) Since the last visit, have you instituted a planned out-patient visit schedule on a less frequent basis than the required monthly visit schedule? No (1) Yes (2)

b) Have you instructed this patient to perform self blood glucose monitoring on a less frequent daily schedule than the required minimum of four times a day, including three pre-prandial and one bedtime sample? No (1) Yes (2)

If yes, record frequency __ / day

c) Have you instructed this patient to use less stringent goals of therapy? No (1) Yes (2)

(i) Specify the new goals:

HbA1c (range) __ __.__ to __ __.__

Blood glucose (range):

Preprandial __ __ __ to __ __ __

Postprandial __ __ __ to __ __ __

3:00 a.m. __ __ __ to __ __ __

(ii) Specify the reason and situation for modification of goals of therapy in this patient:

_____

_____

_____

(iii) Specify the date that the new goal(s) became effective: __ __ Month __ __ Day __ __ Year

(iv) Are the stated goals in effect at present? No (1) Yes (2)

If NO, enter the date that the patient returned to the goals of the experimental treatment group set forth in the Protocol: __ __ Month __ __ Day __ __ Year

d) Other modification; specify: No (1) Yes (2)

_____

_____

K. DIABETES MONITORING - ANSWER FOR PATIENTS CURRENTLY ON 3 OR MORE INJECTIONS OR PUMP

1. Summarize the patient's performance of glucose monitoring. Use the patient's "Daily Diabetes Monitoring Record" to do this. The "number should have done" is the *number* of tests you instructed the patient to do. Record performance of these prescribed tests only; do not record extra tests performed.

	BLOOD	
Testing Required by Protocol	Number Actually Done	Number Should Have Done
Before breakfast	_ _ _	_ _ _
Before lunch	_ _ _	_ _ _
Before dinner	_ _ _	_ _ _
Bedtime	_ _ _	_ _ _
3:00 a.m.	_ _ _	_ _ _

2. Is the patient performing more self blood glucose monitoring than prescribed? No (1) Yes (2) Uncertain (3)

L. DIABETES MONITORING - ANSWER FOR PATIENTS CURRENTLY ON ONE OR TWO INJECTIONS

1. Summarize the patient's performance of glucose monitoring. Use the patient's "Daily Diabetes Monitoring Record" to do this. The "number should have done" is the *number* of tests you instructed the patient to do. Record performance of these prescribed tests only; do not record extra tests performed.

	URINE		BLOOD	
Testing Required by Protocol	Number Actually Done	Number Should Have Done	Number Actually Done	Number Should Have Done
Before breakfast	_ _ _	_ _ _	_ _ _	_ _ _
Before lunch	_ _ _	_ _ _	_ _ _	_ _ _
Before dinner	_ _ _	_ _ _	_ _ _	_ _ _
Bedtime	_ _ _	_ _ _	_ _ _	_ _ _

2. Is the patient performing more glucose monitoring (urine or blood) than prescribed? No (1) Yes (2) Uncertain (3)

M. INDICATIONS OF NON-ADHERENCE TO TREATMENT PROTOCOL

1. Answer a) - i) for all patients.

a) How often has the patient claimed to have followed the meal plan?

Not applicable	(0)
Never followed meal plan	(1)
Very infrequently (less than 10% of the time)	(2)
Infrequently (10-44% of the time)	(3)
About half the time (45-55% of the time)	(4)
Most of the time (56-90% of the time)	(5)
Almost all of the time (more than 90% of the time)	(6)
Always followed meal plan	(7)

	No	Yes	Uncertain
b) Has the patient followed a pattern of eating suggestive of an eating disorder (e.g., history of bulimia, vomiting, anorexia)?	(1)	(2)	(3)
c) (i) How many illnesses (intercurrent events or not) has the patient experienced? (If none, enter 00 and proceed to 1.d)	__ __		
(ii) During how many of these illnesses has the patient been known to have failed to adjust the insulin dose as prescribed?	__ __		
d) Has the patient used a type of insulin which has not been prescribed?	(1)	(2)	(3)
e) Has the patient been rotating the site of injection (or, in pump patients, the site of infusion)?	(1)	(2)	(3)
f) Has the patient completed less than all seven of the capillary blood collections required for the Profiset?	(1)	(2)	(3)
g) (i) How many intercurrent events (as defined in Chapter 10 of the Manual of Operations) has the patient experienced? (If none, enter 00)	__ __		
(ii) How many of these intercurrent events has the patient failed to report in the appropriate time window? (If none, enter 00)	__ __		
h) Has the patient failed to bring in his/her daily record?	(1)	(2)	(3)
i) Does the patient perform self blood glucose monitoring? (If no or uncertain, proceed to Question M.2)	(1)	(2)	(3)
If yes: (i) Has the patient been using self blood glucose monitoring to adjust his/her insulin dosage?	(1)	(2)	(3)
(ii) Does the patient perform self blood glucose monitoring more than once per day?	(1)	(2)	(3)

Patient ID _____

2. ANSWER (a) - (f) FOR PATIENTS RANDOMIZED TO THE STANDARD TREATMENT GROUP

On how many days has the patient . . .

a) taken more than the prescribed units of insulin (excluding sick days)? __ __

b) taken extra injections of insulin? __ __

c) taken fewer injections of insulin? __ __

d) failed to take his/her prescribed insulin dose? __ __

e) failed to perform and record at least two urine tests or one blood glucose test a day? __ __

f)(i) been ill? __ __

(ii) failed to test and record urine acetone during an illness? __ __

3. ANSWER (a) - (d) FOR PATIENTS RANDOMIZED TO THE EXPERIMENTAL TREATMENT GROUP

a) On how many days has the patient not followed the prescribed algorithm for insulin delivery? __ __

b) How many times has the patient failed to do the prescribed 3:00 a.m. blood tests? __ __

c) How many times has the patient failed to promptly report a low 3:00 a.m. blood glucose to the clinic? __ __

d) How many times has the patient failed to monitor urine acetone when blood glucose was >240 mg/dl or during an illness? __ __

4. ANSWER (a) - (c) FOR PATIENTS RANDOMIZED TO THE EXPERIMENTAL TREATMENT GROUP AND USING INSULIN INFUSION PUMPS

a) How many times has the patient failed to follow instructions for changing batteries? __ __

b) How many times has the patient failed to follow instructions for changing catheters? __ __

c) How many times has the patient failed to follow instructions for changing syringes? __ __

N. DIABETES CONTROL - ANSWER FOR ALL PATIENTS

1. Symptoms of hyperglycemia (Std pts priority 1 goals)

a) How many nights in the past week did the patient wake up ONCE to urinate? __

b) How many nights in the past week did the patient wake up TWO OR MORE times to urinate? __

c) On the average, how many 8 ounce glasses of fluid did the patient drink per day? __ __

d) How many times did the patient experience DKA? __ __
(As defined in Chapter 10 of the Manual of Operations)

If the patient has had DKA, complete the Notification of Intercurrent Event (Form 020) if it has not previously been completed for this event.

e) Did the patient experience other symptoms of hyperglycemia? No (1) Yes (2)

If YES, specify: _____

_____

2. How many days has the patient had moderate or large ketonuria? __ __
(If none, enter 00 and proceed to Question N.3.)

How many of these were . . .

a) explained by change in routine? __ __

b) due to illness? __ __

c) due to medical equipment failure? __ __

d) spontaneous or unexplained? __ __

Patient ID _____

3. a) Is the patient female? No (1) Yes (2)

Proceed to Question N.4 _____|

b)(i) Has the patient had any vaginal itching or discharge? No (1) Yes (2)

Proceed to Question N.3.c _____|

(ii) Was the patient treated for this? No (1) Yes (2)

(iii) Specify treatment: _____

_____

c)(i) Does the patient menstruate? No (1) Yes (2)

Proceed to Question N.4 _____|

(ii) Enter date of start of last menstrual period:

__ __ __ __ __ __
Month Day Year

d)(i) Was the last menstrual period more than five weeks ago? No (1) Yes (2)

Proceed to Question N.4 _____|

(ii) Was a pregnancy test performed? No (1) Yes (2)

If no, why not? _____

_____

If yes, did the test indicate pregnancy? No (1) Yes (2)

Complete the Notification of Intercurrent Event (Form 020) if it has not previously been completed for this pregnancy. _____|

4. Symptoms of hypoglycemia since last QV

a) Number of hospitalizations for hypoglycemia. (Hospitalization implies overnight admission to the hospital; an emergency ward visit that did not result in hospitalization does not apply.) __ __

If the patient has been hospitalized for hypoglycemia, complete Notification of Intercurrent Event (Form 020), the Notification of Hypoglycemic Intercurrent Event (Form 083), and Further Details (Form 092) if not previously completed for this hospitalization.

If any hospitalizations, give specific reasons:

_____

_____

b) How many times did the patient experience hypoglycemia of such severity that the patient . . .

(i) lost consciousness without seizure __ __

(ii) lost consciousness with seizure __ __

c) How many times did the patient experience hypoglycemia of such severity . . .

(i) that the patient required professional medical assistance, including placement of an IV or an intravenous injection of glucose? __ __

(ii) as to require the assistance of another person, such as the administration of glucagon, but did not require any of the assistance described in (i)? __ __

(iii) as to require the assistance of another person but did not require any of the help described in (i) or (ii)? __ __

d) Complete only if severe hypoglycemia which the patient could not treat himself/herself has occurred:

(i) How many times has the patient received glucagon? __ __

(ii) How many times has the patient received IV glucose to treat hypoglycemia? __ __

(iii) Did any episodes result in injury to the patient or others? No (1) Yes (2)

If YES, specify: _____

_____

If the patient has experienced severe hypoglycemia which he/she could not treat himself/herself, please complete Notification of Intercurrent Event (Form 020), Notification of Hypoglycemic Intercurrent Event (Form 083) and Further Details (Form 092) for for any episodes for which this has not previously been done.

e) How many times in the past seven days did the patient experience hypoglycemia which was mild enough for the patient to treat himself/herself? __ __

f) If the patient has experienced hypoglycemia in the past seven days which was mild enough for the patient to treat himself/herself, answer Items (i) through (iii) below. Otherwise, skip to Section O.

(i) Did mild hypoglycemia occur:

While the patient was awake (1)

While the patient was asleep (2)

Both (3)

(ii) What was the usual reason for the mild hypoglycemia? (CHECK ALL THAT APPLY)

Missed meal or snack (1)

Decreased food intake at meal or snack (1)

Increased exercise level (1)

Too much insulin taken (1)

Lack of early warning signs of low blood glucose (1)

Other; specify: _____ (1)

_____

Unexplained (1)

(iii) What symptoms does the patient have with mild hypoglycemia? (CHECK ALL THAT APPLY)

Adrenergic warning symptoms (1)

Diaphoresis (sweating) (1)

Altered mental status (1)

Other (1)

None (1)

Patient ID _____

O. DIABETES RELATED COMPLICATIONS AND/OR CATEGORY 3 INTERCURRENT EVENTS

If the patient has been hospitalized (overnight) to treat any of the following diabetes-related complications or Category 3 events, the Notification of Intercurrent Event (Form 020) must be completed for each hospitalization (see Chapter 10 of the Manual of Operations).

If no hospitalization occurred, Category 3 Intercurrent Events are reported on this form only; Form 20 is not required.

1. OPHTHALMIC

	Right Eye	Left Eye
a) Has the patient had blurred or reduced vision?	No (1) Yes (2)	No (1) Yes (2)
If YES, explain: _____		
b) Has the patient experienced floaters or flashing lights?	No (1) Yes (2)	No (1) Yes (2)
c) Has the patient had any other eye problems?	No (1) Yes (2)	No (1) Yes (2)
If YES, specify: _____		
d) Will the patient be sent to the ophthalmologist for a special visit?		No (1) Yes (2)

2. NEUROLOGIC

Has the patient had any of the following?

a) Paresthesias (pain or numbness) in hands or feet	No (1) Yes (2)
b) Unexplained muscle weakness	(1) (2)
c) Vomiting or bloating after meals	(1) (2)
d) Bouts of persistent or recurrent diarrhea	(1) (2)
e) Bouts of urinary retention	(1) (2)
f) Dizziness or lightheadedness (not associated with hypoglycemia)	(1) (2)
g) Fainting (not associated with hypoglycemia)	(1) (2)
h) Seizure (not due to hypoglycemia)	(1) (2)

If YES, complete the Notification of Intercurrent Events (Form 020) if it has not already been completed for this condition.

i) Impotence	No (1)	Yes (2)	Not Applicable (3)
j) Has the patient developed symptoms compatible with a focal neuropathy (described as sudden onset, asymmetrical and self-limited, i.e., cranial mononeuropathy, proximal motor neuropathy, truncal neuropathy)?	No (1)	Yes (2)	
k) Other neurologic problem ?	No (1)	Yes (2)	
If YES, specify: _____			
l) Will the patient be sent to the neurologist for a special visit?	No (1)	Yes (2)	

Patient ID _____

3. RENAL

Has the patient had any of the following?

	No	Yes
a) Edema (of renal etiology only)	(1)	(2)
b) Other renal problem	(1)	(2)

If YES, specify: _____

4. VASCULAR

Has the patient had any of the following?

	No	Yes
a) Shortness of breath	(1)	(2)
b) Symptoms of congestive heart disease	(1)	(2)
c) Impaired peripheral vascular circulation (e.g., intermittent claudication)	(1)	(2)
d) Chest pain	(1)	(2)
(i) If yes, is this clinical angina? (As defined in Chapter 10 of the Manual of Operations)	(1)	(2)
e) Other symptoms suggestive of a suspected non-acute MI (as defined MOO Chapter 10)	No (1)	Yes (2)

If Yes to d)i or e) complete the Notification of Intercurrent Events (Form 020) if it has not already been completed for this condition.

f) Symptoms suggestive of transient ischemic attack(s) (As defined in Chapter 10 of the Manual of Operations)	(1)	(2)
g) Other vascular problem	(1)	(2)

If YES, specify: _____

5. INFECTIONS

Has the patient had any of the following?
(As defined in Chapter 10 of the Manual of Operations)

	No	Yes
a) Urinary tract infection (e.g., cystitis, pyelonephritis, perinephric abscess)	(1)	(2)
b) Upper or lower respiratory tract infection	(1)	(2)
c) Gastroenteritis with fever	(1)	(2)
d) Cutaneous (non-infusion site) or mucocutaneous (e.g., Candida vulvo-vaginitis, furunculosis, dental abscess) infection	No (1)	Yes (2)

If YES, specify: _____

e) Post-operative or deep wound infection	(1)	(2)
f) Gangrene	(1)	(2)
g) Other infections not specifically defined in the Manual of Operations (i.e., mononucleosis, epididymitis, measles, chicken pox)	(1)	(2)

If YES, specify: _____

ANSWER THE FOLLOWING ONLY FOR PATIENTS WHO USE AN INDWELLING NEEDLE OR CATHETER FOR INSULIN ADMINISTRATION.

h) Has the patient had infection at the insertion site (e.g., >1.5 cm erythema and purulence)?	No (1)	Yes (2)

Complete the Notification of Intercurrent Event (Form 020).

6. MINOR OUTPATIENT SURGERY OR INCIDENTAL TRAUMA (e.g., simple fracture, uncomplicated laceration). No (1) Yes (2)

If YES, specify: _____

Patient ID _____

7. INTERCURRENT ENDOCRINE EVENT

(e.g., hypothyroidism, Grave's disease, Cushing's disease) No (1) Yes (2)

If YES, specify: _____

_____

8. ADVERSE PSYCHOSOCIAL REACTION No (1) Yes (2)

If YES, specify: _____

_____

9. OTHER

a) Has the patient experienced any other medical problems or difficulties in carrying out the diabetes treatment regimen (includes imprisonment)? No (1) Yes (2)

If YES, explain: _____

_____

P. MEDICATIONS

1. On the average, how many aspirin-containing tablets or other prostaglandin inhibitors does the patient use each month? (IF NONE, ENTER 000) ___

2. Has the patient used or is he/she currently using any prescription drug on a regular basis other than insulin? No (1) Yes (2)

Specify: _____

_____

_____

3. Has the patient used any over-the-counter drugs? No (1) Yes (2)

Specify: _____

_____

4. Does the patient use vitamin supplements on a regular basis? No (1) Yes (2)

Specify: _____

_____

Q. PHYSICAL EXAMINATION

1. Date of last physical examination — Month __ Day __ Year __ __

2. Current weight (kg) (To convert pounds to kilograms, multiply by 0.454.) — __ __ __ . __

3. Change in weight since previous exam (kg) (CIRCLE + OR -) + - __ __ . __

4. What is the patient's desired weight (kg)? __ __ __ . __

5. Is the patient less than 18 years old? If NO, skip to Question Q.8. — No (1) Yes (2)

6. Current height (cm) (To convert inches to centimeters, multiply by 2.54.) — __ __ __ . __

7. Has patient failed to maintain normal growth and development (see Manual of Operations Chapter for definition)? — No (1) Yes (2)

8. Pulse (bpm) — __ __ __

9. Sitting blood pressure (RIGHT ARM)

   a) Systolic (mm Hg) — __ __ __

   b) Diastolic (mm Hg) — __ __ __

   c) Has hypertension been previously documented and has the Notification of Intercurrent Form been completed and sent to the Coordinating Center? — No (1) Yes (2)

   SKIP TO QUESTION Q.10 _____|

   d) Is the current systolic or diastolic blood pressure so high as to be above the normal range as stated in Chapter 10 of the Manual of Operations i.e., ≥ 140 systolic or ≥ 90 diastolic? — No (1) Yes (2)

   IF YES, PATIENT SHOULD RETURN ON ANOTHER DAY WITHIN ONE MONTH FOR A SECOND DETERMINATION OF BLOOD PRESSURE. COMPLETE ITEMS e) THROUGH g) AT THAT TIME.

   e) Date of second sitting blood pressure determination — Month __ Day __ Year __ __

   f) Sitting blood pressure:

   Systolic (mm Hg) __ __ __

   Diastolic (mm Hg) __ __ __

   g) Does the systolic or diastolic blood pressure indicate hypertension as defined in the MOO, Chapter 10 i.e, ≥ 140 systolic or ≥ 90 diastolic? — No (1) Yes (2)

   Complete the Notification of Intercurrent Event (DCCT Form 020). _____|

10. Injection sites (INCLUDING CATHETER SITES):

	Absent	Present
a) Lipoatrophy	(1)	(2)
b) Lipohypertrophy	(1)	(2)
c) Inflammation	(1)	(2)

11. Abdomen:

	Absent	Present
a) Hepatomegaly	(1)	(2)
b) If present, how large (span)?		__ __ cm

12. Feet:

	Absent	Present
a) Ulcers	(1)	(2)
b) Infection	(1)	(2)
c) Abnormal toenails	(1)	(2)

Pulse -- Dorsalis pedis

d) Right			e) Left		
Normal	Diminished	Absent	Normal	Diminished	Absent
(1)	(2)	(3)	(1)	(2)	(3)

Pulse -- Posterior tibial

f) Right			g) Left		
Normal	Diminished	Absent	Normal	Diminished	Absent
(1)	(2)	(3)	(1)	(2)	(3)

13. Were any other abnormalities noted on physical examination? No (1) Yes (2)

Specify: _____

_____

R. BLOOD GLUCOSE PROFILE, HEMOGLOBIN A1c, LIPID AND RENAL STUDIES

1. Will the Profiliset be mailed to the Central Biochemistry Laboratory? No (1) Yes (2)

2. Why not? (CHECK ALL THAT APPLY THEN SKIP TO QUESTION R.9)

   Kit damaged after collection (1)
   Patient forgot to do collection (1)
   Patient lost kit (1)
   Patient refused to do collection (1)
   Other or unknown (1)

3. On what date were the collections performed? __ __ Month __ __ Day __ __ Year

4. On what date will the Profiliset be mailed? __ __ Month __ __ Day __ __ Year

5. What accession number will be used on the Profiliset? BGP1 thru BGP7 - _ _ _ _ _ _ _

6. a. Was this profiliset supposed to have been quality-controlled? No (1) Yes (2)

   (i) If yes, which stick number did the patient *duplicate*? _____ stick
   (If not done, answer 0)

   (ii) Was this the correct stick number? No (1) Yes (2)

If the patient is randomized to the Experimental Treatment Group, answer Questions R.7 and R.8; otherwise, *proceed* to Question R.9.

7. Did the patient perform self blood glucose monitoring on the day he/she obtained the Profiliset specimens? No (1) Yes (2)

Proceed to Question R.9

8. Using the patient's "Daily Diabetes Monitoring Record", specify the results of the self blood glucose monitoring performed on that day:

Prebreakfast	___	mg/dl
90 min. p.c.	___	mg/dl
Prelunch	___	mg/dl
90 min. p.c.	___	mg/dl
Presupper	___	mg/dl
90 min. p.c.	___	mg/dl
Bedtime	___	mg/dl

9. The quarterly blood sample is to be taken for HbAlc measurement.

a) HbAlc accession number: H - _____

b) Date specimen collected: ____ ____ ____
Month Day Year

10. Will lipid specimens be mailed to the Central Biochemistry Laboratory for annual visit? No ( ) Yes (2)

Proceed to Question R.13

11. On what date will the specimens be drawn? ____ ____ ____
Month Day Year

12. What accession number will be used? L - _____

13. Will renal studies specimens be mailed to the Central Biochemistry Laboratory for annual visit? No (1) Yes (2)

Process to end of form and sign

14. On what date will the specimens be collected? ____ ____ ____
Month Day Year

15. What accession number will be used? S and U - _____

Name of person responsible for information on this form: Certification Number

_____ ___ - ___

REMINDER: The Notification of Intercurrent Event (DCCT Form 020) must be completed if the patient has experienced any of the intercurrent events Category 1 or Category 2 listed in Chapter 10 of the DCCT Manual of Operations For hypoglycemia episodes, complete the Notification of Hypoglycemic Intercurrent Event (DCCT Form 083) and Further Details of Hypoglycemic Event (Form 092) as well.

DCCT Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Locally-Performed Blood Count and Chemistry

The appropriate area of this form is to be completed whenever a blood sample from a DCCT patient is analyzed by the clinic's laboratory as part of an eligibility evaluation or for the annual follow-up evaluation of the patient.

Canadian and other clinics which use S.I. units may write the blood analysis results in the space between the item description and the boxes.

If these procedures are being performed for an eligibility evaluation, the patient cannot be randomized if any STOP items are checked. See Chapter 8 of the Manual of Operations for clarification of these exclusion criteria.

At annual visits, only the hemoglobin test need be performed. (Investigators are free to measure annually other blood chemistries or blood cells that they consider part of routine general medical care, but the expense for such laboratory work should not be justified as a DCCT-required expense and should be met in other ways.)

When the form has been completed, a copy is to be sent to the Coordinating Center in the weekly forms mailing.

A. IDENTIFYING INFORMATION

1. Clinic Number ___ ___

2. Patient ID Number ___ ___ ___ ___ ___

3. Patient's Initials ___ ___ ___

4. Date form completed __ __ / __ __ / __ __ (Month / Day / Year)

5a) Enter the visit number: (IF AN ELIGIBILITY VISIT, ENTER 00) ___ ___

b) Is the visit being held within the time window? No (1) Yes (2)

6. Indicate patient's gender: Male (1) Female (2)

B. CHEMISTRY ANALYSIS

1. Date of collection __ __ / __ __ / __ __ (Month / Day / Year)

2. Date of analysis __ __ / __ __ / __ __ (Month / Day / Year)

3. Na^+ (mEq/L) ___ ___ ___

4. K^+ (mEq/L) ___ . ___

5. Cl^- (mEq/L) ___ ___ ___

6. Uric acid (mg/dl) ___ ___ . ___

7. Ca^{++} (mg/dl) ___ ___ . ___

8. PO_4^{--} (mg/dl) ___ . ___

9. SGOT (International Units) ___ ___ ___

10. Alkaline phosphatase (International Units) ___ ___ ___

11. Total protein (gm/dl) ___ . ___

12. Albumin (gm/dl) ___ . ___

13. Creatinine (mg/dl) ___ . ___

14. Total cholesterol (mg/dl) ___ ___ ___

15. Total triglycerides (mg/dl) ___ ___ ___

C. BLOOD COUNT

1. Date blood sample drawn __ __ / __ __ / __ __ (Month / Day / Year)

2. Hemoglobin (gm/dl) ___ ___ . ___

3. Hematocrit (%) ___ ___ . ___

4. RBC count (million per cu mm) __ __ . __

5. WBC count (thousand per cu mm) __ __ . __

% Neutrophils (ENTER 99 IF NOT DONE) __ __

% Polymorphonuclear (ENTER 99 IF NOT DONE) __ __

% Band forms (ENTER 99 IF NOT DONE) __ __

% Lymphocytes (ENTER 99 IF NOT DONE) __ __

% Monocytes (ENTER 99 IF NOT DONE) __ __

% Eosinophils (ENTER 99 IF NOT DONE) __ __

% Others (ENTER 99 IF NOT DONE) __ __

6. Platelet count (thousand per cu mm) __ __ __

D. SPECIAL BLOOD TESTS

	Check Here If Not Applicable	Date Performed Month Day Year	Pregnant STOP	Not Pregnant	
1. Pregnancy test	(1)	__ __ __ __ __ __	(1)	(2)	
			Abnormal STOP	Normal	Actual Value
2. Hb electrophoresis	(1)	__ __ __ __ __ __	(1)	(2)	
3. T4 (µg/dl)	(1)	__ __ __ __ __ __	(1)	(2)	__ __ . __

If there are special circumstances why the T4 value is not necessarily abnormal, explain:

_____

_____

	Not Applicable	Month Day Year	Abnormal STOP	Normal	Actual Value
4. TSH (µu/ml)	(1)	__ __ __ __ __ __	(1)	(2)	__ __ . __

Type or print name of person who completed this form:

_____

Certification Number (if any)

__ __ - __ __

Type or print name of DCCT physician who reviewed these results:

_____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Neurological History and Examination

The neurological history and examination should be carried out to permit answering certain specific questions. First, is there neurological evidence of a systemic disorder that could jeopardize the patient's ability to participate in the DCCT study? Second, is there clinical evidence of a peripheral nervous system disorder? If so, is it distal symmetrical polyneuropathy, a proximal motor neuropathy, a mononeuropathy or some other disorder that is unlikely to be related to diabetes? Third, if there is evidence of a polyneuropathy, what is the extent of the neurologic deficit at the time of examination? Decisions should be based on the history and physical findings, and must be made independent from the results of any neurophysiological testing.

The physical examination should be carried out in a quiet comfortable room such as an outpatient examining room or an EMG suite.

This form is completed for examinations performed for baseline assessment and for annual follow-up evaluations. A copy of this form is to be sent to the Coordinating Center in the weekly forms mailing.

A. IDENTIFYING INFORMATION

1. Clinic Number ☐☐ 5–6
2. Patient ID Number ☐☐☐☐☐ 7–11
3. Patient's Initials ☐☐☐ 12–14
4. Date of examination ☐☐/☐☐/☐☐ (Month / Day / Year) 15–20
5. If this is a baseline examination, check here: ☐1 21

   Otherwise,

   (i) specify which follow-up visit this is ☐☐ 22–23

   (ii) is this visit being held within the time window? No ☐1 Yes ☐2 24

B. NEUROLOGICAL HISTORY

NOTE: Your standard neurological history should be performed. The history should include an inquiry into possible exposure to neurotoxic drugs or chemicals, and a family history of neurologic disease, weakness, or arthritis and joint deformities. Also make specific and detailed inquiry about symptoms of sensory, motor and autonomic dysfunction.

1. Based on your history, does the patient have:

   a) A condition other than diabetes which could cause neuropathy? No ☐1 Yes ☐2 25

   If YES, specify: _____

   _____

   _____

1. (Continued)

   b) Exposure to known neurotoxins? No ☐1 Yes ☐2 26

   If YES, specify:

Toxin	Date of Exposure
_____	_____
_____	_____
_____	_____
_____	_____

   c) A family history of neuromuscular disorders? No ☐1 Yes ☐2 27

   If YES, specify: _____

   _____

2. Are any of the following sensory symptoms present in the hands or feet?

	No	Both Hands and Feet	Hands Only	Feet Only	
a) Numbness	☐1	☐2	☐3	☐4	28
b) Dysesthesias, paresthesias	☐1	☐2	☐3	☐4	29
c) Hypersensitivity to touch	☐1	☐2	☐3	☐4	30
d) Burning/aching stabbing pain	☐1	☐2	☐3	☐4	31

3. Are any of the following motor symptoms present?

	No	Yes	
a) Ankle weakness	☐1	☐2	32
b) Cramps	☐1	☐2	33

4. Are any of the following autonomic symptoms present? (Before they are ascribed to diabetic autonomic neuropathy, the symptoms must have been present for at least 30 days and should not be attributable to other conditions to the best of the physician's knowledge.)

Postural hypotension

	No	Yes	
a) Weakness on standing relieved by lying down	☐1	☐2	34
b) Fainting on standing relieved by lying down	☐1	☐2	35

Gastroparesis

	No	Yes	
c) Dysphagia (difficulty in swallowing)	☐1	☐2	36
d) Anorexia	☐1	☐2	37
e) Nausea	☐1	☐2	38
f) Vomiting	☐1	☐2	39
g) Vague fullness after meal	☐1	☐2	40

Diabetic Diarrhea

	No	Yes	
h) Nocturnal diarrhea	☐1	☐2	41
i) Fecal incontinence	☐1	☐2	42
j) More than 20 bowel movements/day	☐1	☐2	43

Colonic Atony

	No	Yes	
k) Less than 2 bowel movements/week	☐1	☐2	44
l) Less than 1 bowel movement/3 days	☐1	☐2	45

Genitourinary

	No	Yes	
m) Impotence (not due to other causes)	☐1	☐2	46
n) Retrograde ejaculation	☐1	☐2	47
o) Overflow bladder incontinence	☐1	☐2	48
p) Urinary dribbling	☐1	☐2	49
q) Incomplete bladder emptying	☐1	☐2	50
r) Increased urinary volume	☐1	☐2	51
s) Decreased urinary frequency	☐1	☐2	52

Sudomotor Abnormality

	No	Yes	
t) Diminished sweating of legs	☐1	☐2	53
u) Feeling of increased sweating elsewhere	☐1	☐2	54

Hypoglycemic Unawareness

	No	Yes	
v) Decreased adrenergic awareness of hypoglycemia	☐1	☐2	55

C. NEUROLOGICAL EXAMINATION

NOTE: Your standard neurological examination should be performed. Special attention should be paid to the peripheral nervous system.

The recommended method for testing small-diameter sensory fibers is to begin with evaluation of cold perception. A dense metal object such as the weight at the end of a 128 Hz tuning fork serves as a good cold stimulus. Begin by asking the patient to compare the temperature of this object as perceived over the dorsum of the foot and the top of the thigh. If the more proximal stimulus is colder, then starting on the dorsum of the toes, slowly move the object proximalward until the level of change to normal is found. Pin prick should be used to verify this level, since patients without neuropathy may report a change in temperature if they are examined in a cool room. The level at which the pin prick feels normal (compared with the upper thigh or face), and not just "sharp", should be recorded. To examine large fiber functions, the ability to detect the direction of the small upward or downward movements of the great toe should be determined, as well as the ability to perceive a low amplitude 128 Hz vibration at the first metatarsal-phalangeal joint, using your personal experience with individuals without neuropathy as a control.

For the most part, strength will be normal in this group of patients. To look for evidence of distal weakness, test the strength of great toe dorsiflexion (extensor hallucis longus muscle) and the strength of small toe dorsiflexion (extensor digitorum brevis). In addition, look for evidence of atrophy of intrinsic foot muscles and evaluate the size of the contracting EHL muscle for atrophy.

Reflexes should be elicited in your usual way. In this study we will be especially interested in the knee and ankle jerks. Reflexes should be graded as ++++ (very brisk with clonus), +++ (brisk), ++ and + (normal), +/- (elicited only with the Jendrassik maneuver) or 0 (cannot be elicited).

Patient ID _____

C. NEUROLOGICAL EXAMINATION (Continued)

1. Based on the physical examination, are there abnormalities of:

	No	Yes	
a) Mental status *(Normal mental status is defined as a score of 14 or more on the Glasgow Scale)*	☐1	☐2	56
b) Cranial nerves	☐1	☐2	* 57
c) Proximal or distal muscles	☐1	☐2	* 58
d) Sensory function of small fibers (decreased pin or temperature)	☐1	☐2	* 59
e) Sensory function of large fibers	☐1	☐2	* 60
f) Gait and coordination	☐1	☐2	* 61

*If any of the above abnormalities are present, explain:

_____

_____

_____

2. Reflex Pattern (use the number in parentheses to record the reflex pattern)

++++ brisk with clonus (5)
+++ brisk-normal (4)
++ normal (3)
+ normal (2)
± present with reinforcement (1)
0 unobtainable (0)

	Right	Left	
a) Biceps	☐☐		62–63
b) Triceps	☐☐		64–65
c) Brachioradialis	☐☐		66–67
d) Quadriceps	☐☐		68–69
e) Gastroc/soleus	☐☐		70–71

D. CONCLUSIONS FROM NEUROLOGICAL HISTORY AND EXAMINATION

1. Based on your completed neurological history and physical examination, does this patient have:

	No	Yes	
a) Symptoms consistent with a distal symmetrical polyneuropathy?	☐1	☐2	72
b) Abnormal sensory exam consistent with a distal symmetrical polyneuropathy?	☐1	☐2	73
c) Decreased or absent deep tendon reflexes?	☐1	☐2	74

2. Does this patient have clincially-evident diabetic peripheral neuropathy?

Definite yes (at least two of the three responses to Question D.1 must be positive) ☐1 75

Possible yes (one of the three responses to Question D.1 must be positive) ☐2

No ☐3

If NO, skip to Question D.4.

3. If the patient has a diabetic neuropathy, is it primarily:

Diffuse (distal symmetrical sensory-motor and/or autonomic) ☐1 76

Focal (proximal motor neuropathy, mononeuropathy, mononeuropathy multiplex)? ☐2

4. Based on your completed neurological history and physical examination, is there evidence of a neurological disorder other than diabetic symmetrical sensory-motor polyneuropathy?

No	Yes	
☐1	☐2	77

Type or print name of person completing this form:

_____

Certification Number (if any)

☐☐-☐☐ 78–81

DIABETES CONTROL AND COMPLICATIONS TRIAL

Locally-Performed Urinalysis and Urine Culture

The appropriate section of this form is to be completed whenever a urine sample has been collected from a DCCT patient for locally-performed urinalysis and urine culture for the annual follow-up evaluation of the patient.

Chapter 10 of the Manual of Operations gives procedures for identifying and treating various infections. At annual visits, the only tests to be performed are urinalysis and, for female patients, urine culture.

Once the form has been completed, a copy is to be sent to the DCCT Coordinating Center in the weekly forms mailing.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date form completed __ __ __ __ __ __ (Month Day Year)
5a) Enter the visit number: (IF AN ELIGIBILITY VISIT, ENTER 00) __ __
b) Is the visit being held within the time window? No (1) Yes (2)

B. URINALYSIS

1. Date of urinalysis __ __ __ __ __ __ (Month Day Year)

2. Indicate amounts of the following. (CHECK ONLY ONE BOX)

	None	Trace	+1	+2	+3
Hematuria (Hemastix)	(1)	(2)	(3)	(4)	(5)

3. If Hemastix is positive, Indicate numbers of the following (IF NONE, ENTER 00. IF TOO NUMBEROUS TO COUNT, ENTER 99.

a) RBC/hpf __ __
b) WBC/hpf __ __
c) RBC casts/hpf __ __
d) WBC casts/hpf __ __
e) Cellular, granular, broad or waxy casts/hpf (DO NOT INCLUDE HYALINE OR OTHER CASTS) __ __

	No	Yes
4. Are greater than 5 RBC, WBC, cellular, granular, broad or waxy casts present?	(1)	(2)
5. Is the patient female?	(1)	(2)
a) If YES, was the urine collected on a day outside of the patient's menstrual period?	(1)	(2)
b) If YES to (a), were there more than 5 RBC/hpf?	(1)	(2)

C. URINE CULTURE

A QUANTITATIVE URINE CULTURE MUST BE PERFORMED FOR ALL FEMALE PATIENTS. FOR MALES, IT NEED BE PERFORMED ONLY IF THERE WERE GREATER THAN OR EQUAL TO 2-4 WBC/hpf (Item B.6.d).

	No	Yes
1. Was a urine culture performed?	(1)	(2)
If YES, (a) enter date of urine culture:	Month __ __ Day __ __ Year __ __	
(b) if the subject is an outpatient or non-catheterized inpatient, is there a single culture of >100000/ml of one organism, OR two cultures of >100 colonies/ml Candida species?	(1)	(2)
OR		
if the subject is a catheterized inpatient, is there a single culture with one or two organisms, either of which is >100000 colonies/ml, OR a single culture of >100 colonies/ml Candida species?	(1)	(2)

Type of print name of person completing this form:

_____

Certification Number (if any)

__ __ - __ __

Type or print name of individual who reviewed these results:

_____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Documentation of Local Laboratory Certification

LABORATORY NAME AND ADDRESS:

_____

_____

_____

_____

_____

CERTIFICATION AGENCY:

_____

_____

_____

Test Procedure	Method	Certification (yes/no)	Is there an observed male/female difference?	Normal Range Values: Male (or both if no diff.) Upper Limit	Male (or both if no diff.) Lower Limit	Female Upper Limit	Female Lower Limit
HbA1							
Hb electrophoresis							
CBC							
Reticulocytes							
Sickle prep							
T4							
TSH							
Multichannel analysis							
Na							
K							
CL							
Ca							
PO_4							
Uric acid							
SGOT							
Alkaline phosphatase							
Total protein							
Albumin							
Serum bilirubin							
Total							
Indirect							
Pregnancy test							
Renal function - Serum creatinine							
Urinalysis							
Appearance							
Specific gravity							
Dipstick for							
Protein							
Sugar							
PH							
Microscopic sediment							

Please mail to:

Ms. Tina Johnson, Research Assistant
DCCT, Coordinating Center
The Biostatistics Center
7979 Old Georgetown Road, Suite 500
Bethesda, Maryland 20814

DIRECTOR'S SIGNATURE: _____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Baseline Ophthalmic Examination
and Ocular History

This form is to be used to document the initial ophthalmic assessment of patient eligibility for the DCCT. Chapter 13 of the DCCT Manual of Operations should be consulted for procedures for completing this examination. Chapter 8 should be consulted for eligibility criteria.

If a box with STOP is checked, an exclusion criterion has been encountered and the patient is ineligible for participation in the DCCT. You should continue to complete the examination, however, so that the baseline ophthalmic data will be complete for this excluded patient.

The Principal Investigator must review this form and sign it (Section I). If the patient was found to be ineligible at this visit, the Principal Investigator should explain this to the patient. A copy of this form is to be sent to the DCCT Coordinating Center.

A. IDENTIFYING INFORMATION

1. Clinic Number [ ][ ] 5-6
2. Patient ID Number [ ][ ][ ][ ][ ] 7-11
3. Patient's Initials [ ][ ][ ] 12-14
4. Date of examination [ ][ ] / [ ][ ] / [ ][ ] 15-20
   Month Day Year

B. OCULAR HISTORY

	No	Yes	
1. History of ocular surgery other than strabismus or lid surgery	[1]	Stop [2]	21
2. History of glaucoma requiring medication	[1]	Stop [2]	22
3. History of chronic requirement for any ocular medication	[1]	Stop [2]	23
4. History of photocoagulation	[1]	Stop [2]	24
5. History of any other ocular condition which may interfere with assessment of ophthalmic endpoints	[1]	Stop [2]	25

C. INTRAOCULAR PRESSURE MEASUREMENT

Use Goldmann applanation tonometry

1. Intraocular pressure in right eye: [ ][ ] mm Hg 26-27
2. Intraocular pressure in left eye: [ ][ ] mm Hg 28-29

	No	Yes	
3. Is the intraocular pressure in one or both eyes greater than or equal to 23 mm Hg?	[1]	Stop [2]	30

D. SLIT-LAMP EXAMINATION

	No	Yes	
1. Is either lens missing?	[1]	Stop [2]	31
2. Is there evidence of definite iris neovascularization in either eye?	[1]	Stop [2]	32

E. DISTANCE SUBJECTIVE REFRACTION

Use any visual acuity chart other than ETDRS Visual Acuity Chart 1 or 2

1. Corrective lenses obtained by subjective refraction for distance:

Indicate whether plus or minus spheres or cylinders were used by circling the appropriate signs. If no lens corrections are required, record a check mark (√) in the box for "No Corrections"

	Right Eye	Left Eye	
Sphere	± [ ][ ].[ ][ ]	± [ ][ ].[ ][ ]	33-36
Cylinder	± [ ][ ].[ ][ ]	± [ ][ ].[ ][ ]	37-40
Axis	[ ][ ][ ]	[ ][ ][ ]	41-42
No corrections	[1]	[1]	43-44

	No	Yes	
2. Is there myopia greater than 7 diopters in one or both eyes?	[1]	Stop [2]	45

Patient ID _____

F. VISUAL ACUITY MEASUREMENTS

The patient's BEST-CORRECTED visual acuity in each eye should be determined with the lens corrections obtained by subjective refraction and recorded in Question 1 of Section E. One of the standard ETDRS Charts should be used to determine for each eye the number of letters the patient is able to read on each line of the chart. CHART 1 should be used for the RIGHT EYE and CHART 2 should be used for the LEFT EYE.

1. Distance between the patient and the chart (record in meters to nearest 1/10 meter): [.] meters 66-68

2. Letters correct at four meters distance:

Circle each letter the patient identifies correctly and write the total correct for that row in column at right. Each row total must be entered.

RIGHT EYE - CHART 1

Acuity Equivalent	Chart 1 Letters	Number Correct
20/200	N C K Z O	___
20/160	R H S D K	___
20/125	D O V H R	___
20/100	C Z R H S	___
20/80	O N H R C	___
20/63	D K S N V	___
20/50	Z S O K N	___
20/40	C K D N R	___
20/32	S R Z K D	___
20/25	H Z O V C	___
20/20	N V D O K	___
20/16	V H C N O	___
20/13	S V H C Z	___
20/10	O Z D V K	___

Total number correct at four meters: [ ] 69-70

Is the total number of letters read correctly with the right eye at four meters greater than or equal to 45? No (Stop) 1 Yes [ ] 2 71

LEFT EYE - CHART 2

Acuity Equivalent	Chart 2 Letters	Number Correct
20/200	D S R K N	___
20/160	C K Z O H	___
20/125	O N R K D	___
20/100	K Z V D C	___
20/80	V S H Z O	___
20/63	H D K C R	___
20/50	C S R H N	___
20/40	S V Z D K	___
20/32	N C V O Z	___
20/25	R H S D V	___
20/20	S N R O H	___
20/16	O D H K R	___
20/13	Z K C S N	___
20/10	C R H D V	___

Total number correct at four meters: [ ] 72-73

Is the total number of letters read correctly with the left eye at four meters greater than or equal to 45? No (Stop) 1 Yes [ ] 2 74

3. The visual acuity score is the number of letters read correctly at four meters plus 30.

Right Eye
Visual acuity score [:] 75-77

Left Eye
Visual acuity score [ ] 78-80

Patient ID _____

OPHTHALMOSCOPIC EXAMINATION

1. Is there evidence of prior photocoagulation? No ☐1 Yes Stop ☐2 81

2. Is there evidence of significant chorioretinal scars, optic atrophy, retinal degeneration, or other conditions which might confound the assessment of ocular status? No ☐1 Yes Stop ☐2 82

3. Is there evidence of diabetic retinopathy?

Right Eye			Left Eye		
No	Yes		No	Yes	
☐1	☐2	83	☐1	☐2	84

4. If Question 3 is answered NO for either eye, is the total number of letters read correctly greater than or equal to 50?

Right Eye			Left Eye		
No*	Yes		No*	Yes	
☐1	☐2	85	☐1	☐2	86

*If NO, do not exclude the patient unless the degree of retinopathy is confirmed by grading of stereo fundus photographs by the Central Ophthalmologic Reading Unit.

5. If Question 3 is answered YES for either eye, is the degree of retinopathy less than that which would characterize the eye as P2 or worse?

Right Eye			Left Eye		
No**	Yes		No**	Yes	
☐1	☐2	87	☐1	☐2	88

**If NO, do not exclude the patient unless this is confirmed by grading of stereo fundus photographs by the Central Ophthalmologic Reading Unit.

H. FUNDUS PHOTOGRAPHY

1. As far as you can determine from this examination, is there any reason why adequate quality stereo fundus photographs cannot be obtained for this patient? No ☐1 Yes Stop ☐2 89

If YES, specify reason:

_____

_____

If NO, the patient should be sent to the ophthalmic photographers to have fundus photographs and fluorescein angiograms taken. These procedures are described in the Manual of Operations, Chapter 13.

I. CONCLUSION OF VISIT

1. Was the patient deemed ineligible for any reason at this visit? No ☐1 Yes ☐2 90

Certification Numbers (if any)

Type or print name of ophthalmologist performing this examination:

_____ ☐☐-☐☐ 91-94

Type or print name of person performing visual acuity examination:

_____ ☐☐-☐☐ 95-98

Type or print name of DCCT Clinic Coordinator:

_____ ☐☐-☐☐ 99-102

Signature of Principal Investigator:

_____

OCULAR ELIGIBILITY (P-III) RECORD LAYOUT

Position	Description
1-2	Clinic number
3-7	Patient identification number
8-10	Patient initials
11-16	Random accession number for color photo set (eg. F-12345 appears as 112345)
17-22	Date color photos were taken (MMDDYY)
23-28	Date this patients photos were mailed by clinic (MMDDYY)
29-34	Date CORU sent eligibility record
35	Submission type 1 - Original photos 2 - Retakes
36	Right eye eligibility code (Same code table as left eye below)
37	Left eye eligibility code 0 - No Retinopathy 1 - Retinopathy < ETDRS P2 2 - Retinopathy ≥ ETDRS P2 3 - Retinopathy without Ma 4 - Other exclusion criteria 8 - Cannot grade BLANK if requesting retakes
38	Patient eligibility code 0 - No Retinopathy in either eye 1 - Retinopaty < ETDRS P2 including ≥ 1 Ma in either eye 2 - Ineligible in either or both eyes 8 - Cannot grade BLANK if requesting retakes
39	Retake indicator 0 - Retakes not requested 1 - Retakes requested
40	Correction code 0 - Original transmission of record 1 - First correction 2 - Second correction and so on

DCCTELG3.DOC 2/28/85

DIABETES CONTROL AND COMPLICATIONS TRIAL

Neurobehavioral Assessment (Complete Battery)

This form is to be completed by the staff of the DCCT Central Neurobehavioral Coding Unit to report the results of a neurobehavioral assessment.

A completed copy of the form is to be sent to the DCCT Coordinating Center.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date Tests Administered __ __ / __ __ / __ __ (Month / Day / Year)
5. If a baseline visit, check here: (1)

   Otherwise, (i) specify which follow-up visit this was: __ __

   (ii) was the visit held within the time window? No (1) Yes (2)
6. Date Assessment Coded __ __ / __ __ / __ __ (Month / Day / Year)
7. Coder's ID __ __
8. Neurobehavioralist's Certification Number __ __ - __ __
9. Dominant hand Right (1) Left (2) Ambidextrous (3)

B. WAIS PICTURE COMPLETION

1. Total correct: 0-21 __ __
   a. Scaled score: 0-19 __ __
   b. Age-corrected scaled score: 0-19 __ __
2. Mean latency for correct responses: 0-20 __ __

C. WISC-R PICTURE COMPLETION

1. Total correct: 0-26 __ __
   a. Age-corrected scaled score: 0-19 __ __
2. Mean latency for correct responses: 0-20 __ __

D. LOGICAL MEMORY -- IMMEDIATE RECALL

1. Total number of units recalled -- Story 1: 0-25 __ __.__
2. Total number of units recalled -- Story 2: 0-21 __ __.__

E. LOGICAL MEMORY -- DELAYED RECALL

1. Total number of units recalled -- Story 1: 0-25 __ __.__
2. Hint given? No (1) Yes (2)
3. Total number of units recalled -- Story 2: 0-21 __ __.__
4. Hint given? No (1) Yes (2)

F. WAIS OBJECT ASSEMBLY

1. Total number of points: 0-44 __ __
   a. Scaled score: 0-19 __ __
   b. Age-corrected scaled score: 0-19 __ __

Patient ID _____

G. WISC-OBJECT ASSEMBLY

1. Total number of points: 0-33 — —

a. Age-corrected scaled score: 0-19 — —

H. DIGIT SYMBOL SUBSTITUTION TEST

1. Total number of symbols completed within each 30 second interval:

30": 0-50 — —

60": 0-50 — —

90": 0-50 — —

120": 0-50 — —

150": 0-50 — —

180": 0-50 — —

210": 0-50 — —

240": 0-50 — —

270": 0-50 — —

300": 0-50 — —

2. Total time to complete grid: 0-360 — — —

3. Total number correct within first 90 seconds: 0-90 — —

a. Scaled score (for subjects 16 years old and over): 0-19 — —

b. Age-corrected scaled score: 0-19 — —

4. Incidental recall: 0-9 —

I. WAIS INFORMATION

1. Total number correct: 0-29 — —

a. Scaled score: 0-19 — —

b. Age-corrected scaled score: 0-19 — —

J. WISC-R INFORMATION

1. Total number correct: 0-30 — —

a. Age-corrected scaled score: 0-19 — —

K. EMBEDDED FIGURES TEST

1. Total number correct: 0-10 — —

2. Mean latency for correct responses: 0-60 — —

L. STAR DRAWING - DOMINANT HAND

1. Total time: 0-90 — —

2. Number of errors: 0-90 — —

3. Direction taken Left (1) Right (2)

M. STAR DRAWING - NON-DOMINANT HAND

1. Total time: 0-90 — —

2. Number of errors: 0-90 — —

3. Direction taken Left (1) Right (2)

N. WAIS ARITHMETIC

1. Number of points: 0-18 — —

a. Scaled score: 0-19 — —

b. Age-corrected scaled score: 0-19 — —

2. Mean latency for correct responses: 0-120 — — —

O. WISC-R ARITHMETIC

1. Number of points: 0-18 — —

a. Age-corrected scaled score: 0-19 — —

2. Mean latency for correct responses: 0-75 — —

Patient ID _____

P. WAIS SIMILARITIES

1. Number of points: 0-26 ___
   a. Scaled score: 0-19 ___
   b. Age-corrected scaled score: 0-19 ___

Q. WISC-R SIMILARITIES

1. Number of points: 0-30 ___
   a. Age-corrected scaled score: 0-19 ___

R. VISUAL REPRODUCTIONS - IMMEDIATE RECALL

1. Design A -- total points: 0-4 ___
2. Design A -- segmentation score: 0-5 ___
3. Design B -- total points: 0-5 ___
4. Design B -- segmentation score: 0-9 ___
5. Design C1 -- total points: 0-4 ___
6. Design C1 -- segmentation score: 0-7 ___
7. Design C2 -- total points: 0-4 ___
8. Design C2 -- segmentation score: 0-7 ___

S. VISUAL REPRODUCTIONS - COPY

1. Design A -- total points: 0-4 ___
2. Design A -- segmentation score: 0-5 ___
3. Design B -- total points: 0-5 ___
4. Design B -- segmentation score: 0-9 ___
5. Design C1 -- total points: 0-4 ___
6. Design C1 -- segmentation score: 0-7 ___
7. Design C2 -- total points: 0-4 ___
8. Design C2 -- segmentation score: 0-7 ___

T. VISUAL REPRODUCTIONS - DELAY

1. Design A -- total points: 0-4 ___
2. Design A -- segmentation score: 0-5 ___
3. Hint given? No (1) Yes (2)
4. Design B -- total points: 0-5 ___
5. Design B -- segmentation score: 0-9 ___
6. Hint given? No (1) Yes (2)
7. Design C1 -- total points: 0-4 ___
8. Design C1 -- segmentation score: 0-7 ___
9. Hint given? No (1) Yes (2)
10. Design C2 -- total points: 0-4 ___
11. Design C2 -- segmentation score: 0-7 ___
12. Hint given? No (1) Yes (2)

U. WAIS COMPREHENSION

1. Number of points: 0-28 ___
   a. Scaled score: 0-19 ___
   b. Age-corrected scaled score: 0-19 ___

V. WISC-R COMPREHENSION

1. Number of points: 0-34 ___
   a. Age-corrected scaled score: 0-19 ___

W. DIGIT VIGILANCE

1. Time to complete page 1: 0-400 ___
2. Number of omission errors -- page 1: 0-103 ___
3. Number of comission errors -- page 1: 0-99 ___
4. Number of correct responses -- page 1: 0-103 ___
5. Time to complete page 2: 0-400 ___
6. Number of omission errors -- page 2: 0-103 ___

Patient ID _____

7. Number of comission errors -- page 2: 0-99 __

8. Number of correct responses -- page 2: 0-103 ___

X. WAIS PICTURE ARRANGEMENT

1. Number of points: 0-36 __

a. Scaled score: 0-19 __

b. Age-corrected scaled score: 0-19 __

Y. WISC-R PICTURE ARRANGEMENT

1. Number of points: 0-48 __

a. Age-corrected scaled score: 0-19 __

Z. WAIS DIGIT SPAN

1. Number of points: 0-17 __

2. Number of digits repeated forward: 0-9 _

3. Number of digits repeated backward: 0-8 _

a. Scaled score: 0-19 __

b. Age-corrected scaled score: 0-19 __

AA. WISC-R DIGIT SPAN

1. Number of points: 0-28 __

2. Number of digits repeated forward: 0-9 _

3. Number of digits repeated backward: 0-8 _

a. Age-corrected scaled score: 0-19 __

BB. CATEGORY TEST

1. Number of errors -- subtest 1: 0-8 _

2. Number of errors -- subtest 2: 0-20 __

3. Number of errors -- subtest 3: 0-40 __

4. Number of errors -- subtest 4: 0-40 __

5. Number of errors -- subtest 5: 0-40 __

6. Number of errors -- subtest 6: 0-40 __

7. Number of errors -- subtest 7: 0-20 __

8. Time to complete task: 0-1800 ____

CC. GROOVED PEGBOARD - DOMINANT HAND

1. Time to insert pegs: 0-180 ___

2. Time to remove pegs: 0-180 ___

3. Number of pegs dropped: 0-25 __

DD. GROOVED PEGBOARD - NON-DOMINANT HAND

1. Time to insert pegs: 0-180 ___

2. Time to remove pegs: 0-180 ___

3. Number of pegs dropped: 0-25 __

EE. FINGER TAPPING - DOMINANT HAND

1. Number of trials administered: 0-10 __

2. Mean tapping rate per 10 second trial: 0-60.0 ___

FF. FINGER TAPPING - NON-DOMINANT HAND

1. Number of trials administered: 0-10 __

2. Mean tapping rate per 10 second trial: 0-80.0 ___

GG. SYMBOL-DIGIT PAIRED-ASSOCIATE LEARNING TEST

1. Number correct -- trial 1: 0-7 _

2. Number correct -- trial 2: 0-7 _

3. Number correct -- trial 3: 0-7 _

4. Number correct -- trial 4: 0-7 _

5. Number correct -- delayed recall: 0-7 _

HH. WAIS VOCABULARY

1. Number correct: 0-80 __

a. Scaled score: 0-19 __

b. Age-corrected scaled score: 0-19 __

Patient ID _____

II. WISC-R VOCABULARY

1. Number correct: 0-64 — —

   a. Age-corrected scaled score: 0-19 — —

JJ. TRAILMAKING

1. Sample A Time: 0-60 — —

2. Sample A Errors: 0-8 —

3. Trails A Time: 0-99 — —

4. Trails A Errors: 0-25 — —

5. Sample B Time: 0-60 — —

6. Sample B Errors: 0-8 —

7. Trails B Time: 0-300 — — —

8. Trails B Errors: 0-25 — —

KK. WAIS BLOCK DESIGN

1. Number of points: 0-48 — —

   a. Scaled score: 0-19 — —

   b. Age-corrected scaled score: 0-19 — —

2. Number of rotations: 0-25 — —

3. Number of broken configurations: 0-25 — —

4. Number of reversals: 0-25 — —

FOR ITEMS 5-10, CODE
99 IF CORRECT BUT OVERTIME
98 IF INCORRECT AND OVERTIME

5. Time to complete Design 1 correctly: 0-60 — —

6. Time to complete Design 2 correctly: 0-60 — —

7. Time to complete Design 3 correctly: 0-60 — —

8. Time to complete Design 4 correctly: 0-60 — —

9. Time to complete Design 5 correctly: 0-60 — —

10. Time to complete Design 6 correctly: 0-60 — —

FOR ITEMS 11-14, CODE
999 IF CORRECT BUT OVERTIME
998 IF INCORRECT AND OVERTIME

11. Time to complete Design 7 correctly: 0-120 — — —

12. Time to complete Design 8 correctly: 0-120 — — —

13. Time to complete Design 9 correctly: 0-120 — — —

14. Time to complete Design 10 correctly: 0-120 — — —

LL. WISC-R BLOCK DESIGN

1. Number of points: 0-62 — —

   a. Age-corrected scaled score: 0-19 — —

2. Number of rotations: 0-25 — —

3. Number of broken configurations: 0-25 — —

4. Number of reversals: 0-25 — —

FOR ITEMS 5-12, CODE
99 IF CORRECT BUT OVERTIME
98 IF INCORRECT AND OVERTIME

5. Time to complete Design 1 correctly: 0-45 — —

6. Time to complete Design 2 correctly: 0-45 — —

7. Time to complete Design 3 correctly: 0-45 — —

8. Time to complete Design 4 correctly: 0-45 — —

9. Time to complete Design 5 correctly: 0-75 — —

10. Time to complete Design 6 correctly: 0-75 — —

11. Time to complete Design 7 correctly: 0-75 — —

Patient ID _____

12. Time to complete Design 8 correctly: 0-75 ___

FOR ITEMS 13-15, CODE 999 IF CORRECT BUT OVERTIME 998 IF CORRECT AND OVERTIME

13. Time to complete Design 9 correctly: 0-120 ___
14. Time to complete Design 10 correctly: 0-120 ___
15. Time to complete Design 11 correctly: 0-120 ___

MM. SHORT-TERM MEMORY

1. Number of words correctly recalled after 5 seconds: 0-20 ___
2. Number of words correctly recalled after 15 seconds: 0-20 ___
3. Number of words correctly recalled after 30 seconds: 0-20 ___
4. Number of prior-trial intrusion errors: 0-60 ___
5. Number of intra-list intrusion errors: 0-60 ___
6. Number of extra-list intrusion errors: 0-99 ___

NN. WRAT ARITHMETIC

1. Raw Score: 0-57 ___
   a. Grade rating: 0.0-16.8 ___.___
   b. Standard score: 48-155 ___
   c. Percentile: 1-99.9 ___.___

OO. VERBAL FLUENCY

1. Number of "F" words in first quarter (0-15 seconds): 0-25 ___
2. Number of "F" words in second quarter (16-30 seconds): 0-25 ___
3. Number of "F" words in third quarter (31-45 seconds): 0-25 ___
4. Number of "F" words in fourth quarter (46-60 seconds): 0-25 ___
5. Number of illegitimate words: 0-25 ___
6. Number of "A" words in first quarter (0-15 seconds): 0-25 ___
7. Number of "A" words in second quarter (16-30 seconds): 0-25 ___
8. Number of "A" words in third quarter (31-45 seconds): 0-25 ___
9. Number of "A" words in fourth quarter (46-60 seconds): 0-25 ___
10. Number of illegitimate words: 0-25 ___
11. Number of "S" words in first quarter (0-15 seconds): 0-25 ___
12. Number of "S" words in second quarter (16-30 seconds): 0-25 ___
13. Number of "S" words in third quarter (31-45 seconds): 0-25 ___
14. Number of "S" words in fourth quarter (46-60 seconds): 0-25 ___
15. Number of illegitimate words: 0-25 ___
16. Total number of words: 0-300 ___

PP. TACTUAL PERFORMANCE TEST

1. Total time with dominant hand: 0-600 ___
2. Total time with non-dominant hand: 0-600 ___
3. Total time with both hands: 0-600 ___
4. Total time for recall: 0-600 ___
5. Memory score: 0-10 ___
6. Location score: 0-10 ___

QQ. INTELLIGENCE QUOTIENTS (IQ)

1. Verbal IQ ___
2. Performance IQ ___
3. Full Scale IQ ___

RR. QUALITY OF NEUROBEHAVIORAL TESTING

1. How willing was this subject to try his or her best?

Very willing	(1)
Somewhat willing	(2)
Not too willing	(3)
Very unwilling	(4)

2. Overall, how much did distractions and interruptions affect the session?

Very much	(1)
Much	(2)
Somewhat	(3)
Little	(4)
Very little	(5)

3. To what extent do you feel the information obtained is accurate?

Completely	(1)
Mostly	(2)
Moderately	(3)
Somewhat	(4)
Not very	(5)

4. Quality Grade:

Satisfactory	(1)
Acceptable with minor problems	(2)
Unacceptable	(3)

DIABETES CONTROL AND COMPLICATIONS TRIAL

Randomization Report

Once a patient has been found to be eligible for participation in the DCCT, this form is to be completed. The form will document the results of the final eligibility examinations and the baseline assessments. (The Eligibility and Exclusion Checklist, Form 038, recorded the results of the initial eligibility screens; it should already be on file at the Coordinating Center.)

After completing Sections A-C of this form, the clinic coordinator should telephone the DCCT Research Assistant at the Coordinating Center to receive the patient's treatment assignment. The telephone number is (301) 657-2376. Complete Section D of this form after speaking with the Research Assistant. Note that if any boxes marked "HOLD" are checked, the patient is not ready to be randomized.

Send a copy of this form to the Coordinating Center in the weekly forms mailing.

A. IDENTIFYING INFORMATION

1. Clinic Number [ ][ ] 5-6
2. Patient ID Number [ ][ ][ ][ ][ ] 7-11
3. Patient's Initials [ ][ ][ ] 12-14
4. Date of Randomization [ ][ ] / [ ][ ] / [ ][ ] 15-20 (Month / Day / Year)

B. FINAL ELIGIBILITY EXAMINATIONS

1. Did the patient complete the Volunteer's Understanding Questionnaire (Form 045 or 046)? No (Hold) 1 / Yes 2 — 21

   If YES, did the patient correctly answer all of the questions? No 1 / Yes 2 — 22

   If NO, did the Principal Investigator consider the patient to have an adequate understanding of the DCCT objectives and design? No (Stop) 1 / Yes 2 — 23

2. Is the patient female? No 1 / Yes 2 — 24

   If YES, enter date of final pregnancy test: [ ][ ] / [ ][ ] / [ ][ ] 25-30 (Month / Day / Year)

3. Has the patient signed the second Informed Consent form, giving permission to be randomized and to participate in the trial? No (Hold) 1 / Yes 2 — 31

4. Will the patient be less than eighteen years of age when randomized? No 1 / Yes 2 — 32

   If YES, has the patient's parent or guardian also signed the second Informed Consent form? No (Hold) 1 / Yes 2 — 33

C. BASELINE ASSESSMENTS

1. Was a blood sample mailed to the Hemoglobin A_{1c} Laboratory for baseline HbA_{1c} determination? No (Hold) 1 / Yes 2 — 34

   If YES,

   i) On what date was the sample sent? [ ][ ] / [ ][ ] / [ ][ ] 35-40 (Month / Day / Year)

   ii) What was the accession number? H - [ ][ ][ ][ ][ ][ ][ ] 41-47

2. Was a capillary blood glucose set mailed to the Central Biochemistry Laboratory for baseline blood glucose profile determination? No (Hold) 1 / Yes 2 — 48

   If YES,

   i) On what date was the set mailed? [ ][ ] / [ ][ ] / [ ][ ] 49-54 (Month / Day / Year)

   ii) What was the accession number? BGP - [ ][ ][ ][ ][ ][ ][ ] 55-61

3. Was a serum specimen mailed to the Central Biochemistry Laboratory for baseline measurement of lipids? No (Hold) 1 / Yes 2 — 62

   If YES,

   i) On what date was the serum sent? [ ][ ] / [ ][ ] / [ ][ ] 63-68 (Month / Day / Year)

   ii) What was the accession number? S - [ ][ ][ ][ ][ ][ ][ ] 69-75

Patient ID _____

4. Was a creatinine clearance performed and was a urine specimen mailed to the Central Biochemistry Laboratory? No (Hold) 1 Yes 2 — 76

If YES,

i) On what date was the urine specimen sent? Month / Day / Year — 77–82

ii) What was the accession number? U - _____ — 83–89

5. Was extra serum drawn and mailed to the Central Biochemistry Laboratory for possible future determinations? No (Hold) 1 Yes 2 — 90

6. Were fluorescein angiograms taken and mailed to the Central Ophthalmologic Reading Unit? No 1 Yes 2 — 91

If YES,

i) On what date were the angiograms sent? Month / Day / Year — 92–97

ii) What was the accession number? A - _____ — 98–102

7. Was an EKG obtained to measure baseline R-R variation and was it mailed to the Autonomic Neuropathy Coding Unit? No (Hold) 1 Yes 2 — 103

If YES, on what date was the EKG sent? Month / Day / Year — 104–109

8. Was a baseline neurobehavioral assessment performed? No (Hold) 1 Yes 2 — 110

9. Were the following forms completed and mailed to the Coordinating Center?

	No (Hold) 1	Yes 2	
Neurological History and Examination (Form 005)			111
Diet History (Form 018)			112
Quarterly Clinic Visit (Form 021)			113
Symptom Checklist-90-R (Form 035)			114
Quality of Life Questionnaire (Form 036)			115
Nerve Conduction Studies (Form 037)			116
Family Understanding and Expectation Interview (Form 048)			117

10. Were the behavioral tasks completed? No (Hold) 1 Yes 2 — 118

If YES, on what date were the tasks completed? Month / Day / Year — 119–124

D. TREATMENT ASSESSMENT

To be completed after telephoning the Coordinating Center for the patient's treatment assignment.

1. To which treatment group is the patient randomized?

Standard Therapy 1 — 125

Experimental Therapy 2

2. If the patient is randomized to the Experimental Treatment Group, when will he/she be hospitalized for initiation of therapy?

If unknown, check here: 1 — 126

This hospitalization should occur as soon as possible. You will be queried later concerning the date of hospitalization.

Otherwise, enter date: Month / Day / Year — 127–132

Type or print name of person completing this form: _____

Certification Number (if any) _____ — 133–136

DIABETES CONTROL AND COMPLICATIONS TRIAL

Personal Information on Study Volunteer

This form is to be completed for every patient who has been randomized to one of the two treatment regimens of the DCCT. It must be completed at the time of randomization and every 12 months thereafter.

The originals of this form (on blue paper) are to be sent to the Coordinating Center in the weekly forms mailing.

A. IDENTIFYING INFORMATION

1. Clinic Number ☐☐
2. Patient ID Number ☐☐☐☐☐
3. Patient's Initials ☐☐☐
4. Date form completed ☐☐/☐☐/☐☐ (Month / Day / Year)

B. PATIENT INFORMATION

1. Patient's full name: _____ (Last) _____ (First) _____ (Middle)
2. Last name of patient's father (enter even if it's the same as the patient's last name): _____
3. Date of birth: ☐☐/☐☐/☐☐ (Month / Day / Year)
4. Place of birth: _____ (City) _____ (State or Province)
5. Sex: Male ☐ 1 Female ☐ 2
6. Does the patient have a Social Security Number or, for Canadians, a Social Insurance Number? No ☐ 1 Yes ☐ 2

   If YES, enter Social Security (or Social Insurance) Number: ☐☐☐☐☐☐☐☐☐
7. Does the patient have a driver's license number? No ☐ 1 Yes ☐ 2

   If YES, (a) enter license number (may be the same as Social Security Number): _____

   (b) from which state or province was the driver's license granted? _____
8. Patient's home address: _____ (Number and Street)

   _____ (City) _____ (State or Province) _____ (Zip Code)
9. Patient's State or Province of legal residence (enter even if it's the same as given in Question 8): _____
10. Is the patient married? No ☐ 1 Yes ☐ 2

    If YES, enter full name of spouse:

    _____ (Last) _____ (First) _____ (Middle)

B. PATIENT INFORMATION (Continued)

11. If the patient is/was under 18 years of age at randomization, enter name and address of parent or guardian (address may be the same as the patient):

_____ Last , _____ First _____ Middle

_____ Number and Street

_____ City _____ State or Province _____ Zip Code

Telephone number: ( ) _____ Area Code

12. Enter name and address of a close relative or friend not living at the same address given in Questions 8 or 11:

_____ Last , _____ First _____ Middle

_____ Number and Street

_____ City _____ State or Province _____ Zip Code

Telephone number: ( ) _____ Area Code

13. Enter name and address of employer or, if student, name and address of school currently attending:

_____ Name of Employer (Company, etc.) or Name of School

_____ Number and Street (if known)

_____ City _____ State or Province _____ Zip Code

Telephone number (if known): ( ) _____ Area Code

14. Patient's medical center/clinic/hospital ID number (if any): _____

Name of medical center/clinic/hospital: _____

15. Did a physician refer the patient to the DCCT clinic? No ☐ 1 Yes ☐ 2

If YES, enter physician's name and address:

_____ Last , _____ First

_____ Number and Street (if known)

_____ City _____ State or Province _____ Zip Code

Telephone number (if known): ( ) _____ Area Code

16. Does the patient have health insurance? No ☐ 1 Yes ☐ 2

If YES, enter (a) name of insurance company _____

(b) policy number _____

Signature of person who completed this form:

_____

Certification Number (if any)

☐☐ - ☐☐

DIABETES CONTROL AND COMPLICATIONS TRIAL

Neurobehavioral Studies Demographic Questionnaire

This questionnaire should be administered by the neurobehavioral examiner after making his/her opening remarks introducing the session. These straightforward questions will provide the Central Neurobehavioral Coding Unit with important information and will give the examiner and subject an opportunity to get to know each other better in a non-threatening situation.

Send the original of this questionnaire to the Coordinating Center in the regular weekly mailing. Also send a copy to the Central Neurobehavioral Coding Unit along with the test results.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number ___ ___
2. Patient ID Number ___ ___ ___ ___ ___
3. Patient's Initials ___ ___ ___
4. Date form completed ___ ___ ___ ___ ___ ___ (Month Day Year)
5. Examiner's Certification Number ___ ___ - ___ ___
6. Follow-up visit number (if baseline visit enter 00) ___ ___

B. DEMOGRAPHIC QUESTIONS

THE EXAMINER SHOULD SAY: "BEFORE WE BEGIN, I WOULD LIKE TO ASK YOU A FEW GENERAL QUESTIONS." THEN ASK THE FOLLOWING QUESTIONS:

1. How old are you now? (years) ___ ___
2. When were you born? ___ ___ ___ ___ ___ ___ (Month Day Year)
3. Are you in school now? No (1) Yes (2)

   If YES, what grade (year) are you in?

   Enter year in elementary or secondary school ___ ___

   or year in college ___

   or year in graduate school ___

   If NO, how many years of school did you complete? ___ ___

   If adult with less than 12 years, did you receive a G.E.D.? No (1) Yes (2)

4. Which hand do you prefer to write with? Right (1) Left (2) Both equally well (3)
5. Do you have any problems now using any of your fingers? No (1) Yes (2)

   If YES, which fingers?

Left					Right				
L	R	M	I	T	T	I	M	R	L

   What is the problem? _____

   _____
6. Can you move both wrists freely? No (1) Yes (2)

   If NOT, which one do you have trouble with? Right (1) Left (2) Both (3)

   What is the problem? _____

   _____
7. Is English your native language? No (1) Yes (2)

   If NO, what is your native language?

   _____

   At what age did you learn English? ___ ___ years

		No	Yes
8.	Do you wear glasses or contact lenses?	(1)	(2)
	If YES, do you have them with you?	(1)	(2)
9.	Do you have any problems with your hearing?	(1)	(2)

If YES, what is the problem?

_____

		No	Yes
10.	Have you taken any medications or drugs (aside from insulin) in the past 48 hours?	(1)	(2)

If YES, list drug, approximate quantity, reason for taking drug, and time drug taken:

_____

_____

11. Have you had any beer or other alcohol in the past 48 hours?

	No	Yes	If yes, when	Quantity
Beer	(1)	(2)	_____	_____
Wine	(1)	(2)	_____	_____
Hard liquor/mixed drinks:	(1)	(2)	_____	_____

C. BLOOD GLUCOSE LEVELS

		No	Yes
1.	Were blood glucose levels checked at appropriate times during the session?	(1)	(2)
2.	(IF YES) Were the blood glucose levels acceptable for neurobehavioral testing purposes?	(1)	(2)

If blood glucose levels were not acceptable, explain:

_____

_____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Notification of Missed Clinic Visit or Modification of Follow-up Schedule

This form is to be completed whenever a randomized patient fails to keep an endpoint or interim clinic visit within the "time window" allowed or fails to undergo any scheduled procedure.

The original of this form is to be sent to the Coordinating Center in the weekly forms mailing. Retain a copy in the clinic files.

A. IDENTIFYING INFORMATION

1. Clinic Number ___ ___
2. Patient ID Number ___ ___ ___ ___ ___
3. Patient's Initials ___ ___ ___
4. Date form completed ___ ___ ___ ___ ___ ___
   Month Day Year

B. VISIT INFORMATION

1. Target date for missed visit ___ ___ ___ ___ ___ ___
   Month Day Year
2. If the missed appointment was an interim management visit, check here: (1)

   Otherwise, indicate which endpoint visit this was to be: ___ ___
3. Indicate which (if any) of the following procedures were to have been completed at this visit but were not completed inside the window:
   (CHECK ALL THAT APPLY. NUMBERS IN PARENTHESES INDICATE FORMS TO BE COMPLETED FOR THE PROCEDURE.)

   Annual Medical History and Physical Examination (003) (1)

   Quarterly Visit (021) (1)

   Hemoglobin A1c Specimen Mailing List (055) (1)

   Blood Glucose Profile Specimen Mailing List (050) (1)

   Endpoint Visit Ophthalmic Examination (027) (1)

   Fundus Photography (025) and Fundus Photograph Mailing List (042) (1)

   Fluorescein Angiography (026) and Fundus Photograph Mailing List (042) (1)

   Renal Studies Specimen Mailing List (044) (1)

   Neurological History and Examination (005) (1)

   ANS Tape and Documentation Sheet, ANS Testing Eligibility (081) and ANS Mailing List (054) (1) (1)

   Nerve Conduction Studies (037) (1)

   Resting EKG and Resting Electrocardiogram Mailing List (053) (1)

   Lipid Specimen Mailing List (058) (1)

   Locally-Performed Blood Count and Chemistry (004) (1)

   Locally-Performed Urinalysis and Urine Culture (006) (1)

   Neurobehavioral Assessment (010), Neurobehavioral Studies Demographic Questionnaire (013) and Neurobehavioral Assessment Mailing List (051) (1)

   Symptom Checklist-90-R (035) (1)

   Quality of Life Questionnaire (036) (1)

   Diet History (018) and Diet History Mailing List (052) (1)

   Assessment of Adherence (1)

   Other; specify: _____ (1)

   _____

4. Has the patient been in contact with or been contacted by the DCCT clinic concerning his/her missed visit? No (1) Yes (2)

If YES, in your opinion, what is the main reason for the missed visit? (CHECK ONLY ONE)

- Patient refuses to undergo these endpoint examinations but is willing to undergo others (1)
- Moved to a less convenient location (2)
- Illness/surgery/hospitalization (3)
  (IF SO, YOU MAY ALSO NEED TO COMPLETE NOTIFICATION OF INTERCURRENT EVENT, DCCT FORM 020.)
- General decline in motivation (4)
- Conflicting responsibilities (job, birthday, family) (5)
- Scheduling error (6)
- Other; specify: _____ (7)

_____

5. Will any of the missed procedures be completed at a later date? No (1) Yes (2) Uncertain (3)

If YES, which ones and when? _____

_____

Signature of Trial Coordinator: _____

Certification Number (if any) __ __ - __ __

DIABETES CONTROL AND COMPLICATIONS TRIAL

Notification of Death

Immediately upon learning of the death of a DCCT patient, the clinic coordinator should notify the DCCT Research Assistant at the Coordinating Center by telephone. The telephone number is (301) 657-2376. After discussion with the patient's family and personal physician, the DCCT physician should complete a copy of this form to record the probable underlying cause of death. Every effort must be made to obtain a copy of the autopsy report and death certificate. If not available at the time this form is completed, they must be mailed to the Coordinating Center as soon as possible.

A. IDENTIFYING INFORMATION

1. Clinic Number [ ][ ] 5-6
2. Patient ID Number [ ][ ][ ][ ][ ] 7-11
3. Patient's Initials [ ][ ][ ] 12-14
4. Date form completed [ ][ ] / [ ][ ] / [ ][ ] 15-20
   Month Day Year

B. GENERAL INFORMATION

1. Date of death [ ][ ] / [ ][ ] / [ ][ ] 21-26
   Month Day Year
2. Place of death: *(Check only one)*
   - Hospital [1] 27
   - Home [2]
   - Long-term care institution [3]
   - Other; specify _____ [4]
   - Unknown [5]
3. Was the death: *(Check only one)*
   - Sudden, explained [1] 28
   - Sudden, unexplained [2]
   - Following illness [3]
4. Do you consider the death to be diabetes related? No [1] Yes [2] 29
5. Was the patient using the insulin-infusion pump? No [1] Yes [2] 30
6. Was an autopsy performed? No [1] Yes [2] 31
   If YES, is the autopsy report enclosed? No [1] Yes [2] 32
   If NO, the autopsy report must be forwarded to the Coordinating Center as soon as possible.
7. Is the death certificate enclosed? No [1] Yes [2] 33
   If NO, the death certificate must be forwarded to the Coordinating Center as soon as possible.
8. Specify which sources of information were used in completing this form: *(Answer each)*

	No	Yes	
Death certificate	[1]	[2]	34
Autopsy report	[1]	[2]	35
Hospital report of final illness	[1]	[2]	36
Interview of the attending physician at time of death	[1]	[2]	37
Interview of a family member	[1]	[2]	38
Other (specify):	[1]	[2]	39

_____
_____
_____

1. Immediate cause of death:
   _____
   _____
   _____
2. Underlying cause of death: *(May be the same as immediate cause of death; please specify)*
   _____
   _____
   _____
3. Specify any contributory causes of death:
   _____
   _____
   _____

Signature of Principal Investigator:

_____

FOR COORDINATING CENTER USE ONLY

Reviewed: [ ][ ] / [ ][ ] / [ ][ ] 40-45
Month Day Year

DIABETES CONTROL AND COMPLICATIONS TRIAL

Application for Transfer to Inactive Status

This form must be completed whenever a Principal Investigator seeks permission from the Clinic Monitoring Group (CMG) to transfer a randomized patient to inactive status. Transfer to inactive status implies a temporary or permanent moritorium on all efforts to involve the patient in any DCCT activities whatsoever (either treatment or endpoint determination). The clinical center must notify the Chairman of the CMG at the time of any potential transfer to inactive status. The Chairman of the CMG will advise the clinical center of the appropriate action. The Treatment Committee will also review all transfers to inactive status.

The original of this form is to be sent to the Coordinating Center in the weekly forms mailing. Retain a copy in the clinic files.

A. IDENTIFYING INFORMATION

1. Clinic Number ___ ___
2. Patient ID Number ___ ___ ___ ___ ___
3. Patient's Initials ___ ___ ___
4. Date form completed ___ ___ ___ ___
   Month Day Year

B. INFORMATION ON TRANSFER TO INACTIVE STATUS

1. Specify the reason for the request for transfer to inactive status; (CHECK ALL THAT APPLY)
   to inactive status: (CHECK ALL THAT APPLY)

   a) Judgment of Principal Investigator and mental health consultants that any manner of participation in the study could no longer be considered informed or would be directly injurious to the patient's well-being (1)

   b) Catastrophic injury or illness leading to coma, dementia, blindness, or insbility to monitor diabetic retinopathy adequately (1)

   c) Complete inaccessibility to metabolic monitoring or to monitoring of endpoints (for example, long-term imprisonment) (1)

   d) Patient has withdrawn consent for continued participation (1)

   e) Other (specify in Question 2) (1)

2. Explain in detail reason for request for transfer. (USE EXTRA SHEET IF NECESSARY)

_____

_____

3. On what date would the proposed transfer to inactive status become effective? (IF IMMEDIATELY, ENTER TODAY'S DATE.) __ __ Month __ __ Day __ __ Year

If uncertain, check here: (1)

C. PLANS FOR FUTURE CONTACT

	No	Yes	Uncertain
1. Do you believe you will attempt to contact the patient in the future?	(1)	(2)	(3)

If NO, give reasons: _____

_____

	No	Yes	Uncertain
2. Do you believe that the patient would be willing and able to return to a DCCT clinic for at least some endpoint evaluations?	(1)	(2)	(3)

If YES or UNCERTAIN, specify plans for future patient followup:

_____

_____

3. Who will be delivering the patient's diabetes care? (Specify names, addresses and phone numbers if known)

_____

_____

Signature of Principal Investigator:

_____

FOR COORDINATING CENTER USE ONLY

1. Reviewed by Clinic Monitoring Group:		__ __ Month __ __ Day __ __ Year
2. Reviewed by Treatment Committee:		__ __ Month __ __ Day __ __ Year
3. Recommendation:	Transfer (1)	Deny Transfer (2)
4. Clinic notified:		__ __ Month __ __ Day __ __ Year

DIABETES CONTROL AND COMPLICATIONS TRIAL

Bradburn Affect Balance Scale

Clinic Number __ __ Patient's Initials __ __ __

Patient ID Number __ __ __ __ __ Today's Date __ __ / __ __ / __ __
Month Day Year

	Very happy	Pretty happy	Not too happy
I. Taking all things together, how would you say things are these days? Would you say you are very happy, pretty happy, or not too happy?	(1)	(2)	(3)

II. Below are some of the ways people feel at different times. Indicate whether you felt like that during the PAST FEW WEEKS by checking the box that applies.

	Often	Sometimes	Never
On top of the world	(1)	(2)	(3)
Very lonely or remote from other people	(1)	(2)	(3)
That things were going your way	(1)	(2)	(3)
Upset because someone criticized you	(1)	(2)	(3)
Particularly excited or interested in something	(1)	(2)	(3)
Depressed or very unhappy	(1)	(2)	(3)
Pleased about having accomplished something	(1)	(2)	(3)
Bored	(1)	(2)	(3)
Proud because someone complimented you on something you had done	(1)	(2)	(3)
So restless you couldn't sit long in a chair	(1)	(2)	(3)

Diabetes Control and Complications Trial

DIET HISTORY

DCCT FORM 018.2

DCN940100

DATE FORM COMPLETED (MONTH - DAY - YEAR) ☐☐-☐☐-☐☐

CLINIC ☐☐

PATIENT'S NAME

PATIENT'S ID # ☐☐☐☐☐

PATIENT'S INITIALS ☐☐☐

ROUTINELY TAKES VITAMIN/MINERAL OR OTHER SUPPLEMENTS
0 = No
1 = Yes ☐

RELIABILITY: 0 = No 1 = Yes
Recalls all meals ____
Not Yea-saying ____
Cross-check validates ____
Rating (total above) ☐

EXERCISE LEVEL
1 = Sedentary
2 = Moderate
3 = Heavy ☐

VISIT
If this is a baseline visit check here ☐
Otherwise, i) specify which follow-up visit this is ☐☐
ii) is the visit being held within the time window? ☐ 0 = No 1 = Yes

FOR NCC USE
BATCH NO.: ____
INITIALS
CODER'S ID ☐☐
DATE CODED ☐☐-☐☐-☐☐
EDITION NO ☐☐
NO RECORDS ☐☐☐

Page ☐ of ☐

Type or print name of Dietitian: 004242
Certification Number ☐☐-☐☐

Type or print name of Clinic Coordinator:
Certification Number ☐☐-☐☐

DCN940200
Dup 10-29

MEAL: 1 = AM meal, 2 = AM snack, 3 = Noon meal, 4 = Aft snack, 5 = Eve meal, 6 = Eve snack
PREPARED: 1 = Home 2 = Restaurant

SALT IN PREP? 0 = No 1 = Yes 9 = Unkn
FAT IN PREP? 0 = No 1 = Yes 9 = Unkn

SALT AT TABLE? 0 = No 1 = Light 2 = Medium 3 = Heavy 9 = Unkn

LINE NO.	Weekday	Saturday	Sunday	MEAL	FOODS and BEVERAGES DESCRIPTION	AMOUNT	FREQ.	FOOD CODE	AMOUNT	FOOD UNIT	FREQUENCY	PREP. CODE	FAT CODE	DO NOT USE
01														
02														
03														
04														
05														
06														
07														
08														
09														
10														
11														
12														
13														
14														

DIABETES CONTROL AND COMPLICATIONS TRIAL

Notification of Intercurrent Event

This form must be completed each time a patient who has been randomized or is undergoing eligibility screening experiences a major intercurrent event. These events are listed and defined in Chapter 10 of the DCCT Manual of Operations. Definitions of the time frame categories are given in the same chapter.

This form should be completed according to the time frames given in Chapter 10 and mailed to this address: DCCT Morbidity/Mortality Classification Committee, The Biostatistics Center, 6110 Executive Boulevard, Suite 750, Rockville, Maryland 20852. A copy of the form is to be kept in the clinic's files. On the Clinic Forms Inventory and Forms Mailing List (DCCT Forms 040 and 041), you should list the Form 020 which was mailed to the Coordinating Center.

A. IDENTIFYING INFORMATION

1. Clinic Number ___ ___
2. Patient ID Number ___ ___ ___ ___ ___
3. Patient's Initials ___ ___ ___
4. Date form completed ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)
5. Has the patient been randomized? No (1) Yes (2)

B. RECOGNITION OF INTERCURRENT EVENT

1a) Specify date of occurrence or recognition of intercurrent event: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)

OR

b) If date uncertain, check here: (1)

2. Specify date DCCT clinic learned of the intercurrent event: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)

3. How did the clinic learn of the intercurrent event?

Patient or patient's family/friends contacted clinic (1)

Third party contacted clinic (2)

Clinic recognized event and informed the patient (3)

Patient informs clinic at follow-up visit (4)

C. NATURE OF INTERCURRENT EVENT

1. Indicate diagnosis. (CHECK ALL THAT APPLY).

Diabetic Intercurrent Events		Time Frame Category
a) Ketoacidosis	(1)	2
b) Hyperglycemic, hyperosmolar, nonketotic coma	(1)	2
c) Definite catastrophic hypoglycemia*	(1)	1
d) Suspected catastrophic hypoglycemia*	(1)	1
e) Definite severe hypoglycemia*	(1)	2
f) Suspected severe hypoglycemia*	(1)	2

*Be certain to complete Question 3 below and Form 083.

Patient ID _____

		Time Frame Category
Ocular Intercurrent Events		
g) Loss of vision	(1)	2
h) High risk characteristics (HRC)	(1)	2
i) Ocular disease (OTHER THAN RETINOPATHY) that may influence visual acuity or require surgery or medical treatment for >3 months (SPECIFY UNDER QUESTION 2)	(1)	2
j) Photocoagulation	(1)	2
Cardiovascular Intercurrent Events		
k) Definite acute myocardial infarction	(1)	2
l) Suspected acute myocardial infarction	(1)	2
m) Angina pectoris	(1)	2
n) Arrhythmia	(1)	2
o) Congestive heart failure	(1)	2
p) Initial diagnosis of hypertension	(1)	2
q) CVA with permanent neurological deficit	(1)	2
r) CVA without permanent neurological deficit	(1)	2
Renal Intercurrent Events		
s) Renal insufficiency	(1)	2
Other Intercurrent Events		
t) Infusion catheter infection	(1)	2
u) Amputation (traumatic)	(1)	2
v) Amputation (surgical)	(1)	2
w) Major accident not requiring hospitalization but requring medical attention	(1)	2
x) Major accident requiring hospitalization	(1)	2
y) Overnight hospitalization (SPECIFY UNDER QUESTION 2)	(1)	2
z) Psychiatric disease requiring treatment	(1)	2
aa) Other (SPECIFY UNDER QUESTION 2)	(1)	2
Pregnancy Related Intercurrent Events		
bb) Pregnancy (to be completed when patient is diagnosed)	(1)	2
cc) Abortion (spontaneous)	(1)	2
dd) Abortion (induced)	(1)	2
ee) Live birth:		
Birth weight (grams)	_ _ _	
Gestational age (wks)	_ _ _	
Apgar Score.	_ _ _	
ff) Discharged alive with congenital malformation (SPECIFY UNDER QUESTION 2)	(1)	2
gg) Discharged alive without congenital malformation	(1)	2
hh) Neonatal death with congenital malformation (SPECIFY UNDER QUESTION 2)	(1)	2
ii) Neonatal death with other complications (SPECIFY UNDER QUESTION 2)	(1)	2
jj) Still birth with congenital malformation (SPECIFY UNDER QUESTION 2)	(1)	2
kk) Still birth with other complications (SPECIFY UNDER QUESTION 2)	(1)	2

Patient ID _____

Central Unit Notification

Check here if in response to central unit notification, then check one of the responses below, and then proceed to Section D. (1)

		Time Frame Category
ll) Notification of pre-proliferative or proliferative characteristics	(1)	2
mm) Notification of clinically significant macular edema	(1)	2
nn) Notification of hypercholesterolemia	(1)	2
oo) Notification of hypertriglyceridemia	(1)	2
pp) Notification of neuropsychological deterioration	(1)	2

2. Give diagnosis or describe condition, symptoms and suspected causes.

3. Complete this question only if catastrophic or severe hypoglycemia is being reported.* Otherwise proceed to Question 4.

Indicate symptoms or signs of hypoglycemia which occurred. (CHECK ALL THAT APPLY)

a) Death	(1)
b) Neurological insult requiring hospitalization	(1)
c) Myocardial infarction	(1)
d) Stroke	(1)
e) Injury to the patient requiring hospitalization	(1)
f) Injury to another person	(1)
g) Property damage	(1)
h) Traffic violation	(1)
i) Loss of consciousness	(1)
j) Seizure	(1)
k) Suspected seizure	(1)
l) Unusual difficulty in awakening	(1)
m) Irrational	(1)
n) Uncontrollable behavior	(1)
o) Confusion	(1)
p) Memory loss	(1)
q) Other; specify: _____	(1)

_____

*Be sure to complete a Form 083.

Patient ID _____

4. If a specific diagnosis was made, how was it established? (SEE THE CRITERIA IN CHAPTER 10 OF THE MANUAL OF OPERATIONS)

D. TREATMENT OF INTERCURRENT EVENT

1. Where was (is) the intercurrent event (being) treated? (CHECK ALL THAT APPLY)

a) Emergency room (1)

b) Hospital inpatient ward (1)

c) Office visit (1)

d) Long-term care institution (1)

e) DCCT clinic (1)

f) Other; SPECIFY: (1)

_____

_____

_____

	No	Yes
2. Did the DCCT clinic staff treat the patient for this event?	(1)	(2)
3. Were any medications prescribed to treat this event?	(1)	(2)

If YES, list medications, doses and use duration:

_____

_____

	No	Yes
4. Was any operation performed to treat this event?	(1)	(2)

If YES, specify operation and results:

_____

_____

	No	Yes
5. Did the patient receive psychiatric counseling?	(1)	(2)
6. Were other forms of treatment used for this event?	(1)	(2)

If YES, specify:

_____

_____

7. Specify the period of treatment for the intercurrent event:

a) Date of admission or start of treatment: __Month __Day __Year

b) (i) If treatment is still in progress, check here: (1)

(ii) Otherwise, enter date of discharge or conclusion of treatment: __Month __Day __Year

Patient ID _____

E. EFFECT ON DIABETIC CONTROL

COMPLETE THIS SECTION ONLY IF THE PATIENT HAS BEEN RANDOMIZED

1. Was diabetic control influenced by the intercurrent event or treatment? No (1) Yes (2) Unknown (3)

   If YES, in what way?

2. Was the diabetes treatment altered to an extent that it did not conform to the usual treatment (as specified in the Protocol and Manual of Operations) for patients in that study group? No (1) Yes (2)

   If YES, (a) in what way?

b) (i) Enter the date the diabetes treatment was altered

Month Day Year

OR

(ii) If date uncertain, check here: (1)

c) (i) Enter the date the patient returned to a diabetes treatment that conformed with protocol-specified therapy

Month Day Year

OR

(ii) If the patient has not yet returned to the protocol required treatment, check here: (1)

NOTE: IF THE EVENT OR ITS THERAPY WILL INVOLVE DEVIATION FROM THE DCCT TREATMENT, COMPLETE THE NOTIFICATION OF DEVIATION FROM ASSIGNED TREATMENT (DCCT FORM 022).

IF THE EVENT OR ITS THERAPY WILL PRECLUDE COLLECTION OF ENDPOINT DATA FOR A PROLONGED PERIOD OF TIME, COMPLETE THE NOTIFICATION OF MISSED VISIT OR MODIFICATION OF FOLLOWUP SCHEDULE (DCCT FORM 14)

Type or print name of person completing this form:

_____

Certification Number (if any)

__ __ - __ __

Signature of Principal Investigator:

_____

FOR COORDINATING CENTER USE ONLY

1. Reviewed: __ __ __ __ __ __
   Month Day Year
2. Recommendations: (if any):

   _____

   _____

   _____
3. Clinic notified: __ __ __ __ __ __
   Month Day Year

Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Quarterly Visit

This form is to be completed at the randomization visit and each of the scheduled quarterly follow-up clinic visits. For visits occurring yearly post-randomization, complete the Annual Medical History and Physical Examination (DCCT Form 003) in lieu of this form. At the time of the quarterly visit, data will be collected on this form to document modifications of therapy and to update information on the status of patients on deviations from assigned treatment and transfers to inactive status.

All questions on this form refer to the patient's experience since the last completed quarterly, annual or randomization visit. If the form is being completed at the randomization visit, the questions refer to the patient's experience since the Baseline Medical History and Physical Examination (DCCT Form 002) was completed.

If in completing this evaluation it is found that the patient has experienced an intercurrent event, complete the Notification of Intercurrent Event Form (DCCT Form 020) and, if applicable, the Notification of Hypoglycemic Intercurrent Event (DCCT Form 083) and Further Details of Hypoglycemic Event (Form 092).

Send the completed form to the Coordinating Center in the weekly forms mailing, retaining a copy in the clinic files.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date of Visit
   Month __ Day __ Year __
5a) Was it necessary to reschedule the patient for this visit for any reason? No (1) Yes (2)
   b) How many times? __ __ _____|
6. What is the follow-up visit number? (For the randomization visit, enter 00.) __ __
7. Enter the date of the LAST COMPLETED visit (baseline, randomization, quarterly or annual, whichever is most recent). All questions on this form refer to the patient's experience since this date. (For the randomization visit, enter the date the Baseline Medical History and Physical Exam (DCCT Form 002) was completed.)
   Month __ Day __ Year __

B. DIABETES MANAGEMENT

Answer Section B for all patients except where specified. Do not complete this section at the randomization visit. When completing this section, refer to the previous day's insulin dosage only. However, if in your judgement the previous day's dosage was atypical of the patient's regimen, use another recent day that you would consider typical.

1. Specify types of insulins used by this patient: (CHECK ALL THOSE THAT APPLY)

Human regular	(1)	Pork Regular	(1)
Human Semilente	(1)	Pork Semilente	(1)
Human NPH	(1)	Pork NPH	(1)
Human Lente	(1)	Pork Lente	(1)
Human Ultralente	(1)	Pork 70/30	(1)
Human 70/30	(1)		
Beef/pork Regular	(1)		
Beef/pork Semilente	(1)		
Beef/pork NPH	(1)		
Beef/pork Lente	(1)		
Beef/pork Ultralente	(1)		

2. To what group was this patient randomized?

   Standard (1) Experimental (2)

3. a) What insulin regimen is currently being used by this patient?

   insulin infusion pump (1)
   three or more daily injections (2)
   one or two daily injections (3)
   other: (4)
   (describe the regimen in Question Number 5)

   b) Is this the regimen prescribed by the DCCT clinic? No (1) Yes (2)

4. Please summarize this patient's usual insulin regimen here. (Refer to the previous day's insulin dosage only. However, if the previous day's dosage was atypical, use the most recent day that you would consider typical. Round off to the nearest whole unit.)

   a) Total number of units per day: __ __ __

   b) Number of:

Units Used	Breakfast	Lunch	Supper	Bedtime	Other
Regular	__ __	__ __	__ __	__ __	__ __
Semilente	__ __	__ __	__ __	__ __	__ __
NPH	__ __	__ __	__ __	__ __	__ __
Lente	__ __	__ __	__ __	__ __	__ __
Ultralente	__ __	__ __	__ __	__ __	__ __
70/30	__ __	__ __	__ __	__ __	__ __

   NOTE: When filling out this table, consider all insulin given between breakfast and lunch as part of the lunch dose. All insulin between lunch and supper is part of the supper dose. All insulin between supper and bedtime snack is part of the snack dose. If a patient gives a prescribed mealtime dose which happened to be zero on the day recorded, record "0" in the appropriate space. If no dose was prescribed for a given time of day, leave the space blank. If a patient is on a pump, do not record basal here. Meal insulin only refers to bolus doses. Capture basal in number 6 following.

5. If the insulin regimen used by this patient on a typical day cannot accurately be recorded on the table (question 4) please leave the table blank and describe the regimen here:

   Answer if #4 is blank: No (1) Yes (2)
   I am describing the insulin regimen here:

   If yes, specify:

   _____

   _____

6. COMPLETE ONLY FOR PATIENTS USING AN INSULIN INFUSION PUMP

   Total number of UNITS BASAL insulin infused per day: __ __

   Total number of different BASAL RATES used per day: __ __

   Has the patient had any technical problems with the insulin infusion pump? No (1) Yes (2)

   If YES, specify: _____

   _____

7. COMPLETE THIS QUESTION ONLY FOR PATIENTS CURRENTLY ON ONE OR TWO DAILY INJECTIONS:

   a) Have you prescribed a change in the insulin regimen or dose since the last visit? No (1) Yes (2)

   If YES, please indicate the reason.

	No	Yes
Symptomatic polyuria/polydipsia/nocturia	(1)	(2)
Unacceptable degree of hypoglycemia	(1)	(2)
Recurrrent ketonuria	(1)	(2)
Hemoglobin A1c above the action limit	(1)	(2)
Pregnancy	(1)	(2)
Other:	(1)	(2)

   Specify _____

   b) How is this patient monitoring his/her diabetes?

	No	Yes	Uncertain
Self blood glucose monitoring	(1)	(2)	(3)
Urine glucose monitoring	(1)	(2)	(3)

B. COMPLETE THIS QUESTION FOR PATIENTS IN BOTH GROUPS:

Do you suspect that this patient's reported glucose (urine and/or blood) monitoring results are inaccurate or fictitious?

No	Yes	Not Sure
(1)	(2)	(3)

Explain: _____

_____

C. DEVIATIONS FROM ASSIGNED TREATMENT

1. Since the last visit, has the patient been on a "deviation from treatment" (as defined in Section 12.5 of the Protocol) at any time? No (1) Yes (2)

   a. If yes, is the patient currently on deviation from treatment? No (1) Yes (2)

      (i) If NO, enter date of termination of deviation: __ __ Month __ __ Day __ __ Year

      (ii) If this is a new (started since last QV) deviation: enter date of DCCT Form 022, Notification of Deviation from Assigned Treatment: __ __ Month __ __ Day __ __ Year

D. TRANSFER TO INACTIVE STATUS

1. Since the last visit, has the patient been on inactive status at any time? (as defined in Section 12.7 of the Protocol) No (1) Yes (2)

   a. If yes, is the patient currently on transfer to inactive status? No (1) Yes (2)

      (i) If NO, enter date of return to active status: __ __ Month __ __ Day __ __ Year

      (ii) If this is a new transfer to inactive status, enter date of DCCT Form 016, Application for Transfer to Inactive Status: __ __ Month __ __ Day __ __ Year

E. MODIFICATIONS OF FOLLOW-UP SCHEDULE FOR ENDPOINT ASSESSMENTS

(See Manual of Operations Chapter 11)

1. Since the last visit, has the patient been on a modified follow-up schedule at any time? No (1) Yes (2)

   If YES, indicate which assessments:

   _____

   _____

2. Is the patient currently on a modified follow-up schedule? No (1) Yes (2)

F. MODIFICATIONS OF THERAPY FOR PATIENTS RANDOMIZED TO THE STANDARD GROUP ONLY

1. Since the last visit, has the patient been on a modified therapy at any time? No (1) Yes (2)

   Proceed to Question G.1 _____

   a) Since the last visit, has this patient used glucose monitoring at greater frequency than specified in the Protocol (urine testing 4x/day or self blood glucose monitoring once per day) at your direction? No (1) Yes (2)

      IF YES, record frequency: SBGM __/day

      UGM __/day

b) Since the last visit has this patient used more than two injections of insulin per day or used an insulin pump to achieve first or second priority standard treatment group goals at your direction at any time?

(NOTE: PERMISSION OF THE TREATMENT COMMITTEE IS REQUIRED PRIOR TO INSTITUTING THIS MODIFICATION OF THERAPY)

No (1) Yes (2)

Proceed to question d) _____|

If this modification was started since the last visit:

(i) Enter date permission was received from the Treatment Committee to institute the regimen in this patient Month __ Day __ Year __

(ii) Enter date that new regimen was started Month __ Day __ Year __

c) Is the patient currently using more than two injections per day or an insulin pump to achieve first or second priority treatment goals for the standard treatment group? No (1) Yes (2)

If NO, enter date of return to one or two injections of insulin per day Month __ Day __ Year __

If this patient is using more than two injections per day or an insulin pump for reasons other than instructed by you to achieve first and second priority goal for the Standard Group, this represents a deviation from assigned treatment, and should be recorded in Section C and on Form 022.

d) Other modification; specify: No (1) Yes (2)

_____

_____

FOR PATIENTS RANDOMIZED TO THE EXPERIMENTAL GROUP ONLY

2. Since the last visit, has the patient been on a modified treatment protocol? No (1) Yes (2)

Proceed to Question G.1 _____|

a) Since the last visit, have you instituted a planned out-patient visit schedule on a less frequent basis than the required monthly visit schedule? No (1) Yes (2)

b) Have you instructed this patient to perform self blood glucose monitoring on a less frequent daily schedule than the required minimum of four times a day, including three pre-prandial and one bedtime sample? No (1) Yes (2)

If yes, record frequency __ / day

c) Have you instructed this patient to use less stringent goals of therapy? No (1) Yes (2)

(i) Specify the new goals:

HbAlc (range) __ __.__ to __ __.__

Blood glucose (range):

Preprandial __ __ __ to __ __ __

Postprandial __ __ __ to __ __ __

3:00 a.m. __ __ __ to __ __ __

(ii) Specify the reason and situation for modification of goals of therapy in this patient:

_____

_____

_____

(iii) Specify the date that the new goal(s) became effective: Month __ Day __ Year __

(iv) Are the stated goals in effect at present? No (1) Yes (2)

If NO, enter the date that the patient returned to the goals of the experimental treatment group set forth in the Protocol: Month __ Day __ Year __

d) Other modification; specify: No (1) Yes (2)

_____

_____

G. DIABETES MONITORING - ANSWER FOR PATIENTS CURRENTLY ON 3 OR MORE INJECTIONS OR PUMP

1. Summarize the patient's performance of glucose monitoring. Use the patient's "Daily Diabetes Monitoring Record" to do this. The "number should have done" is the number of tests you instructed the patient to do. Record performance of these prescribed tests only; do not record extra tests performed.

Testing Required by Protocol	BLOOD Number Actually Done	Number Should Have Done
Before breakfast	___	___
Before lunch	___	___
Before dinner	___	___
Bedtime	___	___
3:00 a.m.	___	___

2. Is the patient performing more self blood glucose monitoring than prescribed? No (1) Yes (2) Uncertain (3)

H. DIABETES MONITORING - ANSWER FOR PATIENTS CURRENTLY ON ONE OR TWO INJECTIONS

1. Summarize the patient's performance of glucose monitoring. Use the patient's "Daily Diabetes Monitoring Record" to do this. The "number should have done" is the number of tests you instructed the patient to do. Record performance of these prescribed tests only; do not record extra tests performed.

Testing Required by Protocol	URINE Number Actually Done	Number Should Have Done	BLOOD Number Actually Done	Number Should Have Done
Before breakfast	___	___	___	___
Before lunch	___	___	___	___
Before dinner	___	___	___	___
Bedtime	___	___	___	___

2. Is the patient performing more glucose monitoring (urine or blood) than prescribed? No (1) Yes (2) Uncertain (3)

I. INDICATIONS OF NON-ADHERENCE TO TREATMENT PROTOCOL

Do not complete this section at the randomization visit.

1. Answer a) - i) for all patients.

a) How often has the patient claimed to have followed the meal plan?

Not applicable	(0)
Never followed meal plan	(1)
Very infrequently (less than 10% of the time)	(2)
Infrequently (10-44% of the time)	(3)
About half the time (45-55% of the time)	(4)
Most of the time (56-90% of the time)	(5)
Almost all of the time (more than 90% of the time)	(6)
Always followed meal plan	(7)

	No	Yes	Uncertain
b) Has the patient followed a pattern of eating suggestive of an eating disorder (e.g., history of bulimia, vomiting, anorexia)?	(1)	(2)	(3)
c) (i) How many illnesses (intercurrent events or not) has the patient experienced? (If none, enter 00 and proceed to 1.d)	__ __		
(ii) During how many of these illnesses has the patient been known to have failed to adjust the insulin dose as prescribed?	__ __		
d) Has the patient used a type of insulin which has not been prescribed?	(1)	(2)	(3)
e) Has the patient been rotating the site of injection (or, in pump patients, the site of infusion)?	(1)	(2)	(3)
f) Has the patient completed less than all seven of the capillary blood collections required for the Profilset?	(1)	(2)	(3)
g) (i) How many intercurrent events (as defined in Chapter 10 of the Manual of Operations) has the patient experienced? (If none, enter 00)	__ __		
(ii) How many of these intercurrent events has the patient failed to report in the appropriate time window? (If none, enter 00)	__ __		
h) Has the patient failed to bring in his/her daily record?	(1)	(2)	(3)
i) Does the patient perform self blood glucose monitoring? (If no or uncertain, proceed to Question I.2)	(1)	(2)	(3)
If yes: (i) Has the patient been using self blood glucose monitoring to adjust his/her insulin dosage?	(1)	(2)	(3)
(ii) Does the patient perform self blood glucose monitoring more than once per day?	(1)	(2)	(3)

2. ANSWER (a) - (f) FOR PATIENTS RANDOMIZED TO THE STANDARD TREATMENT GROUP.

On how many days has the patient . . .

a) taken more than the prescribed units of insulin (excluding sick days)? __ __

b) taken extra injections of insulin? __ __

c) taken fewer injections of insulin? __ __

d) failed to take his/her prescribed insulin dose? __ __

e) failed to perform and record at least two urine tests or one blood glucose test a day? __ __

f)(i) been ill? __ __

(ii) failed to test and record urine acetone during an illness? __ __

3. ANSWER (a) - (d) FOR PATIENTS RANDOMIZED TO THE EXPERIMENTAL TREATMENT GROUP

a) On how many days has the patient not followed the prescribed algorithm for insulin delivery? __ __

b) How many times has the patient failed to do the prescribed 3:00 a.m. blood tests? __ __

c) How many times has the patient failed to promptly report a low 3:00 a.m. blood glucose to the clinic? __ __

d) How many times has the patient failed to monitor urine acetone when blood glucose was >240 mg/dl or during an illness? __ __

4. ANSWER (a) - (c) FOR PATIENTS RANDOMIZED TO THE EXPERIMENTAL TREATMENT GROUP AND USING INSULIN INFUSION PUMPS.

a) How many times has the patient failed to follow instructions for changing batteries? __ __

b) How many times has the patient failed to follow instructions for changing catheters? __ __

c) How many times has the patient failed to follow instructions for changing syringes? __ __

J. DIABETES CONTROL - ANSWER FOR ALL PATIENTS

If this is the randomization visit, complete this section and Sections K, L and M; then turn to the last page and sign the form.

1. Symptoms of hyperglycemia (Std pts priority 1 goals)

a) How many nights in the past week did the patient wake up ONCE to urinate? __

b) How many nights in the past week did the patient wake up TWO OR MORE times to urinate? __

c) On the average, how many 8 ounce glasses of fluid did the patient drink per day? __ __

d) How many times did the patient experience DKA? __ __
(As defined in Chapter 10 of the Manual of Operations)

If the patient has had DKA, complete the Notification of Intercurrent Event (Form 020) if it has not previously been completed for this event.

e) Did the patient experience other symptoms of hyperglycemia? No (1) Yes (2)

If YES, specify: _____

2. How many days has the patient had moderate or large ketonuria? __ __
(If none, enter 00 and proceed to Question J.3.)

How many of these were . . .

a) explained by change in routine? __ __

b) due to illness? __ __

c) due to medical equipment failure? __ __

d) spontaneous or unexplained? __ __

3. a) Is the patient female? No (1) Yes (2)

Proceed to Question J.4 _____|

b)(i) Has the patient had any vaginal itching or discharge? No (1) Yes (2)

Proceed to Question J.3.c _____|

(ii) Was the patient treated for this? No (1) Yes (2)

(iii) Specify treatment: _____

_____

c)(i) Does the patient menstruate? No (1) Yes (2)

Proceed to Question J.4 _____|

(ii) Enter date of start of last menstrual period:

__ __ __ __ __ __
Month Day Year

d)(i) Was the last menstrual period more than five weeks ago? No (1) Yes (2)

Proceed to Question J.4 _____|

(ii) Was a pregnancy test performed? No (1) Yes (2)

If no, why not? _____

_____

If yes, did the test indicate pregnancy? No (1) Yes (2)

Complete the Notification of Intercurrent Event (Form 020) if it has not previously been completed for this pregnancy. _____|

4. Symptoms of hypoglycemia since last QV

a) Number of hospitalizations for hypoglycemia. (Hospitalization implies overnight admission to the hospital; an emergency ward visit that did not result in hospitalization does not apply.) __ __

If the patient has been hospitalized for hypoglycemia, complete Notification of Intercurrent Event (Form 020), the Notification of Hypoglycemic Intercurrent Event (Form 083), and Further Details (Form 092) if not previously completed for this hospitalization.

If any hospitalizations, give specific reasons:

_____

_____

b) How many times did the patient experience hypoglycemia of such severity that the patient . . .

(i) lost consciousness without seizure __ __

(ii) lost consciousness with seizure __ __

c) How many times did the patient experience hypoglycemia of such severity . . .

(i) that the patient required professional medical assistance, including placement of an IV or an intravenous injection of glucose? __ __

(ii) as to require the assistance of another person, such as the administration of glucagon, but did not require any of the assistance described in (i)? __ __

(iii) as to require the assistance of another person but did not require any of the help described in (i) or (ii)? __ __

d) Complete only if severe hypoglycemia which the patient could not treat himself/herself has occurred:

(i) How many times has the patient received glucagon? __ __

(ii) How many times has the patient received IV glucose to treat hypoglycemia? __ __

(iii) Did any episodes result in injury to the patient or others? No (1) Yes (2)

If YES, specify: _____

_____

If the patient has experienced severe hypoglycemia which he/she could not treat himself/herself, please complete Notification of Intercurrent Event (Form 020), Notification of Hypoglycemic Intercurrent Event (Form 083) and Further Details (Form 092) for for any episodes for which this has not previously been done.

e) How many times in the past seven days did the patient experience hypoglycemia which was mild enough for the patient to treat himself/herself? __ __

f) If the patient has experienced hypoglycemia in the past seven days which was mild enough for the patient to treat himself/herself, answer items (i) through (iii) below. Otherwise, skip to Section K.

(i) Did mild hypoglycemia occur:

While the patient was awake (1)

While the patient was asleep (2)

Both (3)

(ii) What was the usual reason for the mild hypoglycemia? (CHECK ALL THAT APPLY)

Missed meal or snack (1)

Decreased food intake at meal or snack (1)

Increased exercise level (1)

Too much insulin taken (1)

Lack of early warning signs of low blood glucose (1)

Other; specify: _____ (1)

_____

Unexplained (1)

(iii) What symptoms does the patient have with mild hypoglycemia? (CHECK ALL THAT APPLY)

Adrenergic warning symptoms (1)

Diaphoresis (sweating) (1)

Altered mental status (1)

Other (1)

None (1)

K. DIABETES RELATED COMPLICATIONS AND/OR CATEGORY 3 INTERCURRENT EVENTS

If the patient has been hospitalized (overnight) to treat any of the following diabetes-related complications or Category 3 events, the Notification of Intercurrent Event (Form 020) must be completed for each hospitalization (see Chapter 10 of the Manual of Operations).

If no hospitalization occurred, Category 3 Intercurrent Events are reported on this form only; Form 20 is not required.

1. OPHTHALMIC

	Right Eye	Left Eye
a) Has the patient had blurred or reduced vision?	No (1) Yes (2)	No (1) Yes (2)
If YES, explain: _____		
b) Has the patient experienced floaters or flashing lights?	No (1) Yes (2)	No (1) Yes (2)
c) Has the patient had any other eye problems?	No (1) Yes (2)	No (1) Yes (2)
If YES, specify: _____		

d) Will the patient be sent to the ophthalmologist for a special visit? No (1) Yes (2)

2. NEUROLOGIC

Has the patient had any of the following?

a) Paresthesias (pain or numbness) in hands or feet	No (1) Yes (2)
b) Unexplained muscle weakness	(1) (2)
c) Vomiting or bloating after meals	(1) (2)
d) Bouts of persistent or recurrent diarrhea	(1) (2)
e) Bouts of urinary retention	(1) (2)
f) Dizziness or lightheadedness (not associated with hypoglycemia)	(1) (2)
g) Fainting (not associated with hypoglycemia)	(1) (2)
h) Seizure (not due to hypoglycemia)	(1) (2)

If YES, complete the Notification of Intercurrent Events (Form 020) if it has not already been completed for this condition.

i) Impotence	No (1) Yes (2)	Not Applicable (3)
j) Has the patient developed symptoms compatible with a focal neuropathy (described as sudden onset, asymmetrical and self-limited, i.e., cranial mononeuropathy, proximal motor neuropathy, truncal neuropathy)?	No (1) Yes (2)	
k) Other neurologic problem ?	No (1) Yes (2)	

If YES, specify: _____

l) Will the patient be sent to the neurologist for a special visit? No (1) Yes (2)

3. RENAL

Has the patient had any of the following?

	No	Yes
a) Edema (of renal etiology only)	(1)	(2)
b) Other renal problem	(1)	(2)

If YES, specify: _____

4. VASCULAR

Has the patient had any of the following?

	No	Yes
a) Shortness of breath	(1)	(2)
b) Symptoms of congestive heart disease	(1)	(2)
c) Impaired peripheral vascular circulation (e.g., intermittent claudication)	(1)	(2)
d) Chest pain	(1)	(2)
(i) If yes, is this clinical angina? (As defined in Chapter 10 of the Manual of Operations)	(1)	(2)
e) Other symptoms suggestive of a suspected non-acute MI (as defined MOO Chapter 10)	(1)	(2)

If Yes to d)i or e) complete the Notification of Intercurrent Events (Form 020) if it has not already been completed for this condition.

	No	Yes
f) Symptoms suggestive of transient ischemic attack(s) (As defined in Chapter 10 of the Manual of Operations)	(1)	(2)
g) Other vascular problem	(1)	(2)

If YES, specify: _____

5. INFECTIONS

Has the patient had any of the following? (As defined in Chapter 10 of the Manual of Operations)

	No	Yes
a) Urinary tract infection (e.g., cystitis, pyelonephritis, perinephric abscess)	(1)	(2)
b) Upper or lower respiratory tract infection	(1)	(2)
c) Gastroenteritis with fever	(1)	(2)
d) Cutaneous (non-infusion site) or mucocutaneous (e.g., Candida vulvo-vaginitis, furunculosis, dental abscess) infection	(1)	(2)

If YES, specify: _____

	No	Yes
e) Post-operative or deep wound infection	(1)	(2)
f) Gangrene	(1)	(2)
g) Other infections not specifically defined in the Manual of Operations (i.e., mononucleosis, epididymitis, measles, chicken pox)	(1)	(2)

If YES, specify: _____

ANSWER THE FOLLOWING ONLY FOR PATIENTS WHO USE AN INDWELLING NEEDLE OR CATHETER FOR INSULIN ADMINISTRATION.

	No	Yes
h) Has the patient had infection at the insertion site (e.g., >1.5 cm erythema and purulence)?	(1)	(2)

Complete the Notification of Intercurrent Event (Form 020).

6. MINOR OUTPATIENT SURGERY OR INCIDENTAL TRAUMA (e.g., simple fracture, uncomplicated laceration).

	No	Yes
	(1)	(2)

If YES, specify: _____

7. INTERCURRENT ENDOCRINE EVENT

(e.g., hypothyroidism, Grave's disease, Cushing's disease) No (1) Yes (2)

If YES, specify: _____

_____

8. ADVERSE PSYCHOSOCIAL REACTION No (1) Yes (2)

If YES, specify: _____

_____

9. OTHER

a) Has the patient experienced any other medical problems or difficulties in carrying out the diabetes treatment regimen (includes imprisonment)? No (1) Yes (2)

If YES, explain: _____

_____

L. MEDICATIONS

1. On the average, how many aspirin-containing tablets or other prostaglandin inhibitors does the patient use each month? (IF NONE, ENTER 000) ___ ___ ___

2. Has the patient used or is he/she currently using any prescription drug on a regular basis other than insulin? No (1) Yes (2)

_____

Specify: _____

_____

_____

3. Has the patient used any over-the-counter drugs? No (1) Yes (2)

_____

Specify: _____

_____

_____

4. Does the patient use vitamin supplements on a regular basis? No (1) Yes (2)

_____

Specify: _____

_____

_____

M. PHYSICAL EXAMINATION

1. Date of last physical examination — Month __ Day __ Year __

2. Current weight (kg) (To convert pounds to kilograms, multiply by 0.454.) ___.__

3. Change in weight since previous exam (kg) (CIRCLE + OR -) + / - ___.__

4. What is the patient's desired weight (kg)? ___.__

5. Is the patient less than 18 years old? If NO, skip to Question 8. No (1) Yes (2)

6. Current height (cm) (To convert inches to centimeters, multiply by 2.54.) ___.__

7. Has patient failed to maintain normal growth and development (see Manual of Operations Chapter for definition)? No (1) Yes (2)

8. Pulse (bpm) ___

9. Sitting blood pressure (RIGHT ARM)

   a) Systolic (mm Hg) ___

   b) Diastolic (mm Hg) ___

   c) Has hypertension been previously documented and has the Notification of Intercurrent Form been completed and sent to the Coordinating Center? No (1) Yes (2)

   SKIP TO QUESTION M.10 _____|

   d) Is the current systolic or diastolic blood pressure so high as to be above the normal range as stated in Chapter 10 of the Manual of Operations i.e., ≥ 140 systolic or ≥ 90 diastolic? No (1) Yes (2)

   IF YES, PATIENT SHOULD RETURN ON ANOTHER DAY WITHIN ONE MONTH FOR A SECOND DETERMINATION OF BLOOD PRESSURE. COMPLETE ITEMS e) THROUGH g) AT THAT TIME.

   e) Date of second sitting blood pressure determination — Month __ Day __ Year __

   f) Sitting blood pressure:

   Systolic (mm Hg) ___

   Diastolic (mm Hg) ___

   g) Does the systolic or diastolic blood pressure indicate hypertension as defined in the MOO, Chapter 10 i.e. ≥ 140 systolic or ≥ 90 diastolic? No (1) Yes (2)

   Complete the Notification of Intercurrent Event (DCCT Form 020). _____|

10. Injection sites (INCLUDING CATHETER SITES):

	Absent	Present
a) Lipoatrophy	(1)	(2)
b) Lipohypertrophy	(1)	(2)
c) Inflammation	(1)	(2)

11. Abdomen:

	Absent	Present
a) Hepatomegaly	(1)	(2)
b) If present, how large (span)?		__ __ cm

12. Feet:

	Absent	Present
a) Ulcers	(1)	(2)
b) Infection	(1)	(2)
c) Abnormal toenails	(1)	(2)

Pulse -- Dorsalis pedis

d) Right			e) Left		
Normal (1)	Diminished (2)	Absent (3)	Normal (1)	Diminished (2)	Absent (3)

Pulse -- Posterior tibial

f) Right			g) Left		
Normal (1)	Diminished (2)	Absent (3)	Normal (1)	Diminished (2)	Absent (3)

13. Were any other abnormalities noted on physical examination? No (1) Yes (2)

Specify: _____

_____

N. BLOOD GLUCOSE PROFILE, HEMOGLOBIN A1c, LIPID AND RENAL STUDIES

Do not complete this section at the randomization visit.
Turn to the last page and sign the form.

1. Will the Profileset be mailed to the Central Biochemistry Laboratory? No (1) Yes (2)

2. Why not? (CHECK ALL THAT APPLY THEN SKIP TO QUESTION N.7)

   Kit damaged after collection (1)
   Patient forgot to do collection (1)
   Patient lost kit (1)
   Patient refused to do collection (1)
   Other or unknown (1)

3. On what date were the collections performed? Month Day Year

4. On what date will the Profileset be mailed? Month Day Year

5. What accession number will be used on the Profileset? BGP1 thru BGP7 - _ _ _ _ _ _

6. a. Was this profileset supposed to have been quality-controlled? No (1) Yes (2)

   (i) If yes, which stick number did the patient duplicate? (If not done, answer 0) _____ stick

   (ii) Was this the correct stick number? No (1) Yes (2)

If the patient is randomized to the Experimental Treatment Group, answer Questions N.7 and N.8; otherwise, proceed to Question N.9.

7. Did the patient perform self blood glucose monitoring on the day he/she obtained the Profileset specimens? No (1) Yes (2)

Proceed to Question N.9

8. Using the patient's "Daily Diabetes Monitoring Record", specify the results of the self blood glucose monitoring performed on that day:

Prebreakfast	__ __ __	mg/dl
90 min. p.c.	__ __ __	mg/dl
Prelunch	__ __ __	mg/dl
90 min. p.c.	__ __ __	mg/dl
Presupper	__ __ __	mg/dl
90 min. p.c.	__ __ __	mg/dl
Bedtime	__ __ __	mg/dl

9. The quarterly blood sample is to be taken for HbAlc measurement.

a) HbAlc accession number: H - __ __ __ __ __ __

b) Date specimen collected: __/__ __/__ __/__ Month Day Year

10. Will lipid specimens be mailed to the Central Biochemistry Laboratory (due to intercurrent event or additional draw for elevated LDL cholesterol or triglycerides)? No (1) Yes (2)

Proceed to Question N.13

11. On what date will the specimens be drawn? __/__ __/__ __/__ Month Day Year

12. What accession number will be used? L - __ __ __ __ __ ____

13. Will renal studies specimens be mailed to the Central Biochemistry Laboratory (due to intercurrent event)? No (1) Yes (2)

Process to end of form and sign

14. On what date will the specimens be collected? __/__ __/__ __/__ Month Day Year

15. What accession number will be used? S and U - __ __ __ __ __ __

Name of person responsible for information on this form: _____

Certification Number __ __ - __ __

REMINDER: The Notification of Intercurrent Event (DCCT Form 020) must be completed if the patient has experienced any of the intercurrent events Category 1 or Category 2 listed in Chapter 10 of the DCCT Manual of Operations For hypoglycemia episodes, complete the Notification of Hypoglycemic Intercurrent Event (DCCT Form 083) and Further Details of Hypoglycemic Event (Form 092) as well.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Notification of Deviation from Assigned Treatment

This form is to be completed whenever a randomized patient or his/her DCCT physician seeks a deviation from the protocol-specified regimen of the treatment group to which the patient is randomized. Except in urgent circumstances, all such deviations must be approved beforehand by the Treatment Committee. For all deviations, the Treatment Committee and Coordinating Center must be notified as soon as possible. This notification should be in the form of a telephone call to the Treatment Committee Chairman and filing this form with the Coordinating Center.

Deviation from treatment protocol is defined in Protocol Section 12.5 as follows:

1) Deviation from the experimental treatment protocol is defined as withdrawal from the intensive methods of insulin delivery set forth in Protocol Section 8.2.2.
2) Deviation from the standard treatment protocol is defined as institution of insulin delivery by pump or multiple daily injections for any purpose other than meeting the first and second treatment priorities set forth in Protocol Section 8.1.1.

Any other change in treatment is considered a treatment modification and is not reportable on this form.

The original of this form is to be sent to the Coordinating Center in the weekly forms mailing. Retain a copy in the clinic files.

A. IDENTIFYING INFORMATION

1. Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date form completed __ __ __ __ __ __
   Month Day Year
5. To which treatment group is the patient randomized?

   Standard Treatment (1)
   (COMPLETE SECTIONS B AND D)

   Experimental Treatment (2)
   (COMPLETE SECTIONS C AND D)

B. PURPOSE OF PROPOSED DEVIATION IN THE STANDARD TREATMENT GROUP

1. Specify the reasons why the patient will deviate from the regimen of the standard treatment. (CHECK ALL THAT APPLY)

   a) Pregnancy (1)

   b) Purposely seeking conception (1)

   c) Patient insistence (SPECIFY IN QUESTION D.1) (1)

   d) Other reason (SPECIFY IN QUESTION D.1) (1)

Patient ID _____

C. PURPOSE OF PROPOSED DEVIATION IN THE EXPERIMENTAL TREATMENT GROUP

1. Specify the reasons why the patient will deviate from the regimen of the experimental treatment. (CHECK ALL THAT APPLY)

a) Inability to prevent recurrent severe hypoglycemia despite manipulations within the experimental treatment (1)

b) Major sequelae of hypoglycemia such as brain damage or an accident which jeopardizes the patient or others or alters the ability of the patient to continue on intensive methods of insulin delivery (1)

c) Psychiatric disorder or sociopathic behavior affecting judgment or causing risk of suicide (1)

d) Substance abuse (as defined in the Manual of Operations) (1)

e) Inaccessibility of subject to management by DCCT staff or other qualified personnel (1)

f) Blindness (1)

g) Any serious intercurrent illness (example: malignancy with short life expectancy) which would, in the opinion of the investigator, make it unduly burdensome for the patient to continue the experimental treatment methods (1)

h) Ability to meet experimental treatment group goals on less intensive methods of insulin delivery (1)

i) Unavoidable chronic use of beta-blocking drugs for intercurrent illness (1)

j) Adoption of hazardous occupation (1)

k) Patient insistence (SPECIFY IN QUESTION D.1) (1)

l) Other reason (SPECIFY IN QUESTION D.1) (1)

D. DETAILS OF DEVIATION SOUGHT

1. Explain more fully the reason for deviation indicated in Question B.1 or C.1. (Use a separate sheet if necessary)

_____

_____

_____

_____

2. On what date would the proposed deviation be effective? (IF IMMEDIATELY, ENTER TODAY'S DATE) __ __ Month __ __ Day __ __ Year

If uncertain, check here: (1)

3. How long will the proposed deviation be in effect?

Permanent (1)
Temporary (2)

If temporary, what is the expected date of return to the protocol-specified regimen of the assigned treatment group? __ __ Month __ __ Day __ __ Year

If uncertain, check here: (1)

4. Specify the direction of the deviation. (CHECK ONLY ONE)

Standard Treatment Group subject:

Using insulin infusion pump (1)

Using multiple daily injections (3 or more injections of insulin per day) (2)

Experimental Treatment Group subject:

Discontinuing pump (3)

Discontinuing multiple daily injections (3 or more injections of insulin per day) (4)

Patient ID _____

5. Specify who suggested the deviation: (CHECK ONLY ONE)

DCCT medical treatment team	(1)
Non-DCCT physician	(2)
Patient	(3)
Family member or friend of patient	(4)
Other; specify: _____	(5)

_____

6. Will a non-DCCT physician assume management of blood glucose control? No (1) Yes (2)

If YES, enter the physician's name, address and phone number.

_____

_____

Type or print name of individual completing this form:

_____

Certification Number (if any)

__ __ - __ __

Signature of Principal Investigator:

_____

FOR COORDINATING CENTER USE ONLY

1. Reviewed by Treatment Committee: __ __ / __ __ / __ __ (Month / Day / Year)
2. Recommendation: Allow deviation (1) Deny (2)
3. Clinic Notified: __ __ / __ __ / __ __ (Month / Day / Year)

Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL
Central Biochemistry Laboratory Results -- SECTION A (C-peptide)

Each time a new specimen analysis is performed for a given patient, the appropriate area of this form is to be completed by personnel at the Central Biochemistry Laboratory and a copy of the form is mailed to the Coordinating Center.

Clinic Number: __ __ Patient ID Number: __ __ __ __ __ Patient's Initials: __ __ __ Date Reported: __ __ __ __ __ __
Month Day Year

DCCT TEST #	TEST NAME	COLLECTION DATE Mo Da Yr	DATE OF ARRIVAL Mo Da Yr	ANALYSIS DATE Mo Da Yr	ACCESSION NUMBER	RESULTS VALUE	UNITS	CODE
1	C-peptide (serum)-Pre	__ __ __	__ __ __	__ __ __	CP-_____	__ . __ __	PMOL/ML	
2	Glucose (serum)-Pre			__ __ __	CP	__ __ __ __	MG/DL	CP __
3	Creatinine (serum)-Pre			__ __ __	CP	__ __ . __	MG/DL	
4	Cholesterol (serum)-Pre			__ __ __	CP	__ __ __ __	MG/DL	
5	C-peptide (serum) 90 min post			__ __ __	CPT	__ . __ __	PMOL/ML	CPT __
6	Glucose (serum) 90 min post			__ __ __	CPT	__ __ __ __	MG/DL	
	Tests to be performed if cholesterol >265 mg/dl:							
7	Cholesterol (serum)	__ __ __	__ __ __	__ __ __	CP-_____	__ __ __ __	MG/DL	CP __
8	Triglyceride (serum)			__ __ __	CP	__ __ __ __	MG/DL	
9	HDL Cholesterol (serum)			__ __ __	CP	__ __ __ __	MG/DL	
10	LDL Cholesterol (calculated)			__ __ __	CP	__ __ __ __	MG/DL	
	Cholesterol Retake Test (Performed if high cholesterol due to elevated TSH):							
11	Cholesterol (serum)	__ __ __	__ __ __	__ __ __	CP-_____	__ __ __ __	MG/DL	CP __

CODES: IF MORE THAN ONE APPLIES, LIST THE MOST IMPORTANT ONE FIRST

A Specimen lost in transmit--request backup specimen
B Specimen thawed in transit--request backup specimen
C Specimen leaked in transit
D Backup specimen
E Lipemic specimen
F Inadequate mixing of capillary blood
G Probable reversal of basal and stimulated specimens
H Hemolyzed specimen
I Specimen lost due to laboratory accident--request backup specimen
J Unsatisfactory determination--request backup specimen
K Repeat determination requested by CoC
L Repeat determination on backup specimen requested by CoC
M Specimen improperly collected
N Quantity not sufficient--request backup specimen
O Mislabeled specimen--identification questionable
P Unlabeled specimen--identification questionable
Q Test cancelled by clinic
R Test cancelled by CoC
S No specimen received
T Unsatisfactory specimen
U Not collected by patient
V Varying levels of hemolyzing reagent--results questionable
W Inadequate volume of hemolyzing reagent--results questionable
X Inadequate volume of blood--results questionable
Y Glucose non-detectable
Z Excessive volume of hemolyzing reagent--results questionable

DIABETES CONTROL AND COMPLICATIONS TRIAL
Central Biochemistry Laboratory Results -- SECTION B (Renal Studies)

Each time a new specimen analysis is performed for a given patient, the appropriate area of this form is to be completed by personnel at the Central Biochemistry Laboratory and a copy of the form is mailed to the Coordinating Center.

Clinic Number: __ __ Patient ID Number: __ __ __ __ __ Patient's Initials: __ __ __ Date Reported: __ __ __ __ __ __ (Month Day Year)

DCCT TEST #	TEST NAME	COLLECTION DATE Mo Da Yr	DATE OF ARRIVAL Mo Da Yr	ANALYSIS DATE Mo Da Yr	ACCESSION NUMBER	RESULTS	VALUE	UNITS	CODE
12	Albumin (serum)	___ ___ ___	___ ___ ___	___ ___ ___	S-_____		___ . ___ ___	G/DL	
13	Creatinine (serum)			___ ___ ___		S	___ ___ . ___	MG/DL	S ___
14	Albumin (urine)			___ ___ ___		U	___ ___ ___	MG/L	U ___
15	Albumin excretion (urine)			___ ___ ___		U	___ ___ ___ ___	UG/MN	
16	Creatinine (urine)			___ ___ ___		U	___ ___ ___	MG/DL	
17	Height (cm)					U	___ ___ ___ . ___	CM	
18	Weight (kg)					U	___ ___ ___ . ___	KG	
19	Raw clearance			___ ___ ___		U	___ ___ ___	ML/MN	
20	Standard clearance					U	___ ___ ___ ___	ML/MN/1.73M^2	
	Duration (hrs)					U	___ ___	HRS	
	Volume (ml)					U	___ ___ ___ ___	ML	

CODES: IF MORE THAN ONE APPLIES, LIST THE MOST IMPORTANT ONE FIRST

A Specimen lost in transmit--request backup specimen
B Specimen thawed in transit--request backup specimen
C Specimen leaked in transit
D Backup specimen
E Lipemic specimen
F Inadequate mixing--blood in capillary
G Inadequate mixing--blood on side of tube
H Hemolyzed specimen
I Specimen lost due to laboratory accident--request backup specimen
J Unsatisfactory determination--request backup specimen
K Repeat determination requested by CoC
L Repeat determination on backup specimen requested by CoC
M Specimen improperly collected
N Quantity not sufficient--request backup specimen
O Mislabeled specimen--identification questionable
P Unlabeled specimen--identification questionable
Q Test cancelled by clinic
R Test cancelled by CoC
S No specimen received
T Unsatisfactory specimen
U Not collected by patient
V Varying levels of hemolyzing reagent--results questionable
W Inadequate volume of hemolyzing reagent--results questionable
X Inadequate volume of blood--results questionable
Y Glucose non-detectable
Z Excessive volume of hemolyzing reagent--results questionable

DIABETES CONTROL AND COMPLICATIONS TRIAL
Central Biochemistry Laboratory Results -- SECTION C (Lipid Studies)

Each time a new specimen analysis is performed for a given patient, the appropriate area of this form is to be completed by personnel at the Central Biochemistry Laboratory and a copy of the form is mailed to the Coordinating Center.

Clinic Number: __ __ Patient ID Number: __ __ __ __ __ Patient's Initials: __ __ __ Date Reported: __ __ __ __ __ __
Month Day Year

DCCT TEST #	TEST NAME	COLLECTION DATE Mo Da Yr	DATE OF ARRIVAL Mo Da Yr	ANALYSIS DATE Mo Da Yr	ACCESSION NUMBER	RESULTS VALUE	UNITS	CODE
21	Cholesterol (serum)	___ ___ ___	___ ___ ___	___ ___ ___	L-_____	___ ___ ___ ___	MG/DL	L ___
22	Triglyceride (serum)			___ ___ ___		L ___ ___ ___ ___	MG/DL	
23	HDL cholesterol (serum)			___ ___ ___		L ___ ___ ___ ___	MG/DL	
24	LDL cholesterol (serum)			___ ___ ___		L ___ ___ ___ ___	MG/DL	

CODES: IF MORE THAN ONE APPLIES, LIST THE MOST IMPORTANT ONE FIRST

A Specimen lost in transmit--request backup specimen
B Specimen thawed in transit--request backup specimen
C Specimen leaked in transit
D Backup specimen
E Lipemic specimen
F Inadequate mixing--blood in capillary
G Inadequate mixing--blood on side of tube
H Hemolyzed specimen
I Specimen lost due to laboratory accident--request backup specimen
J Unsatisfactory determination--request backup specimen
K Repeat determination requested by CoC
L Repeat determination on backup specimen requested by CoC
M Specimen improperly collected
N Quantity not sufficient--request backup specimen
O Mislabeled specimen--identification questionable
P Unlabeled specimen--identification questionable
Q Test cancelled by clinic
R Test cancelled by CoC
S No specimen received
T Unsatisfactory specimen
U Not collected by patient
V Varying levels of hemolyzing reagent--results questionable
W Inadequate volume of hemolyzing reagent--results questionable
X Inadequate volume of blood--results questionable
Y Glucose non-detectable
Z Excessive volume of hemolyzing reagent--results questionable

DIABETES CONTROL AND COMPLICATIONS TRIAL
Central Biochemistry Laboratory Results -- SECTION D (Blood Glucose Profile)

Each time a new specimen analysis is performed for a given patient, the appropriate area of this form is to be completed by personnel at the Central Biochemistry Laboratory and a copy of the form is mailed to the Coordinating Center.

Clinic Number: __ __ Patient ID Number: __ __ __ __ __ Patient's Initials: __ __ __ Date Reported: __ __ __ __ __ __
Month Day Year

Collection Date: __ __ __ __ __ __
Month Day Year

Arrival Date: __ __ __ __ __ __
Month Day Year

Analysis Date: __ __ __ __ __ __
Month Day Year

BGP1 - _____
Accession Number

BGP8 - _____
QC Accession Number

DCCT TEST #	TEST NAME		BLOOD GLUCOSE (MG/DL)	OPTICAL DENSITY @ 340	CODE
25	Pre-Breakfast	BGP1	___ ___ ___ ___	___ . ___ ___ ___	___
26	Post-Breakfast	BGP2	___ ___ ___ ___	___ . ___ ___ ___	___
27	Pre-Lunch	BGP3	___ ___ ___ ___	___ . ___ ___ ___	___
28	Post-Lunch	BGP4	___ ___ ___ ___	___ . ___ ___ ___	___
29	Pre-Dinner	BGP5	___ ___ ___ ___	___ . ___ ___ ___	___
30	Post-Dinner	BGP6	___ ___ ___ ___	___ . ___ ___ ___	___
31	Bedtime	BGP7	___ ___ ___ ___	___ . ___ ___ ___	___
32	3:00 am		___ ___ ___ ___	___ . ___ ___ ___	___
33	Quality Control	BGP8	___ ___ ___ ___	___ . ___ ___ ___	___

CODES: IF MORE THAN ONE APPLIES, LIST THE MOST IMPORTANT ONE FIRST

A Specimen lost in transmit--request backup specimen
B Specimen thawed in transit--request backup specimen
C Specimen leaked in transit
D Backup specimen
E Lipemic specimen
F Inadequate mixing--blood in capillary
G Inadequate mixing--blood on side of tube
H Hemolyzed specimen
I Specimen lost due to laboratory accident--request backup specimen
J Unsatisfactory determination--request backup specimen
K Repeat determination requested by CoC
L Repeat determination on backup specimen requested by CoC
M Specimen improperly collected
N Quantity not sufficient--request backup specimen
O Mislabeled specimen--identification questionable
P Unlabeled specimen--identification questionable
Q Test cancelled by clinic
R Test cancelled by CoC
S No specimen received
T Unsatisfactory specimen
U Not collected by patient
V Varying levels of hemolyzing reagent--results questionable
W Inadequate volume of hemolyzing reagent--results questionable
X Inadequate volume of blood--results questionable
Y Glucose non-detectable
Z Excessive volume of hemolyzing reagent--results questionable

D

DCCT

DIABETES CONTROL & COMPLICATIONS TRIAL

Resting Electrocardiogram Grading Form

DCCT Form Dec.1 [illegible]
Page 1 of 1

APR 1 1984

1 FORM
2 CLINIC
3 PATIENT
4 INITIAL
5 FORMDATE
6 CERTNO

Area for identification label with Clinic Number, ID Number, Initials, date ECG taken and ECG technician certification number.

9-80

This form is to be completed by the staff of the Central Electrocardiogram Reading Unit upon receipt of a baseline or follow-up resting electrocardiogram.

A completed copy of this form is to be mailed to the DCCT Coordinating Center.

Other variable names are underlined

Q and QS Patterns (18X)

I AVL V_6	2 3 AVF	V_1 V_5
1	2 3-11	5 6

ST Segment Depression (48X)

I AVL V_4	2 3 AVF	V_1 V_5
7	8 9-10	11 12

T Wave Items (5X)

I L V_6	2 3 F	V_2 V_5
13	14	15

ST Segment Elev. (92X)

I L V_6	2 3 F	V_1 V_5
16	17-18	19

R (5X): 20

AV Cond. Defect (6X): 21-22

Vent. Cond. Defect (7X): 23-24

Arrythmias (8X)

1X	2X	3X	4X	5X	6X
24	25	26-27	28	29	

Ectopic Cycles

SVHB	VHB	NHBG	PT	I-R
30	31	32	33-34	35 36-37

Miscellaneous (9X)

1	3	5	4X
38	39	40-41	

Heart Rate per minute: 42-43-44

QRS AXIS: 45 46-47 48

Max. R. Height (mms)

I II III	V_4 V_5 V_6
49	50-51-52

Max. S. Depth (mms)

I II III	V_1 V_2 V_3
53	54-55-56

T Height (mms): V_5 — 57 58-59

R Height (mms): AVL — 60-61

Tech. Prob.: 98X — 62

Clear: 1.0 — 63

Comments:

DATE GRADING MAILED TO DCCT COORDINATING CENTER: ___ / ___ / ___
Month Day Year

64-69

DIABETES CONTROL AND COMPLICATIONS TRIAL

Fundus Photography

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. Date photography completed: __ __ __ __ __ __ Month Day Year
5. Visit Number: __ __ (FOR BASELINE VISIT ENTER 00. IF PRE-PHOTOCOAGULATION VISIT, ENTER 99.)
6. Is this a retake session? No ( ) Yes ( )
   If YES, specify: _____
7. Photo accession number (if any): __ __ __ __ __ __
8. Photographer's Name: _____
9. Certification Status:
   Full ( )
   Provisional ( )
   Uncertified ( )
10. Certification Number (if any): __ __ - __ __
11. Date form and photographs mailed to CORU: __ __ __ __ __ __ Month Day Year

B. PRESENCE OF PHOTOGRAPHS AND QUALITY REVIEW

	Field	Present Yes	Present No	Field Definition Good	Field Definition Fair	Field Definition Poor	Focus and Clarity Good	Focus and Clarity Fair	Focus and Clarity Poor	Stereo Good	Stereo Fair	Stereo Poor	Photographer's Comments
R	1	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
I	2	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
G	3	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
H	4	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
T	5	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
	6	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
E	7	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
Y	8a	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
E	8b	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
	Lens	( )	( )										
	1	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
L	2	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
E	3	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
F	4	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
T	5	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
	6	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
E	7	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
Y	8a	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
E	8b	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
	Lens	( )	( )										

DIABETES CONTROL AND COMPLICATIONS TRIAL

Fluorescein Angiography

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. Date of angiography: Month __ __ Day __ __ Year __ __
5. Visit Number: __ __
(FOR BASELINE VISIT ENTER 00.
IF PRE-PHOTOCOAGULATION VISIT, ENTER 99.)
6. Is this a retake session? No ( ) Yes ( )
If YES, specify: _____
7. Photo accession number (if any): __ __ __ __ __ __
8. Angiographer's Name: _____
9. Certification Status: Full ( )
Provisional ( )
Uncertified ( )
10. Certification Number (if any): __ __ - __ __
11. Date form and photographs mailed to CORU: Month __ __ Day __ __ Year __ __

B. PHOTOGRAPHY SESSION

1. Did any complications occur during the photography session? No ( ) Yes ( )
If YES, check all that occurred:

Nausea	( )	Dyspnea	( )
Vomiting	( )	Hypotension	( )
Urticaria	( )	Other, specify:	( )
Pruritus	( )	_____	

2. Eye to be photographed first: Right ( ) Left ( )

C. PRESENCE OF PHOTOGRAPHS AND QUALITY REVIEW

	Present		Field Definition			Focus and Clarity			Stereo			Photographer's Comments (Enter frame numbers graded)
	Yes	No	Good	Fair	Poor	Good	Fair	Poor	Good	Fair	Poor	
1. First Eye, Field 2F early phase or mid phase	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
2. First Eye, Field 2F mid phase	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
3. Second Eye, Field 2F early phase or mid phase	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
4. Second Eye, Field 1F mid phase	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
5. Second Eye, Field 2F 7-9 min.	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
6. First Eye, Field 2F 7-9 min.	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
7. Color Photos, Right Eye												
Field 1F	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
Field 2F	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____
8. Color Photos, Left Eye												
Field 1F	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	
Field 2F	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	( )	_____

Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Endpoint Visit Ophthalmic Examination

Patients are to undergo eye examinations every 12 months after randomization. If High Risk Characteristics are noted at a nonscheduled follow-up visit, only Sections A, C and D need to be completed. The ophthalmic follow-up visits should be scheduled to correspond with other regularly scheduled visits whenever possible. Visual acuity is measured and stereo fundus photographs are taken at each annual eye examination. The following procedures are also required: measurement of intraocular pressure, slit-lamp examination, ophthalmoscopy. (Fluorescein angiography may be performed at the eye examination visit occurring two years after randomization.) Chapter 13 of the Manual of Operations should be consulted for procedures to follow in completing these examinations. The original of this form is to be completed at each endpoint visit eye examination and sent to the DCCT Coordinating Center; a copy of the form should be kept in the clinic's files.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date of examination __ __ __ __ __ __ (Month Day Year)

5a) Is this a regularly scheduled endpoint visit? No (1) Yes (2)

If NO, specify reason for the visit:

_____

_____

If YES, answer b) and c) below.

b) Which follow-up visit is this? __ __

c) Is the visit being held within the time window? No (1) Yes (2)

B. OCULAR HISTORY

	Right Eye No	Right Eye Yes	Left Eye No	Left Eye Yes
1a,b) Is the eye enucleated?	(1)	(2)	(1)	(2)

IF YES FOR EITHER EYE, ANSWER THE FOLLOWING ITEM FOR THE APPROPRIATE EYE(S).

IF NO FOR BOTH EYES, PROCEED TO QUESTION 2.

	Right Eye No	Right Eye Yes	Left Eye No	Left Eye Yes
c,d) Has enucleation occurred since the Baseline Ophthalmic Examination or the last completed Endpoint Visit Ophthalmic Examination, whichever is more recent?	(1)	(2)	(1)	(2)

IF YES FOR EITHER EYE, COMPLETE THE REMAINDER OF SECTION B FOR THE TIME SINCE THE LAST VISIT AND BEFORE ENUCLEATION.

IF NO, LEAVE BLANK QUESTIONS 2-8 FOR THAT EYE, I.E., EYE ENUCLEATED BEFORE LAST VISIT.

		Right Eye		Left Eye	
		No	Yes	No	Yes
2a,b)	Has the patient had any ocular surgical procedure(s) since the Baseline Ophthalmic Examination or the last completed Endpoint Visit Ophthalmic Examination, whichever is more recent?	(1)	(2)	(1)	(1)

IF YES, IDENTIFY SURGICAL PROCEDURES IN THE FOLLOWING ITEMS FOR APPROPRIATE EYE(S).

IF NO FOR BOTH EYES, PROCEED TO QUESTION 3.

		Right Eye		Left Eye	
		No	Yes	No	Yes
c,d)	External plastic surgery	(1)	(2)	(1)	(2)
e,f)	Extraocular muscle surgery	(1)	(2)	(1)	(2)
g,h)	Corneal transplant	(1)	(2)	(1)	(2)
i,j)	Other corneal surgery	(1)	(2)	(1)	(2)
k,l)	Filtering surgery, cyclocryotherapy, or other operative procedure to lower intraocular pressure	(1)	(2)	(1)	(2)
m,n)	Cataract extraction	(1)	(2)	(1)	(2)
o,p)	Vitrectomy	(1)	(2)	(1)	(2)
q,r)	Retinal detachment surgery	(1)	(2)	(1)	(2)
s,t)	Other surgery (specify below)	(1)	(2)	(1)	(2)

R - _____

L - _____

		Right Eye		Left Eye	
		No	Yes	No	Yes
3a,b)	Has the patient had any photocoagulation since the Baseline Ophthalmic Examination or the last completed Endpoint Visit Ophthalmic Examination, whichever is more recent?	(1)	(2)	(1)	(2)
4a,b)	Has the patient been diagnosed as having glaucoma in either eye since the Baseline Ophthalmic Examination or the last complete Endpoint Visit Ophthalmic Examination, whichever is more recent?	(1)	(2)	(1)	(2)
5a,b)	Has the patient used any ocular medications which require a prescription since the Baseline Ophthalmic Examination or the last completed Endpoint Visit Ophthalmic Examination, whichever is more recent?	(1)	(2)	(1)	(2)

IF YES, INDICATE IN THE FOLLOWING ITEMS ALL PRESCRIPTIONS FOR OCULAR MEDICATIONS.

IF NO, PROCEED TO QUESTION 6.

	Right Eye No	Right Eye Yes	Left Eye No	Left Eye Yes
c,d) Steroid drops	(1)	(2)	(1)	(2
e,f) Glaucoma drops	(1)	(2)	(1)	(2)
g,h) Mydriatics	(1)	(2)	(1)	(2)
i,j) Other (specify below)	(1)	(2)	(1)	(2)

R - _____

L - _____

	Right Eye No	Right Eye Yes	Left Eye No	Left Eye Yes
6a,b) Has the patient received any ocular treatments administered by a physician since the Baseline Ophthalmic Examination or the last completed Endpoint Visit Ophthalmic Examination, whichever is more recent?	(1)	(2)	(1)	(2)

IF YES, INDICATE IN THE FOLLOWING ITEMS ALL SUCH TREATMENTS.

IF NO, PROCEED TO QUESTION 7.

	Right Eye No	Right Eye Yes	Left Eye No	Left Eye Yes
c,d) Retrobulbar steriods	(1)	(2)	(1)	(2)
e,f) Retrobulbar alcohol	(1)	(2)	(1)	(2)
g,h) Other (specify below)	(1)	(2)	(1)	(2)

R - _____

L - _____

	Right Eye No	Right Eye Yes	Left Eye No	Left Eye Yes
7a,b) Does the patient describe symptoms which you believe to be caused by vitreous hemorrhage since the Baseline Ophthalmic Examination or the last completed Endpoint Visit Ophthalmic Examination, whichever is more recent?	(1)	(2)	(1)	(2)

Patient ID _____

C. DISTANCE SUBJECTIVE REFRACTION

Use any visual acuity chart other than ETDRS Visual Acuity Chart 1 or 2.

IF A SUBJECTIVE REFRACTION CANNOT BE PERFORMED IN ONE OR BOTH EYES AT FOUR METERS BECAUSE OF POOR ACUITY, ATTEMPT THE REFRACTION AT ONE METER. IF A ONE METER REFRACTION IS POSSIBLE, SUBTRACT +0.75 SPHERE FROM THE REFRACTION USED AT ONE METER, AND ENTER THIS RESULT IN QUESTION 2.

	No	Yes
1a) Was a refraction performed for both eyes?	(1)	(2)

IF YES, PROCEED TO QUESTION 2.

IF NO, ANSWER THE FOLLOWING ITEMS AND LEAVE BLANK THE RESPONSE TO QUESTION 2 FOR EYE(S) NOT REFRACTED.

Specify reason:

	Right Eye No	Right Eye Yes	Left Eye No	Left Eye Yes
b,c) Poor visual acuity	(1)	(2)	(1)	(2)
d,e) Eye(s) enucleated*	(1)	(2)	(1)	(2)
f,g) Other (specify below)	(1)	(2)	(1)	(2)

R - _____

L - _____

*LEAVE BLANK ALL RESPONSES TO QUESTIONS C-2 THROUGH G-7 FOR ENUCLEATED EYE(S).

2. Corrective lenses obtained by subjective refraction for distance:

IF A SUBJECTIVE REFRACTION WAS NOT PERFORMED AT FOUR OR ONE METERS, ENTER THE DISTANCE SUBJECTIVE REFRACTION FROM EITHER THE BASELINE OPHTHALMIC EXAMINATION OR THE LAST ENDPOINT VISIT OPHTHALMIC EXAMINATION, WHICHEVER IS MORE RECENT. INDICATE WHETHER PLUS OR MINUS SPHERES OR CYLINDERS WERE USED BY CIRCLING THE APPROPRIATE SIGNS. IF SPHERE, CYLINDER, AND AXIS ARE ALL ZERO, RECORD A CHECK MARK ( ) IN THE APPROPRIATE SPACE BELOW:

	Right Eye	Left Eye
a,b) Sphere	+ / - __ __ . __ __	+ / - __ __ . __ __
c,d) Cylinder	+ / - __ __ . __ __	+ / - __ __ . __ __
e,f) Axis	__ __ __	__ __ __
g,h) Sphere, cylinder, and axis all zero	(1)	(1)

	No	Yes
3. Is there myopia greater than 7 diopters in one or both eyes?	(1)	(2)

D. VISUAL ACUITY MEASUREMENTS

Use ETDRS Visual Acuity CHART 1 for the RIGHT EYE and CHART 2 for the LEFT EYE.

1. What is the distance between the patient and the chart (record in meters to nearest 1/10 meter)? __ . __ Meters

2. Letters correct at four meters distance:

CIRCLE EACH LETTER THE PATIENT IDENTIFIES CORRECTLY AND WRITE THE TOTAL CORRECT FOR EACH ROW IN COLUMN AT RIGHT. EACH ROW TOTAL MUST BE ENTERED.

REMEMBER: THE PATIENT STARTS AT THE TOP READING SLOWLY AND GETS ONLY ONE CHANCE AT EACH LETTER. PUSH THE PATIENT UNTIL HE/SHE CLEARLY DEMONSTRATES HE/SHE CANNOT READ OR GUESS LETTERS CORRECTLY.

Patient ID _____

RIGHT EYE - CHART 1

Acuity Equivalent	Chart 1 letters	Number Correct
20/200	N C K Z O	____
20/160	R H S D K	____
20/125	D O V H R	____
20/100	C Z R H S	____
20/80	O N H R C	____
20/63	D K S N V	____
20/50	Z S O K N	____
20/40	C K D N R	____
20/32	S R Z K D	____
20/25	H Z O V C	____
20/20	N V D O K	____
20/16	V H C N O	____
20/13	S V H C Z	____
20/10	O Z D V H	____

a) Total number correct at four meters ___

NOTE; DO NOT CHANGE TO CHART 2 UNTIL YOU HAVE CHANGED THE COVER TO THE PATIENT'S RIGHT EYE.

LEFT EYE - CHART 2

Acuity Equivalent	Chart 2 letters	Number Correct
20/200	D S R K N	____
20/160	C K Z O H	____
20/125	O N R K D	____
20/100	K Z V D C	____
20/80	V S H Z O	____
20/63	H D K C R	____
20/50	C S R H N	____
20/40	S V Z D K	____
20/32	N C V O Z	____
20/25	R H S D V	____
20/20	S N R O H	____
20/16	O D H K R	____
20/13	Z K C S N	____
20/10	C R H O V	____

b) Total number correct at four meters ___

IF THE TOTAL NUMBER OF LETTERS READ CORRECTLY IS GREATER THAN OR EQUAL TO 5 IN EACH EYE, PROCEED TO SECTION E.

IF TOTAL NUMBER OF LETTERS READ CORRECTLY WITH EITHER EYE IS LESS THAN 5, MOVE THE PATIENT TO A DISTANCE OF ONE METER FROM THE CHART AND TEST THE ACUITY AT THIS DISTANCE IN EACH EYE WITH LESS THAN 5 LETTERS CORRECT. ANSWER QUESTIONS 3 AND 4.

Patient ID _____

3. Letters correct at one meter distance:

	No	Yes
a) Will the right eye be tested?	(1)	(2)

IF NO, PROCEED TO QUESTION 4.

PRIOR TO ACTUAL TESTING AT ONE METER, A +0.75 SPHERE SHOULD BE ADDED TO THE DISTANCE CORRECTION IN THE TRIAL FRAME.

CIRCLE EACH LETTER THE PATIENT IDENTIFIES CORRECTLY AND WRITE THE TOTAL CORRECT FOR EACH ROW IN COLUMN AT RIGHT. EACH ROW TOTAL MUST BE ENTERED.

RIGHT EYE - CHART 1

Acuity Equivalent	Chart 1 letters	Number Correct
5/200	N C K Z O	_____
5/160	R H S D K	_____
5/125	D O V H R	_____
10/200	C Z R H S	_____
10/160	O N H R C	_____
10/125	D K S N V	_____
20/200	Z S O K N	_____
20/160	C K D N R	_____
20/125	S R Z K D	_____
20/100	H Z O V C	_____
20/80	N V D O K	_____
20/63	V H C N O	_____
20/50	S V H C Z	_____
20/40	O Z D V H	_____

b) Total number correct at one meter: __ __

	No	Yes
c) If total number correct at one meter is zero, were count fingers, hand motion, or light perception present?	(1)	(2)

	No	Yes
4a) Will the left eye be tested?	(1)	(2)

IF NO, PROCEED TO SECTION E.

PRIOR TO ACTUAL TESTING AT ONE METER, A +0.75 SPHERE SHOULD BE ADDED TO THE DISTANCE CORRECTION IN THE TRIAL FRAME.

CIRCLE EACH LETTER THE PATIENT IDENTIFIES CORRECTLY AND WRITE THE TOTAL CORRECT FOR EACH ROW IN COLUMN AT RIGHT. EACH ROW TOTAL MUST BE ENTERED.

LEFT EYE - CHART 2

Acuity Equivalent	Chart 2 letters	Number Correct
5/200	D S R K N	_____
5/160	C K Z O H	_____
5/125	O N R K D	_____
10/200	K Z V D C	_____
10/160	V S H Z O	_____
10/125	H D K C R	_____
20/200	C S R H N	_____
20/160	S V Z D K	_____
20/125	N C V O Z	_____
20/100	R H S D V	_____
20/80	S N R O H	_____
20/63	O D H K R	_____
20/50	Z K C S N	_____
20/40	C R H D V	_____

b) Total number correct at one meter: __ __

	No	Yes
c) If total number correct at one meter is zero, were count fingers, hand motion, or light perception present?	(1)	(2)

E. INTRAOCULAR PRESSURE

Use Goldmann applanation tonometry

	Right Eye	Left Eye
1a,b) Intraocular pressure:	__ __ mm Hg	__ __ mm Hg

F. SLIT-LAMP EXAMINATION

	Right Eye No	Right Eye Yes	Left Eye No	Left Eye Yes
1a,b) Is the lens missing?	(1)	(2)	(1)	(2)
2a,b) Is there evidence of definite iris neovascularization?	(1)	(2)	(1)	(2)

IF YES, GONIOSCOPY SHOULD BE PERFORMED AND THE FOLLOWING ITEM SHOULD BE ANSWERED FOR THAT EYE.

c,d) Is there evidence of angle neovascularization?	(1)	(2)	(1)	(2)

NOTE: BECAUSE GONIOSCOPY MAY INTERFERE WITH CORNEAL CLARITY AND AFFECT THE ABILITY TO TAKE ADEQUATE QUALITY PHOTOGRAPHS, IT IS RECOMMENDED THAT THE PATIENT RETURN FOR A SEPARATE VISIT IF POSSIBLE, OR THAT GONIOSCOPY BE DEFERRED UNTIL AFTER PUPILLARY DILATION AND FUNDUS PHOTOGRAPHY.

G. OPHTHALMOSCOPIC EXAMINATION

1a,b) Was the ophthalmoscopic examination of the fundus satisfactory?	Right Eye	Left Eye
Yes	(1)	(1)
Not entirely satisfactory, but performed	(2)	(2)
Examination could not be performed	(3)	(3)

IF YES FOR BOTH EYES, PROCEED TO QUESTION 2.

IF NOT ENTIRELY SATISFACTORY FOR EITHER EYE OR IF EXAMINATION WAS NOT PERFORMED FOR EITHER EYE, ANSWER THE FOLLOWING ITEM FOR APPROPRIATE EYE.

c,d) Specify the main reason the fundus examination was unsatisfactory or could not be performed (CHECK ONLY ONE)

	Right Eye	Left Eye
Patient refused	(1)	(1)
Vitreous opacity	(2)	(2)
Vitreous hemmorrhage	(3)	(3)
Lens opacity	(4)	(4)
Corneal opacity secondary to neovascular glaucoma	(5)	(5)
Other corneal opacity	(6)	(6)
Posterior synechia prevent dilation of pupil	(7)	(7)
Other (SPECIFY IN THE SPACE PROVIDED)	(8)	(8)

R - _____

L - _____

IF OPHTHALMOSCOPIC EXAMINATION COULD NOT BE PERFORMED FOR EITHER EYE (I.E., IF QUESTION 1 IS ANSWERED "NOT PERFORMED" FOR BOTH EYES), SKIP QUESTIONS 2 AND 3.

IF THE FUNDUS OF EITHER EYE IS EXAMINED, QUESTIONS 2-7 SHOULD BE ANSWERED FOR THAT EYE.

2a,b) Which statement best describes the clarity of the lens in each eye? (CHECK ONLY ONE)

	Right Eye	Left Eye
No lens opacity or some lens opacity but not sufficient to expect reduced visual acuity	(1)	(1)
Lens opacity sufficient to reduce visual acuity but not to less than 20/100	(2)	(2)
Lens opacity sufficient to reduce visual acuity to less than 20/100	(3)	(3)

	Right Eye	Left Eye
3a,b) Are vitreous or preretinal hemorrhage present in any areas of the fundus?	No (1) Yes (2)	No (1) Yes (2)
IF YES, ANSWER THE FOLLOWING ITEM FOR THAT EYE. IF NO, PROCEED TO QUESTION 4.		
c,d) Does hemorrhage obscure one or more disc areas of retina?	No (1) Yes (2)	No (1) Yes (2)
IF YES, ANSWER THE FOLLOWING ITEMS FOR THAT EYE. IF NO, PROCEED TO QUESTION 4.		
Indicate areas in which vitreous or preretinal hemorrhage obscures one or more disc areas of retina:		
	Right Eye	Left Eye
e,f) Within seven standard fields	(1)	(1)
g,h) Outside seven standard fields but posterior to vortex ampullae	(1)	(1)
i,j) Anterior to vortex ampullae	(1)	(1)
	Right Eye	Left Eye
4a,b) Are new vessels present on or within one disc diameter of the optic nerve head (NVD)?	No (1) Yes (2) Quest. (3)	No (1) Yes (2) Quest. (3)
IF YES, ANSWER THE FOLLOWING ITEM FOR THAT EYE. IF NO, PROCEED TO QUESTION 5.		
c,d) Are the vessels greater than or equal to DRS Standard Photo 10A?	No (1) Yes (2)	No (1) Yes (2)
5a,b) Are new vessels elsewhere present?	No (1) Yes (2) Quest. (3)	No (1) Yes (2) Quest. (3)
IF YES, ANSWER THE FOLLOWING ITEMS FOR THAT EYE. IF NO, PROCEED TO QUESTION 6.		
c,d) Are there new vessels within the seven standard fields?	No (1) Yes (2)	No (1) Yes (2)
e,f) Are there new vessels outside the seven standard fields?	(1) (2)	(1) (2)
g,h) Are the new vessels greater than or equal to 1/2 DA in size in any 30 degree field?	(1) (2)	(1) (2)

	Right Eye			Left Eye		
	No	Yes	Quest.	No	Yes	Quest.
6a,b) Is there retinal thickening within one disc diameter of the center of the macula, i.e., within a circle two disc diameters in diameter centered on the macula?	(1)	(2)	(3)	(1)	(2)	(3)
IF YES OR QUESTIONABLE, ANSWER THE FOLLOWING ITEMS FOR THAT EYE. IF NO, PROCEED TO QUESTION 7.						
c,d) Is the center of the macular involved?	(1)	(2)	(3)	(1)	(2)	(3)
e,f) Are cystoid changes present?	(1)	(2)	(3)	(1)	(2)	(3)

	Right Eye		Left Eye	
	No	Yes	No	Yes
7a,b) Are high risk characteristics present?	(1)	(2)	(1)	(2)
IF YES, ANSWER THE FOLLOWING ITEM FOR THAT EYE. IF NO, PROCEED TO QUESTION 8.				
c,d) Do you plan to perform photocoagulation?	(1)	(2)	(1)	(2)
IF YES, PROCEED TO QUESTION 8. IF NO, ANSWER THE FOLLOWING ITEM FOR THAT EYE.				
e,f) Why do you not plan photocoagulation in the eye(s) with high risk characteristics? (CHECK ALL THAT APPLY)				
Patient refuses	(1)		(1)	
Unable to treat due to hemorrhage	(1)		(1)	
Unable to treat for other reason*	(1)		(1)	
*Specify reason: _____				
_____				
Would prefer not to treat	(1)		(1)	
Other; specify: _____	(1)		(1)	
_____				

8a,b) Is there any other major ophthalmoscopic abnormality such as retinal detachment, photocoagulation scars, fibrous/glial proliferations, vein occlusion, etc.?

Right Eye No (1)	Right Eye Yes (2)	Left Eye No (1)	Left Eye Yes (2)

IF YES, DESCRIBE:

_____

_____

_____

Type or print name of Ophthalmologist performing eye examination:

Certification Numbers (if any)

_____ __ __ - __ __

Type or print name of individual performing visual acuity examination:

_____ __ __ - __ __

Type or print name of Clinic Coordinator or other person who reviewed the form for completeness:

_____ __ __ - __ __

DIABETES CONTROL and COMPLICATIONS TRIAL
Autonomic Neuropathy Studies

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number
2. Patient ID Number
3. Patient's Initials
4. Certification Number of Tester
5. Visit Number

B. SINUS ARRHYTHMIA DURING QUIET RESPIRATION

1. Six Minutes of Recording Available?
2. RR Study Date (mm-dd-yy)
3. RR Receive Date (mm-dd-yy)
4. RR Evaluation Date (mm-dd-yy)
5. Is this a Repeat Evaluation?
6. Is this a Duplicate Evaluation?
7. Mean RR Interval (msec)
8. Standard Deviation
9. RR Variation (x 1000)

C. POSTURAL STUDIES

1. Post. Study Date (mm-dd-yy)
2. Post. Receive Date (mm-dd-yy)
3. Post. Evaluation Date (mm-dd-yy)
4. Is this a Repeat Evaluation?
5. Is this a Duplicate Evaluation?
6. Postural Data:

TIME (minutes)	BLOOD PRESSURE (mm Hg)		HEART RATE (bpm)	PLASMA CATECHOLAMINES (pg/ml)	
	Systolic	Diastolic		Norepi.	Epi.
-6 (supine)			Mean	_____	_____
0 (supine)			SD	_____	_____
1 (standing)				_____	_____
2 (standing)				_____	_____
3 (standing)				_____	_____
4 (standing)				_____	_____
5 (standing)				_____	_____
10 (standing)				_____	_____

PATIENT ID: 01122 DYG

D. VALSALVA MANUEVER

1. Completed?
2. Valsalva Study Date (mm-dd-yy)
3. Valsalva Receive Date (mm-dd-yy)
4. Valsalva Evaluation Date (mm-dd-yy)
5. Is this a Repeat Evaluation?
6. Is this a Duplicate Evaluation?

7. Study 1

    a. Pre-Valsalva

        1. Mean RR Interval (msec)

        2. Standard Deviation

    b. Smallest Valsalva RR Interval (msec)

    c. Largest Post-Valsalva RR Interval (msec)

    d. Valsalva Ratio

    e. Time of Valsalva (sec)

8. Study 2

    a. Pre-Valsalva

        1. Mean RR Interval (msec)

        2. Standard Deviation

    b. Smallest Valsalva RR Interval (msec)

    c. Largest Post-Valsalva RR Interval (msec)

    d. Valsalva Ratio

    e. Time of Valsalva (sec)

E. Quality

F. Subject Preparation Code

G. Overall Duplicate Code

This form was checked by: _____

Diabetes Control and Complications Trial

FOOD PATTERN QUESTIONNAIRE

Diabetes Control and Complications Trial (DCCT)

This questionnaire asks general questions about your food choices and eating habits. Answer as best you can. If you have questions about the form you may call the dietitian. More details will be collected at the clinic visit. Depending upon the instructions from your dietitian, please bring the completed questionnaire with you to your next clinic visit, or mail one week prior to clinic visit. Thank you for your cooperation in providing this information.

NAME _____

DATE _____

_____

DIETITIAN _____

TELEPHONE _____

1. Has your general pattern of eating changed in the last year? [] YES [] NO

   If yes, describe:

2. Are you or have you in the past year been on any special diet in addition to a diabetic diet? (such as low salt, vegetarian, weight reducing, etc.)

   [] YES [] NO

   If yes, describe:

3. Are you currently either increasing or decreasing your intake of any particular foods or beverages (such as foods high in fiber, caffeine, etc.)?

   [] YES [] NO

   If yes, describe:

4. Does your meal pattern tend to vary from week to week? (such as shift work, sports activities, etc.) [] YES [] NO

   If yes, describe:

5. In the last year, have you taken any vitamin and/or mineral preparations? [] YES [] NO

   If yes, specify brand name, amount and frequency:

   Attach label(s) if available.

6. Do you alter your diet for exercise? [] YES [] NO

   If yes, specify how:

7. How do you treat reactions (such as low blood sugar)?

   List item(s) and amount:

8. Do you use sugar or sugar substitute at the table? [] YES [] NO

   Specify which foods/beverages you add it to (such as cereal, coffee, tea, other):

   If sugar substitute, specify brand name:_____

9. Do you salt your food at the table?

   [] always [] occasionally [] never

10. If you add salt, how would you rate yourself in terms of amount of salt added at the table?

    [] light [] moderate [] heavy

11. Do you use a salt substitute at the table such as Lite, Co-salt, No-salt, etc.?

    [] always [] occasionally [] never

    If used, specify brand name:_____

12. Do you regularly use other salt seasonings at the table such as Accent, onion salt, garlic salt? [] YES [] NO

    Specify kind(s):_____

    _____

    _____

13. Indicate below your usual meal and snack patterns:

	Indicate Number of Times Per Week:					
	USUAL TIME	EAT AT HOME	CARRY FROM HOME	CAFETERIA, VENDING MACHINE, RESTAURANT	DO NOT EAT	COMMENTS
Morning meal	_____	____	____	____	____	_____
Morning snack	_____	____	____	____	____	_____
Noon meal	_____	____	____	____	____	_____
Afternoon snack	_____	____	____	____	____	_____
Evening meal	_____	____	____	____	____	_____
Evening snack	_____	____	____	____	____	_____
Additional snack	_____	____	____	____	____	_____

14. Who prepares most of your home-cooked meals?

Self	Parent	Spouse	Other Household Member	Other, Specify
[]	[]	[]	[]	[] _____
				_____

Please estimate how often you eat the following foods by checking the appropriate box. Include diet foods and other special products in the general food categories. For example, include low calorie beer with beer. You may use the Comments Section for details such as whether the food is eaten only at certain times of the year. Feel free to use the bottom of each page for additional comments.

	Daily	4-6 times a week	1-3 times a week	1-3 times a month	Never or Almost never	Comment
BEVERAGES						
Coffee - regular or decaffeinated	[]	[]	[]	[]	[]	
Cereal-type beverage (e.g. Postum)	[]	[]	[]	[]	[]	
Tea - regular, decaf, herbal	[]	[]	[]	[]	[]	
Cocoa	[]	[]	[]	[]	[]	
Beer, ale	[]	[]	[]	[]	[]	
Liquor, cocktails	[]	[]	[]	[]	[]	
Liqueur, cordials, brandy	[]	[]	[]	[]	[]	
Wine, dry or sweet	[]	[]	[]	[]	[]	
Carbonated beverages - cola and non-cola	[]	[]	[]	[]	[]	
Diet carbonated beverages - cola and non-cola	[]	[]	[]	[]	[]	
Kool-Aid, regular or unsweetened	[]	[]	[]	[]	[]	
DAIRY PRODUCTS						
Milk - whole, skim, buttermilk, chocolate, etc.	[]	[]	[]	[]	[]	
Cottage cheese	[]	[]	[]	[]	[]	
Cheese, process cheese, cheese spread	[]	[]	[]	[]	[]	
Yogurt, plain	[]	[]	[]	[]	[]	
Yogurt, sweetened	[]	[]	[]	[]	[]	
Sour cream, dips	[]	[]	[]	[]	[]	

DAIRY PRODUCTS, continued	Daily	4-6 times a week	1-3 times a week	1-3 times a month	Almost never	Comments
Whipped cream	[]	[]	[]	[]	[]	
Half and half cream	[]	[]	[]	[]	[]	
Ice cream	[]	[]	[]	[]	[]	
Sherbet, ice milk	[]	[]	[]	[]	[]	
Milk shakes, malts	[]	[]	[]	[]	[]	
Eggs	[]	[]	[]	[]	[]	
Egg substitutes	[]	[]	[]	[]	[]	
BREADS AND CEREALS						
Bread and rolls - white	[]	[]	[]	[]	[]	
Bread and rolls - whole wheat, whole grain	[]	[]	[]	[]	[]	
Muffins - corn, bran, etc.	[]	[]	[]	[]	[]	
Quick breads - banana, date, nut, etc.	[]	[]	[]	[]	[]	
Biscuits, cornbread	[]	[]	[]	[]	[]	
Bagels, English muffins	[]	[]	[]	[]	[]	
Sweet rolls, Danish, doughnuts	[]	[]	[]	[]	[]	
Pancakes, waffles, French toast	[]	[]	[]	[]	[]	
Cereals - cooked or dry (including grits, granola, etc.)	[]	[]	[]	[]	[]	
Cereals - pre-sweetened	[]	[]	[]	[]	[]	
Noodles, other pasta	[]	[]	[]	[]	[]	
Rice, kasha, bulgur, rice mixes	[]	[]	[]	[]	[]	
Tortillas, pita bread	[]	[]	[]	[]	[]	

	Daily	4-6 times a week	1-3 times a week	1-3 times a month	Almost never	Comments
BREADS AND CEREALS, continued						
Crackers - saltine, soda, wafer, etc.	[]	[]	[]	[]	[]	
Popcorn	[]	[]	[]	[]	[]	
Chips - potato, corn, etc.	[]	[]	[]	[]	[]	
MEAT, POULTRY, FISH						
Beef (including hamburger)	[]	[]	[]	[]	[]	
Pork	[]	[]	[]	[]	[]	
Lamb	[]	[]	[]	[]	[]	
Veal	[]	[]	[]	[]	[]	
Ham or Canadian bacon	[]	[]	[]	[]	[]	
Ham hocks, pigs' feet, salt pork	[]	[]	[]	[]	[]	
Bacon, breakfast sausages	[]	[]	[]	[]	[]	
Frankfurters, Polish sausage, Italian sausage, etc.	[]	[]	[]	[]	[]	
Corned beef, pastrami	[]	[]	[]	[]	[]	
Luncheon meats: bologna, salami, etc.	[]	[]	[]	[]	[]	
Variety/Organ meats - liver, tongue, kidney, etc.	[]	[]	[]	[]	[]	
Chicken, turkey	[]	[]	[]	[]	[]	
Duck, goose, pheasant	[]	[]	[]	[]	[]	
Fish, canned - salmon, tuna sardines, etc.	[]	[]	[]	[]	[]	
Fish, fresh or frozen - perch, salmon, halibut, cod, sole, etc.	[]	[]	[]	[]	[]	
Shellfish, fresh or canned - lobster, shrimp, crab, clams, scallops, etc.	[]	[]	[]	[]	[]	

	Daily	4-6 times a week	1-3 times a week	1-3 times a month	Almost never	Comments
MEAT SUBSTITUTES						
Peanut butter	[]	[]	[]	[]	[]	
Nuts or seeds	[]	[]	[]	[]	[]	
Canned or dried beans, lentils, split peas, lima beans	[]	[]	[]	[]	[]	
Soy protein foods such as tofu, Bacos	[]	[]	[]	[]	[]	
MIXED DISHES, SOUPS						
Pizza, lasagna, manicotti, ravioli, spaghetti	[]	[]	[]	[]	[]	
Tacos, enchiladas, burritos, etc.	[]	[]	[]	[]	[]	
Submarine sandwiches or hoagies	[]	[]	[]	[]	[]	
Stews, pot pies	[]	[]	[]	[]	[]	
Meat balls, meat loaf	[]	[]	[]	[]	[]	
Chili, hash, meat casseroles	[]	[]	[]	[]	[]	
Macaroni and cheese	[]	[]	[]	[]	[]	
Quiche, souffle	[]	[]	[]	[]	[]	
Chow mein, chop suey	[]	[]	[]	[]	[]	
TV dinners, frozen main dishes	[]	[]	[]	[]	[]	
Baked beans	[]	[]	[]	[]	[]	
Soups, including cream soups, chowders	[]	[]	[]	[]	[]	
Other mixed dishes commonly eaten Specify:	[]	[]	[]	[]	[]	
	[]	[]	[]	[]	[]	
	[]	[]	[]	[]	[]	

	Daily	4-6 times a week	1-3 times a week	1-3 times a month	Almost never	Comments
VEGETABLES						
Potatoes - baked, french fries, scalloped, etc.	[]	[]	[]	[]	[]	
Sweet potatoes	[]	[]	[]	[]	[]	
Starchy vegetables - peas, corn, lima beans, winter squash, etc.	[]	[]	[]	[]	[]	
Other cooked vegetables - green beans, cabbage, carrots, broccoli, etc.	[]	[]	[]	[]	[]	
Salads, raw vegetables	[]	[]	[]	[]	[]	
Vegetable juices - V-8, tomato juice	[]	[]	[]	[]	[]	
FRUIT AND FRUIT JUICES						
Fruit Juice	[]	[]	[]	[]	[]	
Fruit-flavored drinks - Tang, Awake, High-C, etc.	[]	[]	[]	[]	[]	
Citrus fruits - oranges, grapefruit	[]	[]	[]	[]	[]	
Berries - strawberries, blueberries, raspberries, etc.	[]	[]	[]	[]	[]	
Melons - cantaloupe, honeydew, watermelon, etc.	[]	[]	[]	[]	[]	
Other fresh fruit - grapes, apples, bananas, etc.	[]	[]	[]	[]	[]	
Canned fruits in syrup peaches, pears, etc.	[]	[]	[]	[]	[]	
Canned fruits - diet pack	[]	[]	[]	[]	[]	
Dried fruits - raisins, dates, prunes, apricots, etc.	[]	[]	[]	[]	[]	
Avocado	[]	[]	[]	[]	[]	

	Daily	4–6 times a week	1–3 times a week	1–3 times a month	Almost never	Comments
DIETETIC PRODUCTS						
Artificial sweeteners	[]	[]	[]	[]	[]	
Candy, gum	[]	[]	[]	[]	[]	
Chocolate candy	[]	[]	[]	[]	[]	
Syrups, jams, jellies	[]	[]	[]	[]	[]	
Ice cream	[]	[]	[]	[]	[]	
Cookies, cake	[]	[]	[]	[]	[]	
Gelatin desserts - D-Zerta, etc.	[]	[]	[]	[]	[]	
Puddings, custards	[]	[]	[]	[]	[]	
DESSERTS						
Puddings, custards	[]	[]	[]	[]	[]	
Cookies, bars, squares, slices	[]	[]	[]	[]	[]	
Cakes	[]	[]	[]	[]	[]	
Pies, cobblers, crisps	[]	[]	[]	[]	[]	
Gelatin desserts - Jello, etc.	[]	[]	[]	[]	[]	
Other, specify	[]	[]	[]	[]	[]	
	[]	[]	[]	[]	[]	
	[]	[]	[]	[]	[]	

	Daily	4-6 times a week	1-3 times a week	1-3 times a month	Almost never	Comments
MISCELLANEOUS						
Olives	[]	[]	[]	[]	[]	
Pickles, relish - sweet or sour	[]	[]	[]	[]	[]	
Steak sauces, mustard	[]	[]	[]	[]	[]	
Catsup, chili sauce	[]	[]	[]	[]	[]	
Soy sauce, teriyaki sauce	[]	[]	[]	[]	[]	
Candy, gum, coughdrops, chocolate bars	[]	[]	[]	[]	[]	
Sweets - jam, honey, syrup, sugar	[]	[]	[]	[]	[]	
DIETARY SUPPLEMENTS						
Vitamins and/or minerals	[]	[]	[]	[]	[]	
Bran	[]	[]	[]	[]	[]	
Lecithin	[]	[]	[]	[]	[]	
Bone meal	[]	[]	[]	[]	[]	
Wheat germ	[]	[]	[]	[]	[]	
Brewers' yeast	[]	[]	[]	[]	[]	
Other (e.g. Geritol, enzymes, protein supplements, dry malt, etc.) Specify:						
_____	[]	[]	[]	[]	[]	
_____	[]	[]	[]	[]	[]	
OTHER COMMONLY CONSUMED FOODS OR BEVERAGES NOT INCLUDED IN PREVIOUS GROUPS						
Specify:						
_____	[]	[]	[]	[]	[]	
_____	[]	[]	[]	[]	[]	
_____	[]	[]	[]	[]	[]	

FOOD PREPARATION QUESTIONNAIRE

Diabetes Control and Complications Trial (DCCT) This questionnaire is to be completed by the person who usually prepares the food in your home. This information is important for analysis of the dietary component of the study. Any questions about the form may be referred to the dietitian. Depending upon the instructions from your dietitian, please bring the completed questionnaire with you to your next clinic visit, or mail to dietitian one week prior to clinic visit. Thank you for your cooperation.	PARTICIPANT'S NAME _____ DATE _____ _____ DIETITIAN _____ TELEPHONE _____

1. What relationship are you to the participant?

   [] self [] parent [] spouse [] other, specify _____

2. Check the type of sweetener usually used in preparing the following foods:

	Sugar Added	Artificial Sweetener Added (give name)	Fructose Added	None Added
Fruit juices	____	_____	_____	_____
Fresh fruit	____	_____	_____	_____
Canned fruit	____	_____	_____	_____
Tomatoes, coleslaw, cucumber	____	_____	_____	_____
Beverages	____	_____	_____	_____
Baked goods	____	_____	_____	_____
Other (specify)				
_____	____	_____	_____	_____
_____	____	_____	_____	_____

3. Check whether salt or a salt substitute is usually added in preparing the following foods:

	salt	salt substitute	seasoning salts	none
Pasta, such as noodles, macaroni, etc.	[]	[]	[]	[]
Rice	[]	[]	[]	[]
Potatoes	[]	[]	[]	[]
Other vegetables	[]	[]	[]	[]
Meat	[]	[]	[]	[]
Fruit	[]	[]	[]	[]
Other, (e.g., coffee)	[]	[]	[]	[]
specify _____	[]	[]	[]	[]
_____	[]	[]	[]	[]

If salt substitute, specify kind/brand _____

4. Are the following table and cooking fats used:

Butter [] yes ——→ Specify: [] regular
[] unsalted
[] no

Margarine [] yes —→ Specify: [] regular
[] unsalted
[] no

Specify brand(s):

_____	[] stick	[] tub	[] diet	[] spread
_____	[] stick	[] tub	[] diet	[] spread
_____	[] stick	[] tub	[] diet	[] spread

Vegetable oil (such as corn, soy, safflower, sunflower, etc.)

[] yes ——————> Specify types and/or brands used:

[] no _____

_____

Spray shortening (such as Pam)

[] yes ——————> Specify brand: _____

[] no

Solid shortening (such as Crisco, Spry, Fluffo, etc.)

[] yes ——————> Specify types and/or brands used:

[] no _____

_____

Other cooking fats (such as lard, bacon drippings, salt pork, poultry fat, etc.)

[] yes ——————> Specify _____

[] no _____

5. Check the fat most often used in preparing each of the following foods:

	Butter	Marg-arine	Spray short-ening	Oil, such as Wesson, Mazola, etc.	Vegetable shortening such as Crisco, Fluffo, Spry, etc.	Bacon fat	Lard	Chicken fat	Beef suet	None
Eggs, fried	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
Eggs, scrambled	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
French toast	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
Cornbread	[]	[]	[]	[]	[]	[]	[]	[]	[]	
Potatoes, mashed	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
Potatoes, french fried	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
Potatoes, pan fried	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
Greens	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
Other vegetables	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
White beans, pinto	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
Gravy	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
White sauce	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]
Pie crust	[]	[]	[]	[]	[]	[]	[]	[]	[]	[]

6. Indicate the most usual method of preparing each of the following. If you fry any of them, comment on whether the item is dipped in flour or batter or breaded before frying and what fat is used for frying. Also check whether gravy is prepared.

ITEM	METHOD OF COOKING such as pan frying, broiling, deep frying	KIND OF FAT USED (if any)	GRAVY yes	GRAVY no
Hamburger				
Steaks				
Chops				
Poultry				
Fish				
Shellfish (shrimp, etc.)				
Liver				
Other, specify				

7. If you prepare gravies, do you usually use: [] cornstarch [] flour

   Is the liquid usually: [] milk [] water [] other, specify:_____

8. Indicate how much fat is usually trimmed from the meat before cooking or eating:

   [] trim most [] trim some [] usually don't trim

9. Check the salad dressing most often used with the following salads:
   (Specify brand)

	Mayonnaise-type such as Miracle Whip, Spin Blend	Regular mayonnaise such as Hellmann's, Kraft	Imitation mayonnaise such as Bright Day	Weight Watchers' Mayonnaise	Other - specify as French, Italian, Ranch-style, etc. Also specify creamy, clear, lo-cal, etc.
Potato salad					
Cole slaw					
Tossed salad					
Macaroni salad					
Other, specify					

Diabetes Control and Complications Trial

DCCT Form 031.3
March 3, 1986

INFORMED CONSENT FORM #1 (PROTOTYPE)

Diabetes Control and Complications Trial (DCCT)

Institution: _____

Principal Investigator: _____

1. I have been told that I may be eligible for participation in the Diabetes Control and Complications Trial (DCCT).

2. I have been given copies of the DCCT Research Volunteer's Information Handbook and the Manual of Diabetes Tests, Terms and Special Procedures. I have read both of these, I have had my questions answered, and I now clearly understand the following:

a) The purpose of the study. (Research Volunteer's Information Handbook, pages 4-6)

b) The nature of a clinical trial. (Research Volunteer's Information Handbook, page 5)

c) The two groups to be studied — the Standard Group and the Experimental Group — and the fact that there is no proven advantage to being placed in one group or the other. (Research Volunteer's Information Handbook, pages 5 and 8)

d) The fact that I shall be assigned to one of these two groups based on a process called random assignment, which means that neither my doctor nor I can choose to which group I will be assigned. Instead, I will be assigned by chance. I am willing to accept an assignment to either of the two treatment groups. (Research Volunteer's Information Handbook, page 5)

e) That blood tests and urine tests (including tests I will perform at home) will be used to measure diabetes control. (Research Volunteer's Information Handbook, pages 8-9; Manual of Diabetes Tests, Terms and Special Procedures, page 12)

f) That special tests of my eyes, kidneys, nervous system, heart, blood vessels, and psychological tests will be conducted to look for the appearance or progress of early diabetes complications. (Research Volunteer's Information Handbook, page 10; Manual of Diabetes Tests, Terms and Special Procedures, pages 4-8)

I have been given a complete description of these special tests in the Manual of Diabetes Tests, Terms and Special Procedures. I understand that if I am eligible to volunteer for this clinical trial, I shall be given a thorough explanation in writing of any tests not covered below before I am asked to sign a second permission form for those tests.

g) The responsibilities I agree to carry out if I decide to be a volunteer for the clinical trial involve my willingness to follow the treatment program of the group to which I have been assigned and to keep my appointments as scheduled. I understand that some of these appointments will take considerable time. (Research Volunteer's Information Handbook, pages 12-13)

I also understand that my responsibilities will include blood tests and urine tests I will do at my home. One of the required blood tests is a 3:00 a.m. sample. I will also keep records of my test results and treatment program, even though this may be time consuming. (Research Volunteer's Information Handbook, pages 8-9; Manual of Diabetes Tests, Terms and Special Procedures, page 12)

3. I have had a chance at this time to ask all questions which I feel are necessary. I now feel I have enough understanding to allow me to make a preliminary decision about my participation in this clinical trial.

4. Understanding the above, and having been made aware of the potential risks and benefits of the overall program (Research Volunteer's Information Handbook, pages 14-15; Manual of Diabetes Tests, Terms and Special Procedures, pages 4-12), I give you my permission to conduct the tests and procedures necessary to see whether I will qualify as a volunteer for the DCCT. I do this because I am willing to consider volunteering for participation in the DCCT if I do qualify.

I understand that if any of the test results show that I am not eligible to be in the trial, the rest of the tests will not be done. If this happens, I will be informed of the reasons why I will not be eligible to participate in the trial. I understand some test results may make me ineligible, even though they have nothing to do with the state of my health.

5. I specifically give my permission at this time for the following:

a) A complete medical history and physical examination. I understand that there is no risk involved in this thorough examination, and that there may be some benefit to me in terms of my being more aware of my exact health.

b) Collection of urine samples at different times; these samples will be used for various tests. There is no risk involved in this procedure. One test involves four hour timed urine collection during a visit to the center.

c) The collection of approximately two ounces of my blood from a vein in my arm, a procedure which will be carried out by a skilled technician. This blood sample will be used for various laboratory tests. I understand that there is a very small risk of a black and blue mark when this procedure is done. One blood sample will be taken after I drink four ounces of a commonly used formula which is not pleasant tasting. This drink may make me sick to my stomach. (For women: I understand that one of the tests which will be performed on a blood or urine sample will tell me whether or not I am pregnant.)

d) A thorough eye examination by an eye specialist using standard techniques. This will include a test of my vision and a measurement of the pressure in my eyes. To carry out these tests, drops will be put in my eyes to make them dilate; I understand some people find this uncomfortable. I know that I will not be able to drive, or read clearly, for a few hours after this test.

Photographs will be taken of my eyes. If I have had diabetes for less than five years, additional photographs of my eyes may be taken after a dye called fluorescein has been injected into a vein in my arm. I understand that both these techniques are used in standard clinical practice, but there may be some discomfort associated with each. With fluorescein I understand that it is also possible that I shall experience some nausea. I have also been told that on rare occasions some people have a very serious allergic reaction to this dye. I understand that trained personnel will be available when I take the test to lessen the possibility of any such reaction, or to treat it should it occur.

e) I agree to undergo evaluation of my nervous system. This evaluation will consist of a thorough physical examination in which my strength, reflexes and sensations will be tested. Then I will undergo a nervous system evaluation (nerve conduction test) to evaluate certain nerve functions. Some people feel a slight pain during this test. In other people, the test produces a temporary numb feeling.

f) I understand that a standard electrocardiogram will be done. There is no risk or discomfort involved in this test.

g) I agree to take several psychological tests. I recognize that this testing is being performed to determine if it is in my best interest to be included in the trial. The tests are designed to be sure I have no problems that could interfere with my participation in the trial. The tests will include:

1) Questionnaires: Several paper and pencil tests will be given to me to complete.

2) A formal interview with a member of the health care team.

I agree to participate in other meetings, which will include my family or a person I live with, in which the various procedures involved in this clinical trial will be discussed.

A few people find some of the questions embarrassing. I understand that I may refuse to answer such a question.

I understand that all information obtained during these interviews will be confidential. The results will be given to my doctor only if the results will have an effect on my participation in the study. No information will be released to anyone else without my specific consent.

6. I also agree to carry out to the best of my abilities several tasks, some at home, as part of this program to see if I qualify to be a participant in the DCCT. These include:

a) Keeping records about my current treatment program for two weeks.

b) Meeting with members of the health care team to review my program.

c) Collecting blood samples at home. (Two 3:00 a.m. self blood glucose monitoring samples will be required during this two-week period.)

7. I understand that I will be given a questionnaire to test my understanding of the objectives and nature of the DCCT. I understand that I must answer 100% of these questions correctly before I will be considered qualified to be a participant in the DCCT. If I give the wrong answer to any of the questions, I understand that I must come back another day to retake the questionnaire. If I feel that I would benefit from viewing the orientation slide show or by re-reading the Research Volunteer's Handbook, I may do so. If I have any questions regarding my incorrect answers, I would be able to discuss them with a member of the team before taking the questionnaire again. If I do not answer correctly all the questions on the second test, I understand the DCCT physician will decide whether I understand the objectives and nature of the DCCT.

8. I understand that during the period of this study (if I am accepted as a volunteer), my doctor at the center will be made aware of all information that may affect my personal care. However, I also understand that my doctor may not be aware of possible beneficial or detrimental results from my involvement in the study, until it is determined by an independent group of experts that these data are conclusive and meaningful. The results of some tests may not be made known to my physician or to me unless a change in my treatment is needed. (Research Volunteer's Information Handbook, pages 5 and 11)

9. I understand that the choice I have is to volunteer to participate in the DCCT and have the DCCT health care team take care of me or to

continue in my present program for diabetes management with my current doctor.

10. I understand that I may choose not to participate in the DCCT, or that I may change my mind at any time concerning participation, without placing in jeopardy my continuing medical care.

11. I understand that the information concerning my diabetes will be combined with that of many other volunteers, and that I will not be personally identified in any publications or public documents which result from this study.

12. Neither this institution nor the government agency funding this research project will automatically provide special services, free care, or compensation for any injuries or adverse reactions resulting from this research. Treatment for such injuries or adverse reactions will be provided under the same financial arranagement as those under which treatment is usually provided.

If I believe that I may have suffered any injury or adverse reaction as a result of participating in this research, or have questions about my rights as a research subject, I may contact Dr. _____ (_____) or the Associate Vice President of this medical center (_____). They can review the matter with me, identify other resources that may be available to me, and provide me with further information as to how to proceed.

Signature _____

Date _____

Witness _____

(IN THE CASE OF A VOLUNTEER UNDER 18 YEARS OF AGE)

We, as parents or legal guardians of _____, have read and understand this material, have had our questions answered, and give our permission for our child to participate in this clinical trial. (Both parents should sign, if available.)

Signature _____

Date _____

Witness _____

Signature of
Principal Investigator _____

Date _____

Witness _____

Diabetes Control and Complications Trial

DCCT Form 032.3
February 6, 1987

INFORMED CONSENT FORM #2 (PROTOTYPE)

Diabetes Control and Complications Trial (DCCT)

Institution: _____

Principal Investigator: _____

1. I have been told that I am eligible to participate in the Diabetes Control and Complications Trial (DCCT).

2. I have been given copies of the DCCT Research Volunteer's Information Handbook and the Manual of Diabetes Tests, Terms and Special Procedures. I have read both of these, I have had my questions answered, and I now clearly understand the following:

   a) The purpose of the study. (Research Volunteer's Information Handbook, pages 4-6)

   b) The nature of a clinical trial. (Research Volunteer's Information Handbook, page 5)

   c) The two groups to be studied -- the Standard Group and the Experimental Group -- and the fact that there is no proven advantage to being placed in one group or the other. (Research Volunteer's Information Handbook, pages 5 and 8)

   d) The possible risks and benefits of being assigned to the Standard Group or the Experimental Group. (Research Volunteer's Information Handbook, pages 14-15; Manual of Diabetes Tests, Terms and Special Procedures, pages 4-12)

   e) The fact that I shall be assigned to one of these two groups based on a process called random assignment, which means that neither my doctor nor I can choose to which group I will be assigned. Instead, I will be assigned by chance. I am willing to accept an assignment to either of the two treatment groups. (Research Volunteer's Information Handbook, page 5)

   f) That blood tests and urine tests (including tests I will perform at home) will be used to measure diabetes control. (Research Volunteer's Information Handbook, pages 8-9; Manual of Diabetes Tests, Terms and Special Procedures, page 12)

g) That special tests of my eyes, kidneys, nervous system, heart, blood vessels, and psychological tests will be conducted during the trial to look for the appearance or progress of early diabetes complications. I have been given a complete description of these special tests in the Manual of Diabetes Tests, Terms and Special Procedures. (Research Volunteer's Information Handbook, page 10; Manual of Diabetes, Tests, Terms and Special Procedures, pages 4-8)

h) I understand the extent of the responsibilities I agree to carry out if I agree to be a volunteer for the clinical trial. These involve my willingness to follow the treatment program of the group to which I have been assigned and to keep my appointments as scheduled. I understand that some of these appointments will take considerable time. (Research Volunteer's Information Handbook, pages 12-13)

I also understand that my responsibilities will include blood tests and urine tests I will do at my home. One of the required blood tests may be a 3:00 a.m. sample once a week. I will also keep records of my test results and treatment program, even though this may be time consuming.

i) I am agreeing to participate in a clinical trial that may last for seven years. I understand that the study could end early if the study questions have been answered or for reasons of safety. (Research Volunteer's Information Handbook, pages 12-13)

3. I have had a chance at this time to ask all questions which I feel are necessary. I now feel I have enough understanding to allow me to decide to participate in this clinical trial.

4. Understanding the above, and having been made aware of the potential risks and benefits of the overall program, I give you my permission to conduct the tests and procedures listed below during the clinical trial. I further understand that if any new tests are required, I shall be given a thorough explanation in writing before I am asked to sign another permission form covering these new tests.

5. I specifically give my permission at this time for the following tests and examinations:

a) A complete medical history and physical examination. I understand that there is no risk involved in this thorough examination, and that there may be some benefit to me in terms of my being more aware of my exact health. This examination will be done once a year.

b) Collection of urine samples once a year; these samples will be used for various tests. There is no risk involved in this procedure. One test involves a four hour timed urine collection during a visit to the Center once a year. Another test requires a 24 hour collection of urine at home.

c) The collection of blood from a vein in my arm, a procedure which will be carried out by a skilled technician. These blood samples will be used for various laboratory tests. I understand that there is a very small risk of a black and blue mark when this procedure is done. These blood tests which will require about one tablespoon of blood will be done routinely at three-month intervals in the Standard Treatment Group and monthly in the Experimental Treatment Group. At the annual clinic visit, an additional two tablespoons of blood will be taken.

d) A complete and thorough eye examination by an eye specialist using standard techniques. This will include a test of my vision every year and a measurement of the pressure in my eyes every year. To carry out these tests, drops will be put in my eyes to make them dilate; I understand some people find this uncomfortable. I know that I will not be able to drive, or read clearly, for a few hours after this test.

Photographs will be taken of my eyes at six-month intervals. If I have had diabetes for less than five years, a set of additional photographs of my eyes may be taken in five years and at the conclusion of the study and for this a dye called fluorescein will be injected into a vein in my arm. I understand that both these techniques are used in standard clinical practice, but there may be some discomfort associated with each. With fluorescein I understand that it is also possible that I shall experience some nausea. I have also been told that on rare occasions some people have a very serious allergic reaction to this dye. I understand that trained personnel will be available when I take the test to lessen the possibility of any such reaction, or to treat it should it occur.

e) I agree to undergo evaluation of my nervous system in five years and at the conclusion of the study. This evaluation will consist of a thorough physical examination in which my strength, reflexes and sensations will be tested. Then I will undergo a peripheral nervous system evaluation (nerve conduction test) to evaluate certain nerve functions. Some people feel a slight pain during this test. In other people, the test produces a temporary numb feeling. Every two years, I agree to undergo a test of my autonomic nervous system.

f) I understand that a standard electrocardiogram will be done. There is no risk or discomfort involved in this test. The electrocardiogram will be done every two years.

g) I agree to take several psychological tests. The tests will include:

1) Questionnaires: Several paper and pencil tests will be given to me to complete every year.

2) A series of tests (neurobehavioral assessment) of my intelligence, memory, problem-solving ability, motor coordination and attention will be performed at the beginning of the trial and every year thereafter.

A few people find some of these questions embarrassing. I understand that I may refuse to answer such questions.

I understand that all information obtained during these interviews and tests will be confidential. The results will be given to my doctor only if the results will have an effect on my personal care. No information will be released to anyone else without my specific consent.

h) The investigators of this trial are asking me to participate in a new and more accurate means of measuring my kidney function that has become available. This is called the 125-I Iothalamate Flomerular Filtration Rate Determination. This test involves a subcutaneous injection (given just like insulin) of a compound that contains a small amount of radioactive iodine. This substance is absorbed and will be measured in my blood and urine (five times) over a period of several hours. This study will be done as part of the baseline examination, the three-year annual examination and at the end of the study.

125-I Iothalamate has been approved for intravenous injection in humans by the Food and Drug Administration (FDA). Subcutaneous injection has been approved for investigative purposes by the FDA. However, subcutaneous injection has been extensively used in many centers in the United States. The administered dose contains less than 35 microcuries. The total amount of radiation is less than 1/100 of a chest x-ray. The compound 125-I Iothalamate is efficiently excreted by the kidneys and is not stored in the body. At the end of 24 hours, less than 1/10,000 of a dose will remain in the body. The risks involved are those of having blood drawn and possible allergic reactions to the iodine or iothalamate. I will be given a few drops of inorganic iodine prior to the test to block any uptake by the thyroid. If I am a woman, I should not be pregnant at the time of the test and will have a serum pregnancy test performed within 72 hours prior to the test. I understand that the choice I have is to volunteer for this part of the DCCT or refuse this test. I can still participate in the DCCT even if I do not agree to have this test performed.

6. I understand that if I am a woman, I am not planning to become pregnant in the next 2 years.

7. I understand that during the period of this study my doctor at the center will be made aware of all information that may affect my personal care. However, I also understand that my doctor may not be aware of possible beneficial or detrimental results from my involvement in the study until it is determined by an independent

group of experts that these data are conclusive and meaningful. The results of some tests may not be made known to my physician or to me unless a change in my treatment is needed. (Research Volunteer's Information Handbook, pages 5 and 11)

8. I understand that the choice I have is to volunteer to participate in the DCCT and have the DCCT health care team take care of me or to continue in my present program for diabetes management with my current doctor.

9. I understand that I may choose not to participate in the DCCT, or that I may change my mind at any time concerning participation, without in any way placing in jeopardy my continuing medical care or incurring any danger or health risk provided I continue on an appropriate insulin regimen.

10. I understand that the information concerning my diabetes will be combined with that of many other volunteers, and that I will not be personally identified in any publications or public documents which result from this study.

11. Neither this institution nor the government agency funding this research project will automatically provide special services, free care, or compensation for any injuries or adverse reactions resulting from this research. Treatment for such injuries or adverse reactions will be provided under the same financial arranagement as those under which treatment is usually provided.

If I believe that I may have suffered any injury or adverse reaction as a result of participating in this research, or have questions about my rights as a research subject, I may contact Dr. _____ (_____) or the Associate Vice President of this medical center (_____). They can review the matter with me, identify other resources that may be available to me, and provide me with further information as to how to proceed.

Signature _____

Date _____

Witness _____

My signature below also signifies my willingness to participate in the 125-I Iothalamate study.

Signature _____

Date _____

Witness _____

(IN THE CASE OF A VOLUNTEER UNDER 18 YEARS OF AGE)

We, as parents or legal guardians of _____, have read and understand this material, have had our questions answered, and give our permission for our child to participate in this clinical trial. (Both parents should sign, if available.)

Signature _____

Date _____

Witness _____

Signature of
Principal Investigator _____

Date _____

Witness _____

Diabetes Control and Complications Trial

DCCT Form 33.1

FUNDUS PHOTOGRAPH DETAILED GRADING

RAN 1-[ ][ ][ ][ ][ ] [ ] R-0 L-1

PATIENT ID [ ][ ][ ][ ][ ] Date of Grading [ ][ ] [ ][ ] [ ][ ] Reading List [ ][ ][ ] [ ] GRADER [ ][ ]

NAMECODE [ ][ ][ ] Graders Initials _____

87 FORM LEVEL SELECTED

SHORT FORM S-1

Answers recorded for MA, CTMA, HMA, DRU, AN and Other Nondiabetic Lesions. All other lesions judged absent.

MEDIUM FORM M-2

Answers recorded for MA, CTMA, HMA, DRU, HE, SE, IRMA, VLR, AN, AS, AVN, HERG, HEMC, HECR, Retinal Thickening, Macular Region (Cyst and Z), and Other Nondiabetic Ocular Lesions. All other lesions judged absent.

FULL FORM F-3

88 X OTHER NONDIABETIC LESIONS

Any definitely or questionably present? N-0 Y-2
If so, indicate below.

28	B	Asteroid Hyalosis	Q-1	Y-2
29	C	Central Vein Occlusion	Q-1	Y-2
30	D	Branch Vein Occlusion	Q-1	Y-2
31	E	Central Artery Occlusion	Q-1	Y-2
32	F	Branch Artery Occlusion	Q-1	Y-2
33	G	Macular Degeneration	Q-1	Y-2
34	H	Chorioretinal Scar	Q-1	Y-2
36	I	Nevus	Q-1	Y-2
37	J	Subretinal Fibrous Tissue	Q-1	Y-2
38	K	Coloboma or Staphyloma	Q-1	Y-2
35	L	Other	Q-1	Y-2

91 W FUNDUS REFLEX

0 - no opacity
1 - Q, lens opacity or ctr. not involved
2 - lens opacity, center involved
3 - lens opacity, precludes photos
4 - vitreous opacity, precludes photos
5 - other changes
8 - photos absent or inadequate

89 Y GLOBAL SCARS/OBSCURITIES

0 - no evidence
2 - present
8 - all retina obscured

If answer is 2, complete for all fields.

D 1
CHECK IF FIELD MISSING 1 [ ]

101 RH — Retinal Hem.

0 - no evidence 0
1 - questionable 1
2 - 1 retinal hem. 2
3 - ≥ 2 retinal hem. 3
8 - can't grade 8

104 CTMA — Count of Ma

0 - no evidence 0
Q - questionable 0
number if ≤ 5 Ma [ ] Q
6 - > 5 Ma 6
8 - can't grade 8

105 SE — Soft Exudate

0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #8A 2
3 - < Std. Photo #5 3
4 - ≥ Std. Photo #5 4
8 - can't grade 8

106 PRH — Preretinal Hemorrhage

0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #9 or #13 2
3 - < 1/2 field 3
4 - ≥ 1/2 field 4
8 - can't grade 8

111 VH — Vitreous Hemorrhage

0 - no evidence 0
1 - questionable 1
2 - < 1 DA 2
3 - < 1/2 field 3
4 - ≥ 1/2 field 4
5 - obscures all 5
8 - can't grade 8

140 NVD — New Vessels on Disc

0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #10A 2
3 - < Std. Photo #10C 3
4 - ≥ Std. Photo #10C 4
8 - can't grade 8

141 DLTD — Dilated Tips

If NVD > 0.
0 - no evidence 0
1 - Q, or < 2x proximal 1
2 - ≥ 2x proximal 2
8 - can't grade 8

142 FPD — Fibrous Prolif. on Disc

0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #10B 2
3 - < 2 DA 3
4 - ≥ 2 DA 4
8 - can't grade 8

143 PPD — Place of Prolif. on Disc

If NVD > 0 or FPD > 0.
0 - no evidence 0
1 - Q, or < 1/4 DD 1
2 - < 1 DD 2
3 - < 2 DD 3
4 - ≥ 2 DD 4
8 - can't grade 8

144 PS — Papillary Scarring

0 - no evidence 0
1 - questionable 1
2 - Ex. A, B, C, D 2
3 - Ex. E, F 3
8 - can't grade 8

115 NVE — New Vessels Elsewhere

0 - no evidence 0
1 - questionable 1
2 - < 1/2 DA 2
3 - < Std. Photo #7 3
4 - ≥ Std. Photo #7 4
8 - can't grade 8

116 DLTE — Dilated Tips

If NVE > 0.
0 - no evidence 0
1 - Q, or < 2x proximal 1
2 - ≥ 2x proximal 2
8 - can't grade 8

117 FPE — Fibrous Prolif. Elsewhere

0 - no evidence 0
1 - questionable 1
2 - < 1/2 DA 2
3 - < Std. Photo #11 3
4 - ≥ Std. Photo #11 4
8 - can't grade 8

118 PPE — Place of Prolif. Elsewhere

If NVE > 0 or FPE > 0.
0 - no evidence 0
1 - Q or < 1/4 DD 1
2 - < 1 DD 2
3 - < 2 DD 3
4 - ≥ 2 DD 4
8 - can't grade 8

122 Scars (plc) %

[ ][ ]

123 Obscurities %

[ ][ ]

ELD 2
HECK IF FIELD MISSING 1 ☐

H
0 - no evidence 0
1 - questionable 1
2 - 1 retinal hem. 2
3 - ≥ 2 retinal hem. 3
8 - can't grade 8
11

TMA 0 - no evidence 0
Q - questionable number if ≤ 5 Ma Q ☐
6 - > 5 Ma 6
8 - can't grade 8
Ma

MA 0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #1 2
3 - < Std. Photo #2A 3
4 - < Std. Photo #2B 4
5 - ≥ Std. Photo #2B 5
8 - can't grade 8
Micro-aneurysms

RU 0 - no evidence 0
1 - Q or < Std. Photo #1 1
2 - < Std. Photo #20 2
3 - < Std. Photo #21 3
4 - ≥ Std. Photo #21 4
8 - can't grade 8

E 0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #3 2
3 - < Std. Photo #5 3
4 - < Std. Photo #4 4
5 - ≥ Std. Photo #4 5
8 - can't grade 8

HE > 1. assess
ERQ 0 - no evidence 0
1 - questionable 1
2 - < 10% 2
3 - < 50% 3
4 - < 90% 4
5 - ≥ 90% 5
8 - can't grade 8

HE > 0. assess
EMC 0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #3 2
3 - < Std. Photo #5 3
4 - < Std. Photo #4 4
5 - ≥ Std. Photo #4 5
8 - can't grade 8
Center of Macula

HEMC > 0. assess
ECR 0 - no evidence 0
1 - questionable 1
2 - present 2
8 - can't grade 8
Center

E 0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #8A 2
3 - < Std. Photo #5 3
4 - ≥ Std. Photo #5 4
8 - can't grade 8
Exudate

RMA 0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #8A 2
3 - < Std. Photo #8B 3
4 - ≥ Std. Photo #8B 4
8 - can't grade 8
11

Scars (pic) %
12

Obscurities %
13

RETINAL THICKENING

FTSZ 0 - no evidence 0
1 - questionable 1
2 - < 1/2 DA 2
3 - < 1 DA 3
4 - < 2 DA 4
5 - < 1/4 field 5
6 - < 1/2 field 6
7 - ≥ 1/2 field 7
8 - can't grade 8
All of Field Presence and Area
252

If FTSZ > 1. assess
FDTK 2 - < 1x reference 2
3 - < 2x reference 3
4 - < 1/2 DD 4
5 - ≥ 1/2 DD 5
7 - CG, poor stereo 7
8 - can't grade, other 8
All of Field Max. Thickness
253

If FTSZ > 0. assess
MTSZ 0 - no evidence 0
1 - questionable 1
2 - < 1/2 DA 2
3 - < 1 DA 3
4 - < 2 DA 4
5 - ≥ 2 DA 5
8 - can't grade 8
< 1 DD from Center Presence and Area
254

If MTSZ > 1. assess
MCTK 2 - < 1x reference 2
3 - < 2x reference 3
4 - < 1/2 DD 4
5 - ≥ 1/2 DD 5
7 - CG, poor stereo 7
8 - can't grade, other 8
< 1 DD from Center Max. Thickness
255

If MTSZ > 0. assess
CRTK 0 - no evidence 0
1 - questionable 1
2 - < 1x reference 2
3 - < 2x reference 3
4 - < 1/2 DD 4
5 - ≥ 1/2 DD 5
7 - CG, poor stereo 7
8 - can't grade 8
Center of Macula Max. Thickness
256

PVDT 0 - no evidence 0
1 - questionable 1
2 - inferred, other lesions 2
3 - visible, thin 3
4 - visible, thick 4
8 - can't grade 8
Post. Vitreous Detachment
231

REL 0 - no evidence 0
1 - questionable 1
2 - < 1 DA/vessel elevated 2
3 - < Std. Photo #12 3
4 - ≥ Std. Photo #12 4
8 - can't grade 8
Retinal Elevation
219

PRH 0 - no evidence 0
1 - questionable 1
2 - < Std. Photo #9 or #13 2
3 - < 1/2 field 3
4 - ≥ 1/2 field 4
8 - can't grade 8
Preretinal Hemorrhage
220

VH 0 - no evidence 0
1 - questionable 1
2 - < 1 DA 2
3 - < 1/2 field 3
4 - ≥ 1/2 field 4
5 - obscures all 5
8 - can't grade 8
Vitreous Hemorrhage
221

MACULAR REGION

If MTSZ > 0. assess
CSME 0 - no evidence 0
1 - questionable 1
2 - ≥ 1 DA, part < 1 DD 2
3 - thickening/HE < 500 u 3
8 - can't grade 8
Clin. Sig. Macular Edema
282

If MTSZ > 0. assess
261 CYST 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG

2 Are any macular lesions below > 0?
90 0 ☐ N 2 ☐ Y
If yes, complete all

Assess following within 1 DD of center of macula.

263 NV on retinal surface 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
264 FP on retinal surface 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
265 NV on det. post. hyaloid 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
266 FP on det. post. hyaloid 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG

267 Pigment disturbance 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
268 Tension lines 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
269 Macular hole 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG

Assess following at center of macula

270 New vessels 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
271 Fibrous proliferation 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG

272 Retinal detachment 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
273 Ret. distortion-tension lines 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
274 Dragged macula 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG

275 Retinal hemorrhage 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
276 Preretinal hemorrhage 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
277 Subretinal hemorrhage 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG

278 Exudate plaque, organized exudate, "fibrous scar" 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
279 Deep white spot-choroid/RPE 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG

280 Obscured by VH 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG

SP1 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
SP2 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
SP3 0 ☐ N 1 ☐ Q 2 ☐ Y 8 ☐ CG
SP4A ☐☐ SP4B ☐☐

SP5A	SP5B
0	0
1	1
2	2
3	3
8	8

SP6A	SP6B
0	0
1	1
2	2
3	3
4	4
8	8

SP7A	SP7B
0	0
1	1
2	2
3	3
4	4
5	5
8	8

	CHECK IF FIELD MISSING	FIELD 3 1 ☐	FIELD 4 1 ☐	FIELD 5 1 ☐	FIELD 6 1 ☐	FIELD 7 1 ☐		FIELD 8A 1 ☐	FIELD 8B 1 ☐
RH Retinal Hem. 01	0 - no evidence 1 - questionable 2 - 1 retinal hem. 3 - ≥ 2 retinal hem. 8 - can't grade	0 1 2 3 8	0 1 2 3 8	0 1 2 3 8	0 1 2 3 8	0 1 2 3 8		0 1 2 3 8	0 1 2 3 8
CTMA Count of Ma 04	0 - no evidence Q - questionable number if ≤ 5 Ma 6 - > 5 Ma 8 - can't grade	0 Q 6 8	0 Q 6 8	0 Q 6 8	0 Q 6 8	0 Q 6 8	TMA Eye Total of Mas 05	0 - no evidence Q - questionable number if ≤ 20 Ma 21 - > 20 Ma 88 - can't grade	0 Q 21 88
HMA Hemorrhages/ Microaneurysms 02	0 - no evidence 1 - questionable 2 - < Std. Photo #1 3 - < Std. Photo #2A 4 - < Std. Photo #2B 5 - ≥ Std. Photo #2B 8 - can't grade	0 1 2 3 4 5 8	0 1 2 3 4 5 8	0 1 2 3 4 5 8	0 1 2 3 4 5 8	0 1 2 3 4 5 8		0 1 2 3 4 5 8	0 1 2 3 4 5 8
DRU Drusen 03	0 - no evidence 1 - Q or < Std. Photo #1 2 - < Std. Photo #20 3 - < Std. Photo #21 4 - ≥ Std. Photo #21 8 - can't grade	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8		0 1 2 3 4 8	0 1 2 3 4 8
HE Hard Exudate	0 - no evidence 1 - questionable 2 - < Std. Photo #3 3 - < Std. Photo #5 4 - < Std. Photo #4 5 - ≥ Std. Photo #4 8 - can't grade	0 1 2 3 4 5 8	0 1 2 3 4 5 8	0 1 2 3 4 5 8	0 1 2 3 4 5 8	0 1 2 3 4 5 8		0 1 2 3 4 5 8	0 1 2 3 4 5 8
SE Soft Exudate 06	0 - no evidence 1 - questionable 2 - < Std. Photo #8A 3 - < Std. Photo #5 4 - ≥ Std. Photo #5 8 - can't grade	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8		0 1 2 3 4 8	0 1 2 3 4 8
IRMA 11	0 - no evidence 1 - questionable 2 - < Std. Photo #8A 3 - < Std. Photo #8B 4 - ≥ Std. Photo #8B 8 - can't grade	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8		0 1 2 3 4 8	0 1 2 3 4 8
VLR Venous Loop Redup. 08	0 - no evidence 1 - < 3/2 width and < 31u 2 - ≥ 3/2 width or ≥ 31u 3 - < 31u 4 - ≥ 31u 8 - can't grade	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8		0 1 2 3 4 8	0 1 2 3 4 8
VB Venous Beading 09	0 - no evidence 1 - questionable 2 - < Std. Photo #8A 3 - < Std. Photo #8B 4 - ≥ Std. Photo #8B 8 - can't grade	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8		0 1 2 3 4 8	0 1 2 3 4 8
VN Venous Narrowing 07	0 - no evidence 1 - Q, or < 125u 2 - < 1500u 3 - ≥ 1500u 4 - general 8 - can't grade	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8	0 1 2 3 4 8		0 1 2 3 4 8	0 1 2 3 4 8
Venous Sheathing 09	0 - no evidence 1 - Q, or < 125u 2 - < 1500u 3 - ≥ 1500u 8 - can't grade	0 1 2 3 8	0 1 2 3 8	0 1 2 3 8	0 1 2 3 8	0 1 2 3 8		0 1 2 3 8	0 1 2 3 8
PVEX Peri-venous Exudate	0 - no evidence 1 - Q, or < 1/8 DD 2 - ≥ 1/8 DD 8 - can't grade	0 1 2 8	0 1 2 8	0 1 2 8	0 1 2 8	0 1 2 8		0 1 2 8	0 1 2 8

		FIELD 3	FIELD 4	FIELD 5	FIELD 6	FIELD 7		FIELD 8A	FIELD 8B
AN Arteriolar Narrowing 2	0 - no evidence	0	0	0	0	0		0	0
	1 - questionable	1	1	1	1	1		1	1
	2 - < Std. Photo #1	2	2	2	2	2		2	2
	3 - < Std. Photo #7	3	3	3	3	3		3	3
	4 - ≥ Std. Photo #7	4	4	4	4	4		4	4
	8 - can't grade	8	8	8	8	8		8	8
AS Arteriolar Sheathing 3	0 - no evidence	0	0	0	0	0		0	0
	1 - Q. or < 125u	1	1	1	1	1		1	1
	2 - < Std. Photo #5	2	2	2	2	2		2	2
	3 - < Std. Photo #7	3	3	3	3	3		3	3
	4 - ≥ Std. Photo #7	4	4	4	4	4		4	4
	8 - can't grade	8	8	8	8	8		8	8
AVN Arterio-venous Nicking 4	0 - no evidence	0	0	0	0	0		0	0
	1 - questionable	1	1	1	1	1		1	1
	2 - < Std. Photo #9	2	2	2	2	2		2	2
	3 - ≥ Std. Photo #9	3	3	3	3	3		3	3
	8 - can't grade	8	8	8	8	8		8	8
PROLIFERATIVE LESIONS									
NVE New Vessels Elsewhere 5	0 - no evidence	0	0	0	0	0		0	0
	1 - questionable	1	1	1	1	1		1	1
	2 - < 1/2 DA	2	2	2	2	2		2	2
	3 - < Std. Photo #7	3	3	3	3	3		3	3
	4 - ≥ Std. Photo #7	4	4	4	4	4		4	4
	8 - can't grade	8	8	8	8	8		8	8
If NVE > 0, assess									
DLTE Dilated Tips 6	0 - no evidence	0	0	0	0	0		0	0
	1 - Q. or < 2x proximal	1	1	1	1	1		1	1
	2 - ≥ 2x proximal	2	2	2	2	2		2	2
	8 - can't grade	8	8	8	8	8		8	8
FPE Fibrous Prolif. Elsewhere 7	0 - no evidence	0	0	0	0	0		0	0
	1 - questionable	1	1	1	1	1		1	1
	2 - < 1/2 DA	2	2	2	2	2		2	2
	3 - < Std. Photo #1	3	3	3	3	3		3	3
	4 - ≥ Std. Photo #1	4	4	4	4	4		4	4
	8 - can't grade	8	8	8	8	8		8	8
If NVE > 0 or FPE > 0, assess									
PPE Preret. Prolif. Elsewhere 8	0 - no evidence	0	0	0	0	0		0	0
	1 - Q. or < 1/4 DD	1	1	1	1	1		1	1
	2 - < 1 DD	2	2	2	2	2		2	2
	3 - < 2 DD	3	3	3	3	3		3	3
	4 - ≥ 2 DD	4	4	4	4	4		4	4
	8 - can't grade	8	8	8	8	8		8	8
REL Retinal Elevation 9	0 - no evidence	0	0	0	0	0		0	0
	1 - questionable	1	1	1	1	1		1	1
	2 - < 1 DA/vessel elevated	2	2	2	2	2		2	2
	3 - < Std. Photo #12	3	3	3	3	3		3	3
	4 - ≥ Std. Photo #12	4	4	4	4	4		4	4
	8 - can't grade	8	8	8	8	8		8	8
PRH Preretinal Hemorrhage 10	0 - no evidence	0	0	0	0	0		0	0
	1 - questionable	1	1	1	1	1		1	1
	2 - < Std. Photo #9 or #13	2	2	2	2	2		2	2
	3 - < 1/2 field	3	3	3	3	3		3	3
	4 - ≥ 1/2 field	4	4	4	4	4		4	4
	8 - can't grade	8	8	8	8	8		8	8
VH Vitreous Hemorrhage 11	0 - no evidence	0	0	0	0	0		0	0
	1 - questionable	1	1	1	1	1		1	1
	2 - < 1 DA	2	2	2	2	2		2	2
	3 - < 1/2 field	3	3	3	3	3		3	3
	4 - ≥ 1/2 field	4	4	4	4	4		4	4
	5 - obscures all	5	5	5	5	5		5	5
	8 - can't grade	8	8	8	8	8		8	8
22 Scars (p/c) %									
23 Obscurities %									
SPM		0	0	0	0	0		0	0
		1	1	1	1	1		1	1
		2	2	2	2	2		2	2
		3	3	3	3	3		3	3
		4	4	4	4	4		4	4
		8	8	8	8	8		8	8

Diabetes Control and Complications Trial

Fundus Photo Reading Center
November 5, 1987

DCCT Detailed Fluorescein Angiogram Grading Record Structure

Character	Information
	Identifying Information
1-6	accession number
7	eye
8-9	clinic
10-14	patient ID
15-17	patient initials
18-19	visit
20-25	date of angiography: MMDDYY
26	rapid series eye: 0 = RE, 1 = LE
27	unscheduled visit indicator: 0 = original, 2 = retake
	Photographic Quality (0,1,2,3)
32	Fld. 2F, early/mid phase, central subfield
33	Fld. 2F, early/mid phase, inner subfields
34	Fld. 2F, early/mid phase, outer subfields
35	Fld. 2F, early/mid phase, far temporal subfield
36	Fld. 2F, late phase, central subfield
37	Fld. 2F, late phase, inner subfields
38	Fld. 2F, late phase, outer subfields
39	Fld. 2F, late phase, far temporal subfield
40	Fld. 1F, mid phase
	Grading Information
41	outline of foveal avascular zone (0,1,2,3,8)
42	size of foveal avascular zone (0,1,2,3,4,8)
	capillary loss (0,1,2,3,4,5,7,8)
43	Fld. 2F, central subfield
44	Fld. 2F, inner superior subfield
45	Fld. 2F, inner nasal subfield
46	Fld. 2F, inner inferior subfield
47	Fld. 2F, inner temporal subfield
48	Fld. 2F, outer superior subfield
49	Fld. 2F, outer nasal subfield
50	Fld. 2F, outer inferior subfield
51	Fld. 2F, outer temporal subfield
52	Fld. 2F, far temporal subfield
53	Fld. 1F

capillary dilatation (0,1,2,3,4,7,8)

54 Fld. 2F, central subfield
55 Fld. 2F, inner superior subfield
56 Fld. 2F, inner nasal subfield
57 Fld. 2F, inner inferior subfield
58 Fld. 2F, inner temporal subfield
59 Fld. 2F, outer superior subfield
60 Fld. 2F, outer nasal subfield
61 Fld. 2F, outer inferior subfield
62 Fld. 2F, outer temporal subfield
63 Fld. 2F, far temporal subfield
64 Fld. 1F

retinal pigment epithelial abnormalities (0,1,2,3,4,5,7,8)

65 Fld. 2F, central subfield
66 Fld. 2F, inner superior subfield
67 Fld. 2F, inner nasal subfield
68 Fld. 2F, inner inferior subfield
69 Fld. 2F, inner temporal subfield
70 Fld. 2F, outer superior subfield
71 Fld. 2F, outer nasal subfield
72 Fld. 2F, outer inferior subfield
73 Fld. 2F, outer temporal subfield
74 Fld. 2F, far temporal subfield

fluorescein leakage (0,1,2,3,4,5,7,8)

75 Fld. 2F, central point
76 Fld. 2F, central subfield
77 Fld. 2F, inner superior subfield
78 Fld. 2F, inner nasal subfield
79 Fld. 2F, inner inferior subfield
80 Fld. 2F, inner temporal subfield
81 Fld. 2F, outer superior subfield
82 Fld. 2F, outer nasal subfield
83 Fld. 2F, outer inferior subfield
84 Fld. 2F, outer temporal subfield
85 Fld. 2F, far temporal subfield

source of leakage (0,1,2,3,4,5,7,8)

86 Fld. 2F, central subfield
87 Fld. 2F, inner superior subfield
88 Fld. 2F, inner nasal subfield
89 Fld. 2F, inner inferior subfield
90 Fld. 2F, inner temporal subfield
91 Fld. 2F, outer superior subfield
92 Fld. 2F, outer nasal subfield
93 Fld. 2F, outer inferior subfield
94 Fld. 2F, outer temporal subfield
95 Fld. 2F, far temporal subfield

cystoid changes (0,1,2,3,7,8)

96 Fld. 2F, central subfield
97 Fld. 2F, inner superior subfield
98 Fld. 2F, inner nasal subfield
99 Fld. 2F, inner inferior subfield
100 Fld. 2F, inner temporal subfield
101 Fld. 2F, outer superior subfield
102 Fld. 2F, outer nasal subfield
103 Fld. 2F, outer inferior subfield
104 Fld. 2F, outer temporal subfield
105 Fld. 2F, far temporal subfield

focal narrowing of arterioles (0,1,2,3,7,8)

106 Fld. 2F, inner superior subfield
107 Fld. 2F, inner nasal subfield
108 Fld. 2F, inner inferior subfield
109 Fld. 2F, inner temporal subfield
110 Fld. 2F, outer superior subfield
111 Fld. 2F, outer nasal subfield
112 Fld. 2F, outer inferior subfield
113 Fld. 2F, outer temporal subfield
114 Fld. 2F, far temporal subfield
115 Fld. 2F, other area
116 Fld. 1F

narrowing/pruning of arterioles (0,1,2,3,7,8)

117 Fld. 2F, inner superior subfield
118 Fld. 2F, inner nasal subfield
119 Fld. 2F, inner inferior subfield
120 Fld. 2F, inner temporal subfield
121 Fld. 2F, outer superior subfield
122 Fld. 2F, outer nasal subfield
123 Fld. 2F, outer inferior subfield
124 Fld. 2F, outer temporal subfield
125 Fld. 2F, far temporal subfield
126 Fld. 2F, other area
127 Fld. 1F

staining/broadening of arterioles (0,1,2,3,7,8)

128 Fld. 2F, inner superior subfield
129 Fld. 2F, inner nasal subfield
130 Fld. 2F, inner inferior subfield
131 Fld. 2F, inner temporal subfield
132 Fld. 2F, outer superior subfield
133 Fld. 2F, outer nasal subfield
134 Fld. 2F, outer inferior subfield
135 Fld. 2F, outer temporal subfield
136 Fld. 2F, far temporal subfield
137 Fld. 2F, other area
138 Fld. 1F

contour of arterioles (0,1,2,3,7,8)

139 Fld. 2F, inner superior subfield
140 Fld. 2F, inner nasal subfield
141 Fld. 2F, inner inferior subfield
142 Fld. 2F, inner temporal subfield
143 Fld. 2F, outer superior subfield
144 Fld. 2F, outer nasal subfield
145 Fld. 2F, outer inferior subfield
146 Fld. 2F, outer temporal subfield
147 Fld. 2F, far temporal subfield
148 Fld. 2F, other area
149 Fld. 1F

other abnormalities (0,1,2,8)

150 filling delay
151 choroidal leakage
152 macular hole
153 other

count of microaneurysms (0,Q,1...11,88)

154-155 Fld. 2F
156-157 Fld. 1F

Summary Information

capillary loss, all subfields of Fld. 2F plus 1F

161 maximum grade
162-163 number of subfields with maximum (1...11)

capillary loss, center and inner subfields of Fld. 2F

164 maximum grade
165 number of subfields with maximum (1...5)

capillary dilatation, all subfields of Fld. 2F plus 1F

166 maximum grade
167-168 number of subfields with maximum (1...11)

retinal pigment epithelial abnormalities, all subfields of Fld. 2F

169 maximum grade
170-171 number of subfields with maximum grade (1...10)

fluorescein leakage, all subfields of Fld. 2F

172 maximum grade
173-174 number of subfields with maximum (1...10)

fluorescein leakage, center and inner subfields of Fld. 2F

175 maximum grade
176 number of subfields with maximum grade (1...5)

source of leakage (percent of leakage from microaneurysms), all subfields of Fld. 2F

177 maximum grade (code '5' ignored)
178-179 number of subfields with maximum grade (1...10)

cystoid changes, all subfields of Fld. 2F excluding central subfield

180 maximum grade
181-182 number of subfields with maximum grade (1...9)

cystoid changes, inner subfields, excluding central subfield

183 maximum grade
184 number of subfields with maximum grade (1...4)

focal narrowing of arterioles, all subfields of Fld. 2F plus Fld. 1F

185 maximum grade
186-187 number of subfields with maximum grade (1...12*)

narrowing/pruning of arterioles, all subfields of Fld. 2F plus Fld. 1F

188 maximum grade
189-190 number of subfields with maximum grade (1...11)

staining/broadening of arterioles, all subfields of Fld. 2F plus 1F

191 maximum grade
192-193 number of subfields with maximum grade (1...12*)

contour of arterioles, all subfields of Fld. 2F plus Fld. 1F

194 maximum grade
195-196 number of subfields with maximum grade (1...12*)

count of microaneurysms (0,Q,1...11,88)

197-198 total for eye

other information
199-200 angiographic quality

201-206 date angiograms received at CCRU (mmddyy)

207-209 blanks

210 correction code: 0 = original, 1-9 = sequence number of correction

*Code 3 in Field 1F denotes definite presence in two subfields.

SCL-90-R

Name:_____ Technician:_____ Ident. No._____

Location:_____ Visit No.:_____ Mode: S-R_____ Nar_____

Age:_____ Sex: M_____ F_____ Date:_____ Remarks:_____

INSTRUCTIONS

Below is a list of problems and complaints that people sometimes have. Read each one carefully, and select one of the numbered descriptors that best describes HOW MUCH DISCOMFORT THAT PROBLEM HAS CAUSED YOU DURING THE PAST_____INCLUDING TODAY. Place that number in the open block to the right of the problem. Do not skip any items, and print your number clearly. If you change your mind, erase your first number completely. Read the example below before beginning, and if you have any questions please ask the technician.

EXAMPLE

HOW MUCH WERE YOU DISTRESSED BY:	Answer	Descriptors
Ex. Body Aches.....	Ex. [3]	0 Not at all 1 A little bit 2 Moderately 3 Quite a bit 4 Extremely

HOW MUCH WERE YOU DISTRESSED BY:	Descriptors
	0 Not at all 1 A little bit 2 Moderately 3 Quite a bit 4 Extremely

NOTE. The holder of the copyright for the "Symptoms Checklist 90, revised (SCL-90r)" did not grant permission to reproduce this form. Persons interested in reviewing copies of this form should contact Pearsons at: www.pearsonassessments.com. In the following pages we summarize the variables included in the DCCT dataset derived using this form.

VARIABLES	DESCRIPTION
fsasdate	Form date as SAS date value
form	DCCT form number
cevsitno	Follow-up visit number
agegrp	Patient's age group (1=adult, 2=adolescent)
age	Patient's age
testage	Patient's age at time of test, based on visit
sex	Patient's gender (form 001); M=Male;F=Female
mask_pat	Patient ID number
cewindow	Visit held within time window, 1=YES

Scale and Subscale Scores

tscanx	T-score - anxiety
tscdep	T-score - depression
tschos	T-score - hostility
tscint	T-score - interpersonal sensitivity
tscobs	T-score - obsessive-compulsive behavior
tscpar	T-score - paranoid ideation
tscpho	T-score - phobic anxiety
tscpsy	T-score - psychoticism
tscsom	T-score - somatization
tscgsi	T-score - global severity index
tscpsdi	T-score - positive symptom - distress index
tscpst	T-score - positive symptom - total
pst	Positive symptoms - total
psdi	Positive symptoms - distress index
naddi	Number of questions answered - additional items
nanx	Number of questions answered - anxiety
ndep	Number of questions answered - depression
nhos	Number of questions answered - hostility
nint	Number of questions answered - interpersonal sensitivity
nobs	Number of questions answered - obsessive - compuls
npar	Number of questions answered - paranoid ideation
npho	Number of questions answered - phobic anxiety
npsy	Number of questions answered - psychoticism
nsom	Number of questions answered - somatization
ntotal	Number of questions answered - total
totaddi	Total score - additional item(s)
totanx	Total score - anxiety
totdep	Total score - depression
tothos	Total score - hostility
totint	Total score - interpersonal sensitivity
totobs	Total score - obsessive-compulsive
totpar	Total score - paranoid ideation
totpho	Total score - phobic anxiety
totpsy	Total score - psychoticism
totsom	Total score - somatization
total	Total score - 90 items
rawaddi	Raw score - additional item
rawanx	Raw score - anxiety
rawdep	Raw score - depression

rawhos	Raw score - hostility
rawint	Raw score - interpersonal sensitivity
rawobs	Raw score - obsessive-compulsive
rawpar	Raw score - paranoid ideation
rawpho	Raw score - phobic anxiety
rawpsy	Raw score - psychoticism
rawsom	Raw score - somatization

Individual questions (CEQ1 - CEQ90) ask about extent of distress caused by 90 factors.

Responses are coded: 0=not at all; 1=a little;2=moderately; 3=quite a bit; 4=extremely

ceq1	distressed by headaches
ceq2	distressed by nervousness or shakiness inside
ceq3	distressed by repeated unpleasant thoughts
ceq4	distressed by feeling faint or dizzy
ceq5	distressed by loss of sexual interest/pleasure
ceq6	distressed by feeling critical of others
ceq7	distressed by the idea that someone else controls thoughts
ceq8	distressed by feeling others are to blame for most troubles
ceq9	distressed by trouble remembering things
ceq10	distressed by worried about sloppiness or carelessness
ceq11	distressed by feeling easily annoyed
ceq12	distressed by pains in heart/chest
ceq13	distressed by feeling afraid in open spaces or on street
ceq14	distressed by feeling low in energy - slowed down
ceq15	distressed by suicidal thoughts
ceq16	distressed by hearing voices that others do not hear
ceq17	distressed by trembling
ceq18	distressed by feeling that most people cannot be trusted
ceq19	distressed by poor appetite
ceq20	distressed by crying easily
ceq21	distressed by feeling shy or uneasy with opposite sex
ceq22	distressed by feelings of being trapped
ceq23	distressed by being suddenly scared for no reason
ceq24	distressed by temper outbursts you could not control
ceq25	distressed by feeling afraid to leave the house alone
ceq26	distressed by blaming yourself for things
ceq27	distressed by pains in lower back
ceq28	distressed by feeling blocked in getting things done
ceq29	distressed by feeling lonely
ceq30	distressed by feeling blue
ceq31	distressed by worrying too much about things
ceq32	distressed by feeling no interest in things
ceq33	distressed by feeling fearful
ceq34	distressed by your feelings being easily hurt
ceq35	distressed by other people being aware of your private thoughts
ceq36	distressed by feeling others do not understand you or are unsympathetic
ceq37	distressed by feeling that people are unfriendly or dislike you
ceq38	distressed by having to do things very slowly to do them correctly
ceq39	distressed by heart pounding or racing
ceq40	distressed by nausea or up-set stomach

ceq41	distressed by feeling inferior to others
ceq42	distressed by muscle soreness
ceq43	distressed by feeling watched and talked about by others
ceq44	distressed by trouble falling asleep
ceq45	distressed by having to check and double-check what you do
ceq46	distressed by difficulty making decisions
ceq47	distressed by feeling afraid to travel on buses / subways / trains
ceq48	distressed by trouble catching your breath
ceq49	distressed by hot or cold spells
ceq50	distressed by having to avoid certain things / places / activities because they frighten you
ceq51	distressed by your mind going blank
ceq52	distressed by numbness and tingling in parts of your body
ceq53	distressed by a lump in your throat
ceq54	distressed by feeling hopeless about the future
ceq55	distressed by trouble concentrating
ceq56	distressed by feeling weak in parts of your body
ceq57	distressed by feeling tense or keyed up
ceq58	distressed by heavy feelings in your arms or legs
ceq59	distressed by thoughts of death or dying
ceq60	distressed by overeating
ceq61	distressed by feeling uneasy when people are watching or talking about you
ceq62	distressed by having thoughts that are not your own
ceq63	distressed by having urges to beat / injure / or harm someone
ceq64	distressed by awakening in the early morning
ceq65	distressed by having to repeat the same action -- such as touching / counting / washing
ceq66	distressed by sleep that is restless or disturbed
ceq67	distressed by having urges to break or smash things
ceq68	distressed by having ideas or believes that others do not share
ceq69	distressed by feeling very self-conscious with others
ceq70	distressed by feeling uneasy in crowds -- e.g. in shopping areas or at a movie
ceq71	distressed by feeling everything is an effort
ceq72	distressed by spells of terror or panic
ceq73	distressed by feeling uncomfortable about eating or drinking in public
ceq74	distressed by getting into frequent arguments
ceq75	distressed by feeling nervous when left alone
ceq76	distressed by others not giving proper credits for your achievements
ceq77	distressed by feeling lonely even when you are with people
ceq78	distressed by feeling so restless you could not sit still
ceq79	distressed by feelings of worthlessness
ceq80	distressed by the feeling that something bad is going to happen to you
ceq81	distressed by shouting or throwing things
ceq82	distressed by feeling afraid you will faint in public
ceq83	distressed by feeling that people will take advantage of you if you let them
ceq84	distressed by having thoughts about sex that bother you a lot
ceq85	distressed by the idea that you should be punished for sins
ceq86	distressed by thoughts or images of a frightening nature
ceq87	distressed by the idea that something serious is wrong with your body
ceq88	distressed by never feeling close to another person
ceq89	distressed by feelings of guilt
ceq90	distressed by the idea that something is wrong with your mind

DIABETES CONTROL AND COMPLICATIONS TRIAL

Quality of Life Questionnaire

INSTRUCTIONS TO CLINIC COORDINATOR --

This questionnaire is to be completed by the study participant during the baseline visit, at the first and second quarterly endpoint visits, and every six months thereafter.

A copy of this form is to be sent to the DCCT Coordinating Center in the weekly forms mailing.

INFORMATION TO BE SUPPLIED BY CLINIC COORDINATOR:

1. Clinic Number: [ ][ ] 5-6
2. Patient ID Number: [ ][ ][ ][ ][ ] 7-11
3. Patient's Initials: [ ][ ][ ] 12-14
4. Today's Date: [ ][ ] / [ ][ ] / [ ][ ] 15-20
   Month Day Year
5. If this is a baseline visit, check here: [ ] 21

   Otherwise, (i) specify which follow-up visit this is: [ ][ ] 22-23

   (ii) Is the visit being held within the time window? No [ ] Yes [ ] 24

A. DIRECTIONS: *Read each statement carefully. Please indicate how satisfied or dissatisfied you currently are with the aspect of your life described in the statement. Check (√) the box that corresponds to how satisfied or dissatisfied you feel. There are no right or wrong answers to these questions. We are interested in your opinion.*

		Satisfied			Dissatisfied		
		Very	Moderately	Neither	Moderately	Very	
A1.	How satisfied are you with the amount of time it takes to manage your diabetes?	[1]	[2]	[3]	[4]	[5]	25
A2.	How satisfied are you with the amount of time you spend getting checkups?	[1]	[2]	[3]	[4]	[5]	26
A3.	How satisfied are you with the time it takes to determine your sugar level?	[1]	[2]	[3]	[4]	[5]	27
A4.	How satisfied are you with your current treatment?	[1]	[2]	[3]	[4]	[5]	28
A5.	How satisfied are you with the flexibility you have in your diet?	[1]	[2]	[3]	[4]	[5]	29
A6.	How satisfied are you with the burden your diabetes is placing on your family?	[1]	[2]	[3]	[4]	[5]	30
A7.	How satisfied are you with your knowledge about your diabetes?	[1]	[2]	[3]	[4]	[5]	31

	Satisfied			Dissatisfied		
	Very	Moderately	Neither	Moderately	Very	
Speaking generally:						
A8. How satisfied are you with your sleep?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	32
A9. How satisfied are you with your social relationships and friendships?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	33
A10. How satisfied are you with your sex life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	34
A11. How satisfied are you with your work, school, and household activities?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	35
A12. How satisfied are you with the appearance of your body?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	36
A13. How satisfied are you with the time you spend exercising?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	37
A14. How satisfied are you with your leisure time?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	38
A15. How satisfied are you with life in general?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	39
Answer the next questions if you attend school:						
A16. How satisfied are you with your performance in school?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	60
A17. How satisfied are you with how your classmates treat you?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	61
A18. How satisfied are you with your attendance in school?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	62

Everyone answer the next question:

A19. Compared to other persons your age, would you say your health is: *(Check one)*

- Excellent ☐ 1 63
- Good ☐ 2
- Fair ☐ 3
- Poor ☐ 4

B. DIRECTIONS: *Read each statement carefully. Please indicate how often the following events happen to you. Check (√) the appropriate box. There are no right or wrong answers to these questions. We are interested in your opinion.*

	Never	Very Seldom	Some-times	Often	All the Time	
B1. How often do you feel pain associated with the treatment for your diabetes?	☐1	☐2	☐3	☐4	☐5	44
B2. How often are you embarrassed by having to deal with your diabetes in public?	☐1	☐2	☐3	☐4	☐5	45
B3. How often do you have low blood sugar?	☐1	☐2	☐3	☐4	☐5	46
B4. How often do you feel physically ill?	☐1	☐2	☐3	☐4	☐5	47
B5. How often does your diabetes interfere with your family life?	☐1	☐2	☐3	☐4	☐5	48
B6. How often do you have a bad nights sleep?	☐1	☐2	☐3	☐4	☐5	49
B7. How often do you find your diabetes limiting your social relationships and friendships?	☐1	☐2	☐3	☐4	☐5	50
B8. How often do you feel good about yourself?	☐1	☐2	☐3	☐4	☐5	51
B9. How often do you feel restricted by your diet?	☐1	☐2	☐3	☐4	☐5	52
B10. How often does your diabetes interfere with your sex life?	☐1	☐2	☐3	☐4	☐5	53
B11. How often does your diabetes keep you from driving a car or using a machine (for example, a typewriter)?	☐1	☐2	☐3	☐4	☐5	54
B12. How often does your diabetes interfere with your exercising?	☐1	☐2	☐3	☐4	☐5	55
B13. How often do you miss work, school or household duties because of your diabetes?	☐1	☐2	☐3	☐4	☐5	56
B14. How often do you find yourself explaining what it means to have diabetes?	☐1	☐2	☐3	☐4	☐5	57
B15. How often do you find that your diabetes interrupts your leisure time activities?	☐1	☐2	☐3	☐4	☐5	58

Patient ID _____

B. (Continued)

	Never	Seldom	Some-times	Often	All the Time	
B16. How often do you tell others about your diabetes?	☐1	☐2	☐3	☐4	☐5	59
B17. How often are you teased because you have diabetes?	☐1	☐2	☐3	☐4	☐5	60
B18. How often do you feel that because of your diabetes you go to the bathroom more than others?	☐1	☐2	☐3	☐4	☐5	61
B19. How often do you find you eat something you shouldn't rather than tell someone that you have diabetes?	☐1	☐2	☐3	☐4	☐5	62
B20. How often do you hide from others the fact that you are having an insulin reaction?	☐1	☐2	☐3	☐4	☐5	63
Answer the next questions if you attend school:						
B21. How often do you find that your diabetes prevents you from participating in school activities (for example, being active in a school play, being on a sports team, being in a school band, etc.)?	☐1	☐2	☐3	☐4	☐5	64
B22. How often do you find that your diabetes prevents you from going out to eat with your school friends?	☐1	☐2	☐3	☐4	☐5	65
B23. How often do you feel that your diabetes is limiting your career or what you will be able to do in the future?	☐1	☐2	☐3	☐4	☐5	66
Answer the next questions if you are living with your parents:						
B24. How often do you find that your parents are too protective of you?	☐1	☐2	☐3	☐4	☐5	67
B25. How often do you feel that your parents worry too much about your diabetes?	☐1	☐2	☐3	☐4	☐5	68
B26. How often do you find that close family members, (for example, brothers, sisters, cousins), tease you about your diabetes?	☐1	☐2	☐3	☐4	☐5	69
B27. How often do you find that your parents act like diabetes is <u>their</u> disease, not yours?	☐1	☐2	☐3	☐4	☐5	70

Patient ID _____

C. DIRECTIONS: *Read each statement carefully. Please indicate how often the following events happen to you. Check (/) the appropriate box. There are no right or wrong answers to these questions. If the question is not relevant to you, check non-applicable.*

	Does Not Apply	Never	Seldom	Some-times	Often	All the Time	
C1. How often do you worry about whether you will get married?	☐	☐	☐	☐	☐	☐	71
C2. How often do you worry about whether you will have children?	☐	☐	☐	☐	☐	☐	72
C3. How often do you worry about whether you will not get a job you want?	☐	☐	☐	☐	☐	☐	73
C4. How often do you worry about whether you will pass out?	☐	☐	☐	☐	☐	☐	74
C5. How often do you worry about whether you will be denied insurance?	☐	☐	☐	☐	☐	☐	75
C6. How often do you worry about whether you will be able to complete your education?	☐	☐	☐	☐	☐	☐	76
C7. How often do you worry about whether you will miss work?	☐	☐	☐	☐	☐	☐	77
C8. How often do you worry about whether you will be able to take a vacation or a trip?	☐	☐	☐	☐	☐	☐	78
C9. How often do you worry that your body looks different because you have diabetes?	☐	☐	☐	☐	☐	☐	79
C10. How often do you worry that you will get complications from your diabetes?	☐	☐	☐	☐	☐	☐	80
C11. How often do you worry about whether someone will not go out with you because you have diabetes?	☐	☐	☐	☐	☐	☐	81
Answer the next questions if you attend school:							
C12. How often do you worry that your teachers treat you differently because of your diabetes?	☐	☐	☐	☐	☐	☐	82
C13. How often do you worry that your diabetes will disrupt something you currently are doing in school (for example, act in a play, continue on a sports team, be in the school band, etc.)?	☐	☐	☐	☐	☐	☐	83
C14. How often do you worry that because of your diabetes you are behind in terms of dating, going to parties, and keeping up with your friends?	☐	☐	☐	☐	☐	☐	84

DIABETES CONTROL AND COMPLICATIONS TRIAL

Nerve Conduction Studies

Patients should be scheduled one to two hours after a regular meal. Outpatients should be scheduled at least 30 minutes before the actual test in order to accommodate to the temperature of the laboratory.

Serial studies on any one patient should be performed under the direct supervision of the same trained electromyographer (M.D.).

Nerve conduction studies in the individual patients should be performed under similar temperature conditions, as close as possible. If necessary, the extremity should be heated to the temperature of the previous examination. Temperature measurements are performed with surface thermistors throughout. The temperature is recorded before and after the actual nerve conduction study in each nerve, and both values are reported. Note that the nerve conduction velocities should be reported as the actually recorded values without temperature corrections.

If any sensory or motor response is absent, enter "00.0" for amplitude and "NR" for latency and conduction velocity. If the F-response is absent, enter "NR" for F-wave latency.

Send a copy of this form to the Coordinating Center in the weekly forms mailing.

A. IDENTIFYING INFORMATION

1. Clinic Number |__|__| 5-6
2. Patient ID Number |__|__|__|__|__| 7-11
3. Patient's Initials |__|__|__| 12-14
4. Date of Studies |__ __|__ __|__ __| 15-20 (Month / Day / Year)
5. If a baseline visit, check here: (1) 21

   Otherwise, (i) specify which follow-up visit this is: |__|__| 22-23

   (ii) is the visit being held within the time window? No (1) Yes (2) 24
6. Date of Birth |__ __|__ __|__ __| 25-30 (Month / Day / Year)
7. Indicate patient's dominant side Left (1) Right (2) 31

B. NERVE SITES (ALL OF THE FOLLOWING TESTS SHOULD BE PERFORMED ON THE INDICATED DOMINANT SIDE)

1. Median Nerve Motor Conduction

   Wrist-abd. poll. brev. muscle

   a) Distance (mm) |__|__|__| 32-34
   b) Latency to onset (msec) |__|__|.|__| 35-38
   c) Amplitude (mv) (baseline to negative peak) |__|__|.|__| 39-42

   F-Wave-Wrist

   d) Latency (shortest of 8 - msec) |__|__|.|__| 43-46

   Elbow-wrist

   e) Temperature before (C degrees) |__|__|.|__| 47-50
   f) Distance (elbow to wrist - mm) |__|__|__| 51-53
   g) Latency to onset (msec) |__|__|.|__| 54-57
   h) Conduction Velocity (m/sec) |__|__|.|__| 58-61
   i) Amplitude (mV) (baseline to negative peak) |__|__|.|__| 62-65
   j) Temperature after (C degrees) |__|__|.|__| 66-69

2. Median Nerve Sensory Conduction (orthodromic)

Digit II-wrist

a) Temperature before (C degrees)	|__|__|.|__|	70-73
b) Distance (mm)	|__|__|__|	74-76
c) Latency to onset (msec) (Not peak)	|__|__|.|__|	77-80
d) Conduction Velocity (m/sec)	|__|__|.|__|	81-84
e) Amplitude (V) (baseline to negative peak)	|__|__|	85-88
f) Temperature after (C degrees)	|__|__|.|__|	87-90

3. Peroneal Nerve Motor Conduction

Ankle-ext. dig. brev.

a) Distance (mm)	|__|__|__|	91-93
b) Latency to onset (msec)	|__|__|.|__|	94-97
c) Amplitude (mV) (baseline to negative peak)	|__|__|.|__|	98-101

Below cap. fib.-ankle

d) Temperature before (C degrees)	|__|__|.|__|	102-105
e) Distance (knee to ankle - mm)	|__|__|__|	106-108
f) Latency to onset (msec)	|__|__|.|__|	109-112
g) Conduction Velocity (m/sec)	|__|__|.|__|	113-116
h) Amplitude (mV) (baseline to negative peak)	|__|__|.|__|	117-120
i) Temperature after (C degrees)	|__|__|.|__|	121-124

F-Wave-Ankle

j) Latency (shortest of 8 - msec)	|__|__|.|__|	125-128

4. Sural Sensory Conduction

Calf-lateral malleous (14 cm proximal to the active electrode)

a) Temperature before (C degrees)	|__|__|.|__|	129-132
b) Distance (mm)	|__|__|__|	133-135
c) Latency to onset (msec) (Not peak)	|__|__|.|__|	136-139
d) Conduction Velocity (m/sec)	|__|__|.|__|	140-143
e) Amplitude (V) (baseline to negative peak)	|__|__|	144-145
f) Temperature after (C degrees)	|__|__|.|__|	146-149

Type or print name of electromyographer:

_____

Certification Number (if any)

\|__\|__\|-\|__\|__\| 150-153

Type or print name of Clinic Coordinator:

_____

\|__\|__\|-\|__\|__\| 154-157

Patient ID _____

D. EXCLUSION CRITERIA

1. Was a STOP condition (exclusion criterion) reached on the Baseline Medical History and Physical Examination Form (DCCT Form 002)? — No (1) Yes STOP (2) Not Done (3)

2. Date of DCCT Form 002: — Month ___ Day ___ Year ___

3. Was the patient excluded on the basis of a STOP condition on the Locally-Performed Urinalysis and Urine Culture Form (DCCT Form 008) or because of a renal condition? — No (1) Yes STOP (2) Not Done (3)

4. Date of DCCT Form 008: — Month ___ Day ___ Year ___

5. Was the patient excluded on the basis of a STOP condition on the Locally-Performed Blood Count and Chemistry Form (DCCT Form 004) or because of a blood condition? — No (1) Yes STOP (2) Not Done (3)

6. Date of DCCT Form 004: — Month ___ Day ___ Year ___

7. Were the following specimens sent to the Central Biochemistry Laboratory?

a) Serum for C-peptide, cholesterol and creatinine — No (1) Yes (2)

If YES,

i) Date collected: — Month ___ Day ___ Year ___

ii) Accession number:

Cp and Cpt - _ _ _ _ _ _ _

iii) Are these retake specimens? — No (1) Yes (2)

iv) To your knowledge, was the patient excluded due to a serum value? — No (1) Yes STOP (2)

b) Urine and serum for renal studies — No (1) Yes (2)

If YES,

i) Date collected: — Month ___ Day ___ Year ___

ii) Accession number:

S and U - _ _ _ _ _ _ _

iii) Are these retake specimens? — No (1) Yes (2)

iv) To your knowledge, was the patient excluded due to a renal value? — No (1) Yes STOP (2)

8. Was a blood specimen sent to the Hemoglobin A1c Laboratory? — No (1) Yes (2)

If YES,

a) Date collected: — Month ___ Day ___ Year ___

b) Accession number: H - _ _ _ _ _ _ _

c) Is this a retake specimen? — No (1) Yes (2)

d) To your knowledge, was the patient excluded due to the HbA1c value? — No (1) Yes STOP (2)

9. Was the patient excluded on the basis of a STOP condition on the Baseline Ophthalmic Examination and Ocular History Form (DCCT Form 008)? — No (1) Yes STOP (2) Not Done (3)

10. Date of DCCT Form 008: — Month ___ Day ___ Year ___

11. Were fundus stereophotographs (of adequate quality) sent to the Central Ophthalmologic Reading Unit? — No (1) Yes (2)

If YES,

a) Date photos were made: — Month ___ Day ___ Year ___

b) Accession number: F - _ _ _ _ _ _

c) Is this a reread of these photos? — No (1) Yes (2)

d) To your knowledge, was the patient excluded due to a finding by the Central Ophthalmologic Reading Unit? — No (1) Yes STOP (2)

DCCT Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Eligibility and Exclusion Checklist

If a patient volunteer appears to be eligible on the basis of the initial review (DCCT Form 001), the Trial Coordinator should begin completing this checklist for the patient. The checklist summarizes the results of each of the pre-randomization eligibility modules and documents the patient's eligibility or ineligibility. Results of the baseline examinations, if performed, and some of the eligibility examinations which are given late in the screening program are summarized on the Randomization Report (DCCT Form 011). If a box marked "STOP" is checked, the patient is ineligible for the study; continue to complete the form so that there will be a complete record of which evaluations were done and what the results were. If a patient is restarted after being excluded, the patient should be given a new ID Number and the previous ID Number should be coded in Section B to facilitate tracking restarts.

Once the form has been completed, send the original to the Coordinating Center in the weekly forms mailing. Retain a copy in the clinic files. This form must be on file at the Coordinating Center before a patient may be randomized.

A. IDENTIFYING INFORMATION

1. Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. Date this form started: Month __ __ Day __ __ Year __ __
5. Date form completed: Month __ __ Day __ __ Year __ __
6. Patient's date of birth: Month __ __ Day __ __ Year __ __
7. Patient's gender: Male (1) Female (2)

B. PREVIOUS SCREENING

1. Is the patient a "restart," i.e., was the patient previously screened for eligibility? No (1) Yes (2)

2. Previous ID Number: __ __ __ __ __
3. Previous Initials: __ __ __
4. Reason for not being enrolled:

_____

_____

C. INFORMED CONSENT

1. Does the patient understand random assignment and does he/she agree to be randomly assigned to either treatment group? (SEE QUESTION D.2 ON DCCT FORM 047) No STOP (1) Yes (2)
2. Did the patient sign the first Informed Consent form, giving permission to be evaluated for eligibility for the DCCT? No STOP (1) Yes (2)
3. FOR PATIENTS LESS THAN 18 YEARS OLD: Did a parent or guardian sign the first Informed Consent form? No STOP (1) Yes (2)
4. If the answer to either Question 2 or 3 is NO, state reason for refusal to give informed consent:

_____

_____

NOTE: IF THE PATIENT OR HIS/HER PARENT OR GUARDIAN REFUSED TO GIVE INFORMED CONSENT, DO NOT COMPLETE ANY MORE OF THIS FORM. SIGN ON THE LAST PAGE, HOWEVER.

DIABETES CONTROL AND COMPLICATIONS TRIAL
Notification of Patient Transfer or Move

When responsibility for the clinical management of a DCCT patient needs to be transferred to another treatment center (e.g., when a patient is moving to a new state), the DCCT clinic staff should make the necessary arrangements. The details of these arrangements are specified in Chapter 24 of the DCCT Manual of Operations. This form is used to document the transfer. Copies of this form should be sent to the Coordinating Center and the new treatment center. Complete Form 105, DCCT Resource Registry, for any patient making visits to a non-DCCT health care provider for diabetes care or DCCT followup.

A. IDENTIFYING INFORMATION

1. Current Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date form completed __ __ Month __ __ Day __ __ Year

B. ARRANGEMENTS FOR PATIENT TRANSFER OR MOVE

1. What is the reason for the transfer?

Permanent: Patient is changing residence (1)

Patient is not changing residence, but wishes to attend another DCCT clinic near his home (2)

Other reason; specify:_____ (3)

_____

_____

Temporary: Patient will make visits to another clinic temporarily (4)

IF THE PATIENT IS CHANGING RESIDENCE AND THE NEW ADDRESS IS KNOWN, COMPLETE THE PERSONAL INFORMATION ON STUDY VOLUNTEER (DCCT FORM 012) TO RECORD THE NEW ADDRESS AND TELEPHONE NUMBER. SEND A COPY OF THIS FORM TO THE NEW TREATMENT CENTER; KEEP THE ORIGINAL IN THE PATIENT'S FILE.

2. On what date will copies of DCCT forms and other relevant records and materials be mailed to the new treatment center? __ __ Month __ __ Day __ __ Year

3. a. On what date will the patient first visit the new treatment center? __ __ Month __ __ Day __ __ Year

b. (Temporary move): On what date will the patient stop visits to the new treatment center? __ __ Month __ __ Day __ __ Year

4. If the patient is transferring to a DCCT clinical center, enter that center's number; if a non-DCCT treatment center will care for the patient, enter 00 and complete form 105. __ __

5. Indicate the patient's treatment group assignment:

Not randomized (1)

Experimental (2)

Standard (3)

6. If the patient is transferring to a non-DCCT treatment center, specify on the reverse side of this form any procedures which will continue to be performed at a DCCT clinical center (either the original center or one closer to the patient's new residence).

Type or print name of person completing this form:

_____

Certification Number (if any)

__ __ - __ __

Patient ID ______________

12. Was a resting ECG obtained and read locally? No (1) Yes (2)

If YES,

a) Was an abnormality detected? No (1) Yes (2)

b) Date ECG was obtained: __ __ Month __ __ Day __ __ Year

c) Date mailed to Coordinating Center: __ __ Month __ __ Day __ __ Year

13a) Has the Clinic Evaluation of Volunteer's Performance on Behavioral Tasks I (Clinic) (DCCT Form 056) been completed? No (1) Yes (2)

b) If YES to a), date of DCCT Form 056: __ __ Month __ __ Day __ __ Year

c) Has the Clinic Evaluation of Volunteer's Performance on Behavioral Tasks II (Home) (DCCT Form 057) been completed? No (1) Yes (2)

d) If YES to c), date of DCCT Form 057: __ __ Month __ __ Day __ __ Year

e) If YES to either a) or c),

i) Was the patient's performance on these tasks so poor that the patient will be excluded? No (1) Yes (2)

ii) Did the patient decide, due in part to the behavioral tasks, that the requirements of the trial would be too demanding that he/she should not participate? No (1) Yes (2)

14a) Has the patient undergone the Confidence and Adherence Interview (DCCT Form 049) before the behavioral tasks? No (1) Yes (2)

b) If YES to a), date of DCCT Form 049: __ __ Month __ __ Day __ __ Year

c) After the behavioral tasks? No (1) Yes (2)

d) If YES to c), date of DCCT Form 049: __ __ Month __ __ Day __ __ Year

e) If YES to either a) or c), has the patient's estimates of his/her confidence in his/her ability to do these tasks and the estimates of his/her adherence to the treatment regimen caused the clinic to decide to exclude the patient? No (1) Yes STOP (2)

15. To your knowledge, is there any other reason why the patient should be excluded? No (1) Yes STOP (2)

16. If the patient has been found to be ineligible, briefly state the reason (USE ONE BOX FOR EACH LETTER):

|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|_|

Type or print name of person completing this form: ______________________________

Certification Number (if any) __ __ - __ __

Signature of Principal Investigator: ______________________________

DIABETES CONTROL AND COMPLICATIONS TRIAL

Clinic Forms Inventory

Every Thursday afternoon, the originals of all forms completed during the preceding week should be collected and sorted by Form Number and by Patient ID within the Form Number. Then, in the space provided below, list the forms which are being mailed. Use extra pages of this form if necessary.

The Study Week Number to be used is for the Thursday on which the forms are batched; if for some reason, the forms will not be mailed on the Thursday when they were to be batched and mailed, you should still enter the Study Week Number for that Thursday, but enter today's date.

After completing this form, you should complete the Forms Mailing List (DCCT Form 041). If there are no forms to be mailed this week, complete only the Forms Mailing List.

Send the original (WHITE) copy of this form to the Coordinating Center. Retain the duplicate (GOLDENROD) copy in the clinic files.

Clinic Number __ __

Study Week Number __ __ __

Number of Forms Mailed __ __ __

Mailing Date __ __ / __ __ / __ __ (Month / Day / Year)

	FORM NUMBER	DATE OF FORM Month Day Year	PATIENT ID NUMBER	PATIENT'S INITIALS		FORM NUMBER	DATE OF FORM Month Day Year	PATIENT ID NUMBER	PATIENT'S INITIALS
1)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	16)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
2)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	17)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
3)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	18)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
4)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	19)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
5)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	20)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
6)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	21)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
7)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	22)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
8)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	23)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
9)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	24)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
10)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	25)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
11)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	26)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
12)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	27)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
13)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	28)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
14)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	29)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __
15)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __	30)	__ __ __.__	__ __ __ __ __ __	__ __ __ __ __	__ __ __

Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Forms Mailing List

This Forms Mailing List is used by the Trial Coordinator to inventory the weekly batch of forms being sent to the Coordinating Center. The number of each type of form included in the batch is indicated. The forms should be sorted by ascending DCCT Form Number, and by ascending Patient ID within form number. If X number of envelopes are required to mail the week's forms, indicate on the bottom left hand corner of each envelope front whether it is number 1 of X, 2 of X, etc. The Forms Mailing List and the Clinic Forms Inventory (DCCT Form 040) must be placed on the top of the stack in envelope number 1. Forms should be mailed on Thursday of each week. Another copy of the Forms Mailing List is to be sent to the Coordinating Center in a separate envelope. If there are no forms to be mailed, check the appropriate box below and mail this form alone.

DCCT Clinic Number ___ ___ Check here if there are no forms this week ___

Mailing Date ___ ___ ___ ___ ___ ___ Number of envelopes mailed ___ ___
Month Day Year

FORM NUMBER	NAME	To be Filled Out by Clinic	To be Filled Out by CoC
001	Initial Clinic Visit	____	____
002	Baseline Medical History and Physical Examination	____	____
003	Annual Medical History and Physical Examination	____	____
004	Locally-Performed Blood Count and Chemistry	____	____
005	Neurological History and Examination	____	____
006	Locally-Performed Urinalysis and Urine Culture	____	____
008	Baseline Ophthalmic Examination and Ocular History	____	____
011	Randomization Report	____	____
012	Personal Information on Study Volunteer	____	____
014	Notification of Missed Clinic Visit	____	____
016	Notification of Transfer to Inactive Status	____	____
020	Notification of Intercurrent Event	____	____
021	Quarterly Clinic Visit	____	____
022	Notification of Deviation from Assigned Treatment or Goals	____	____
025	Fundus Photography	____	____
026	Fluorescein Angiography	____	____
027	Endpoint Visit Ophthalmic Examination	____	____
031	Informed Consent #1 (for Eligibility Exams)	____	____
032	Informed Consent #2 (for Randomization)	____	____
035	Symptom Checklist-90-R (SCL-90-R)	____	____
036	Quality of Life Questionnaire	____	____
037	Nerve Conduction Studies	____	____
038	Eligibility and Exclusion Checklist	____	____
039	Notification of Clinic Transfer	____	____
042	Fundus Photograph Mailing List	____	____
043	C-Peptide Specimen Mailing List	____	____
044	Urine and Serum Specimen Mailing List (Renal Studies)	____	____

FORM NUMBER	NAME	To be Filled Out by Clinic	CoC
045	Volunteer Understanding Questionnaire (Version A)	____	____
046	Volunteer Understanding Questionnaire (Version B)	____	____
047	Availability, Adherence and Expectation Interview	____	____
048	Family Understanding and Expectation Interview	____	____
049	Request Behaviors Confidence Questionnaire	____	____
050	Glucose Profile (Blood) Specimen Mailing List	____	____
051	Neurobehavioral Assessment Mailing List	____	____
052	Diet History Mailing List	____	____
053	Resting Electrocardiogram Mailing List	____	____
054	R-R Interval Electrocardiogram Mailing List	____	____
055	Hemoglobin A1c Mailing List	____	____
056	Clinic Evaluation of Volunteer's Performance on Behavioral Tasks I (Clinic)	____	____
057	Clinic Evaluation of Volunteer's Performance on Behavioral Tasks II (Home)	____	____
058	Lipid Specimen Mailing List	____	____
067	Request for Certification of ECG Technician	____	____
078	Documentation of Interim Contact with Standard Group Patient	____	____
OTHERS:			
___	_____	____	____
___	_____	____	____
___	_____	____	____
___	_____	____	____
___	_____	____	____
___	_____	____	____
	• • • TOTAL • • •	____	____

Type or print name of person completing this form:

_____

Certification Number (if any)

__ __ - __ __

Diabetes Control and Complications Trial

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DCCT Form 042.2
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DIABETES CONTROL AND COMPLICATIONS TRIAL

Fundus Photograph Mailing List

This mailing list is to be completed whenever the clinic mails a package of fundus stereophotographs and/or fluorescein angiograms to the Central Ophthalmologic Reading Unit. Prepare four copies of this form to distribute as follows:

(1) WHITE -- Complete and place inside package with photographs.

Mail to:
DCCT Central Ophthalmologic Reading Unit
Department of Ophthalmology, Box 5240
University of Wisconsin
Madison, WI 53705

WHEN USING OTHER THAN REGULAR MAIL,
Delete: Box 5240
Add: 610 N. Walnut Street, Room 417

(2) YELLOW -- Send separately to the address above.
(3) PINK -- Send to the Coordinating Center in the weekly forms mailing.
(4) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Transmission Number: __ __ - __ __ __

Date Shipped: __ __ / __ __ / __ __ (Month Day Year)

(A SHIPMENT ACCESSION NUMBER. FOR CLINIC XX, THE FIRST TRANSMISSION NUMBER IS XX-001, THE SECOND XX-002, ETC.)

Person Completing Form: ______________________________

PATIENT ID NUMBER	PATIENT'S INITIALS F M L	FORM NUMBER	DATE OF PHOTOS Month Day Year	IF A BASELINE/ELIGIBILITY VISIT, ENTER 00. IF A FOLLOW-UP VISIT, ENTER VISIT NUMBER	CIRCLE EYE	ACCESSION NUMBER
__ __ __ __ __	__ __ __	0 2 5 . __	__ __/__ __/__ __	__ __	RE LE	F - __ __ __ __ __ __ __
__ __ __ __ __	__ __ __	0 2 6 . __	__ __/__ __/__ __	__ __	FLR ANG	A - __ __ __ __ __ __ __
__ __ __ __ __	__ __ __	0 2 5 . __	__ __/__ __/__ __	__ __	RE LE	F - __ __ __ __ __ __ __
__ __ __ __ __	__ __ __	0 2 6 . __	__ __/__ __/__ __	__ __	FLR ANG	A - __ __ __ __ __ __ __
__ __ __ __ __	__ __ __	0 2 5 . __	__ __/__ __/__ __	__ __	RE LE	F - __ __ __ __ __ __ __
__ __ __ __ __	__ __ __	0 2 6 . __	__ __/__ __/__ __	__ __	FLR ANG	A - __ __ __ __ __ __ __
__ __ __ __ __	__ __ __	0 2 5 . __	__ __/__ __/__ __	__ __	RE LE	F - __ __ __ __ __ __ __
__ __ __ __ __	__ __ __	0 2 6 . __	__ __/__ __/__ __	__ __	FLR ANG	A - __ __ __ __ __ __ __

FOR CENTRAL OPHTHALMOLOGIC READING UNIT USE ONLY

Person receiving: ______________________________

Card Sent: __

Date received: __ __/__ __/__ __ (Month Day Year)

Comments: ______________________________

Entered: __ __/__ __/__ __ (Month Day Year) By: ____________________

Verified: __ __/__ __/__ __ (Month Day Year) By: ____________________

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DIABETES CONTROL AND COMPLICATIONS TRIAL

C-Peptide Specimen Mailing List

This mailing list is used whenever the DCCT clinic ships a container of serum specimens to the Central Biochemistry Laboratory (CBL) for analysis for C-peptide, glucose, cholesterol and creatinine for eligibility. Specimens with the accession number prefix "CP" represent pre-Sustocal specimens and these specimens will be analyzed for C-peptide, glucose, cholesterol and creatinine. Specimens with the accession number prefix "Cpt" are post-Sustocal specimens and these will be analyzed for C-peptide and glucose. The four copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside insulated shipping container with specimens.
Mail to: DCCT Central Biochemistry Laboratory
ATTN: L262, Mayo 376-5187
University of Minnesota Hospital
Receiving Unit K/E
425 East River Road
Minneapolis, MN 55455

(2) YELLOW -- Send separately to the address above.

(3) PINK -- Send to the Coordinating Center in the weekly forms mailing.

(4) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Specimens Shipped on: __ __ / __ __ / __ __ (Month / Day / Year)

Specimens Collected From: __ __ / __ __ / __ __ (Month / Day / Year) through __ __ / __ __ / __ __ (Month / Day / Year)

SERUM FOR C-PEPTIDE

ACCESSION NUMBER	PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE SPECIMEN DRAWN Month Day Year	COMMENTS (Indicate if this is a back-up sample or if only some determinations are to be made.)
CP & CPT __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
CP & CPT __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
CP & CPT __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
CP & CPT __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
CP & CPT __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
CP & CPT __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
CP & CPT __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	

Diabetes Control and Complications Trial

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DCCT Form 044.2
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DIABETES CONTROL AND COMPLICATIONS TRIAL

Renal Studies Specimen Mailing List

This mailing list is used whenever the DCCT clinic ships a container of urine and serum specimens to the Central Biochemistry Laboratory (CBL) for renal studies. Urine specimens have accession numbers with the prefix "U." Serum specimens have the same five-digit accession numbers as the corresponding urine specimens, but have prefix "S." Height in centimeters and weight in kilograms are recorded in order to calculate albumin excretion and creatinine clearance. Chapter 6 of the Manual of Operations describes how height and weight must be measured. The four copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside insulated shipping container with specimens.
Mail to:
DCCT Central Biochemistry Laboratory
ATTN: L282, Mayo 376-5187
University of Minnesota Hospital
Receiving Unit K/E
425 East River Road
Minneapolis, MN 55455

(2) YELLOW -- Send separately to the address above.

(3) PINK -- Send to the Coordinating Center in the weekly forms mailing.

(4) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Specimens Shipped on: __ __ / __ __ / __ __ (Month / Day / Year)

Specimens Collected From: __ __ / __ __ / __ __ (Month / Day / Year) through __ __ / __ __ / __ __ (Month / Day / Year)

RENAL SPECIMENS

ACCESSION NUMBER S & U	PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE SPECIMEN COLLECTED Month Day Year	TIME COLLECTION STARTED	TIME COLLECTION ENDED	TOTAL URINE VOLUME (ml)	# OF TUBES	HEIGHT (cm)	WEIGHT (kg)
								.	.
								.	.
								.	.
								.	.
								.	.
								.	.
								.	.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Volunteer Understanding Questionnaire
(Version A)

INSTRUCTIONS TO TRIAL COORDINATOR

This form is to be completed prior to the baseline visit at which the Informed Consent for Randomization (DCCT Form 032) is signed. The patient should

-- be given a pencil with an eraser with which to complete the form

-- be allowed as much time as he/she needs to complete the form

-- complete the form himself/herself without help from another person and without looking at the Research Volunteer's Information Handbook.

When the patient has completed the questionnaire, you should review the questions with him/her to clarify any items to which the patient gave an incorrect answer. Do NOT change any of the responses which the patient gave, however.

If the patient gives the wrong answer to any ONE of the questions, he/she CANNOT be randomized, but must come back another day to take Version B of the questionnaire. If you feel that the patient would benefit from viewing the orientation audiovisual presentation or by re-reading the Research Volunteer's Information Handbook, encourage him/her to do so, and again inform the patient that he/she should ask for clarification of any point he/she does not understand.

Mail the questionnaire to the DCCT Coordinating Center. Retain a copy in the clinic files.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Today's Date __ __ / __ __ / __ __
Month Day Year

INSTRUCTIONS TO RESEARCH VOLUNTEER

The Volunteer Understanding Questionnaire is based on the Research Volunteer's Information Handbook. The purpose of the questionnaire is to be sure that we have adequately informed you about this study. You should check (✓) the box next to the ONE best answer to each of the questions.

1. Doctors specializing in the treatment of diabetes

a) have proven that keeping blood glucose levels as close as possible to the levels of people without diabetes will prevent complications (1)

b) have proven that blood glucose levels are unrelated to complications (2)

c) do not agree that the relationship of blood glucose levels to complications has been proven and further research is needed (3)

d) believe that the relationship of blood glucose levels to complications is not an important issue keeping in mind all the questions that still have to be answered about diabetes (4)

2. One of the purposes of this study is to determine

a) if a new treatment designed to cure diabetes will be practical and safe over a long period of time (1)

b) if it is practical and safe to try and keep the blood glucose levels of people with diabetes as close as possible to the levels of non-diabetics over a long period of time (2)

Patient ID _____

c) if the use of the insulin pump is as practical and safe over a long period of time as 3-4 daily injections of insulin (3)

d) if self blood glucose monitoring is as accurate as urine testing over a long period of time (4)

3. Random assignment means that

a) the volunteer has an approximately equal chance of being placed in either treatment group (1)

b) the volunteer can decide which treatment group he or she wishes to be in (2)

c) the doctor decides which treatment group the volunteer will be assigned to (3)

d) the volunteer will be assigned to the treatment group which is best (4)

4. The Standard Treatment Group in this study will receive, in addition to diet instruction and diabetes education,

a) either an insulin pump or three or four injections of insulin a day and will be expected to do daily self blood glucose monitoring (1)

b) either an insulin pump or three or four injections of insulin a day and will be expected to do daily urine testing only (2)

c) one or two injections of insulin a day and will be expected to do daily self blood glucose monitoring (3)

d) one or two injections of insulin a day and will be expected to do daily urine testing (4)

5. The Experimental Treatment Group in this study will receive, in addition to diet instruction and diabetes education,

a) either an insulin pump or three or four injections of insulin a day and will be expected to do daily self blood glucose monitoring (1)

b) either an insulin pump or three or four injections of insulin a day and will be expected to do daily urine testing only (2)

c) one or two injections of insulin a day and will be expected to do daily self blood glucose monitoring (3)

d) one or two injections of insulin a day and will be expected to do daily urine testing (4)

6. As compared to my current treatment, being in the Standard Treatment Group

a) will increase my risk for complications (1)

b) will increase my risk of having high blood sugar (2)

c) will increase my risk of having low blood sugar (3)

d) none of the above (4)

7. As compared to my current treatment, being in the Experimental Treatment Group

a) will have the added risk of an increased number, and possible increased severity, of hypoglycemic (low blood glucose) reactions (1)

b) will have the added risk, if I am on the pump, of high blood sugar levels caused by a malfunction of the pump (2)

c) will have the added risk, if I am on the pump, of developing infections where the needle is inserted (3)

d) all of the above (4)

8. If I volunteer for this study, I will be expected to participate

a) possibly one year (1)

b) possibly three years (2)

c) possibly eight years (3)

d) possibly ten years (4)

Patient ID _____

9. If I am assigned to the Standard Treatment Group, I can expect to make visits to the center

   a) at least every month (1)

   b) at least every three months (2)

   c) at least every six months (3)

   d) at least every twelve months (4)

10. If I am assigned to the Experimental Treatment Group, I can expect to make visits to the center

   a) at least every month (1)

   b) at least every three months (2)

   c) at least every six months (3)

   d) at least every twelve months (4)

11. Which of the following is NOT expected from you if you agree to participate in this study?

   a) to choose whether you want to be assigned to the Experimental or the Standard Treatment Group (1)

   b) to stay in whichever treatment group you are assigned to (2)

   c) to keep all appointments in the clinic and keep all the home records required (3)

   d) (if you are a woman) to avoid planning on becoming pregnant in the next two years (4)

12. If I am in the Experimental Treatment Group, I can expect to be initially hospitalized

   a) not at all (1)

   b) one or two days (2)

   c) three to ten days (3)

   d) eleven to fifteen days (4)

13. Which of the following complications of diabetes will NOT be measured in this trial?

   a) complications of the eye (1)

   b) complications of the lung (2)

   c) complications of the nerve system (3)

   d) complications of the kidney (4)

14. A potential risk of fluorescein angiography (eye photography using colored dye) is

   a) nausea (1)

   b) discoloration of urine (2)

   c) serious allergic reaction (3)

   d) all of the above (4)

DIABETES CONTROL AND COMPLICATIONS TRIAL

Volunteer Understanding Questionnaire
(Version B)

INSTRUCTIONS TO TRIAL COORDINATOR

This version of the form is administered only if the patient failed to correctly answer 100% of the questions on Version A (DCCT Form 045). This form is to be completed prior to the baseline visit at which the Informed Consent for Randomization (DCCT Form 032) is signed. The patient should

-- be given a pencil with an eraser with which to complete the form

-- be allowed as much time as he/she needs to complete the form

-- complete the form himself/herself without help from another person and without looking at the Research Volunteer's Information Handbook.

When the patient has completed the questionnaire, you should review the questions with him/her to clarify any items to which the patient gave an incorrect answer. Do NOT change any of the responses which the patient gave, however.

If the patient gives the wrong answer to any ONE of the questions, he/she should not be randomized, unless, in the opinion of the clinic staff, the patient has an adequate understanding of the purpose and requirements of the study.

Mail the questionnaire to the DCCT Coordinating Center. Retain a copy in the clinic files.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number ___

2. Patient ID Number _____

3. Patient's Initials ___

4. Today's Date ___/___/___
Month Day Year

INSTRUCTIONS TO RESEARCH VOLUNTEER

The Volunteer Understanding Questionnaire is based on the Research Volunteer's Information Handbook. The purpose of the questionnaire is to be sure that we have adequately informed you about this study. You should check (✓) the box next to the ONE best answer to each of the questions.

1. One of the purposes of this study is to determine

a) if a new treatment designed to cure diabetes will be practical and safe over a long period of time (1)

b) if it is practical and safe to try and keep the blood glucose levels of people with diabetes as close as possible to the levels of non-diabetics over a long period of time (2)

c) if the use of the insulin pump is as practical and safe over a long period of time as 3-4 daily injections of insulin (3)

d) if self blood glucose monitoring is as accurate as urine testing over a long period of time (4)

2. Doctors specializing in the treatment of diabetes

a) have proven that keeping blood glucose levels as close as possible to the levels of people without diabetes will prevent complications (1)

b) have proven that blood glucose levels are unrelated to complications (2)

Patient ID _____

c) do not agree that the relationship of blood glucose levels to complications' has been proven and further research is needed (3)

d) believe that the relationship of blood glucose levels to complications is not an important issue keeping in mind all the questions that still have to be answered about diabetes (4)

3. The Experimental Treatment Group in this study will receive, in addition to diet instruction and diabetes education,

a) either an insulin pump or three or four injections of insulin a day and will be expected to do daily self blood glucose monitoring (1)

b) either an insulin pump or three or four injections of insulin a day and will be expected to do daily urine testing only (2)

c) one or two injections of insulin a day and will be expected to do daily self blood glucose monitoring (3)

d) one or two injections of insulin a day and will be expected to do daily urine testing (4)

4. The Standard Treatment Group in this study will receive, in addition to diet instruction and diabetes education,

a) either an insulin pump or three or four injections of insulin a day and will be expected to do daily self blood glucose monitoring (1)

b) either an insulin pump or three or four injections of insulin a day and will be expected to do daily urine testing only (2)

c) one or two injections of insulin a day and will be expected to do daily self blood glucose monitoring (3)

d) one or two injections of insulin a day and will be expected to do daily urine testing (4)

5. Random assignment means that

a) the volunteer has an approximately equal chance of being placed in either treatment group (1)

b) the volunteer can decide which treatment group he or she wishes to be in (2)

c) the doctor decides which treatment group the volunteer will be assigned to (3)

d) the volunteer will be assigned to the treatment group which is best (4)

6. If I volunteer for this study, I will be expected to participate

a) possibly one year (1)

b) possibly three years (2)

c) possibly eight years (3)

d) possibly ten years (4)

7. Which of the following is NOT expected from you if you agree to participate in this study?

a) to choose whether you want to be assigned to the Experimental or the Standard Treatment Group (1)

b) to stay in whichever treatment group you are assigned to (2)

c) to keep all appointments in the clinic and keep all the home records required (3)

d) (if you are a woman) to avoid planning on becoming pregnant in the next two years (4)

Patient ID _____

8. As compared to my current treatment, being in the Experimental Treatment Group

   a) will have the added risk of an increased number, and possible increased severity, of hypoglycemic (low blood glucose) reactions (1)

   b) will have the added risk, if I am on the pump, of high blood sugar levels caused by a malfunction of the pump (2)

   c) will have the added risk, if I am on the pump, of developing infections where the needle is inserted (3)

   d) all of the above (4)

9. As compared to my current treatment, being in the Standard Treatment Group

   a) will increase my risk for complications (1)

   b) will increase my risk of having high blood sugar (2)

   c) will increase my risk of having low blood sugar (3)

   d) none of the above (4)

10. If I am assigned to the Standard Treatment Group, I can expect to make visits to the center

   a) at least every month (1)

   b) at least every three months (2)

   c) at least every six months (3)

   d) at least every twelve months (4)

11. If I am assigned to the Experimental Treatment Group, I can expect to make visits to the center

   a) at least every month (1)

   b) at least every three months (2)

   c) at least every six months (3)

   d) at least every twelve months (4)

12. A potential risk of fluorescein angiography (eye photography using colored dye) is

   a) nausea (1)

   b) discoloration of urine (2)

   c) serious allergic reaction (3)

   d) all of the above (4)

13. Which of the following complications of diabetes will NOT be measured in this trial?

   a) complications of the eye (1)

   b) complications of the lung (2)

   c) complications of the nerve system (3)

   d) complications of the kidney (4)

14. If I am in the Experimental Treatment Group, I can expect to be initially hospitalized

   a) not at all (1)

   b) one or two days (2)

   c) three to ten days (3)

   d) eleven to fifteen days (4)

DIABETES CONTROL AND COMPLICATIONS TRIAL

Availability, Adherence and Expectation Interview

This interview of the DCCT subject is used (1) to determine the subject's ability to keep the follow-up appointments which would be required of him/her should he/she be randomized, (2) to assess the subject's knowledge of and adherence to his/her current treatment regimen, and (3) to discover if the subject has unrealistic expectations about what he/she will gain from participating in the study.

The interview should be given by the clinic coordinator during the visit when the Informed Consent for Baseline Examinations (DCCT Form 031.1) is to be signed.

The information from this interview will primarily be used by the clinic coordinator to better understand the subject and his/her particular schedule and needs, and to aid in scheduling clinic visits and providing assistance (if possible) in areas such as child care, nutrition counseling, etc. But the information should also be reviewed by the Principal Investigator, for it may suggest that the subject would have poor compliance and would not be suitable for the trial.

Most of the questions provide space for write-in responses as well as multiple-choice check-boxes. The Coordinating Center will tabulate only the check-box items, so be sure that these are completed, but try to avoid using them to suggest answers to the subject. Send a completed copy of this form to the Coordinating Center in the weekly forms mailing.

A. IDENTIFYING INFORMATION

1. Clinic Number [ ][ ] 5-6
2. Patient ID Number [ ][ ][ ][ ][ ] 7-11
3. Patient's Initials [ ][ ][ ] 12-14
4. Date of Interview [ ][ ] / [ ][ ] / [ ][ ] 15-20
   Month Day Year

B. AVAILABILITY ASSESSMENT

1. Do you plan to move out of town in the near future? (*If subject is an adolescent, you may also ask:* Do you plan to leave home after you graduate?)

   No [ ]1 21
   Yes [ ]2
   Not Certain [ ]3

   If YES, ask: Where do you plan to go and when will you be leaving?

   _____ Anticipated Place Month [ ][ ] Year [ ][ ] Anticipated Date 22-25

AVAILABILITY ASSESSMENT (cont'd.)

If the location is nearby, ask: Can you return to the center once a week if required?

Yes [ ]1 26
No [ ]2
Not certain [ ]3

If No or Not certain, ask: How often can you come in? _____

If the location is not nearby, but is close to another DCCT center ask: There is a DCCT center in (place). Do you think that if you were enrolled into the study here that you could continue to participate in the study by being treated at our center in (place)?

No [ ]1 27
Yes [ ]2
Not certain [ ]3

2. Can you currently come in at least once a week if required?

   Yes [ ]1 28
   No [ ]2
   Not certain [ ]3

   If No or Not certain, ask: How often can you come in? _____

3. How did you get to the center today?

Car	☐ 1	29
Taxi	☐ 2	
Bus/Subway	☐ 3	
Walked	☐ 4	
Other; specify: _____	☐ 5	

4. Did you have any trouble getting to the center today?

No	☐ 1	30
Yes	☐ 2	

If Yes, explain:

_____

_____

_____

5. Do you ever have any transportation problems?

No	☐ 1	31
Yes	☐ 2	

If Yes, explain:

_____

_____

_____

6. Do you have any children?

No	☐ 1	32
Yes	☐ 2	

If Yes, do you ever have any trouble getting someone to care for your children when you come in to the center?

No (or not relevant)	☐ 1	33
Yes	☐ 2	

If Yes, elaborate:

_____

_____

_____

AVAILABILITY ASSESSMENT (cont'd)

7. What times are most convenient for you to come to the center?

_____

_____

_____

At what times will it be impossible for you to come to the center?

_____

_____

_____

If there is a discrepancy between when the subject is available and the center's hours of operation, try to arrange some mutually acceptable times. List them below:

_____

_____

_____

8. How flexible is your employer (school) about giving you time off to keep doctor's appointments?

Fairly flexible	☐ 1	34
Fairly inflexible	☐ 2	
Not applicable	☐ 3	

9. Will you have to take vacation or sick time at work to come to the center?

No	☐ 1	35
Yes	☐ 2	
Not applicable (student, homemaker, unemployed, etc.)	☐ 3	

10. Do you have a telephone number where you can be reached during the day?

No	☐ 1	36
Yes	☐ 2	

(Number: _____)

Patient ID _____

C. ADHERENCE ASSESSMENT

1. What is your current diabetes treatment plan? *(Allow the subject to describe the regimen. If the subject does not address all the areas, ask specifically about the items listed below.)*

   Insulin Schedule: _____

   _____

   _____

   Urine (or blood glucose) testing: ____

   _____

   _____

   Diet: _____

   _____

   Exercise: _____

   _____

2. During the past month, how often have you not followed your insulin injection plan?

Never	☐ 1	77
Very infrequently (less than 10% of the time)	☐ 2	
Infrequently (10-44% of the time)	☐ 3	
About half the time (45-55% of the time)	☐ 4	
Most of the time (56-90% of the time)	☐ 5	
Almost all of the time (more than 90% of the time)	☐ 6	
Always	☐ 7	

   When and where do you have the most difficulty staying on your insulin injection schedule?

   _____

   _____

   _____

   _____

ADHERENCE ASSESSMENT (Cont'd.)

3. During the past month, how often did you purposely decide not to take your insulin injection:

Never	☐ 1	88
Very infrequently (less than 10% of the time)	☐ 2	
Infrequently (10-44% of the time)	☐ 3	
About half the time (45-55% of the time)	☐ 4	
Most of the time (56-90% of the time)	☐ 5	
Almost all of the time (more than 90% of the time)	☐ 6	
Always	☐ 7	

   Why do you decide not to take your insulin injection?

   _____

   _____

   _____

   _____

4. During the past month, how often have you gone a whole day without testing your urine or blood for glucose?

Never	☐ 1	99
Very infrequently (less than 10% of the time)	☐ 2	
Infrequently (10-44% of the time)	☐ 3	
About half the time (45-55% of the time)	☐ 4	
Most of the time (56-90% of the time)	☐ 5	
Almost all of the time (more than 90% of the time)	☐ 6	
Always	☐ 7	

   When and where do you have the most difficulty performing the blood or urine tests?

   _____

   _____

   _____

   _____

Patient ID _____

ADHERENCE ASSESSMENT (cont'd.)

5. During the past month, how often did you purposely decide not to follow your urine blood testing schedule?

- ☐ Never 0
- ☐ Very infrequently (less than 10% of the time) 1
- ☐ Infrequently (10-44% of the time) 2
- ☐ About half the time (45-55% of the time) 3
- ☐ Most of the time (56-90% of the time) 4
- ☐ Almost all of the time (more than 90% of the time) 5
- ☐ Always 6

Why do you decide not to follow your urine or blood testing schedule?

_____

_____

_____

_____

6. During the past month, how often did you not follow your meal plan?

- ☐ Never 1
- ☐ Very infrequently (less than 10% of the time) 2
- ☐ Infrequently (10-44% of the time) 3
- ☐ About half the time (45-55% of the time) 4
- ☐ Most of the time (56-90% of the time) 5
- ☐ Almost all of the time (more than 90% of the time) 6
- ☐ Always 7

When and where do you have the most difficulty following your meal plan?

_____

_____

_____

_____

7. During the past month, how often did you purposely decide not to follow your meal plan?

- ☐ Never 2
- ☐ Very infrequently (less than 10% of the time) 1
- ☐ Infrequently (10-44% of the time) 2
- ☐ About half the time (45-55% of the time) 3
- ☐ Most of the time (56-90% of the time) 4
- ☐ Almost all of the time (more than 90% of the time) 5
- ☐ Always 6

Why do you decide not to follow your meal plan?

_____

_____

_____

_____

8. Does being at work (or school) interfere with following your diabetes treatment plan?

- ☐ Yes 1
- ☐ No 2

If YES, What difficulties does work (or school) cause you?

_____

_____

_____

9. Does being on vacation ever interfere with following your diabetes treatment plan?

- ☐ Yes 1
- ☐ No 2

If YES, What difficulties does being on vacation cause you?

_____

_____

_____

_____

ADHERENCE ASSESSMENT (cont'd.)

10. Do social situations (being at a friend's house, at a party, in a restaurant, etc.) ever interfere with following your diabetes treatment plan?

Yes ☐ 1 → 11

No ☐ 2

If YES, What difficulties do you usually have in social situations?

_____

_____

_____

_____

11. Does your family life ever interfere with following your diabetes treatment plan?

Yes ☐ 1 → 12

No ☐ 2

If YES, In what ways does your family life interfere?

_____

_____

_____

_____

12. How often during the past <u>year</u> have you <u>not</u> followed your diabetes treatment plan because of illness?

Never ☐ 1 → 12

Very infrequently (less than 10% of the time) ☐ 2

Infrequently (10-44% of the time) ☐ 3

About half the time (45-55% of the time) ☐ 4

Most of the time (56-90% of the time) ☐ 5

Almost all of the time (more than 90% of the time) ☐ 6

Always ☐ 7

12. (Cont'd.)

What illnesses did you have and which aspects of your treatment plan were interrupted?

_____

_____

_____

_____

D. ASSESSMENT OF EXPECTATIONS

1. Do you have a strong preference for being assigned to one treatment group over the other? If so, which do you prefer and why?

No, has no strong preference ☐ 1 → 2

Yes, has strong preference for Standard Treatment Group ☐ 2

Yes, has strong preference for Experimental Treatment Group ☐ 3

Reason for preference: _____

_____

_____

2. Would you be willing to accept being randomly assigned to either of the treatment groups?

Yes, certainly ☐ 1 → 3

Yes, probably ☐ 2

No ☐ STOP 1

<u>IMPORTANT NOTE</u>: If the subject states that he/she would not be willing to be randomly assigned to either treatment group, he/she is <u>ineligible</u> for the study. Bring this information to the attention of the Clinic Coordinator or the Principal Investigator as soon as the interview is over.

ASSESSMENT OF EXPECTATIONS (cont'd.)

3. What do you think you will gain from the study?

Let the subject generate responses but be sure that the following areas are addressed and correct any misconceptions.

Rate the subject's understanding:

- *blood sugar*

  Realistic ☐1 s0
  Somewhat unrealistic ☐2
  Very unrealistic ☐3

- *complications*

  Realistic ☐1 s1
  Somewhat unrealistic ☐2
  Very unrealistic ☐3

- *general well-being*

  Realistic ☐1 s2
  Somewhat unrealistic ☐2
  Very unrealistic ☐3

Comments: _____

_____

_____

4. You may find that in order to perform the urine or blood glucose tests you will need to use certain pieces of medical equipment in public. How do you feel about using the necessary medical equipment in public?

Check the statement that best describes the patient's feelings:

Does not at all mind using the equipment in public ☐1 s3
Somewhat minds using the equipment in public ☐2
Very much minds using the equipment in public ☐3

5. What effect do you expect this study to have on your current daily routine?

Check the statement that best describes the patient's feelings:

Should have minimal adverse effect or no effect at all ☐1 s4
Should have considerable adverse effect ☐2
Should have a positive effect ☐3

6. How do you expect this study to affect your family?

Check the statement that best describes the patient's expectations:

Should have minimal adverse effect or no effect at all ☐1 s5
Should have considerable adverse effect ☐2
Should have a positive effect ☐3

Type or print name of Clinic Coordinator:

_____

Certification Numbers (if any)

☐☐ ☐☐ s6-s9

DIABETES CONTROL AND COMPLICATIONS TRIAL

Family Understanding and Expectation Interview

This interview is to be given by the clinic coordinator to any family members or friends who may have accompanied the subject to the clinic. It should be given after the assessment of the behavioral tasks. The subject should not be present during this interview of his/her family or friends.

The interview is used (1) to assess the family's/friend's understanding of the treatments used in the trial, (2) to ascertain whether they have a strong preference for the subject being assigned to one treatment over the other, and (3) to determine whether they have any inaccurate or unrealistic expectations regarding the risks, inconveniences and benefits that may result from the subject's participation.

Most of the questions provide space for write-in responses as well as multiple-choice check-boxes. The Coordinating Center can tabulate only the check-box items, so be sure that these are completed, but try to avoid using them to suggest answers to the interviewees. Send a completed copy of this form to the Coordinating Center in the weekly forms mailing.

A. IDENTIFYING INFORMATION

1. Clinic Number [ ][ ] 5-6
2. Patient ID Number [ ][ ][ ][ ][ ] 7-11
3. Patient's Initials [ ][ ][ ] 12-14
4. Date of Interview [ ][ ] / [ ][ ] / [ ][ ] 15-20
   Month Day Year

B. FAMILY ADAPTATION TO THE PROTOCOL

1. Can you tell me what you understand to be the purpose of the Diabetes Control and Complications Trial?

   The family members should say something to the extent that the study will compare the effect of an experimental and a standard approach to the control of blood glucose on early vascular complications in persons with insulin-dependent diabetes mellitus.

   Rate their understanding:

   Good [1] 21
   Fair [2]
   Poor [3]

2. Can you tell me how insulin will be used in the Standard Treatment Group?

   They should state that the standard treatment consists of one or two daily injections of insulin.

   Rate their understanding:

   Good [1] 22
   Fair [2]
   Poor [3]

3. Can you tell me how insulin will be used in the Experimental Treatment Group?

   They should state that the Experimental Treatment consists of a choice of either multiple daily injections of insulin or use of an insulin infusion pump.

   Rate their understanding:

   Good [1] 23
   Fair [2]
   Poor [3]

4. Can you tell me what is meant by randomization?

   They should state that randomization is the process that will be used to assign the subject to treatment group; neither the subject nor his/her physician can choose the treatment group. Under randomization, there is a 50% chance that the subject will be assigned to either one of the two treatment groups.

   Rate their understanding:

   Good [1] 24
   Fair [2]
   Poor [3]

Patient ID _____

5. Do you have a strong preference for *(name of subject)* being assigned to one treatment group over the other? If so, which do you prefer and why?

No, has no strong preference	1	25
Yes, has strong preference for Standard Treatment Group	2	
Yes, has strong preference for Experimental Treatment Group	3	
There is disagreement among the family members and friends as to which treatment is to be preferred	4	

Reasons for preferences:

_____

_____

_____

_____

6. Would you be willing to support the decision of *(name of subject)* to be randomized into either of the treatment groups?

No *(at least one would not be willing)*	1	26
Yes *(all agree)*	2	

7. What do you think *(name of subject)* will gain from the study?

Let them generate responses but be sure that the following areas are addressed and correct any misconceptions.

Rate their expectations:

• *blood sugar*

Realistic	1	27
Somewhat unrealistic	2	
Very unrealistic	3	

• *complications*

Realistic	1	28
Somewhat unrealistic	2	
Very unrealistic	3	

7. (continued)

• *general well-being*

Realistic	1	29
Somewhat unrealistic	2	
Very unrealistic	3	

Comments: _____

_____

_____

_____

8. If *(name of subject)* is assigned to the Standard Treatment Group, how often will he/she need to come in to the clinic for routine follow-up appointments?

They should answer that the appointments will be every three months.

Rate their response:

Overestimate	1	30
Accurate answer	2	
Underestimate	3	

9. If *(name of subject)* is assigned to the Experimental Treatment Group, he/she will need to spend 3-10 days in the hospital and then he/she will need to come to the clinic weekly until he/she has become accustomed to the new therapy. Following this, how often will he/she need to come in to the clinic for routine follow-up appointments?

They should state that the appointments will be once per month, and could be as often as once per week.

Rate their response:

Overestimate	1	31
Accurate answer	2	
Underestimate	3	

Patient ID _____

10. Do you realize that many times *(name of subject)* may have to give priority to this study, causing other family members and friends to change their plans? Do you understand that *(name of subject)* may have some expenses for transportation, telephoning the clinic, or hiring a babysitter? He/she may have to use vacation or sick days to keep clinic appointments. What kinds of problems will this cause?

Rate their response:

They appear to understand the problems involved and agree that a considerable amount of inconvenience may result ☐ 1 — 32

They appear to understand the problems involved but do not believe that they will experience undue hardship ☐ 2

They do not appear to understand the problems that may arise by giving priority to the study protocol ☐ 3

11. How do you feel about *(name of subject)* using the insulin infusion pump? Would any of you have a problem (e.g., be annoyed) with him/her using the pump?

No one expects to have a problem with the subject's use of a pump ☐ 1 — 33

Someone expects to have a problem with the subject's use of a pump ☐ 2

12. How do you feel about *(name of subject)* performing home blood glucose monitoring, which will have to be done several times each day if he/she is assigned to the Experimental Treatment Group? Would you have problems with him/her doing this?

No one expects to have a problem with the subject performing home blood glucose monitoring ☐ 1 — 34

Someone expects to have a problem with the subject performing home blood glucose monitoring ☐ 2

13. How do you feel about *(name of subject)* performing urine tests several times per day, as he/she will have to do if he/she is assigned to the Standard Treatment Group? Would any of you have problems with him/her doing this?

No one expects to have a problem with the subject performing urine testing ☐ 1 — 35

Someone expects to have a problem with the subject performing urine testing ☐ 2

14. How would you feel about *(name of subject)* using the blood or urine testing equipment in public, as he/she may have to do when at work or school? Would any of you object to him/her doing this?

No one would object to public use of testing equipment ☐ 1 — 36

Someone would object to public use of testing equipment ☐ 2

15. Some aspects of this study, such as using diabetes supplies in public and having a less flexible lifestyle, may identify *(name of subject)* as having diabetes to people who otherwise might not have known. Would this be a problem for you?

No one would object to the subject following the treatment protocol simply because it may identify the subject as having diabetes ☐ 1 — 37

Someone would object to the subject following the treatment protocol because it may identify the subject as having diabetes ☐ 2

16. If *(name of subject)* were to become ill or injured, do you feel you could help him/her to carry out the treatment program?

Yes ☐ 1 — 38

No ☐ 2

Please indicate who was interviewed: *(Check all that apply)*

Subject's father	☐ 1	39
Subject's mother	☐ 1	40
Subject's guardian	☐ 1	41
Subject's spouse	☐ 1	42
Subject's sibling	☐ 1	43
Subject's child	☐ 1	44
Subject's other relative	☐ 1	45
Subject's friend	☐ 1	46

Type or print name of Clinic Coordinator: _____

Certification Numbers (if any) ☐☐-☐☐ 47

DIABETES CONTROL AND COMPLICATIONS TRIAL

Request Behaviors Confidence Questionnaire

A. IDENTIFYING INFORMATION (TO BE COMPLETED BY CLINIC STAFF)

1. Clinic Number ___
2. Patient ID Number _____
3. Patient's Initials ___
4. Date questionnaire completed: ___ ___ ___ (Month Day Year)
5. Administration sequence:
   First administration (1)
   Second administration (2)

Dear Volunteer:

As you progress through the pre-randomization phase of the DCCT, we are interested in how you see your ability to carry out the various treatment tasks that may be asked of you as well as how frequently you think you would be able to carry out the tasks. We will ask this of you at more than one time during this pre-randomization period. Please respond with your most realistic estimate. Thank you.

B. DEGREE OF CONFIDENCE IN ABILITY TO CARRY OUT TREATMENT TASKS

In the boxes to the right, please indicate how certain you are that you will be able to carry out each of the following treatment tasks. First, indicate whether or not you believe you will be able to perform the task as it is described by placing a number in the appropriate box. Using the 11 point scale below, write the number which best matches your degree of confidence in your ability to do that task. Please note that 0 on the scale means that you are quite uncertain that you will be able to do the task described, while a 10 means that you are quite certain that you will be able to do the task.

0 1 2 3 4 5 6 7 8 9 10

VERY UNCERTAIN — MODERATELY CERTAIN — VERY CERTAIN

How certain are you that you will be able to:

1. Test your urine for glucose (sugar) three or four times a day ___
2. Test your urine for glucose at least twice a day ___
3. Test your urine for glucose at least once a day ___
4. Test your urine for acetone at least once a day ___
5. Test your blood for glucose seven times a day by sticking your finger, collecting a drop of blood, and evaluating its its reaction on a test strip ___
6. Test your blood for glucose before each meal and at bedtime (four times a day) ___
7. Test your blood for glucose one or two times a day ___
8. Test your blood for glucose at 3:00 a.m. once a week ___
9. Test your blood for glucose at 3:00 a.m. once a month ___
10. Test your blood for glucose at 3:00 a.m. every three months ___
11. Collect capillary blood specimens by sticking your finger and putting some blood in a tube, seven times in one day, once every three months ___
12. Give yourself insulin one or two times a day ___
13. Give yourself insulin three times a day ___
14. Give yourself insulin four times a day ___
15. Give insulin to yourself by using an insulin pump which involves inserting and wearing a needle in your abdomen which is connected to an insulin delivery pump you wear in or on your clothing ___

Patient ID _____

16. Follow your diet every day __ __
17. Follow your diet most days __ __
18. Follow your diet every meal __ __
19. Follow your diet two meals a day __ __
20. Follow your diet one meal a day __ __
21. Return to the clinic every three months for the next several years __ __
22. Return to the clinic every month for the next several years __ __
23. Return to the clinic every week for the next several years __ __
24. Keep daily records of your glucose readings, insulin administration, diet, and hypoglycemic episodes __ __
25. Keep periodic daily records of your glucose readings, insulin administration, diet, and hypoglycemic episodes __ __

C. ESTIMATE OF HOW OFTEN TASKS WILL BE PERFORMED

In this section, we would like you to indicate the percent of time that you realistically believe that you will be able to carry out each of the following tasks if you are assigned to one or the other treatment groups. We do not expect that a person would be able to perform the treatment tasks 100% of the time. Please be realistic in your estimates. The percent time could range from 0% (never) to 50% (half of the time) to 100% (always).

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

NEVER — HALF THE TIME — ALWAYS

If you are assigned to the standard care group, how often would you probably do each of the following treatment tasks?

1. Test your urine for glucose three or four times a day __ __ __ %
2. Give yourself one or two injections of insulin a day __ __ __ %
3. Keep daily records of glucose readings, insulin injections, and hypoglycemic episodes __ __ __ %
4. Return to the clinic for visits every three months __ __ __ %
5. Collect capillary blood specimens seven times in one day every three months __ __ __ %
6. Follow your diet __ __ __ %

If you are assigned to the experimental group, how often would you probably perform each of the following tasks?

1. Test your blood for glucose seven times a day __ __ __ %
2. Test your blood for glucose four times a day __ __ __ %
3. Test your blood for glucose at 3:00 a.m. __ __ __ %
4. Give yourself three or four injections of insulin each day __ __ __ %
5. Wear an insulin pump for 24 hours each day __ __ __ %
6. Keep a daily record of your glucose readings, insulin administration, diet, and hypoglycemic reactions
7. Return to the clinic for visits every three months __ __ __ %
8. Return to the clinic for monthly visits __ __ __ %
9. Return to the clinic for weekly visits __ __ __ %
10. Collect capillary blood specimens seven times in one day every three months __ __ __ %
11. Follow your diet __ __ __ %

№ 2340

July 18, 1985
DCCT Form 060.2
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Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Blood Glucose Profile Specimen Mailing List

This mailing list is used whenever the DCCT clinic ships a container of capillary blood glucose specimens to the Central Biochemistry Laboratory (CBL). The four copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside insulated shipping container with specimens.
Mail to: DCCT Central Biochemistry Laboratory
ATTN: L262, Mayo 376-5187
University of Minnesota Hospital
Receiving Unit K/E
425 East River Road
Minneapolis, MN 55455

(2) YELLOW -- Send separately to the address above.

(3) PINK -- Send to the Coordinating Center in the weekly forms mailing.

(4) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Specimens Shipped on: __ __ / __ __ / __ __ (Month / Day / Year)

Specimens Collected From: __ __ / __ __ / __ __ (Month / Day / Year) through __ __ / __ __ / __ __ (Month / Day / Year)

PROFILSETS

ACCESSION NUMBER	PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE SPECIMEN DRAWN Month Day Year	COMMENTS (Indicate if any vials are missing or if BGP8 is included.)
BGP1 thru BGP7 __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
BGP1 thru BGP7 __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
BGP1 thru BGP7 __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
BGP1 thru BGP7 __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
BGP1 thru BGP7 __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
BGP1 thru BGP7 __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
BGP1 thru BGP7 __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
BGP1 thru BGP7 __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	
BGP1 thru BGP7 __ __ __ __ __ __	__ __ __ __ __	__ __ __	__ __/__ __/__ __	

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DIABETES CONTROL AND COMPLICATIONS TRIAL

Neurobehavioral Assessment Mailing List

This mailing list is used whenever the DCCT clinic mails the results of a neurobehavioral evaluation to the Central Neurobehavioral Coding Unit. The four copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside package with assessments.
Mail to: Christopher Ryan, Ph.D.
DCCT Central Neurobehavioral Coding Unit
University of Pittsburgh
Western Psychiatric Institute and Clinic
3811 O'Hara Street
Pittsburgh, PA 15261

(2) YELLOW -- Send separately to the address above.

(3) PINK -- Send to the Coordinating Center in the weekly forms mailing.

(4) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Assessments Mailed on: __ __ / __ __ / __ __ (Month / Day / Year)

Assessments Performed From: __ __ / __ __ / __ __ (Month / Day / Year) through __ __ / __ __ / __ __ (Month / Day / Year)

NEUROBEHAVIORAL ASSESSMENTS

PATIENT ID NUMBER	PATIENT'S INITIALS F M L	VISIT NUMBER (00 = BASELINE)	DATE ASSESSMENT PERFORMED Month Day Year	COMMENTS
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________
__ __ __ __ __	__ __ __	__ __	__ __/__ __/__ __	__________

DCCT Diabetes Control and Complications Trial

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DCCT Form 052.2
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DIABETES CONTROL AND COMPLICATIONS TRIAL

Diet History Mailing List

This mailing list is used whenever the DCCT clinic mails a package of diet histories to the Central Nutrition Coding Unit (CNCU). The four copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside package with diet histories.
Mail to: DCCT Central Nutrition Coding Unit
University of Minnesota
2829 University Avenue, S.E., Suite 526
Minneapolis, MN 55414

(2) YELLOW -- Send separately to the address above.

(3) PINK -- Send to the Coordinating Center in the weekly forms mailing.

(4) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Histories Mailed on: __ __ / __ __ / __ __ (Month / Day / Year)

Histories Taken From: __ __ / __ __ / __ __ (Month / Day / Year) through __ __ / __ __ / __ __ (Month / Day / Year)

DIET HISTORIES

PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE DIET HISTORY TAKEN Month Day Year	CNCU USE ONLY Orig	CNCU USE ONLY Dup	COMMENTS
__ __ __ __ __	__ __ __	__ __ / __ __ / __ __	__	__	______
__ __ __ __ __	__ __ __	__ __ / __ __ / __ __	__	__	______
__ __ __ __ __	__ __ __	__ __ / __ __ / __ __	__	__	______
__ __ __ __ __	__ __ __	__ __ / __ __ / __ __	__	__	______
__ __ __ __ __	__ __ __	__ __ / __ __ / __ __	__	__	______
__ __ __ __ __	__ __ __	__ __ / __ __ / __ __	__	__	______
__ __ __ __ __	__ __ __	__ __ / __ __ / __ __	__	__	______
__ __ __ __ __	__ __ __	__ __ / __ __ / __ __	__	__	______
__ __ __ __ __	__ __ __	__ __ / __ __ / __ __	__	__	______
TOTAL NUMBER LISTED ON THIS PAGE		____	__	__	

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September 30, 1988
DCCT Form 053.3
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DIABETES CONTROL AND COMPLICATIONS TRIAL

Resting Electrocardiogram Mailing List

This mailing list is used whenever the DCCT clinic mails resting electrocardiograms to the Coordinating Center. Baseline ECG's thought to show an excluding abnormality on the basis of local reading will be forwarded by the Coordinating Center to the Central ECG Coding Unit for confirmation of ineligibility. Indicate on this form if an excluding abnormality is seen. The three copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside package with the ECG's.

(2) PINK -- Send to the Coordinating Center in the weekly forms mailing.

(3) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Date ECG's mailed: __ __ / __ __ / __ __ (Month / Day / Year)

ECG's obtained from: __ __ / __ __ / __ __ (Month / Day / Year) through __ __ / __ __ / __ __ (Month / Day / Year)

RESTING ECG's

PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE OF ECG Month Day Year	CHECK HERE IF AN EXCLUDING ABNORMALITY WAS DETECTED	DESCRIPTION OF ABNORMALITY

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May 15, 1992
DCCT Form 054.3
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DIABETES CONTROL AND COMPLICATIONS TRIAL

Autonomic Neuropathy Studies Mailing List

This mailing list is used whenever the DCCT clinic mails ANS tapes to the Central Autonomic Coding Unit for analysis. ANS tapes should be sent to the CACU as soon as possible after their creation in order for deficient tapes to be identified and redone promptly. It is best to send only a few tapes in each mailing in case the package is lost. The four copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside package with tapes.
Mail to: Mary Schumer
DCCT Central Autonomic Coding Unit
301 N. 8th Street
Room 4B137
Springfield, Illinois 62702

(2) YELLOW -- Send separately to the address above.

(3) PINK -- Send to the Coordinating Center in the weekly forms mailing.

(4) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Tapes Mailed on: __ __ / __ __ / __ __ (Month / Day / Year)

Tapes Created From: __ __ / __ __ / __ __ (Month / Day / Year) through __ __ / __ __ / __ __ (Month / Day / Year)

ANS TAPES

PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE TAPES CREATED Month Day Year	VISIT NUMBER (If baseline, enter 00)	COMMENTS (Indicate if practice patient for certification normal control, etc.)
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	________
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	________
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	________
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	________
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	________
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	________
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	________
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	________
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	________

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№ 4[illegible]2
March 10, 1983
DCCT Form 055.1
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DIABETES CONTROL AND COMPLICATIONS TRIAL

Hemoglobin A1c Specimen Mailing List

This mailing list is used whenever the DCCT clinic ships a container of blood samples to the Hemoglobin A1c Laboratory. Prepare four copies of this form to distribute as follows:

1. *ORIGINAL -- Complete and place inside insulated shipping container with specimens.*
2. DUPLICATE -- Send separately to:

   Jack England
   University Missouri/Health Science Center
   Child Health - Room M770
   1 Hospital Drive
   Columbia, Missouri 65201

3. TRIPLICATE -- Send to the Coordinating Center in the weekly forms mailing.
4. QUADRUPLICATE -- Retain in clinic files.

Clinic Number: _ _

Specimens Mailed on: _ _ / _ _ / _ _ (Month / Day / Year)

Specimens Collected on: _ _ / _ _ / _ _ (Month / Day / Year) through _ _ / _ _ / _ _ (Month / Day / Year)

HbA1c

ACCESSION NUMBER	PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE SPECIMEN DRAWN Month Day Year	QUANTITY SHIPPED (ml)	COMMENTS (Indicate if this is a back-up sample.)
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________
H - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	______	______________

DIABETES CONTROL AND COMPLICATIONS TRIAL

Clinic Evaluation of Volunteer's Performance on Behavioral Tasks I (Clinic)

This rating of the volunteer's performance on the in-clinic behavioral tasks, part of the screening program, is to be completed by the clinic coordinator or the behavioral scientist using the guidelines given in Chapter 20 of the Manual of Operations.

A copy of this form is to be sent to the Coordinating Center in the weekly forms mailing.

A. IDENTIFYING INFORMATION

1. Clinic Number ☐☐ 5–6
2. Patient ID Number ☐☐☐☐☐ 7–11
3. Patient's Initials ☐☐☐ 12–14
4. Date of evaluation ☐☐/☐☐/☐☐ (Month / Day / Year) 15–20

B. IN-CLINIC DEMONSTRATION

1. Rate the patient's performance on the first five behavioral tasks for Trial 1 and Trial 2. *(If second trial was not done, leave Trial 2 box blank.)*

	Trial 1	Specify Instruction or Prompt	Trial 2
a) Task 1: Draw up 9 U in a 0.5 cc syringe	☐ 21	_____	☐ 22
b) Task 2: Draw up 16 U in a 1.0 cc syringe	☐ 23	_____	☐ 24
c) Task 3: Mix 14 U with 6 U	☐ 25	_____	☐ 26
d) Task 4: Test urine glucose *(complete for method used)*			
i) Clinitest	☐ 27	_____	☐ 28
ii) Diastik	☐ 29	_____	☐ 30
iii) Testape	☐ 31	_____	☐ 32
e) Task 5: Collect capillary blood	☐ 33	_____	☐ 34

2. Task 6: How many (0 to 6) of these were correctly matched as being related to hyperglycemia or hypoglycemia on Trial 1 and Trial 2? *(If second trial was not done, leave Trial 2 box blank)*

Trial 1	Trial 2
☐ 35	☐ 36

Comments:

_____

_____

_____

_____

Patient ID _____

3. Task 7: Did the patient state the following on Trial 1 and Trial 2? *(If second trial was not done, leave Trial 2 boxes blank.)*

	Trial 1 No	Trial 1 Yes		Trial 2 No	Trial 2 Yes	
a) leave game	☐1	☐2	37	☐1	☐2	38
b) take simple carbohydrates	☐1	☐2	39	☐1	☐2	40
c) check blood sugar	☐1	☐2	41	☐1	☐2	42
d) other proper action; specify:	☐1	☐2	43	☐1	☐2	44

_____

_____

Comments:

_____

_____

4. Task 8: Did the patient correctly identify the following as common causes of ketoacidosis on Trial 1 and Trial 2? *(If second trial was not done, leave Trial 2 boxes blank.)*

	Trial 1 No	Trial 1 Yes		Trial 2 No	Trial 2 Yes	
a) failure to take insulin	☐1	☐2	45	☐1	☐2	46
b) infection	☐1	☐2	47	☐1	☐2	48
c) other common cause; specify:	☐1	☐2	49	☐1	☐2	50

_____

_____

Comments:

_____

_____

5. Task 9: Did the patient state the following on Trial 1 and Trial 2? *(If second trial was not done, leave Trial 2 boxes blank.)*

	Trial 1 No	Trial 1 Yes		Trial 2 No	Trial 2 Yes	
a) check urine fpr acetone	☐1	☐2	51	☐1	☐2	52
b) call doctor	☐1	☐2	53	☐1	☐2	54
c) other proper action; specify:	☐1	☐2	55	☐1	☐2	56

_____

Comments:

_____

6. Task 10: Did the patient correctly solve the following? *(If second trial was not done, leave Trial 2 boxes blank.)*

	Trial 1		Trial 2	
	No	Yes	No	Yes
a) the number of units A.B. should take in the morning	☐1	☐2 57	☐1	☐2 58
b) the number of units A.B. should take in the evening	☐1	☐2 59	☐1	☐2 60
c) the time the insulin will peak for C.D.	☐1	☐2 61	☐1	☐2 62

Comments: _____

_____

_____

Type or print name of person completing this form:

_____

Certification Number (if any)

☐☐-☐☐ 63 66

DIABETES CONTROL AND COMPLICATIONS TRIAL

Clinic Evaluation of Volunteer's Performance on Behavioral Tasks II (Home)

This form is to be completed by the clinic staff to evaluate the patient's performance on the at-home behavioral tasks. Mail the original of this form to the Coordinating Center. Retain a copy in the clinic files.

A. IDENTIFYING INFORMATION

1. Clinic Number __ __ Patient's Initials __ __ __
2. Patient ID Number __ __ __ __ __ Date form completed __ __ / __ __ / __ __ (Month / Day / Year)

B. PERFORMANCE ON HOME BEHAVIORAL TASKS

1. Date home behavioral tasks started: __ __ / __ __ / __ __ (Month / Day / Year)

2. Urine testing (NOTE: Only the second sample from the morning double void is tested. Then three more urine tests are are performed each day (*before lunch, supper, bedtime*). This totals 4 tests x 14 days = 56 tests.)

   a) Number of times compliant with double void procedure __ __ ÷ 14 x 100 = __ __ __ . __ % compliance

   b) Number of times urine tests performed __ __ ÷ 56 x 100 = __ __ __ . __ % compliance

   c) Number of positive urine tests (out of 56 tests) __ __

   d) Note any reasons for missed tests:

3. Capillary blood collections

   a) Number of times compliant with *pre-breakfast* tests __ ÷ 4 x 100 = __ __ __ . __ % compliance

   b) Number of times compliant with post-breakfast tests __ ÷ 2 x 100 = __ __ __ . __ % compliance

   c) Number of times compliant with pre-lunch tests __ ÷ 4 x 100 = __ __ __ . __ % compliance

   d) Number of times compliant with post-lunch tests __ ÷ 2 x 100 = __ __ __ . __ % compliance

   e) Number of times compliant with pre-supper tests __ ÷ 4 x 100 = __ __ __ . __ % compliance

   f) Number of times compliant with post-supper tests __ ÷ 2 x 100 = __ __ __ . __ % compliance

   g) Number of times compliant with bedtime tests __ ÷ 4 x 100 = __ __ __ . __ % compliance

   h) Number of times compliant with 3:00 a.m. tests __ ÷ 2 x 100 = __ __ __ . __ % compliance

   i) Note any reasons for missed tests collection:

4. Insulin Administration

a) Number of times insulin injection was done within a 1/2 hour time frame each day (degree of consistency in insulin administration) __ __ ÷ 14 or 28 x 100 = ___ ___ ___ . __ % consistent

(CIRCLE ONE) (14 if one injection/day or 28 if two injections/day)

b) Did patient rotate the injection site? No (1) Yes (2)

5. Three-Day Food Record

Number of days completed a food record __ ÷ 3 x 100 = ___ ___ ___ . __ % compliance

6. Meals

a) Number of times ate breakfast __ __

b) Number of times ate morning snack __ __

c) Number of times ate lunch __ __

d) Number of times ate afternoon snack __ __

e) Number of times ate dinner __ __

f) Number of times ate evening snack __ __

7. Physical Activity

a) Number of days engaged in physical activity __ __

b) List usual types of physical activity and time spent per day:

8. Comments on quality of completion of daily log:

Type of print name of person completing this form:

_____

Certification Number (if any)

__ __ - __ __

DCCT Diabetes Control and Complications Trial

July 18, 1985
DCCT Form 058.2
Page 1 of 1

DIABETES CONTROL AND COMPLICATIONS TRIAL

Lipid Specimen Mailing List

This mailing list is used whenever the DCCT clinic ships a container of serum specimens to the Central Biochemistry Laboratory (CBL) for baseline lipid assessment, for annual lipid analysis, or for saved specimens. The four copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside insulated shipping container with specimens.
Mail to: DCCT Central Biochemistry Laboratory
ATTN: L262, Mayo 376-6187
University of Minnesota Hospital
Receiving Unit K/E
425 East River Road
Minneapolis, MN 55455

(2) YELLOW -- Send separately to the address above.

(3) PINK -- Send to the Coordinating Center in the weekly forms mailing.

(4) GOLDENROD -- Retain in clinic files.

Clinic Number: _ _

Specimens Shipped on: _ _ / _ _ / _ _ (Month / Day / Year)

Specimens Collected From: _ _ / _ _ / _ _ (Month / Day / Year) through _ _ / _ _ / _ _ (Month / Day / Year)

LIPID SPECIMENS

ACCESSION NUMBER	PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE SPECIMEN DRAWN Month Day Year	SAVED SPECIMEN INCLUDED? (Y or N)	COMMENTS (Indicate if this is a back-up sample or if only some determinations are to be made.)
L - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	____	____________
L - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	____	____________
L - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	____	____________
L - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	____	____________
L - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	____	____________
L - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	____	____________
L - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	____	____________
L - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	____	____________
L - _ _ _ _ _ _ _	_ _ _ _ _	_ _ _	_ _ / _ _ / _ _	____	____________

DIABETES CONTROL AND COMPLICATIONS TRIAL

Certification of Visual Acuity Examiner

Name of Visual Acuity Examiner: _____

Title: _____

Phone Number: _____ _____
(Area Code)

Clinic: _____

A. Certification for completion of the Baseline Ophthalmic Examination and Ocular History Form (DCCT Form 008): (INDICATE ONE)

Pass without comment (1)

Pass with comment (1)

Fail — resubmit (1)

B. Review of Refraction and Visual Acuity Procedures (Manual of Operations, Chapter 13.3): (INDICATE ONE)

Satisfactory — certified (1)

Unsatisfactory — hold (1)

Date of Telephone Review: __ __ __ __ __ __
Month Day Year

If status of B is unsatisfactory, what is the date of scheduled review? __ __ __ __ __ __
Month Day Year

Signature of DCCT Certification Examiner: _____

Print Name of DCCT Certification Examiner: _____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Screening Log

Clinic No. ☐☐

Use this form to record the initial screening contact which a potential patient has with your clinic. If the patient is found to be ineligible for the study during this contact, record the reasons for the exclusion using the exclusion codes listed on the following page. Use the lines for "comments" to elaborate on the excluding condition and, if only temporarily excluded, note the date when the subject is expected to be eligible.

Each week during the period when your clinic is recruiting patients, you should use a new copy of this form. Send a copy of the previous week's form to the Coordinating Center in the weekly forms mailing. The Coordinating Center should not receive the information on the patient's name, address, and telephone number, so cut that information off of the Coordinating Center's copy.

	Subject's Name	Address	Telephone Number	Date of Contact (Month / Day / Year)	Is the patient ineligible? No	Yes, temporarily	Yes, Permanently	If temporarily or permanently ineligible, specify reasons for ineligibility *(up to 4) (See page 2 for codes)*	Comments
1)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	
2)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	
3)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	
4)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	
5)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	
6)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	
7)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	
8)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	
9)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	
10)				☐☐/☐☐/☐☐	☐ 1	☐ 2	☐ 3	☐☐ ☐☐ ☐☐ ☐☐	

EXCLUSION CODE	REASON FOR PERMANENT INELIGIBILITY
01	Age over 40 years
02	Duration of insulin-dependent diabetes over 15 years
03	Has history of treatment for IDDM with 3 or more daily injections or insulin infusion pump (except for periods of less than 2 weeks to manage an intercurrent illness or to determine optimal blood glucose control)
04	Has history of photocoagulation (laser treatment of the eyes)
05	Has had 3 or more documented episodes of diabetic ketoacidosis (DKA) requiring hospitalization during the past year
06	Has been treated for hypertension during the past 2 years
07	Has had chronic disease requiring prescription medication for more than a total of 4 months during the past year
08	Has sibling, parent, child or spouse participating in the DCCT
09	Has had cataract extraction in one or both eyes
10	Has glaucoma requiring medication
11	Has chronic requirement for an ocular medication
12	Has a non-diabetic condition that limits life-expectancy or that will interfere with DCCT participation

EXCLUSION CODE	REASON FOR TEMPORARY INELIGIBILITY
13	Age less than 13 years
14	Duration of insulin-dependent diabetes less than 1 year
15	Pregnant or plans or desires a pregnancy within next 2 years
16	Resides at a distance from the clinic that presents a likely impediment to completed followup
17	Plans a permanent move outside of North America during the next 2 years
18	Current participation in another clinical trial or any study which may interfere with participation in the DCCT

DIABETES CONTROL AND COMPLICATIONS TRIAL

Daily Behavioral Tasks Log

Name: _____

Date: ___ / ___ / ___
Month Day Year

Please complete all of the boxes. If you omitted a test, meal or insulin dose, please explain why in the comments column.

URINE TESTS

Procedure	Time Done	Result
1st Morning Void		
Water Drunk		How much did you drink?
2nd Morning Void		
Before Lunch		
Before Supper		
Before Bedtime		

COMMENTS

INSULIN ADMINISTRATION (enter each injection according to prescription)

Insulin Type	Time Done	Dose	Injection Site

COMMENTS

PHYSICAL ACTIVITY

Type of Activity	Time Started	Hours and minutes spent in this activity

COMMENTS

(For two days, please complete the four boxes identified by an asterisk(*). For two other days, complete all boxes.)

MEALTIMES

Meal	Time	Comments
Breakfast		
Snack		
Lunch		
Snack		
Supper		
Snack		

CAPILLARY BLOOD COLLECTIONS

Procedure	Time Done	Tube Number
30 min. Before Breakfast*		
90 min. After Breakfast		
30 min. Before Lunch*		
90 min. After Lunch		
30 min. Before Supper*		
90 min. After Supper		
Bedtime*		

DIABETES CONTROL AND COMPLICATIONS TRIAL

Three-Day Food Record

NAME: _____

Instructions: For three consecutive days you are to list on this form all the foods you eat and all the fluids you drink. Record the amount of each item you consumed and time of day that you consumed it. Record the brand name of the product, if any, and how it was prepared. Please include in the three-day food record one day during the weekend. BRING THESE SHEETS WITH YOU TO YOUR NEXT CLINIC APPOINTMENT.

DAY 1: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)	TIME
BREAKFAST:	
SNACK:	
LUNCH:	
SNACK:	
SUPPER:	
SNACK:	

NAME: _____

DAY 2: ___ ___ / ___ ___ / ___ ___ (Month / Day / Year)	TIME
BREAKFAST:	
SNACK:	
LUNCH:	
SNACK:	
SUPPER:	
SNACK:	

NAME: _____

DAY 3: ___Month___ / ___Day___ / ___Year___	TIME
BREAKFAST:	
SNACK:	
LUNCH:	
SNACK:	
SUPPER:	
SNACK:	

DIABETES CONTROL AND COMPLICATIONS TRIAL

Daily Diabetes Monitoring Record

Standard Treatment

INSTRUCTIONS: Use this form to record: (1) the results of your daily urine tests, (2) insulin doses, and (3) other important information as follows:

URINE TESTS

- You should test your urine 4 times each day: Before Breakfast, Before Lunch, Before Dinner, and at Bedtime.

- To perform these tests, follow these steps:

  1.) Empty your bladder 20 to 30 minutes before you are going to do the test. Discard this urine.

  2.) Drink a glass of water.

  3.) In 20 to 30 minutes, or as soon as you are able, empty your bladder again. Test this urine for glucose using tape, strips or tablets according to instructions.

  4.) Record the results on the next page.

- If the glucose value is 2% or greater, or if you are not feeling well, you should also test the urine for ketones (acetone) using acetest tablets according to instructions. Record the amount of ketones as follows: none (N), small (S), or large (L).

INSULIN DOSES:

- Record the amount of long-, intermediate-, and short-acting insulin used in the morning and afternoon, and the time of these injections.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Daily Diabetes Monitoring Record

Standard Treatment

Name: _____

WEEK OF: ___/___/___	URINE TEST RESULTS Record glucose and, if done, acetone				INSULIN DOSES (Record time, type and amount)		NOTES: Record any sickness, reactions, infection, strenuous activity, exercise, large meals, emotional stress, etc.
DAY DATE	Before Breakfast	Before Lunch	Before Supper	Bedtime	A.M.	P.M.	
Sunday							
Monday							
Tuesday							
Wednesday							
Thursday							
Friday							
Saturday							

DIABETES CONTROL AND COMPLICATIONS TRIAL

Daily Diabetes Monitoring Record

Multiple Daily Injection Users

INSTRUCTIONS: Use this form to record: (1) the results of your blood glucose tests, (2) insulin doses, (3) urine tests for acetone (when done) and (4) other important information as follows:

BLOOD GLUCOSE TESTS

- You should test your blood for glucose 4 times each day: Before Breakfast, Before Lunch, Before Dinner, and at Bedtime.

- The 3 AM blood glucose test is to be done once per week. If it is less than 65 mg/dl, it must be done the following night as well. If on the second night the blood glucose is again less than 65 mg/dl, the clinic should be notified promptly.

- Every three months, the day before a clinic visit, you are to obtain three before-meal, three after-meal, and one bedtime blood sample using the capillary blood glucose profile set which the clinic provides. On these days you should also test your blood for glucose at these same times and record the results on this form.

*****Whenever possible, you should use the reflectance meter to read the test strip. If the strip must be read visually, you should use a chemstrip rather than a dextrostrip for more accurate results.

URINE TESTS

- If a blood glucose result is greater than 300 mg/dl, or if you are not feeling well, you should also test your urine for ketones (acetone) using acetest tablets according to instructions. Record the amount of ketones as follows: none (N), small (S), moderate (M), or large (L).

INSULIN DOSES

- Record the amounts of long-, intermediate-, and short-acting insulin used and the time of these injections.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Daily Diabetes Monitoring Record

Multiple Daily Injection Users

Name: _____

WEEK OF: ___/___/___	BLOOD AND/OR URINE TEST RESULTS									INSULIN DOSES (Record Time, Type, and Amt.)				NOTES:
DAY DATE	Before Breakfast	After Breakfast	Before Lunch	After Lunch	Before Supper	After Supper	At Bedtime	Other (record time)	**3:00am**	Before Breakfast	Before Lunch	Before Supper	Other	Record any sickness, reactions, infection, strenuous activity, exercise, large meal, emotional stress, etc.
Sunday														
Monday														
Tuesday														
Wednesday														
Thursday														
Friday														
Saturday														

DIABETES CONTROL AND COMPLICATIONS TRIAL

Daily Diabetes Monitoring Record

Pump Users

INSTRUCTIONS: Use this form to record: (1) the results of your blood glucose tests, (2) insulin doses, (3) urine tests for acetone (when done) and (4) other important information as follows:

BLOOD GLUCOSE TESTS

- You should test your blood for glucose 4 times each day: Before Breakfast, Before Lunch, Before Dinner, and at Bedtime.

- The 3 AM blood glucose test is to be done once per week. If it is less than 65 mg/dl, it must be done the following night as well. If on the second night the blood glucose is again less than 65 mg/dl, the clinic should be notified promptly.

- Every three months, the day before a clinic visit, you are to obtain three before-meal, three after-meal, and one bedtime blood sample using the capillary blood glucose profile set which the clinic provides. On these days you should also test your blood for glucose at these same times and record the results on this form.

*****Whenever possible, you should use the reflectance meter to read the test strip. If the strip must be read visually, you should use a chemstrip rather than a dextrostrip for more accurate results.

URINE TESTS

- If a blood glucose result is greater than 300 mg/dl, or if you are not feeling well, you should also test your urine for ketones (acetone) using acetest tablets according to instructions. Record the amount of ketones as follows: none (N), small (S), moderate (M), or large (L).

INSULIN DOSES

- Record the time and amount of all pre-meal doses as well as the Basal Infusion Rate(s) at which your pump is set. If more than one Basal Rate is used, record the time span during which the recorded rate is infused.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Daily Diabetes Monitoring Record

Pump Users

Name: _____

WEEK OF: ___/___/___	BLOOD AND/OR URINE TEST RESULTS									PRE-MEAL INSULIN DOSES (Record Time and Amount)						BASAL RATE (record time span with rate if more than one rate used.)	NOTES: Record any sickness, reactions, infection, strenuous activity, exercise, large meals, emotional stress, etc.
DAY DATE	Before Breakfast	After Breakfast	Before Lunch	After Lunch	Before Supper	After Supper	At Bedtime	Other (record time)	**3:00am**	Before Breakfast	Before Snack	Before Lunch	Before Snack	Before Supper	At Bedtime		
Sunday																	
Monday																	
Tuesday																	
Wednesday																	
Thursday																	
Friday																	
Saturday																	

Diabetes Control and Complications Trial

March 26, 1987
DCCT Form 066.4
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DIABETES CONTROL AND COMPLICATIONS TRIAL

Hemoglobin A1c Reporting Log

Analyses Performed From

__ __|__ __|__ __ TO __ __|__ __|__ __
Month Day Year Month Day Year

COLLECTION DATE MO DA YR	DATE OF ARRIVAL MO DA YR	DATE OF ANALYSIS MO DA YR	REPEAT CODE*	ACCESSION NUMBER	CLINIC NUMBER	PATIENT ID NUMBER	PATIENT'S INITIALS F M L	FETAL HEMOGLOBIN	HEMOGLOBIN A1c RESULTS	CONDITION CODES**
				H-				.	.	
				H-				.	.	
				H-				.	.	
				H-				.	.	
				H-				.	.	
				H-				.	.	
				H-				.	.	
				H-				.	.	
				H-				.	.	
				H-				.	.	
				H-				.	.	

* REPEAT CODES: R =Repeat Specimen M =Medical Management

** CONDITION CODES: *(If more than one code applies, list the most important one first.)*

A =Specimen lost in transit - request backup specimen
B =Specimen thawed in transit - request backup specimen
C =Specimen leaked in transit
D =Backup specimen
F =Frozen
HS=Slight hemolysis
H =Visible hemolysis
HM=Marked hemolysis
I =Specimen lost due to laboratory accident - request backup specimen
J =Unsatisfactory determination - request backup specimen
K =Repeat determination requested by CoC
L =Repeat determination on backup specimen request by CoC
M =Specimen improperly collected
N =Quantity not sufficient - request backup specimen
O =Mislabeled specimen - identification questionable
P =Unlabeled specimen - identification questionable
Q =Test cancelled by clinic
R =Test cancelled by CoC
S =No specimen received
T =Arrival T + 8° C
U =Shipment delay due to carrier
X =Repeat determination by laboratory
Z =A1c did not separate well from A1a and A1b
AB=Abnormal hemoglobin, A1c not determinable

DIABETES CONTROL AND COMPLICATIONS TRIAL

Request for Certification of ECG Technician

This form is used by the DCCT Trial Coordinator to request certification of a technician, a cardiology laboratory or internist to obtain electrocardiograms on DCCT patients. Details of the certification procedures are given in Chapter 10 of the DCCT Manual of Operations.

Be certain that each ECG is placed in a separate envelope with a completed certification label listing the DCCT clinic number, the name of the person obtaining the ECG, the date of the ECG, and some identifier of the patient (e.g., Patient 08C). In addition, two labels should be completed and enclosed in the envelope with the tracing.

Mail this form and the ECGs to the Coordinating Center using Form 053.

1. Clinic Number: __ __

2. Clinic Name: _____

3. Certification as an ECG technician is requested for:

   Name: _____

4. Date request mailed:

   Month Day Year
   __ __ __ __ __ __

5. The individual named in Question 3 . . . (complete a, b, or c)

   a) has submitted three 12 standard lead ECGs to the Coordinating Center for review. The ECGs are identified as follows:

Patient Identifier	Date of ECG Month	Day	Year
_____	__ __	__ __	__ __
_____	__ __	__ __	__ __
_____	__ __	__ __	__ __

   b) is on the staff of the cardiology laboratory has submitted one 12 standard lead ECG to the Coordinating Center for review. The ECG is identified as follows:

Patient Identifier	Date of ECG Month	Day	Year
_____	__ __	__ __	__ __

   c) is an internist and has submitted one 12 standard lead ECG to the Coordinating Center for review. The ECG is identified as follows:

Patient Identifier	Date of ECG Month	Day	Year
_____	__ __	__ __	__ __

6. Signature of Trial Coordinator:

   _____

THIS SECTION TO BE COMPLETED BY CENTRAL ECG READING UNIT

1. Date request received:

   Month Day Year
   __ __ __ __ __ __

2. Action recommended:

   Pass without comment ___

   Pass with comment ___

   Fail; resubmit ___

3. Comments:

4. Signature of DCCT Certification Examiner:

   _____

5. Date:

   Month Day Year
   __ __ __ __ __ __

DIABETES CONTROL AND COMPLICATIONS TRIAL

Supplies* Order Form

STAMP # _____

Please request a three-months' supply at a time and order at least six weeks prior to actual need. (Never let supply drop below half without placing an order regardless of time frame.)

MATERIAL WILL BE SHIPPED TO:

Clinic Coordinator: _____

Clinic Number: _____

Date: _____

ENTER CHANGE OF ADDRESS HERE:

_____

_____

This address change is: Permanent ___ For this order only ___

MAIL COMPLETED FORM TO:

Mr. Saddiq Abdul-Baaqiy
The Biostatistics Center
6110 Executive Blvd, Suite 750
Rockville, MD 20852

FOR COORDINATING CENTER USE ONLY	CoC Code	Quantity	Item
			INSULINS (Lilly)
	04	___ vials	(HI210) Regular Humulin
	05	___ vials	(HI310) NPH Humulin
	06	___ vials	(HI410) Lente Humulin
	07	___ vials	(CP210) Regular beef/pork insulin
	08	___ vials	(CP310) NPH beef/pork insulin
	09	___ vials	(CP410) Lente beef/pork insulin
	10	___ vials	(CP210P) Regular pork insulin
	11	___ vials	(CP310P) NPH pork isophane insulin
	12	___ vials	(CP410P) Lente pork insulin zinc
	13	___ vials	(CP610) Ultralente extended beef/pork
	14	___ ampules	(AMP666) Glucagon, 1 mg
	35	___ vials	(HI211) Buffered Regular Humulin
	36	___ vials	(HI610) Ultralente Humulin
			INSULINS (Novo-Nordisk)
	15	___ vials	Novolin, (Human), Regular
	16	___ vials	Novolin, (Human), Lente
	17	___ vials	Novolin, (Human), N.P.H.
	18	___ vials	Standard, (beef/pork), Regular
	19	___ vials	Standard, (beef/pork), Lente
	22	___ vials	Standard, (beef/pork), Semilente
	23	___ vials	Standard, (beef/pork), N.P.H.
	24	___ vials	Purified, (pork), Regular
	25	___ vials	Purified, (pork), Lente
	26	___ vials	Purified, (pork), Semilente
	27	___ vials	Purified, (pork), N.P.H.
	28	___ bxs(5)	(1.5ml cart.) REG Penfill
	29	___ bxs(100)	(27 G 1/2") PenNeedle
	94	___ vials	Novolin 70/30
	95	___ bxs(5)	(1.5ml cart.) Novolin 70/30 Penfill
	97	___ bxs(5)	(1.5ml cart.) NPH Penfill

*These supplies will be used exclusively in the Diabetes Control and Complications Trial.

FOR COORDINATING CENTER USE ONLY	CoC Code	Quantity	Item
			INSULINS (Novo-Nordisk) Cont.
	01	___ each	NovoPen
	02	___ vials	Velosulin (Regular)
	03	___ vials	Insulatard (NPH)
	161	___ vials	Insulatard (Human)
	185	___ vials	Mixtard Human 70/30
	186	___ vials	Velosulin (Human)
	187	___ vials	Standard, (beef), Ultralente
			AUTOSYRINGE AS8MP EUGLY PUMP SUPPLIES
	45/317	___ boxes(30)	Sub-Q-sets 24"
	46/318	___ boxes(30)	Sub-Q-sets 42"
			CPI PUMP 9100 SUPPLIES
	58	___ each	9100 CPI pump batteries
			BETATRON I, II PUMP SUPPLIES
	37	___ boxes(30)	CPI bent infusion sets 40"
	51	___ boxes(30)	CPI infusion sets 40"
	52	___ boxes(30)	CPI infusion sets 20"
	54	___ boxes(30)	CPI extension sets
	55	___ boxes(30)	CPI teflon cannulas
	56	___ boxes(30)	Reservoirs (syringes for Betatrons)
	57	___ each	Betatron back-up batteries
	59	___ each	Betatron batteries (#8130)
			MINIMED PUMP SUPPLIES
	86/307	___ boxes(30)	3.0 cc syringes (Minimed)
	87/308	___ boxes(30)	Infusion sets 42" (Polyfin) Bent Needle
	96/329	___ boxes(30)	Shower-pak (Minimed)
	379	___ boxes(30)	Soft-Sets *** (APPROVALS ONLY)***
	98/382	___ each	Minimed battery (#357)
	387	___ boxes(30)	Infusion sets 24" (Polyfin) Bent Needles
	393	___ each	Shower Pouch
			INSULIN DELIVERY DEVICES
			MEDI-JECTOR SUPPLIES
	61/367	___ boxes(6)	Disposable adapter
	62/368	___ each	Medi-jector holder (Lilly)
	64/369	___ each	Medi-jector holder (Nordisk)
	68/366	___ each	Medi-jector holder (Squibb-Novo)
	63/331	___ each	Bacteriostatic saline solution
	332	___ each	Cleaning solution
	127	___ each	Preci-Jet 50
	128/370	___ boxes(6)	Vial adapter
	333	___ each	0.8 Nozzle
	334	___ each	Preci-jet Solution

Clinic Number _____

FOR COORDINATING CENTER USE ONLY

INSULIN DELIVERY DEVICES

CoC Code	Quantity	Item
		PEN PUMP INFUSER SUPPLIES
66	___ boxes(10)	Infusion sets/syringes for PEN PUMPS (CLINICS PAY)
67	___ boxes(10)	Button infusers (CLINICS PAY)
		BLOOD GLUCOSE MONITORING DEVICES
137	___ btls(100)	Glucostix strips
108/384	___ each	Glucometer II batteries (9 volt)
169	___ each	Glucose Control System (Norm)
172	___ each	Glucose Control System (Low)
174	___ each	Glucose Control System (High)
82	___ btls(100)	Dextrostix strips (Glucometer I)
70	___ boxes(2)	Dextro-chek control (normal)
71	___ boxes(2)	Dextro-chek control (high)
73	___ boxes(2)	Dextro-chek calibrator
81	___ pkg(2)	Dextro-chek control (low)
109/305	___ each	ACCU-CHEK II
300	___ btls(50)	Chemstrips bg (for Accu-chek I)
121/301	___ btls(50)	Chemstrips bg (for Accu-chek II)
74/304	___ box	Glucose control I
330	___ each	ACCU-CHEK II CASE
336	___ box	Glucose control II low/high
105	___ each	GLUCOSCAN 3000
107/383	___ each	N batteries (for 2000 & 3000)
83/385	___ boxes(4)	AA batteries (Accu-chek I & Glucometer I)
103/386	___ each	J batteries (for Accu-Chek II & Glucoscan Plus)
101	___ boxes(5)	Glucoscan control II (for all Lifescan meters)
102/335	___ pkg(100)	Glucoscan Test Strips (for all Lifescan meters)
112/339	___ each	One Touch Meter ***(APPROVALS ONLY)***
113/340	___ boxes(50)	One Touch Strips
342	___ each	One Touch Control
388	___ each	One Touch Meter II ***(APPROVALS ONLY)***
183	___ each	Diascan Meter
326	___ btls(50)	Diascan Strips
343	___ each	Diascan Normal Control
344	___ each	Diascan Elevated Control
337	___ each	Exactech Meter
338	___ boxes(50)	Exactech Test Strips
341	___ each	Exactech Control
389	___ each	Companion II ***(APPROVALS ONLY)***
390	___ boxes(50)	Companion II Sensor Electrodes ***(APPROVALS ONLY)**

FOR COORDINATING CENTER USE ONLY

CoC Code	Quantity	ITEM
		BLOOD GLUCOSE MONITORING SUPPLIES
84	___ btl(100)	Hemastix
111/324	___ each	Autolets
373	___ bxs(200)	Platform (yellow) (Autolet)
374	___ bxs(200)	Platform (orange) (Autolet)
115	___ each	Pen-lets
116/325	___ bxs(200)	Lancets (Autoclix, Hemalets, Pen-lets, Autolets)
117	___ btls(100)	Visidex
118	___ each	Autolance (B/D)
119	___ bxs(100)	Lancets (Autolance)
138	___ each	Glucolet
139	___ bxs(100)	Unilet Lancets (Glucolet)
392	___ each	Pen-lets II
		INSULIN SYRINGES
20	___ cs(500)	0.5 cc syringes, (B/D)
21	___ cs(500)	1.0 cc syringes, (B/D)
129	___ cs(500)	3/10 cc syringes, (B/D)
		URINE TESTING SUPPLIES
130	___ btls(100)	Acetest
131	___ btls(100)	Albustix
132	___ btls(100)	Clinitest tablets (5-drop)
133	___ btls(50)	Diastix
134	___ btls(50)	Keto Diastix
135/302	___ btls(100)	UG strips
136/303	___ btls(100)	UGK strips
		CBL SUPPLIES
151	___ bxs(100)	Profilsets replacement tubes (green tops)
152	___ bxs(100)	Nunc tubes
153	___ bxs(100)	Saved specimen tubes
154	___ vials(100)	Capillary tubes for Profilsets
156	___ each	Trasylol
		BLOOD COLLECTION SUPPLIES
176	___ bx(100)	Lavender top tubes
177	___ bx(100)	Red top tubes
173	___ bx(100)	Needles, multi sample
178	___ each	Tube holders
394	___ bx(100)	Yellow Top Tubes
395	___ bx(100)	Green Top Tubes
		OTHER
150	___ each	Profilsets
155	___ vials(10)	Digitonin (hemolyzing reagent)
160	___ cs(1200)	Alcohol swabs
		HYPOGLYCEMIA SUPPLIES
120	___ cs (12)	Glucose tablets
124	___ Tubes	Insta-glucose
		(see also Lilly glucagon)
162/380	___ each	SLEEP SENTRY
394	___ cs (24 tubes)	Dex4 Tabs

Clinic Number _____

FOR COORDINATING CENTER USE ONLY				CoC Code	Quantity	Item
						COORDINATING CENTER SUPPLIES
				519	___ each	Form 003
				500	___ each	Form 018.2 (Diet History)
				523	___ each	Form 020
				503	___ each	Form 021
				502	___ each	Form 035
				509	___ each	Form 040
				506	___ each	Form 041
				510	___ each	Form 042
				511	___ each	Form 043
				512	___ each	Form 044
				501	___ each	Form 050
				513	___ each	Form 051
				514	___ each	Form 052
				515	___ each	Form 053
				518	___ each	Form 054
				504	___ each	Form 055
				517	___ each	Form 058
				520	___ each	Form 083
				521	___ each	Form 100
				522	___ each	Form 101
				709	___ each	DCCT Notebooks
				704	___ each	Protocol
				705	___ each	Directory
				707	___ each	DCCT ID Cards
				401	___ each	Seasons greeting cards
				402	___ each	Birthday cards
					___ copies	Form __ __ __.__(USE COMMENT SECTION IF
					___ copies	Form __ __ __.__ SPACE HERE IS INSUFFICIENT)

Clinic Number _____

FOR COORDINATING CENTER USE ONLY

CoC Code	Quantity	Item
		COORDINATING CENTER SUPPLIES
		LABELS: FORMS IDENTIFICATION
	___ labels	Resting ECG QV _____ (00,04,08,16,32,etc.)
	___ labels	Form 031, First Informed Consent
	___ labels	Form 032, Second Informed Consent
	___ labels	Form 036, Quality of Life Questionnaire
		LABELS: ACCESSION NUMBERS
	___ sets	50 additional eligibility patients starting with ID Number _____ (fundus photograph, fluorescein angiogram, laboratory specimen)
	___ sets	12 months of followup ID Number _____ Starting Month _____
		LABELS: ADDRESS
	___ sets(48)	Central Autonomic Coding Unit
	___ sets(48)	Central Biochemistry Lab
	___ sets(48)	Central Hemoglobin A1c Lab (Jack England)
	___ sets(48)	Central Neurobehav. Reading Center
	___ sets(48)	Central Ophthalmic Reading Unit
	___ sets(24)	Clarise Williams
	___ sets(24)	DeNyce Becker
	___ sets(24)	Desmond Thompson
	___ sets(24)	Duke Owen
	___ sets(24)	Patricia Cleary
	___ sets(24)	Saddiq Abdul-Baaqiy
	___ sets(24)	Tina Brenneman
	___ sets(24)	Coordinating Center -- Forms
	___ sets(24)	Coordinating Center
	___ sets(24)	Mort/Morb Class. Comm.
	___ sets(48)	Coordinator, Clinic # _____

_____
CLINIC COORDINATOR SIGNATURE

DIABETES CONTROL AND COMPLICATIONS TRIAL

ANS Testing Eligibility

This form is to be completed prior to ANS testing to *ensure* that the subject is properly prepared to undergo the testing. Send the completed form along with the ANS tape to the Central Autonomic Coding Unit.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date of Studies Month __ __ Day __ __ Year __ __
5. Is this subject a normal control? No (1) Yes (2)
6. Is this testing being performed for ANS certification? (1) (2)

B. PREPAREDNESS FOR TESTING
(If YES is answered to any of the questions below, patient is ineligible for ANS testing today. Reschedule the patient for testing another day and discard this form.)

	No	Yes
1. Any food since midnight? (Remember, even a doughnut or toast counts)	(1)	(2)
2. Any liquids since midnight? (except water)	(1)	(2)
3. Any caffeine since midnight?	(1)	(2)
4. Any medication since midnight? (including insulin, except for basal infusion in pump patients)	(1)	(2)
5. Any over-the-counter drugs since midnight? (aspirin, antihistimines, nasal spray, etc.)	(1)	(2)
6. Any alcohol in last 24 hours?	(1)	(2)
7. Any tobacco since midnight?	(1)	(2)
8. Any vigorous exercise in last 24 hours? (Any exercise not part of patient's daily routine, i.e., routine jogging O.K., but marathon running is not. NO exercise morning of test.)	(1)	(2)
9. Any emotional upset in last 24 hours? (Depression, crying episodes, anxiety from personal trauma (death, divorce, car accident, dentist, etc.))	(1)	(2)
10. Acute illness in last 48 hours? (cold, flu, measles, etc.)	(1)	(2)
11. Any hypoglycemic episodes since midnight?	(1)	(2)
12a) Fasting blood sugar value (finger-stick method O.K.) (mg/dl) __ __ __		
b) Below 50 or signs or symptoms of hypoglycemia?	(1)	(2)

C. PHYSICAL CONDITION

1. Height (cm) __ __ __ . __
2. Weight (kg) __ __ __ . __
3. Date of Birth Month __ __ Day __ __ Year __ __
4. Sex Male (1) Female (2)
5. Time of waking (less than 2 hours before test is desirable) __ __ : __ __
6. List any medications taken in the last 2 weeks:

_____

7. List diseases:

	No	Yes
Diabetes	(1)	(2)

Others: _____

Name of individual completing this form: _____

Certification Number (if any) __ __ - __ __

Diabetes
Control and
Complications
Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Hemoglobin A1c Performance Characteristics

July 1, 1990
DCCT Form 069.3
Page 1 of 1

Analyses Performed From

__ __/__ __/__ __ TO __ __/__ __/__ __
Month Day Year Month Day Year

Laboratory: Joslin (1) __
MO (BHL) (2) __
MN (CBL) (3) __

QC Code:
HPLC: Low (1) __
Middle (2) __
High (3) __
LTQC (4) __
Diamat: DN (5) __
DH (6) __
DLTQC (7) __

Instrumentation:

CBL: Diamat 1 (W-2331) (1) __
Diamat 2 (B-1314) (2) __
Other (3) __

BHL: HPLC 1 (4) __
HPLC 2 (5) __
Beckman (6) __

Date QC initiated:

__ __/__ __/__ __

Installed Column (or packed if HPLC) __ __/__ __/__ __
Month Day Year

Column Lot # (Resin) __ __ __ __ __ __ __

Column Serial # (Hardware) __ __ __ __ __

Date of Analysis Month Day Year	Sample Number	Hemoglobin A1c Results	Date of Analysis Month Day Year	Sample Number	Hemoglobin A1c Results	Date of Analysis Month Day Year	Sample Number	Hemoglobin A1c Results
__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __
__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __
__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __
__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __
__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __
__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __
__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __
__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __
__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __	__ __/__ __/__ __	__ __	__ __.__ __

Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

ANS Documentation Sheet

Clinic Number |__|__|

Patient ID Number |__|__|__|__|__|

Patient's Initials |__|__|__|

Date of Studies |__ __|__ __|__ __|
Month Day Year

Was the visit held within the time window? No ( ) Yes ( )

Certification number of person performing the studies: |__|__|-|__|__|

Tape Number: |__|__|

Study Number: |__|__|__|

If a baseline visit, check here: ( )

Otherwise, follow-up visit number: |__|__|

NOTES: _____

TEST	FOOTAGE MARKER	EVENT MARKER	ACTIVITY/COMMENTS (BLOOD PRESSURE)

Patient ID Number ______________

Date of Studies |__ __|__ __|__ __|
Month Day Year

TEST	FOOTAGE MARKER	EVENT MARKER	ACTIVITY/COMMENTS (BLOOD PRESSURE)

DCCT Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Observation of Proliferative or Nonproliferative Diabetic Retinopathy

The Central Ophthalmic Reading Unit (CORU) has observed the following in photographs submitted of this patient indicated below.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number ___
2. Patient ID Number _____
3. Patient's Initials ___
4. Were the photographs taken in conjunction with a regularly scheduled visit? No (1) Yes (2)

   If YES, specify which follow-up visit this is: ___
5. Date of photographs: ___ ___ Month ___ ___ Day ___ ___ Year
6. Date of receipt of photographs at CORU: ___ ___ Month ___ ___ Day ___ ___ Year
7. Date of notification: ___ ___ Month ___ ___ Day ___ ___ Year
8. Person notified: _____
9. CORU Grader: _____
10. Grader Number: ___

B. OBSERVED DIABETIC RETINOPATHY

	Right Eye	Left Eye
1. Moderately severe NPDR		
N/A	(1)	(1)
Moderately severe P2 plus progression of 3 steps or more on the retinopathy classification in the past year	(2)	(2)
2. Severe NPDR		
N/A	(1)	(1)
Severe P2	(2)	(2)
3. Proliferative retinopathy less than DRS High Risk Characteristics:	Right Eye	Left Eye
N/A	(1)	(1)
New vessels elsewhere than disc (NVE)	(2)	(2)
New vessels on or within 1 DD of disc (NVD)	(3)	(3)
Preretinal hemorrhage (PRH)	(4)	(4)
Vitreous hemorrhage (VH)	(5)	(5)
4. DRS High Risk Characteristics:	Right Eye	Left Eye
N/A	(1)	(1)
Possible HRC--PRH or VH could obscure NV	(2)	(2)
Definite HRC--NVE ≥1/2 DA with PRH or VH	(3)	(3)
Definite HRC--NVD < Std. #10A with PRH or VH	(4)	(4)
Definite HRC--NVD ≥ Std. #10A without PRH or VH	(5)	(5)
Definite HRC--NVD ≥ Std. #10A with PRH or VH	(6)	(6)

COMMENTS: _____

NOTE: DCCT guidelines for management of patients with proliferative retinopathy are presented in Chapter 10 of the *Manual of Operations*. Photocoagulation treatment is recommended for occurrence of DRS High Risk Characteristics. For less severe retinopathy, the DCCT Ophthalmic Committee shoud be consulted before any photocoagulation treatment is applied, unless the treating physician thinks that there is a very compelling reason to proceed immediately (such as impending neovascular glaucoma).

DIABETES CONTROL AND COMPLICATIONS TRIAL

Request for Ophthalmic Committee Consultation

This form should be completed whenever a DCCT Ophthalmologist requests the opinion and comments of the Ophthalmic Committee. The left portion of the form is completed by the clinic and then sent to each member of the Ophthalmic Committee for their review and comment. Accompanying this form should be all the information (fundus photos and data forms) necessary to describe the clinical situation. After the Ophthalmic Committee member has recorded his/her comments in the appropriate section, return this form to the Coordinating Center.

1. DCCT Clinic Number |__|__|

2. Patient ID Number |__|__|__|__|__|

3. Patient's Initials |__|__|__|

C L I N I C

4. Date Request Submitted |__ __|__ __|__ __| (Month / Day / Year)

5. Reason for request:

	Eye O.D.	Eye O.S.
To scatter photocoagulate eyes with less than High Risk Characteristics	|__|	|__|
To focal photocoagulate for treatment of macula edema	|__|	|__|
Vitrectomy	|__|	|__|
Cataract extraction	|__|	|__|
Other, specify:	|__|	|__|

_____

_____

C L I N I C

6. (MARK ALL THAT APPLY. SEE CHAPTER 10 OF THE MANUAL OF OPERATIONS FOR DEFINITION.)

	Eye O.D.	Eye O.S.
New vessels elsewhere than disc (NVE)	|__|	|__|
New vessels on or within 1 DD of disc (NVD)	|__|	|__|
Severe P2 retinopathy	|__|	|__|
Clinically significant macular edema	|__|	|__|
Exudates threatening the fovea	|__|	|__|
Other, specify:	|__|	|__|

_____

_____

NOTE

At this point, the Manual of Operations (MOOP) included a copyrighted form: *PAIS, Psychological Adjustment to Illness Scale.* No data are archived for this form, and it is not mentioned in Chapter 19 ("Psychological Procedures") of the MOOP.

Since the form is copyrighted and appears to have been included erroneously in the MOOP, it is not reproduced here.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Documentation of Interim Contact with a Standard Group Patient

This form must be completed each time there is a *telephone contact* or interim visit made with a patient from the Standard Treatment Group, except when the call involves contact with the secretary for scheduling appointments. All completed forms are to be mailed to the *Coordinating Center* at the time of the quarterly or annual visit.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date of Call or Visit __ __ / __ __ / __ __ (Month / Day / Year)
5. This form is being completed to document:
   - a) A phone call ( )
   - b) A clinic visit ( )
   - c) *Other*; specify: _____ ( )
6. This contact was initiated by:
   - a) Patient ( )
   - b) *Clinic Nurse/Coordinator* ( )
   - c) Physician ( )
   - d) Dietitian ( )
   - e) Other; specify: _____ ( )
7. Was the contact initiated because of an intercurrent event? No ( ) Yes ( )

   If YES, date of event: __ __ / __ __ / __ __ (Month / Day / Year)

   (DCCT Form 020.2 should be completed)

B. INDICATIONS FOR CONTACT

Reason for contact: (CHECK ALL THAT APPLY)

- a) To achieve *absence of* symptoms attributable to glycosuria or hyperglycemia ( )
- b) To achieve absence of ketonuria ( )
- c) To maintain normal growth and development and ideal body weight ( )
- d) To avoid frequent and serious *hypoglycemia* ( )
- e) HbAlc exceeds two standard deviations above mean for IDDM population ( )
- f) Patient request ( )
- g) Followup of previously identified problem; *specify on reverse side.* ( )
- h) Other; specify on reverse side. ( )

C. CHANGES TO REGIMEN

		No	Yes
1.	Will the *insulin*, diet or exercise regimen be changed as a result of this contact? If NO, skip Questions C.2-C.7.	( )	( )
2.	Do the proposed changes *constitute* a deviation from therapy?	( )	( )
	If YES, will the deviation last more than 30 days? (If YES, complete the Form 022 for permission for deviation.)	( )	( )
3.	Will the method of insulin administration be changed?	( )	( )
4.	Will the insulin type be changed?	( )	( )
5.	Will the *insulin dose* be changed?	( )	( )

If YES, is the change in insulin dosage an:

- a) Increase ( )
- b) Decrease ( )
- c) Redistribution ( )

		No	Yes
6a)	Will there be a change to the diet regimen? If YES, describe on reverse side.	( )	( )
b)	To the exercise regimen? If YES, *describe* on reverse side.	( )	( )
7)	Will the glucose monitoring be changed?	( )	( )

Type or print the name of the person completing this form: _____

Certification No. __ __ - __ __

DIABETES CONTROL AND COMPLICATIONS TRIAL

Neurobehavioral Assessment (Short Battery)

This form is to be completed by the staff of the DCCT Central Neurobehavioral Coding Unit to report the results of a neurobehavioral assessment (short battery).

A completed copy of the form is to be sent to the DCCT Coordinating Center.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date Tests Administered __ __ / __ __ / __ __ (Month / Day / Year)
5. Follow-up Visit Number __ __
6. Date Assessment Coded __ __ / __ __ / __ __ (Month / Day / Year)
7. Coder's ID __ __
8. Neurobehavioralist's Certification Number __ __ - __ __
9. Dominant hand: Right (1) Left (2) Ambidextrous (3)

B. TRAILMAKING

1. Sample A Time: 0-60 __ __
2. Sample A Errors: 0-8 __
3. Trails A Time: 0-99 __ __
4. Trails A Errors: 0-25 __ __
5. Sample B Time: 0-60 __ __
6. Sample B Errors: 0-8 __
7. Trails B (Form A-1) Time: 0-300 __ __ __
8. Trails B (Form A-1) Time: 0-25 __ __

C. SYMBOL-DIGIT LEARNING (FORM B)

1. Number correct -- trial 1: 0-7 __
2. Number correct -- trial 2: 0-7 __
3. Number correct -- trial 3: 0-7 __
4. Number correct -- trial 4: 0-7 __
5. Number correct -- delayed recall: 0-7 __

D. VERBAL FLUENCY

1. Number of "F" words in first quarter (0-15 seconds): 0-25 __ __
2. Number of "F" words in second quarter (16-30 seconds): 0-25 __ __
3. Number of "F" words in third quarter (31-45 seconds): 0-25 __ __
4. Number of "F" words in fourth quarter (46-60 seconds): 0-25 __ __
5. Number of illegitimate words: 0-25 __ __

Patient ID _____

D. VERBAL FLUENCY (continued)

6. Number of "A" words in first quarter (0-15 seconds): 0-25 __ __
7. Number of "A" words in second quarter (16-30 seconds): 0-25 __ __
8. Number of "A" words in third quarter (31-45 seconds): 0-25 __ __
9. Number of "A" words in fourth quarter (46-60 seconds): 0-25 __ __
10. Number of illegitimate words: 0-25 __ __
11. Number of "S" words in first quarter (0-15 seconds): 0-25 __ __
12. Number of "S" words in second quarter (16-30 seconds): 0-25 __ __
13. Number of "S" words in third quarter (31-45 seconds): 0-25 __ __
14. Number of "S" words in fourth quarter (46-60 seconds): 0-25 __ __
15. Number of illegitimate words: 0-25 __ __
16. Total number of words: 0-300 __ __ __

E. VISUAL REPRODUCTIONS - IMMEDIATE RECALL (FORM B)

1. Design A -- total points: 0-4 __
2. Design A -- segmentation score: 0-5 __
3. Design B -- total points: 0-5 __
4. Design B -- segmentation score: 0-9 __
5. Design C1 -- total points: 0-4 __
6. Design C1 -- segmentation score: 0-7 __
7. Design C2 -- total points: 0-4 __
8. Design C2 -- segmentation score: 0-7 __

F. VISUAL REPRODUCTIONS - COPY (FORM B)

1. Design A -- total points: 0-4 __
2. Design A -- segmentation score: 0-5 __
3. Design B -- total points: 0-5 __
4. Design B -- segmentation score: 0-9 __
5. Design C1 -- total points: 0-4 __
6. Design C1 -- segmentation score: 0-7 __
7. Design C2 -- total points: 0-4 __
8. Design C2 -- segmentation score: 0-7 __

G. VISUAL REPRODUCTIONS - DELAY (FORM B)

1. Design A -- total points: 0-4 __
2. Design A -- segmentation score: 0-5 __
3. Hint given? No (1) Yes (2)
4. Design B -- total points: 0-5 __
5. Design B -- segmentation score: 0-9 __
6. Hint given? No (1) Yes (2)
7. Design C1 -- total points: 0-4 __
8. Design C1 -- segmentation score: 0-7 __
9. Hint given? No (1) Yes (2)
10. Design C2 -- total points: 0-4 __
11. Design C2 -- segmentation score: 0-7 __
12. Hint given? No (1) Yes (2)

Patient ID _____

H. DIGIT VIGILANCE

1. Time to complete page 1: 0-400 ___
2. Number of omission errors -- page 1: 0-103 ___
3. Number of comission errors -- page 1: 0-99 ___
4. Number of correct responses -- page 1: 0-103 ___
5. Time to complete page 2: 0-400 ___
6. Number of omission errors -- page 2: 0-103 ___
7. Number of comission errors -- page 2: 0-99 ___
8. Number of correct responses -- page 2: 0-103 ___

I. SHIPLEY VOCABULARY

1. Number correct: 0-40 ___
2. Total time (minutes): 0-50 ___
3. Estimated verbal IQ ___

J. DIGIT SYMBOL SUBSTITUTION TEST (FORM 2)

1. Total number of symbols completed within each 30 second interval:

30": 0-50 ___
60": 0-50 ___
90": 0-50 ___
120": 0-50 ___
150": 0-50 ___
180": 0-50 ___
210": 0-50 ___
240": 0-50 ___
270": 0-50 ___
300": 0-50 ___

J. DIGIT SYMBOL SUBSTITUTION TEST (Continued)

2. Total time to complete grid: 0-360 ___
3. Total number correct within first 90 seconds: 0-90 ___
   a) Scaled score (for subjects 16 years old and over): 0-19 ___
   b) Age-corrected scaled score: 0-19 ___
4. Incidental recall: 0-9 ___

K. EMBEDDED FIGURES TEST

1. Total number correct: 0-10 ___
2. Mean latency for correct responses: 0-60 ___

L. DIGIT SPAN (FORM B)

1. Number of points: 0-28 ___
2. Number of digits repeated forward: 0-9 ___
3. Number of digits repeated backward: 0-8 ___
4. WAIS age-scaled score: 0-19 ___
5. WISC-R age-scaled score: 0-19 ___

M. FINGER TAPPING - DOMINANT HAND

1. Number of trials administered: 0-10 ___
2. Mean tapping rate per 10 second trial: 0-60.0 ___.___

N. FINGER TAPPING - NON-DOMINANT HAND

1. Number of trials administered: 0-10 ___
2. Mean tapping rate per 10 second trial: 0-80.0 ___.___

Patient ID _____

O. SHIPLEY ABSTRACTION

1. Number correct: 0-20 __ __
2. Total time (minutes): 0-50 __ __
3. Conceptual Quotient: 0-150 __ __ __

P. GROOVED PEGBOARD - DOMINANT HAND

1. Time to insert pegs: 0-180 __ __ __
2. Time to remove pegs: 0-180 __ __ __
3. Number of pegs dropped: 0-25 __ __

Q. GROOVED PEGBOARD - NON-DOMINANT HAND

1. Time to insert pegs: 0-180 __ __ __
2. Time to remove pegs: 0-180 __ __ __
3. Number of pegs dropped: 0-25 __ __

R. SHORT-TERM MEMORY (FORM B)

1. Number of words correctly recalled after 5 seconds: 0-20 __ __
2. Number of words correctly recalled after 15 seconds: 0-20 __ __
3. Number of words correctly recalled after 30 seconds: 0-20 __ __
4. Number of prior-trial intrusion errors: 0-60 __ __
5. Number of intra-list intrusion errors: 0-60 __ __
6. Number of extra-list intrusion errors: 0-60 __ __

S. STAR DRAWING - DOMINANT HAND

1. Total time: 0-90 __ __
2. Number of errors: 0-90 __ __
3. Direction taken: Left (1) Right (2)

T. STAR DRAWING - NON-DOMINANT HAND

1. Total time: 0-90 __ __
2. Number of errors: 0-90 __ __
3. Direction taken: Left (1) Right (2)

U. QUALITY OF NEUROBEHAVIORAL TESTING

1. How willing was this subject to try his or her best?
   - Very willing (1)
   - Somewhat willing (2)
   - Not too willing (3)
   - Very unwilling (4)
2. Overall, how much did distractions and interruptions affect the session?
   - Very much (1)
   - Much (2)
   - Somewhat (3)
   - Little (4)
   - Very little (5)
3. To what extent do you feel the information obtained is accurate?
   - Completely (1)
   - Mostly (2)
   - Moderately (3)
   - Somewhat (4)
   - Not very (5)
4. Quality Grade:
   - Satisfactory (1)
   - Acceptable with minor problems (2)
   - Unacceptable (3)

DIABETES CONTROL AND COMPLICATIONS TRIAL

Next of Kin Interview

D I R E C T I O N S (TO BE DRAFTED)

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date of Interview __ __ __ __ __ __
   Month Day Year

B. GENERAL INFORMATION (ALL PATIENTS)

1. Antecedent MEDICAL problems noted by next of kin:

a) 24 hours prior to death:

	No	Yes
hypoglycemia	(1)	(2)
symptoms of ketosis/ketoacidosis	(1)	(2)
other illness or symptoms (e.g., fever, chest pain, flu, trauma)	(1)	(2)
no apparent illness or symptoms	(1)	(2)

b) 72 hours prior to death:

	No	Yes
hypoglycemia	(1)	(2)
symptoms of ketosis/ketoacidosis	(1)	(2)
other illness or symptoms (e.g., fever, chest pain, flu, trauma)	(1)	(2)
no apparent illness or symptoms	(1)	(2)

c) 10 days prior to death:

	No	Yes
hypoglycemia	(1)	(2)
symptoms of ketosis/ketoacidosis	(1)	(2)
other illness or symptoms (e.g., fever, chest pain, flu, trauma)	(1)	(2)
no apparent illness or symptoms	(1)	(2)

d) Did patient seek medical attention for the above illness or symptoms? (1) (2)

With whom and when (specify):

_____

_____

_____

2. Antecedent PSYCHOSOCIAL problems noted by next of kin:

a) 24 hours prior to death:

	No	Yes
depression or hopelessness	(1)	(2)
family or marital discord	(1)	(2)
loss of job, personal property, etc.	(1)	(2)
trouble sleeping	(1)	(2)
other; specify: _____	(1)	(2)

_____

b) 72 hours prior to death:

	No	Yes
depression or hopelessness	(1)	(2)
family or marital discord	(1)	(2)
loss of job, personal property, etc.	(1)	(2)
trouble sleeping	(1)	(2)
other; specify: _____	(1)	(2)

c) 10 days prior to death:

	No	Yes
depression or hopelessness	(1)	(2)
family or marital discord	(1)	(2)
loss of job, personal property, etc.	(1)	(2)
trouble sleeping	(1)	(2)
other; specify: _____	(1)	(2)

d) Did patient seek counseling or other professional help for any of the above problems? (1) (2)

With whom and when (specify):

B. TREATMENT REGIMEN - STANDARD AND EXPERIMENTAL GROUPS

1. Had patient been taking prescribed insulin dose 72 hours prior to death? No (1) Yes (2) Not Known (3)

Describe: _____

2. Had patient been eating as usual 72 hours prior to death? No (1) Yes (2) Not Known (3)

Describe change in eating pattern (e.g., skipping meals):

3. Had patient been doing unusual or strenuous activity 72 hours prior to death? No (1) Yes (2) Not Known (3)

Describe: _____

4. Was patient monitoring blood glucose or urine 72 hours prior to death? No (1) Yes (2) Not Known (3)

Describe results: _____

5. Was patient using alcohol or non-prescription drugs (including marijuana, cocaine, etc.) 72 hours prior to death? No (1) Yes (2) Not Known (3)

Describe: _____

C. TREATMENT REGIMEN - PUMP PATIENTS ONLY

	No (1)	Yes (2)	Not Known (3)
Was patient wearing his/her pump at the time of death?			

Complete with all available information:

Usual amount of insulin in syringe: __ __ units

Date needle site last changed: __ __ / __ __ / __ __
Month Day Year

Patient's record of monitoring blood glucose:

_____

_____

Data regarding patient's compliance with regimen:

_____

_____

Data regarding patient to adjust insulin, follow regimen, etc.:

_____

_____

Signature of Interviewer:

_____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Patient/Family Group Report

INSTRUCTIONS: Please fill out a report for each group activity held for the DCCT patients in this reporting period.

DCCT Clinic Number __ __

Date of Group Event __ __ / __ __ / __ __
Month Day Year

Reporter _____

1. Group attending:

	Experimental	Standard
Patients	__	__
Family	__	__
Friends	__	__

2. Number of persons attending:

Patients	__
Family/Friends	__
Staff	__

3. Major activity:

Education	__
Support group	__
Recreation	__
Other	__

Specify: _____

_____

4. Group leaders: _____

_____

_____

5. Location of event:

_____

6. Time/duration of event:

_____ a.m. _____ p.m. _____ hours

7. Was transportation or parking provided?

( ) Yes free ( ) Yes for a fee ( ) No

8. Were refreshments provided?

( ) Yes free ( ) Yes for a fee

( ) Yes pot luck ( ) No

9. Please add any further description of the event:

_____

_____

10. How did the patients/families evaluate the event?

_____

_____

11. How did staff evaluate the event?

_____

_____

12. What suggestions would you offer if you were going to do this event again?

_____

_____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Notification of Hypoglycemic Intercurrent Event

This form must be completed by a member of the medical management team each time a patient who has been randomized or is undergoing eligibility screening experiences a hypoglycemic intercurrent event as specified in Chapter 10 of the Manual of Operations.

This form should be completed in accordance with the time frames given in Chapter 10 and mailed to this address: DCCT Morbidity/Mortality Classification Committee, The Biostatistics Center, 6110 Executive Boulevard, Suite 750, Rockville, MD, 20852. A copy of the form is to be kept in the clinic's files. On the Clinic Forms Inventory and Forms Mailing List (DCCT Forms 040 and 041), you should list the Form 083 which was mailed to the Committee.

A. IDENTIFYING INFORMATION

1. Clinic Number ___ ___
2. Patient ID Number ___ ___ ___ ___ ___
3. Patient's Initials ___ ___ ___
4. Date form completed Month ___ ___ Day ___ ___ Year ___ ___
5. Has the patient been randomized? No (1) Yes (2)

B. RECOGNITION OF INTERCURRENT EVENT

1a) Specify date of occurrence or recognition of intercurrent event: Month ___ ___ Day ___ ___ Year ___ ___

OR

b) If date uncertain, check here: (1)

2. Specify date DCCT clinic learned of the intercurrent event: Month ___ ___ Day ___ ___ Year ___ ___

3. How did the clinic learn of the intercurrent event?

a) Patient contacted clinic (1)
b) Patient's family/friends contacted clinic (2)
c) Third party contacted clinic (3)
d) Clinic recognized event and informed the patient (4)
e) Patient informed clinic at follow-up visit (5)
f) Other (6)

4. Onset of hypoglycemia occurred while patient was
asleep (1)
awake (2)

C. CLINICAL MANIFESTATION (Indicate all symptoms or signs which occurred)

1. Loss of consciousness (1)
2. Seizure (1)
3. Suspected seizure (1)
4. Unusual difficulty in awakening (1)
5. Irrational (1)
6. Uncontrollable behavior (1)
7. Confusion (1)
8. Memory loss (1)

D. BLOOD GLUCOSE DETERMINATION

1. Was the blood glucose measured BEFORE treatment? No (1) Yes (2) Unknown (3)

2. By whom?
a) Patient (1)
b) Medical care personnel (2)
c) Other (3)

3a) Record measurement: ___ ___ ___ mg/dl

OR

b) If UNKNOWN, check here: (1)

4. Method used:

a) Blood glucose monitoring -- visual (1)
b) Blood glucose monitoring -- meter (2)
c) Lab determination (plasma) (3)

Patient ID _____

		No	Yes	Unknown
5.	Was the blood glucose measured AFTER treatment?	(1)	(2)	(3)

6. By whom?
   a) Patient (1)
   b) Medical care personnel (2)
   c) Other (3)

7a) Record measurement: __ __ __ mg/dl

OR

b) If UNKNOWN, check here: (1)

8. Method used:
   a) Blood glucose monitoring -- visual (1)
   b) Blood glucose monitoring -- meter (2)
   c) Lab determination (plasma) (3)

E. TREATMENT OF CLINICAL MANIFESTATION

		No	Yes	Unknown
1.	Did the symptoms reverse without treatment?	(1)	(2)	(3)
2.	Did the patient treat SELF?	(1)	(2)	(3)
3a)	Did the patient receive assistance?	(1)	(2)	(3)
b)	Was the patient capable of self treatment?	(1)	(2)	(3)
c)	Was the patient incapable of treating self?	(1)	(2)	(3)
4.	Was the patient hospitalized or treated in an emergency room or other medical facility?	(1)	(2)	(3)

5. Treatment administered: (CHECK ALL THAT APPLY)
   a) intravenous glucose (1)
   b) glucagon (1)
   c) oral carbohydrates (1)
   d) Other, describe: (1)

_____

_____

F. ASSOCIATED EVENTS

		No	Yes
1.	Did any of the following occur with the hypoglycemic event described above?	(1)	(2)

Indicate all that apply:
   a) death (1)
   b) neurological insult requiring hospitalization (1)
   c) myocardial infarction (1)
   d) stroke (1)
   e) injury to the patient requiring hospitalization (1)
   f) injury to another person (1)
   g) property damage (1)
   h) traffic violation (1)

G. USUAL INSULIN TREATMENT

1. On what treatment regimen did the hypoglycemic intercurrent event occur?
   a) pre-randomization (1)
   b) experimental (2)
   c) standard (3)

2. If experimental regimen, was the patient on
   a) MDI (1)
   b) pump (2)
   c) both (3)

		No	Yes	Unknown
3.	If a pump patient, is a pump malfunction suspected?	(1)	(2)	(3)

If YES, describe in detail in a separate report.

Certification Number

Print name of person completing this form:

_____ __ __ - __ __

Signature of Principal Investigator:

_____ __ __ - __ __

DIABETES CONTROL AND COMPLICATIONS TRIAL

Request for Certification of Neurobehavioral Technician

Use this form to request certification of a neurobehavioral technician. Procedures for certification are specified in Chapter 23 of the DCCT Manual of Operations.

Send a copy of this form to Dr. Christopher Ryan at the Central Neurobehavioral Coding Unit. Another copy is to be sent to the Coordinating Center in the regular weekly mailing.

Clinic Number __ __

Date of initial request __ __ Month __ __ Day __ __ Year

1. Person initiating request: _____

2. Reason for change/addition: _____

_____

3. Current technician: _____

4. Proposed technician: _____

5. Qualifications of proposed technician: _____

_____

6. Is current technician willing to train? No ( ) Yes ( )

If NO,

Training session with CNCU personnel scheduled in

_____ (city) on _____ (date)

If YES,

Current technician has trained and observed proposed technician complete entire test battery satisfactorily on __ __ Month __ __ Day __ __ Year

CNCU USE ONLY

7. Proposed technician submitted first practice protocol __ __ Month __ __ Day __ __ Year

Feedback provided on __ __ Month __ __ Day __ __ Year

Comments: _____

_____

8. Proposed technician submitted second practice protocol __ __ Month __ __ Day __ __ Year

Quality of second protocol: Satisfactory ( ) Unsatisfactory ( )

Feedback provided on: __ __ Month __ __ Day __ __ Year

Comments: _____

_____

9. If proposed technician does not meet criteria, what additional steps must be taken?

_____

_____

Technician meets certification criteria as of __ __ Month __ __ Day __ __ Year

Date of this mailing to DCCT Coordinating Center __ __ Month __ __ Day __ __ Year

Signature: _____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Neurobehavioral Consensus Rating

Patient ID _ _ _ _ _ _ Date Rated _ _/_ _/_ _

Follow-up Visit (Baseline = 00) _ _ Rater's Number _

Rater's Initials _ _ _

Test Date _ _/_ _/_ _

For each of the areas listed below, select the rating that best summarizes the current status of that ability. For ratings that seem to fall between categories, use a plus (+) to indicate that the rating is closer to the next higher (somewhat more impaired) category, and a minus (-) to indicate that the rating is closer to the next lower (somewhat less impaired) category.

RATING LIST:

1. above average functioning
2. average functioning
3. borderline; not definitely pathological
4. definite mild impairment
5. definite moderate impairment
6. definite severe impairment
7. not ratable

___	INTELLIGENCE	FSIQ VIQ PIQ (scatter)
___	VERBAL FLUENCY	FAS (Vocabulary)
___	ABSTRACTION	Category TPT-Total-Time (BD,PA,SIM)
___	CALCULATION	Wechsler WRAT
___	LEARNING	Symbol-Digit-Learning
___	SHORT-TERM MEMORY	Imm-VR Imm-LM STM DSST-Recal TPT-Loc
___	LONG-TERM MEMORY	Del-VR Del-LM Delayed-SD-Recall
___	VISUOSPATIAL	Embed PC Copy-Segmentation
___	CONSTRUCTIONAL	BD OA VR-Copy
___	ATTENTION	Dig-Vig-Time Dig-Vig-Errors (Dig-Span Arith)
___	PERCEPTUOMOTOR	Trails-B DSST
___	SPEED & DEXTERITY	Tapping Pegboard Star (worse hand)
___	ASYMMETRY	1=none 2=poss L dysfunction 3=poss R 4=def L dysfunction 5=def R
___	GLOBAL JUDGMENT	
___	CHANGE FROM BASELINE	1=significantly improved 2=slightly improved 3=no change 4=slightly worse 5=significantly worse

NOTE: _____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Request for Certification of Autonomic Nervous System Technician

Use this form to request certification of an autonomic nervous system technician. Procedures for certification are specified in Chapter 23 of the DCCT Manual of Operations.

Send a copy of this form to the Central Autonomic Coding Unit with two tapes on non-DCCT patients. Another copy is to be sent to the Coordinating Center in the regular weekly mailing. Two tapes quality graded "good" are required for certification.

Clinic Number __ __

Date of Initial Request __ __ Month __ __ Day __ __ Year

1. Name of person initiating request: _____

2. Reason for change/addition: _____

_____

3. Name of current ANS technician: _____

4. Name of ANS technician to be certified: _____

	No	Yes
5. Is this an initial request for certification for this person?	( )	( )
Is this a resubmission?	( )	( )
6. Has this person been trained by a certified ANS technician?	( )	( )
Has this person been trained by the CACU staff?	( )	( )

Date of training session: __ __ Month __ __ Day __ __ Year

CACU USE ONLY

7. Date tapes received: Number of tapes received:

Month Day Year	
__ __ __ __ __ __	__ __
__ __ __ __ __ __	__ __
__ __ __ __ __ __	__ __
__ __ __ __ __ __	__ __
__ __ __ __ __ __	__ __

8. Certification Pass: ____ Date: __ __ Month __ __ Day __ __ Year

Comments: _____

_____

_____

_____

_____

Date of this mailing to DCCT Coordinating Center: __ __ Month __ __ Day __ __ Year

Signature: _____

Mail to: Certification
DCCT Coordinating Center
The Biostatistics Center
7979 Old Georgetown Road, Suite 500
Bethesda, MD 20814

Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Request for Certification of Nerve Conduction Technician

Use this form to request certification of a nerve conduction technician. Procedures for certification are specified in Chapter 23 of the DCCT Manual of Operations.

Send a copy of this form along with two DCCT Form 037's and EMG tracings on two non-DCCT patients to:

Dr. James Albers
University of Michigan
Medical Center
Department of Neurology
IC325-UH Box 0032
Ann Arbor, MI 48109

Another copy is to be sent to the Coordinating Center in the regular weekly mailing.

Clinic Number ___ ___

Date of Initial Request ___Month ___Day ___Year

1. Name of person initiating request: _____

2. Reason for change/addition: _____

_____

3. Name of current EMG technician: _____

4. Name of EMG technician to be certified: _____

	No	Yes
5. Is this an initial request for certification for this person?	( )	( )
Is this a resubmission?	( )	( )

7. Date tracings received: ___Month ___Day ___Year

8. Certification: Date: ___Month ___Day ___Year

Pass ____

Fail-resubmit ____

Comments: _____

_____

Date of this mailing to DCCT Coordinating Center: ___Month ___Day ___Year

Signature: _____

Mail to: Certification
DCCT Coordinating Center
The Biostatistics Center
6110 Executive Blvd., Suite 750
Rockville, MD 20852

DIABETES CONTROL AND COMPLICATIONS TRIAL

Request for Certification of Dietitian

Use this form to request certification of a dietitian. Procedures for certification are specified in Chapter 23 of the DCCT Manual of Operations.

Send a copy of this form with the first diet history to the Central Nutrition Coding Unit; send the original to the Coordinating Center.

Clinic Number __ __

Date of Initial Request __ __ / __ __ / __ __ (Month / Day / Year)

1. Name of person initiating request: _____

2. Name of new dietitian: _____

3. Reason for change/addition: _____

_____

4. Date training packet was received from CNCU: __ __ / __ __ / __ __ (Month / Day / Year)

OR

Date person attended training at CNCU: __ __ / __ __ / __ __ (Month / Day / Year)

CNCU USE ONLY

5. Date standard history was received: __ __ / __ __ / __ __ (Month / Day / Year)

6. Date reviewed: __ __ / __ __ / __ __ (Month / Day / Year)

7. Date dietitian contacted: __ __ / __ __ / __ __ (Month / Day / Year)

8. Date three diet histories were received: __ __ / __ __ / __ __ (Month / Day / Year)

8. Certification: Pass _____

Fail _____ (resubmit ___ histories)

Comments: _____

_____

Date: __ __ / __ __ / __ __ (Month / Day / Year)

Signature: _____

Mail to: Certification
DCCT Coordinating Center
The Biostatistics Center
6110 Executive Boulevard, Suite 750
Rockville, MD 20852

DIABETES CONTROL AND COMPLICATIONS TRIAL

Further Details of Hypoglycemic Event

This form captures further details on hypoglycemic events reported on DCCT Forms 020 and 083. The clinic staff should complete this form using the subject's medical records or follow-up conversation with the subject.

Please complete this form in accordance with the time frames given in *Chapter 10 of the Manual of Operations* and mail it along with DCCT Forms 020 and 083 to this address: DCCT Morbidity/Mortality Classification Committee, 6110 Executive Boulevard, Suite 750, Rockville, MD, 20852. A copy of this form is to be kept in the clinic's files. On the Clinic Forms Inventory and Forms Mailing List (DCCT Forms 040 and 041), you should list the DCCT Form 092 which was mailed to the Committee.

A. IDENTIFYING INFORMATION

1. Clinic Number ___ ___
2. Patient ID Number ___ ___ ___ ___ ___
3. Patient's Initials ___ ___ ___
4. Date this form completed ___ ___ ___ ___ ___ ___ (Month Day Year)
5. Date DCCT Forms 020 and/or 083 were completed for this event ___ ___ ___ ___ ___ ___ (Month Day Year)

B. RECOGNITION OF HYPOGLYCEMIC EVENT

1a) Specify date of occurrence or recognition of hypoglycemic event: ___ ___ ___ ___ ___ ___ (Month Day Year)

OR

b) If date uncertain, check here: (1)

2. Specify date DCCT clinic learned of the hypoglycemic event: ___ ___ ___ ___ ___ ___ (Month Day Year)

3. How did the clinic *learn of the hypoglycemic event*?

Patient contacted clinic (1)

Patient's family/friends contacted clinic (2)

Third party contacted clinic (3)

Clinic recognized event and informed the patient (4)

Patient informed clinic at follow-up visit (5)

Other; specify: _____ (6)

C. PRESENCE OF ASSISTANCE

1. Patient's living arrangement at the time of the episode being reported:

With parent or guardian (1)

With other companion/spouse (2)

In dormitory (3)

Alone (4)

Unknown (5)

Other; specify: _____ (6)

2. Who was with the patient at the time of onset of symptoms? (CHECK ALL THAT APPLY)

a) Parent, guardian, spouse, child or other person with whom the patient usually abides (1)

b) School roommate, classmate or teacher (1)

c) Passerby (1)

d) Other person, specify: _____ (1)

e) No one; patient was alone (1)

f) Unknown; patient cannot recall (1)

3. If the patient was not alone (Question 2), was the person who was present during the onset of symptoms capable of recognizing that the patient was experiencing a hypoglycemic reaction? (IF THE PERSON WAS ASLEEP, ANSWER THIS QUESTION "YES" IF THE PERSON WOULD BE CONSIDERED CAPABLE IF AWAKE.)

No	Yes	Unknown
(1)	(2)	(3)

Patient ID _____

4. If YES to Question 3, did this person take any action which might have reduced the severity of this hypoglycemic episode? No (1) Yes (2) Unknown (3)

5. If YES to Question 4, what did this person do? (CHECK ALL THAT APPLY)

a) Administer oral carbohydrates (1)

b) Administer glucagon (1)

c) Unknown (1)

d) Other; specify: _____ (1)

D. DIURNAL FREQUENCY

1. Indicate the time of the onset of the episode (best estimate):

a) 12:00 a.m. -- 4:00 a.m. (1)

4:00 a.m. -- 8:00 a.m. (2)

8:00 a.m. -- 12:00 p.m. (3)

12:00 p.m. -- 4:00 p.m. (4)

4:00 p.m. -- 8:00 p.m. (5)

8:00 p.m. -- 12:00 a.m. (6)

Unknown (7)

b) Record the time if known: __ __:__ __ o'clock

am (1) pm (2)

Or check here if unknown: (3)

E. DESCRIPTION OF EVENT

1. Patient's location at onset of episode:

Home -- awake (1)

asleep (2)

Work (3)

School (4)

Automobile (5)

Leisure activity outside home -- sports (6)

other social activity (7)

Other outside home -- awake (8)

asleep (9)

Unknown (10)

2. If patient was awake,

a) Were the warning signs or symptoms present prior to the episode? No (1) Yes (2) Unknown (3)

b) If YES, were these recognized as symptoms of hypoglycemia by the patient? No (1) Yes (2) Unknown (3)

c) Another person? (1) (2) (3)

F. POTENTIAL CONTRIBUTING FACTORS

1. Characterize the patient's exercise preceding the hypoglycemic event:

	None	Sedentary	Moderate	Strenuous	Unk
a) Exercise during the same four-hour period in D.1	(1)	(2)	(3)	(4)	(5)

	No	Yes	Unk
b) Was this unusual for this patient?	(1)	(2)	(3)

	None	Sedentary	Moderate	Strenuous	Unk
c) Exercise during the previous 24 hours excluding the four-hour period in D.1	(1)	(2)	(3)	(4)	(5)

	No	Yes	Unk
d) Was this unusual for this patient?	(1)	(2)	(3)

2. Characterize the patient's diet preceding this hypoglycemic event: (Check all that apply)

	Missed			Delayed			Ate Less Than Usual		
	Meal	Snack	Unk	Meal	Snack	Unk	No	Yes	Unk
a) During the same four-hour period in D.1	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)
b) Previous 24 hours excluding the four-hour period in D.1	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)

3. a) Were there any deviations from usual insulin dose or algorithm preceding this hypoglycemic event?

	No	Yes	Unk
During the same four-hour period as in D.1	(1)	(2)	(3)
During the previous 24 hours excluding the four-hour period in D.1	(1)	(2)	(3)

b) Were there any deviations from the timing or scheduling of insulin?

	No	Yes	Unk
During the same four-hour period as in D.1	(1)	(2)	(3)
During the previous 24 hours excluding the four-hour period in D.1	(1)	(2)	(3)

4. Was there sexual activity preceding this hypoglycemic event?

	No	Yes	Unk
a) During the same four-hour period period in D.1	(1)	(2)	(3)
b) During the previous 24 hours excluding the four-hour period in D.1	(1)	(2)	(3)

5. Any alcohol or other recreational drug consumption preceding hypoglycemic event?

	No	Yes	Unk
a) During the same four-hour period period in D.1	(1)	(2)	(3)
b) During the previous 24 hours excluding the four-hour period in D.1	(1)	(2)	(3)

6. Glucose monitoring (blood or urine) preceding hypoglycemic event

a) % of expected tests performed during prior week __ __ %

	No	Yes	Unk
b) Were all the expected tests performed during the 24 hours prior to episode?	(1)	(2)	(3)
c) If applicable, did the patient perform 3:00 a.m. blood glucose testing in week prior to episode?	(1)	(2)	(3)

d) Record 3:00 a.m. value __ __ __

Patient ID _____

7. Relationship to menstrual cycle:
(IF NOT APPLICABLE, MALE OR NO MENSES, GO TO QUESTION 8)

	No	Yes	Unk
a) Was the patient menstruating at the time of the episode?	(1)	(2)	(3)
b) Was the patient's usual form of birth control at the time of this episode oral contraceptives?	(1)	(2)	(3)
	Reg	Irreg	Unk
c) Characterize the patient's cycle	(1)	(2)	(3)

If regular, estimate the usual length of cycle (e.g., 28 days) __ __ days

	No	Yes	Unk
d) Did the patient's blood or urine glucose fluctuate around the time of menses?	(1)	(2)	(3)

If YES, explain:

_____

_____

_____

8. Was there any recent stress or other potential psychological disturbances in the week prior to the episode?

No	Yes	Unk
(1)	(2)	(3)

Specify: _____

_____

_____

9. Were other potentially contributing factors present?

No	Yes	Unk
(1)	(2)	(3)

Please list: _____

_____

_____

_____

_____

10a) Did the patient usually carry something to treat reactions?

No	Yes	Unk
(1)	(2)	(3)

Specify: _____

_____

_____

b) Did the patient have something to treat reactions with him at the time of this episode?

No	Yes	Unk
(1)	(2)	(3)

Person completing form:

_____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Random Day Questionnaire

This form was developed for the Ancillary Study of Hypoglycemia in the DCCT. All subjects randomized through December 1, 1985 are to be questionned via a telephone call regarding their activities on the assigned day. Any questions regarding events in the previous week pertain to the seven days prior to the assigned day.

The purpose of these questions is to provide an estimate of prevalence of "risk factors" for hypoglycemia on a randomly chosen day.

A. IDENTIFYING INFORMATION

1. Clinic Number ___

2. Patient ID Number _____

3. Patient's Initials ___

4. Date form completed ___/___/___ (Month Day Year)

5. Assigned day of week about which subject is interviewed

Sunday (1)
Monday (2)
Tuesday (3)
Wednesday (4)
Thursday (5)
Friday (6)
Saturday (7)

B. OCCURRENCE OF MILD HYPOGLYCEMIA DURING PREVIOUS WEEK

1. How many times in the past seven days have you experienced symptomatic hypoglycemia which was mild enough for you to treat yourself? ___

2. If the patient has experienced hypoglycemia in the past seven days which was mild enough for the patient to treat himself/herself, answer Items a) through c) below. Otherwise, skip to Question B.3.

a) When has the above mild hypoglycemia occurred?

While you were awake (1)

While you were asleep (2)

Both (3)

b) What is the usual reason for the mild hypoglycemia? (CHECK ALL THAT APPLY)

(i) Missed meal or snack (1)

(ii) Decreased food intake at meal or snack (1)

(iii) Increased exercise level (1)

(iv) Too much insulin taken (1)

(v) Lack of early warning signs of low blood glucose (1)

(vi) Other; specify: _____ (1)

_____

(vii) Unexplained/Unknown (1)

c) What symptoms do you have with mild hypoglycemia? (CHECK ALL THAT APPLY)

(i) Adrenergic warning symptoms (1)

(ii) Diaphoresis (sweating) (1)

(iii) Altered mental status (1)

(iv) Other; specify: _____ (1)

_____

3. How many times in the past seven days did you experience symptomatic hypoglycemia that you could not treat yourself? ___

Patient ID _____

C. LIFESTYLE ON THE ASSIGNED DAY

1. What are your current living arrangements?

You live with parent or guardian (1)

You live with spouse or other companion (2)

You live in a dormatory (3)

You live alone (4)

Other; specify: _____ (5)

	Sedentary (1)	Moderate (2)	Strenuous (3)	Unk (4)
2. Exercise pattern				

	No (1)	Yes (2)
3. Is this your usual type of exercise?		

4. Were there any diet deviations?

	No (1)	Yes (2)	Unk (3)
Missed meal or snack			
Delayed meal or snack			
Ate less than usual			

	No (1)	Yes (2)
5. Do you usually deviate from your diet?		

6. Amount of sleep in the past 24 hours:

<7 hours (1)
7-8 hours (1)
>8 hours (1)

	No (1)	Yes (2)
7. Is this your usual amount of sleep?		

	No (1)	Yes (2)	Unk (3)
8. Any deviation from usual insulin dose or insulin algorithm?			

	No (1)	Yes (2)	Unk (3)
9. Any deviation (>30 minutes) from timing or schedule of insulin?			

	No (1)	Yes (2)	Unk (3)	NA (4)
10. Any sexual activity in past 24 hours?				

	No (1)	Yes (2)	Unk (3)
11. Any alcohol consumption or recreational drug consumption?			

	No (1)	Yes (2)	NA (3)
12. If applicable, is the patient menstruating?			

13. Glucose monitoring (blood or urine)

Percentage of expected tests performed in previous week ___ ___ ___ %

	No (1)	Yes (2)	Unk (3)
If applicable, did the patient perform 3:00 a.m. blood glucose testing in week prior to episode?			

Record 3:00 a.m. value ___ ___ ___ _____

	No (1)	Yes (2)	Unk (3)
14. For experimental patients only: Did you have any blood glucose reading <50 without symptoms in the past week?			

If YES, how many? ___ ___

	No (1)	Yes (2)	Unk (3)
15. Recent stress or other potential psychological disturbance in previous week			
16. Are you carrying something today to treat a reaction?			
17. Do you usually carry something to treat insulin reaction?			

DCCT Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Observation of Clinically Significant Macular Edema

The Central Ophthalmic Reading Unit (CORU) has observed the following in photographs submitted of this patient indicated below.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Were the photographs taken in conjunction with a regularly scheduled visit? No (1) Yes (2)

   If YES, specify visit: __ __
5. Date of photographs: __ __ Month __ __ Day __ __ Year
6. Date of receipt of photographs at CORU: __ __ Month __ __ Day __ __ Year
7. Date of notification: __ __ Month __ __ Day __ __ Year
8. Person notified: _____
9. CORU Grader: _____
10. Grader Number: __ __

B. OBSERVED MACULAR STATUS

On the basis of these fundus photographs, clinically significant macular edema is:

	Right Eye	Left Eye
Absent	(1)	(1)
Questionable	(2)	(2)
Present, zone of retinal thickening >1 DA, part within 1 DD of center of macula	(3)	(3)
Present, retinal thickening or associated HE within 500 microns of center of macula (center not involved)	(4)	(4)
Present, retinal thickening or associated HE within 500 microns of center of macula (center questionably or definitely involved)	(5)	(5)

COMMENTS: _____

_____

_____

_____

_____

NOTE: DCCT guidelines for management of patients with clinically significant macular edema are presented in Chapter 10 of the Manual of Operations.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Diet Behavior Questionnaire

Instructions to Study Volunteer:

Please read each question completely before recording your answer. Remember there are no right or wrong answers. For each question, check ( ) the answer which most closely describes your situation during the past year.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Today's Date __ __ __ __ __ __
   Month Day Year

B. DIET INFORMATION

There are many ways to teach diet. Which of the following systems does your DCCT dietitian use to teach you your diet? Circle all numbers(s) which precede the systems you have been taught.

1. I have not been taught a diet.
2. The American or Canadian Diabetes Association Exchange Diet. I have been instructed on the number of milk, vegetable, fruit, bread, meat and fat portions to eat each day.
3. To weigh and/or measure foods.
4. I have been taught to estimate food portions.
5. My dietitian asked me to avoid foods with concentrated sugars like candy, regular soda and pie. But, I don't have to follow any other directions.
6. I have been told to count carbohydrate content of foods.
7. I have been taught the Total Available Glucose Method (TAG).

7a. Other, please describe:

How often do you:	Never	Less than half the time	About half the time	More than half the time	Almost Always	Does Not Apply
8. Eat what you feel like	(1)	(2)	(3)	(4)	(5)	(6)
9. Follow the ADA Exchange Diet	(1)	(2)	(3)	(4)	(5)	(6)
10. Weigh and/or measure food	(1)	(2)	(3)	(4)	(5)	(6)
11. Avoid foods with concentrated sugars	(1)	(2)	(3)	(4)	(5)	(6)
12. Estimate food portions	(1)	(2)	(3)	(4)	(5)	(6)
13. Count carbohydrate content of foods	(1)	(2)	(3)	(4)	(5)	(6)
14. Use TAG Method	(1)	(2)	(3)	(4)	(5)	(6)

14a. Other, please describe:

Have you been instructed to eat a snack in the:

	No	Yes
15. Morning	(1)	(2)
16. Afternoon	(1)	(2)
17. Night	(1)	(2)

How often do you eat a snack?

	Less than once a month	1-2 times a week	3-5 times a week	Every day
18. Morning	(1)	(2)	(3)	(4)
19. Afternoon	(1)	(2)	(3)	(4)
20. Night	(1)	(2)	(3)	(4)

How often do you skip a snack because your blood sugar is high?

	Less than once a month	1-2 times a week	3-5 times a week	Every day
21. Morning	(1)	(2)	(3)	(4)
22. Afternoon	(1)	(2)	(3)	(4)
23. Night	(1)	(2)	(3)	(4)

How often do you have an extra snack?
(DO NOT INCLUDE SNACKS TAKEN TO TREAT LOW BLOOD SUGAR)

	Less than once a month	1-2 times a week	3-5 times a week	Every day
24. Morning	(1)	(2)	(3)	(4)
25. Afternoon	(1)	(2)	(3)	(4)
26. Night	(1)	(2)	(3)	(4)

How often do you eat an extra snack when your blood sugar is low (but not having a reaction)?

	Less than once a month	1-2 times a week	3-5 times a week	Every day
27. Morning	(1)	(2)	(3)	(4)
28. Afternoon	(1)	(2)	(3)	(4)
29. Night	(1)	(2)	(3)	(4)

Do you believe eating the following foods raises your blood sugar significantly?

	No	Yes
30. Milk	(1)	(2)
31. Fruits	(1)	(2)
32. Vegetables	(1)	(2)
33. Meats	(1)	(2)
34. Breads	(1)	(2)
35. Fats	(1)	(2)

If your blood glucose is higher than the study goal, do you change your meals so that you eat more/less or the same amount of the following?

	More	Less	Same
36. Milk	(1)	(2)	(3)
37. Fruits	(1)	(2)	(3)
38. Vegetables	(1)	(2)	(3)
39. Meats	(1)	(2)	(3)
40. Breads	(1)	(2)	(3)
41. Fats	(1)	(2)	(3)

Approximately how often do you eat the following?
(DO NOT INCLUDE THOSE TIMES YOU EAT THESE FOODS TO TREAT A LOW BLOOD SUGAR)

	Less than once a week	Once per week	2-5 times per week	Once per day	More than 1 per day
42. Candy (made with sugar)	(1)	(2)	(3)	(4)	(5)
43. Cookies (made with sugar)	(1)	(2)	(3)	(4)	(5)
44. Cake (made with sugar)	(1)	(2)	(3)	(4)	(5)
45. Pie (made with sugar)	(1)	(2)	(3)	(4)	(5)
46. Pastry (sweet rolls, danish, donuts made with sugar)	(1)	(2)	(3)	(4)	(5)
47. Soda pop (made with sugar)	(1)	(2)	(3)	(4)	(5)
48. Other sweets containing concentrated sugar	(1)	(2)	(3)	(4)	(5)

49. If you eat any of the foods listed above 2-5 times per week or more, please list food and amount you eat below.

FOOD	AMOUNT
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

49a. How often do you adjust your insulin dose when you eat any of the foods listed above?

Never (1)	Less than half the time (2)	About half the time (3)	More than half the time (4)	Almost Always (5)

Approximately how often do you skip meals?

	Never	Less than 1 a week	2-3 times a week	4-7 times a week	Daily
50. Breakfast	(1)	(2)	(3)	(4)	(5)
51. Lunch	(1)	(2)	(3)	(4)	(5)
52. Dinner	(1)	(2)	(3)	(4)	(5)

Approximately how often do you allow 30 minutes between injecting your regular insulin and beginning to eat?

	Less than 1 a week	2-3 times a week	4-6 times a week	Daily	Not Applicable
53. Breakfast	(1)	(2)	(3)	(4)	(5)
54. Lunch	(1)	(2)	(3)	(4)	(5)
55. Dinner	(1)	(2)	(3)	(4)	(5)

Approximately how often do you delay your meals more than 45 minutes after you have injected your regular insulin?

	Less than 1 a week	2-3 times a week	4-6 times a week	Daily	Not Applicable
56. Breakfast	(1)	(2)	(3)	(4)	(5)
57. Lunch	(1)	(2)	(3)	(4)	(5)
58. Dinner	(1)	(2)	(3)	(4)	(5)

Approximately how often do you allow less than 20 minutes between injecting regular insulin and beginning to eat?

	Less than 1 a week	2-3 times a week	4-6 times a week	Daily	Does Not Apply
59. Breakfast	(1)	(2)	(3)	(4)	(5)
60. Lunch	(1)	(2)	(3)	(4)	(5)
61. Dinner	(1)	(2)	(3)	(4)	(5)

How often do you omit the prescribed insulin dose before ...

	Never	Less than 1 a week	2-3 times a week	4-7 times a week	Does Not Apply
62. Breakfast	(1)	(2)	(3)	(4)	(5)
63. Lunch	(1)	(2)	(3)	(4)	(5)
64. Supper	(1)	(2)	(3)	(4)	(5)
65. Snacks	(1)	(2)	(3)	(4)	(5)

66. How often do you exercise?

Never	Less than once a week	2-3 times a week	4-7 times a week	More than once a day
(1)	(2)	(3)	(4)	(5)

66a. How often do you test your blood sugar before exercise?

Never	Less than half the time	About half the time	More than half the time	Almost Always
(1)	(2)	(3)	(4)	(5)

67. How often do you have reactions during or after exercise?

Never	Less than half the time	About half the time	More than half the time	Almost Always
(1)	(2)	(3)	(4)	(5)

67a. How often is your blood sugar high after exercise?

Never	Less than 1/2 the time	About 1/2 the time	More than 1/2 the time	Almost Always	Does Not Apply
(1)	(2)	(3)	(4)	(5)	(6)

68. Have you been instructed how to adjust the food you eat when you exercise more than 15 minutes?

Yes	No	Don't Remember
(1)	(2)	(3)

69. How often do you adjust your food when you exercise for more than 15 minutes?

Never	Less than 1/2 the time	About 1/2 the time	More than 1/2 the time	Almost Always	Does Not Apply
(1)	(2)	(3)	(4)	(5)	(6)

70. Have you been instructed how to adjust your insulin when you exercise more than 15 minutes?

Yes	No	Don't Remember
(1)	(2)	(3)

71. How often do you adjust your insulin when you exercise more than 15 minutes?

Never	Less than 1/2 the time	About 1/2 the time	More than 1/2 the time	Almost Always	Does Not Apply
(1)	(2)	(3)	(4)	(5)	(6)

72. How often do you eat more than necessary before or after exercise?

Never	Less than 1/2 the time	About 1/2 the time	More than 1/2 the time	Almost Always	Does Not Apply
(1)	(2)	(3)	(4)	(5)	(6)

73. How often do you use blood sugar results to adjust food for exercise?

Never	Less than 1/2 the time	About 1/2 the time	More than 1/2 the time	Almost Always	Does Not Apply
(1)	(2)	(3)	(4)	(5)	(6)

74. Do you adjust your insulin dose based on what you are going to eat?

a) for meals

Never	Less than half the time	About half the time	More than half the time	Almost Always
(1)	(2)	(3)	(4)	(5)

b) for snacks

Never	Less than half the time	About half the time	More than half the time	Almost Always
(1)	(2)	(3)	(4)	(5)

When my blood sugar is high ...

	Never	Less than half the time	About half the time	More than half the time	Almost always
75. I eat less food at the next meal	(1)	(2)	(3)	(4)	(5)
76. I eat fewer carbohydrates at the next meal	(1)	(2)	(3)	(4)	(5)
77. I skip a snack	(1)	(2)	(3)	(4)	(5)
77a. I take more insulin	(1)	(2)	(3)	(4)	(5)

When treating a reaction, how often do you ...

	Never	Less than half the time	About half the time	More than half the time	Almost always
78. Test your blood sugar before eating	(1)	(2)	(3)	(4)	(5)
79. Eat until you feel better	(1)	(2)	(3)	(4)	(5)
80. Eat a specified amount, wait at least 10-15 minutes, then test your blood sugar before eating again	(1)	(2)	(3)	(4)	(5)
81. Eat a specified amount, wait 10-15 minutes before eating more	(1)	(2)	(3)	(4)	(5)

	Never	Less than half the time	About half the time	More than half the time	Almost always
82. Do you carry a specific food or product to treat reactions?	(1)	(2)	(3)	(4)	(5)

83. Please list food(s) or products used.
(PLEASE INCLUDE TYPE AND AMOUNT OF EACH ITEM)

_____

_____

_____

83a. How often do you eat extra food to prevent hypoglycemia?

Never	Less than half the time	About half the time	More than half the time	Almost Always
(1)	(2)	(3)	(4)	(5)

83b. How often do you eat extra snacks at bedtime to prevent hypoglycemia?

Never	Less than half the time	About half the time	More than half the time	Almost Always
(1)	(2)	(3)	(4)	(5)

83c. How often do you eat something as soon as you feel the first sign of low blood sugar?

Never	Less than half the time	About half the time	More than half the time	Almost Always
(1)	(2)	(3)	(4)	(5)

84. Over the past year I have followed my prescribed meal plan.

Never	(1)
Very infrequently (less than 10% of the time)	(2)
Infrequently (10-44% of the time)	(3)
About half of the time (45-55% of the time)	(4)
More than half the time (56-90% of the time)	(5)
Most of the time (71-90% of the time)	(6)
Almost all of the time (>90% of the time)	(7)
Always	(8)

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE. PLEASE REVIEW IT TO SEE THAT ALL QUESTIONS HAVE BEEN ANSWERED BEFORE MAILING.

DIATETES CONTROL AND COMPLICATIONS TRIAL

Special Forms Inventory

CLINIC NUMBER:

DATE OF MAILING:

THE FOLLOWING FORM(S) ARE BEING MAILED DURING WEEK #_____.

FORM #	PATIENT ID #	FORM DATE

SIGNATURE

DIABETES CONTROL AND COMPLICATIONS TRIAL

GFR Worksheets

INSTRUCTIONS: These worksheets are to be completed and mailed to the CBL accompanying samples for the GFR procedure. Retain a copy for your records and send a copy to the Coordinating Center. Record all times to the nearest minute and volumes to the nearest ml.

A. IDENTIFYING INFORMATION

1. Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date of Test: Month __ __ Day __ __ Year __ __
5. Accession Number: GFR - __ __ __ __ __ __
6. Visit: (00 if in conjunction with baseline) __ __
7. Height __ __ __ . __ cm
8. Weight __ __ . __ kg
9. Began test in the (1) a.m. (2) p.m.
10. Blood glucose (mg/dl)
    a) Pre __ __ __
    b) Midpoint __ __ __
    After collection (0) (1) (2) (3) (4)

	No	Yes
11. Did water load begin at home?	(1)	(2)
12. Did patient comply with dietary restrictions?	(1)	(2)
13. Was the four-hour renal test done simultaneously with the GFR?	(1)	(2)
14. Was a quality control specimen collected?	(1)	(2)
15. Was the study completed?	(1)	(2)

If NO,

a) What was the last collection? (0) (1) (2) (3) (4)

b) Reason for termination: (CHECK MOST SIGNIFICANT REASON)

Hypoglycemia (1)

Vomiting (2)

Other; explain: (3)

Signature of person completing this form:

Certification Number __ __ - __ __

Time:	Background T-Pre	Minimum 30 <--min-->	Minimum 60 <--min-----> T-0	Minimum 20 <--min-->	T-1	Minimum 20 <--min-->	T-2	Minimum 20 <--min-->	T-3	Minimum 20 <--min-->	T-4	End Renal- 240 min. after T-Pre
		SSKI	125-I Iothalamate Injection									
URINE COLLECTION												
Label	U-Pre				U-1		U-2		U-3		U-4	RENAL
Specimen Handling	Void, record time, aliquot, discard			Void, record time (pool for 4-hour renal)	< -----		Void, record time, measure, aliquot, (pool for 4-hour renal)				----- >	Pool all urine, measure volume
Saved Specimens	Freeze 2 1.8 ml aliquots			No saved aliquot	< -----		Freeze 2 1.8 ml aliquots				----- >	Freeze 5 4.5 ml aliquots
Digital[1] Time (hr:min)	_ _:_ _	_ _:_ _	_ _:_ _	__:__	__:__		__:__		__:__		__:__	_ _:_ _
Elapsed Time (minutes)				__:__	__:__		__:__		__:__		__:__	_ _:_ _
Volume (ml)				_____	_____		_____		_____		_____	_____
Flow Rate[2] (ml/min)				_____	_____		_____		_____		_____	
BLOOD COLLECTION												
Label	BACKGROUND B-Pre			B-0	B-1		B-2		B-3		B-4	RENAL
Saved Specimen	Serum frozen- 2 1.8 ml tubes Renal- 2 equal aliquots)			Serum frozen- 2 1.8 ml tubes	<-----		Serum frozen--2 1.8 ml tubes				----- >	None
Time (hr:min)	_____			__:__	__:__		__:__		__:__		__:__	

[1] Record all times to the nearest minute. Digital time is based on the moment of completion of the urine collection.
[2] Urine flow rate at time T-0 must be at least 3 ml/min.

Diabetes Control and Complications Trial

DCCT Form 098.1
December 2, 1986

^{125}I-IOTHALAMATE RENAL FUNCTION STUDY (PROTOTYPE)
(Addendum Consent Form)

Diabetes Control and Complications Trial

Institution: _____

Principal Investigator: _____

1. I am presently enrolled in the Diabetes Control and Complications Trial (DCCT).

2. I clearly understand the purpose and nature of this clinical trial and have previously given my signed consent to participate in the DCCT.

3. I understand that the investigators of this trial have determined that a new and more accurate means of measuring my kidney function has become available. This is called the ^{125}I-Iothalamate Glomerular Filtration Rate Determination. The investigators of the DCCT have asked me to participate in this new study.

4. This test involves the subcutaneous injection (given just like insulin) of a compound that contains a small amount of radioactive iodine. This substance is absorbed and will be measured in my blood and urine (five times) over a period of several hours. This study will be done at the three year annual exam and at the end of the study. Follow-up studies will be done in conjunction with the four-hour timed urine collection.

5. ^{125}I-Iothalamate has been approved for intravenous injection in humans by the Food and Drug Administration (FDA). Subcutaneous injection has been approved for investigative purposes by the FDA. Subcutaneous injection has been extensively used in many centers in the United States. The administered dose contains less than 35 microcuries of radioactive iodine. The total amount of radiation is less than 1/100 of a chest x-ray.

6. The compound ^{125}I-Iothalamate is efficiently excreted by the kidneys and is not stored in the body. At the end of 24 hours, less than 1/10,000 of the dose will remain in the body.

7. The risks involved are those of having blood drawn and possible allergic reactions to the iodine or Iothalamate. I will be given a few drops of inorganic iodine prior to the test to block any uptake by the thyroid. If I am a woman, I should not be pregnant at the time of the test and will have a serum pregnancy test performed within 72 hours prior to the test.

8. I understand that the choice I have is to volunteer for this part of the DCCT or refuse this test. I can still participate in the DCCT even if I do not agree to have this test performed.

9. I understand that study information identifying me will remain confidential and will not be disclosed outside the hospital except with my written permission or as required by law. I understand that the information concerning my diabetes will be combined with that of many other volunteers and that I will not be personally identified in any publications or public documents which result from the study.

10. In the event of a research related injury to me, emergency medical treatment will be rendered. The cost for said treatment may be covered in my medical insurance, however, I understand that there is no federal, state or private program established to provide research subjects with compensation and medical treatment costs for injuries resulting from research procedures.

11. I have discussed this study with _____ and/or _____ and he/she has offered to answer any questions I may have concerning the procedures involved. I am aware that I should contact _____ at _____ and/or _____ at _____ if I have any questions regarding the research, research subjects' rights or my participation in the study and its outcome.

_____ _____
Signature of patient Date

_____ _____
Signature of parent of minor patient or legal guardian Date

_____
Print name if other than patient

_____ _____
Signature of witness Date

_____ _____
Signature of Principal Investigator Date

DIABETES CONTROL AND COMPLICATIONS TRIAL

Neurobehavioral Assessment (Partial Battery at Visit 12)

This form is to be completed by the staff of the DCCT Central Neurobehavioral Coding Unit to report the results of a neurobehavioral assessment at Visit 12.

A completed copy of the form is to be sent to the DCCT Coordinating Center.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date Tests Administered __ __ / __ __ / __ __ (Month / Day / Year)
5. Follow-up Visit Number __ __
6. Date Assessment Coded __ __ / __ __ / __ __ (Month / Day / Year)
7. Coder's ID __ __
8. Neurobehavioralist's Certification Number __ __ - __ __
9. Dominant hand — Right (1) Left (2) Ambidextrous (3)

B. LOGICAL MEMORY (FORM B)

1. Story A -- immediate recall: 0-23 __ __
2. Story B -- immediate recall: 0-23 __ __
3. Story A -- *delayed recall*: 0-23 __ __
4. Story B -- delayed recall: 0-23 __ __

C. DIGIT VIGILANCE (FORM 2)

1. Time to complete page 1: 0-400 __ __ __
2. Number of omission errors -- page 1: 0-112 __ __ __
3. Number of comission errors -- page 1: 0-99 __ __
4. Number of correct responses -- page 1: 0-112 __ __ __
5. Time to complete page 2: 0-400 __ __ __
6. Number of omission errors -- page 2: 0-104 __ __ __
7. Number of comission errors -- page 2: 0-99 __ __
8. Number of correct responses -- page 2: 0-104 __ __ __

D. VISUAL REPRODUCTIONS - IMMEDIATE RECALL (FORM B)

1. Design A -- total points: 0-4 __
2. Design A -- segmentation score: 0-5 __
3. Design B -- total points: 0-5 __
4. Design B -- segmentation score: 0-9 __
5. Design C1 -- total points: 0-4 __
6. Design C1 -- segmentation score: 0-7 __
7. Design C2 -- total points: 0-4 __
8. Design C2 -- segmentation score: 0-7 __

Patient ID _____

E. VISUAL REPRODUCTIONS - COPY (FORM B)

1. Design A -- total points: 0-4 __
2. Design A -- segmentation score: 0-5 __
3. Design B -- total points: 0-5 __
4. Design B -- segmentation score: 0-9 __
5. Design C1 -- total points: 0-4 __
6. Design C1 -- segmentation score: 0-7 __
7. Design C2 -- total points: 0-4 __
8. Design C2 -- segmentation score: 0-7 __

F. VISUAL REPRODUCTIONS - DELAY (FORM B)

1. Design A -- total points: 0-4 __
2. Design A -- segmentation score: 0-5 __
3. Hint given? No (1) Yes (2)
4. Design B -- total points: 0-5 __
5. Design B -- segmentation score: 0-9 __
6. Hint given? No (1) Yes (2)
7. Design C1 -- total points: 0-4 __
8. Design C1 -- segmentation score: 0-7 __
9. Hint given? No (1) Yes (2)
10. Design C2 -- total points: 0-4 __
11. Design C2 -- segmentation score: 0-7 __
12. Hint given? No (1) Yes (2)

G. SYMBOL-DIGIT LEARNING (FORM B)

1. Number correct -- trial 1: 0-7 __
2. Number correct -- trial 2: 0-7 __
3. Number correct -- trial 3: 0-7 __
4. Number correct -- trial 4: 0-7 __
5. Number correct -- delayed recall: 0-7 __

H. VERBAL FLUENCY

1. Number of "C" words in first quarter: 0-25 __ __
2. Number of "C" words in second quarter: 0-25 __ __
3. Number of "C" words in third quarter: 0-25 __ __
4. Number of "C" words in fourth quarter: 0-25 __ __
5. Number of illegitimate words: 0-25 __ __
6. Number of "F" words in first quarter: 0-25 __ __
7. Number of "F" words in second quarter: 0-25 __ __
8. Number of "F" words in third quarter: 0-25 __ __
9. Number of "F" words in fourth quarter: 0-25 __ __
10. Number of illegitimate words: 0-25 __ __
11. Number of "L" words in first quarter: 0-25 __ __
12. Number of "L" words in second quarter: 0-25 __ __
13. Number of "L" words in third quarter: 0-25 __ __
14. Number of "L" words in fourth quarter: 0-25 __ __
15. Number of illegitimate words: 0-25 __ __
16. Total number of words: 0-300 __ __ __

Patient ID _____

I. DIGIT SPAN (FORM B)

1. Number of points: 0-28 __ __
2. Number of digits repeated forward: 0-9 __
3. Number of digits repeated backward: 0-9 __
4. WAIS age-scaled score: 0-19 __ __
5. WISC-R age-scaled score: 0-19 __ __

J. GROOVED PEGBOARD - DOMINANT HAND

1. Time to insert pegs: 0-180 __ __ __
2. Time to remove pegs: 0-180 __ __ __
3. Number of pegs dropped: 0-25 __ __

K. GROOVED PEGBOARD - NON-DOMINANT HAND

1. Time to insert pegs: 0-180 __ __ __
2. Time to remove pegs: 0-180 __ __ __
3. Number of pegs dropped: 0-25 __ __

L. MINNESOTA PAPER FORMBOARD - (FORM 1)

1. Total correct: 0-32 __ __
2. Total time: 0-2000 __ __ __ __

M. DIGIT SYMBOL SUBSTITUTION TEST (FORM 2)

1. Total number of symbols completed within each 30 second interval:

30": 0-50 __ __
60": 0-60 __ __
90": 0-50 __ __
120": 0-50 __ __
150": 0-50 __ __
180": 0-50 __ __
210": 0-50 __ __
240": 0-50 __ __
270": 0-50 __ __
300": 0-50 __ __

M. DIGIT SYMBOL SUBSTITUTION TEST (FORM 2) (Continued)

2. Total time to complete grid: 0-360 __ __ __
3. Total number correct within first 90 seconds: 0-90 __ __
   a) Scaled score (for subjects 16 years old and over): 0-19 __ __
   b) Age-corrected scale score: 0-19 __ __
4. Incidental recall: 0-9 __

N. EMBEDDED FIGURES

1. Total number correct: 0-10 __ __
2. Mean latency for correct responses: 0-60 __ __

O. FINGER TAPPING - DOMINANT HAND

1. Number of trials administered: 0-10 __ __
2. Mean tapping rate per 10 second trial: 0-60.0 __ __ . __

P. FINGER TAPPING - NON-DOMINANT HAND

1. Number of trials administered: 0-10 __ __
2. Mean tapping rate per 10 second trial: 0-80.0 __ __ . __

Q. TRAILMAKING TEST (FORM A-1)

1. Trails A Time: 0-99 __ __
2. Trails A Errors: 0-9 __
3. Trails B Time: 0-300 __ __ __
4. Trails B Errors: 0-25 __ __

R. STAR DRAWING - DOMINANT HAND

1. Total time: 0-90 __ __
2. Number of errors: 0-90 __ __
3. Direction taken: Left (1) Right (2)

Patient ID _____

S. STAR DRAWING - NON-DOMINANT HAND

1. Total time: 0-90 — —

2. Number of errors: 0-80 — —

3. Direction taken:	Left (1)	Right (2)

T. SHORT-TERM MEMORY (FORM B)

1. Number of words correctly recalled after 5 seconds: 0-20 — —

2. Number of words correctly recalled after 15 seconds: 0-20 — —

3. Number of words correctly recalled after 30 seconds: 0-20 — —

4. Number of prior-trial intrusion errors: 0-60 — —

5. Number of intra-list intrusion errors: 0-60 — —

6. Number of extra-list intrusion errors: 0-60 — —

U. QUALITY OF NEUROBEHAVIORAL TESTING

1. How willing was this subject to try his or her best?

Very willing	(1)
Somewhat willing	(2)
Not too willing	(3)
Very unwilling	(4)

2. Overall, how much did distractions and interruptions affect the session?

Very much	(1)
Much	(2)
Somewhat	(3)
Little	(4)
Very little	(5)

3. To what extent do you feel the information obtained is accurate?

Completely	(1)
Mostly	(2)
Moderately	(3)
Somewhat	(4)
Not very	(5)

4. Quality Grade:

Satisfactory	(1)
Acceptable with minor problems	(2)
Unacceptable	(3)

DIABETES CONTROL AND COMPLICATIONS TRIAL

GFR Specimen Mailing List

This mailing list is used whenever the DCCT clinic ships a container of urine and blood specimens to the Central Biochemistry Laboratory (CBL) for the glomerular filtration rate (GFR) study. Urine and blood specimen accession numbers for GFR all have a prefix of "GFR." The four copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside insulated shipping container with specimens.
Mail to: DCCT Central Biochemistry Laboratory
ATTN: L227, Mayo 626-3645
University of Minnesota Hospital and Clinic
425 East River Road
Minneapolis, MN 55455-9980

(2) YELLOW -- Send separately to the address above.

(3) PINK -- Send to the Coordinating Center in the weekly forms mailing; include DCCT Form 097, GFR Worksheet.

(4) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Specimens Shipped on: __ __ | __ __ | __ __
Month | Day | Year

Specimens Collected From: __ __ | __ __ | __ __ through __ __ | __ __ | __ __
Month | Day | Year | Month | Day | Year

GFR SPECIMENS

ACCESSION NUMBER GFR	PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE SPECIMEN COLLECTED Month Day Year	COMMENTS
_ _ _ _ _ _	_ _ _ _ _ _	_ _ _	__ __ | __ __ | __ __	_____
_ _ _ _ _ _	_ _ _ _ _ _	_ _ _	__ __ | __ __ | __ __	_____
_ _ _ _ _ _	_ _ _ _ _ _	_ _ _	__ __ | __ __ | __ __	_____
_ _ _ _ _ _	_ _ _ _ _ _	_ _ _	__ __ | __ __ | __ __	_____
_ _ _ _ _ _	_ _ _ _ _ _	_ _ _	__ __ | __ __ | __ __	_____

Diabetes
Control and
Complications
Trial

September 15, 1987
DCCT Form 101.2
Page 1 of 1

DIABETES CONTROL AND COMPLICATIONS TRIAL

24-Hour Urine Specimen Mailing List

This mailing list is used whenever the DCCT clinic ships a container of frozen aliquots from 24-hour urine collections to the Central Biochemistry Laboratory (CBL) for determination of sodium, creatinine and urea nitrogen for estimation of dietary protein intake. These specimens have accession numbers with the prefix "24H." The four copies of this form are to be distributed as follows:

(1) WHITE -- Complete and place inside insulated shipping container with specimens.
Mail to: DCCT Central Biochemistry Laboratory
ATTN: L227, Mayo 626-3645
University of Minnesota Hospital and Clinic
425 East River Road
Minneapolis, MN 55455-9980

(2) YELLOW -- Send separately to the address above.

(3) PINK -- Send to the Coordinating Center in the weekly forms mailing.

(4) GOLDENROD -- Retain in clinic files.

Clinic Number: __ __

Specimens Shipped on: __ __ / __ __ / __ __ (Month / Day / Year)

Specimens Collected From: __ __ / __ __ / __ __ (Month / Day / Year) through __ __ / __ __ / __ __ (Month / Day / Year)

24-HOUR URINE SPECIMENS

ACCESSION NUMBER 24H	PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE COLLECTION ENDED Month	Day	Year	TIME COLLECTION STARTED	TIME COLLECTION ENDED NEXT DAY	TOTAL VOLUME COLLECTED (ml)	PATIENT'S WEIGHT (kg)
__ __ __ __ __ __	__ __ __ __ __ __	__ __ __	__ __	__ __	__ __	__ __:__ __	__ __:__ __	__ __ __ __	__ __ __.__
__ __ __ __ __ __	__ __ __ __ __ __	__ __ __	__ __	__ __	__ __	__ __:__ __	__ __:__ __	__ __ __ __	__ __ __.__
__ __ __ __ __ __	__ __ __ __ __ __	__ __ __	__ __	__ __	__ __	__ __:__ __	__ __:__ __	__ __ __ __	__ __ __.__
__ __ __ __ __ __	__ __ __ __ __ __	__ __ __	__ __	__ __	__ __	__ __:__ __	__ __:__ __	__ __ __ __	__ __ __.__

COMMENTS: ______________________________

DIABETES CONTROL AND COMPLICATIONS TRIAL

Neurobehavioral Assessment (Partial Battery at Visit 16)

This form is to be completed by the staff of the DCCT Central Neurobehavioral Coding Unit to report the results of a neurobehavioral assessment at Visit 16.

A completed copy of the form is to be sent to the DCCT Coordinating Center.

A. *IDENTIFYING INFORMATION*

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date Tests Administered __ __ __ __ __ __ (Month Day Year)
5. Follow-up Visit Number __ __
6. Date Assessment Coded __ __ __ __ __ __ (Month Day Year)
7. Coder's ID __ __
8. Neurobehavioralist's Certification Number __ __ - __ __
9. Dominant hand — Right (1) Left (2) Ambidextrous (3)

B. LOGICAL MEMORY (FORM C)

1. Story C-1 -- immediate recall: 0-23 __ __
2. Story C-2 -- immediate recall: 0-23 __ __
3. Story C-1 -- delayed recall: 0-23 __ __
4. Story C-2 -- delayed recall: 0-23 __ __

C. DIGIT VIGILANCE (FORM 2)

1. Time to complete page 1: 0-400 __ __ __
2. Number of omission errors -- page 1: 0-112 __ __ __
3. Number of comission errors -- page 1: 0-99 __ __
4. Number of correct responses -- page 1: 0-112 __ __ __
5. Time to complete page 2: 0-400 __ __ __
6. Number of omission errors -- page 2: 0-104 __ __ __
7. Number of comission errors -- page 2: 0-99 __ __
8. Number of correct responses -- page 2: 0-104 __ __ __

D. VISUAL REPRODUCTIONS - IMMEDIATE RECALL (FORM C)

1. Design A -- total points: 0-4 __
2. Design A -- segmentation score: 0-5 __
3. Design B -- total points: 0-5 __
4. Design B -- segmentation score: 0-9 __
5. Design C1 -- total points: 0-4 __
6. Design C1 -- segmentation score: 0-7 __
7. Design C2 -- total points: 0-4 __
8. Design C2 -- segmentation score: 0-7 __

Patient ID _____

E. VISUAL REPRODUCTIONS - COPY (FORM C)

1. Design A -- total points: 0-4 ___
2. Design A -- segmentation score: 0-5 ___
3. Design B -- total points: 0-5 ___
4. Design B -- segmentation score: 0-9 ___
5. Design C1 -- total points: 0-4 ___
6. Design C1 -- segmentation score: 0-7 ___
7. Design C2 -- total points: 0-4 ___
8. Design C2 -- segmentation score: 0-7 ___

F. VISUAL REPRODUCTIONS - DELAY (FORM C)

1. Design A -- total points: 0-4 ___
2. Design A -- segmentation score: 0-5 ___
3. Hint given? No (1) Yes (2)
4. Design B -- total points: 0-5 ___
5. Design B -- segmentation score: 0-9 ___
6. Hint given? No (1) Yes (2)
7. Design C1 -- total points: 0-4 ___
8. Design C1 -- segmentation score: 0-7 ___
9. Hint given? No (1) Yes (2)
10. Design C2 -- total points: 0-4 ___
11. Design C2 -- segmentation score: 0-7 ___
12. Hint given? No (1) Yes (2)

G. ASSOCIATIVE LEARNING (FORM A)

1. Number correct -- trial 1: 0-12 __ __
2. Number correct -- trial 2: 0-12 __ __
3. Number correct -- trial 3: 0-12 __ __
4. Number correct -- trial 4: 0-12 __ __
5. Number correct -- delayed recall: 0-12 __ __

H. VERBAL FLUENCY (FORM 3)

1. Number of "P" words in first quarter: 0-25 __ __
2. Number of "P" words in second quarter: 0-25 __ __
3. Number of "P" words in third quarter: 0-25 __ __
4. Number of "P" words in fourth quarter: 0-25 __ __
5. Number of illegitimate words: 0-25 __ __
6. Number of "R" words in first quarter: 0-25 __ __
7. Number of "R" words in second quarter: 0-25 __ __
8. Number of "R" words in third quarter: 0-25 __ __
9. Number of "R" words in fourth quarter: 0-25 __ __
10. Number of illegitimate words: 0-25 __ __
11. Number of "W" words in first quarter: 0-25 __ __
12. Number of "W" words in second quarter: 0-25 __ __
13. Number of "W" words in third quarter: 0-25 __ __
14. Number of "W" words in fourth quarter: 0-25 __ __
15. Number of illegitimate words: 0-25 __ __
16. Total number of words: 0-300 __ __ __

Patient ID _____

I. DIGIT SPAN (FORM C)

1. Number of points: 0-28 __
2. Number of digits repeated forward: 0-9 _
3. Number of digits repeated backward: 0-9 _
4. WAIS age-scaled score: 0-19 __
5. WISC-R age-scaled score: 0-19 __

J. GROOVED PEGBOARD - DOMINANT HAND

1. Time to insert pegs: 0-180 ___
2. Time to remove pegs: 0-180 ___
3. Number of pegs dropped: 0-25 __

K. GROOVED PEGBOARD - NON-DOMINANT HAND

1. Time to insert pegs: 0-180 ___
2. Time to remove pegs: 0-180 ___
3. Number of pegs dropped: 0-25 __

L. STROOP COLOR/WORD INTERFERENCE TEST

1. Words: Total Correct in 45 Sec (0-150) ___
2. Words: Total Time to Complete Page (0-900) ___
3. Words: Total Number of Errors on Page (0-90) __
1. Colors: Total Correct in 45 Sec (0-150) ___
2. Colors: Total Time to Complete Page (0-900) ___
3. Colors: Total Number of Errors on Page (0-90) __
1. Ink: Total Correct in 45 Sec (0-150) ___
2. Ink: Total Time to Complete Page (0-900) ___
3. Ink: Total Number of Errors on Page (0-90) __

M. DIGIT SYMBOL SUBSTITUTION TEST (FORM A-2)

1. Total number of symbols completed within each 30 second interval:

30": 0-50 __
60": 0-50 __
90": 0-50 __
120": 0-50 __
150": 0-50 __
180": 0-50 __
210": 0-50 __
240": 0-50 __
270": 0-50 __
300": 0-50 __

2. Total time to complete grid: 0-380 ___
3. Total number correct within first 90 seconds: 0-90 __
   a) Scaled score (for subjects 16 years old and over): 0-19 __
   b) Age-corrected scale score: 0-19 __
4. Incidental recall: 0-9 _

N. EMBEDDED FIGURES (FORM 2)

1. Total number correct: 0-10 __
2. Mean latency for correct responses: 0-60 __

O. FINGER TAPPING - DOMINANT HAND

1. Number of trials administered: 0-10 __
2. Mean tapping rate per 10 second trial: 0-80.0 __.__

P. FINGER TAPPING - NON-DOMINANT HAND

1. Number of trials administered: 0-10 __
2. Mean tapping rate per 10 second trial: 0-80.0 __.__

Patient ID _____

Q. TRAILMAKING TEST (FORM A-2)

1. Trails A Time: 0-99 — —
2. Trails A Errors: 0-9 —
3. Trails B Time: 0-300 — — —
4. Trails B Errors: 0-25 — —

R. STAR DRAWING - DOMINANT HAND

1. Total time: 0-90 — —
2. Number of errors: 0-90 — —
3. Direction taken: Left (1) Right (2)

S. STAR DRAWING - NON-DOMINANT HAND

1. Total time: 0-90 — —
2. Number of errors: 0-90 — —
3. Direction taken: Left (1) Right (2)

T. SHORT-TERM MEMORY (FORM C)

1. Number of words correctly recalled after 5 seconds: 0-20 — —
2. Number of words correctly recalled after 15 seconds: 0-20 — —
3. Number of words correctly recalled after 30 seconds: 0-20 — —
4. Number of prior-trial intrusion errors: 0-60 — —
5. Number of intra-list intrusion errors: 0-60 — —
6. Number of extra-list intrusion errors: 0-60 — —

U. QUALITY OF NEUROBEHAVIORAL TESTING

1. How willing was this subject to try his or her best?
   - Very willing (1)
   - Somewhat willing (2)
   - Not too willing (3)
   - Very unwilling (4)
2. Overall, how much did distractions and interruptions affect the session?
   - Very much (1)
   - Much (2)
   - Somewhat (3)
   - Little (4)
   - Very little (5)
3. To what extent do you feel the information obtained is accurate?
   - Completely (1)
   - Mostly (2)
   - Moderately (3)
   - Somewhat (4)
   - Not very (5)
4. Quality Grade:
   - Satisfactory (1)
   - Acceptable with minor problems (2)
   - Unacceptable (3)

Diabetes Control and Complications Trial

DCCT Form 105.1
March 30, 1989

Date Completed ___/___/___

DCCT RESOURCE UPDATE

This form is used to record information on non-DCCT health care providers who are seeing DCCT patients, or have been identified because they might be willing to see DCCT patients. If the provider is not following any DCCT patient, fill out as much information as possible. File one form for each local specialist in #ic. (i.e., one each for diabetes and ophthalmic).

1. Physician (health care provider) information:

   a. Name _____ (LAST) _____ (FIRST) _____ (MIDDLE)

   b. Professional degree _____ (M.D., R.N., etc.)

   c. Type of practice (choose 1):

      (1) Diabetes
      (2) Internal Medicine
      (3) Family Practice
      (4) CRC
      (5) Ophthalmic
      (6) Other _____

   d. Address _____ (STREET and SUITE)

      _____ (CITY) _____ (STATE) _____ (ZIP CODE)

   e. Phone ____ (AREA CODE) _____ (NUMBER)

   f. Has this person indicated that he/she might agree to see (any or additional) DCCT patients? (1) NO (2) YES

   g. Evaluation of this person's performance of DCCT protocol to date:

      (1) Excellent (2) Good/Acceptable (3) Unsatisfactory

   h. Do you recommend for additional DCCT patients? (choose one):

      (1) NO (2) YES (3) STD ONLY (4) EXP ONLY

   i. Referring primary DCCT physician (contact for details):

      _____ (LAST) _____ (FIRST) ____ (MIDDLE) ____ (CLINIC)

2. Patient Information

   a. ID # __ __ __ __ __

   b. Initials __ __ __

   c. Clinic # __ __

   d. Treatment Group (1) Standard (2) Experimental

   e. Current Therapy (1) < 3 Injections (2) MDI (3) CSII

   f. Address _____ (CITY) _____ (STATE) _____ (ZIP)

   g. Relocation (1) Permanent (2) Temporary

   h. Frequency of local visits (choose 1):

      (1) weekly or monthly
      (2) quarterly
      (3) every 6 months
      (4) annual
      (5) other

   i. Patient is making local visits for (choose 1):

      (1) diabetes management
      (2) endpoint collection (i.e., blood draw, QV, etc.)
      (3) management and endpoint collection
      (4) photography/ophthalmic
      (5) other

   j. Financial arrangements with local provider:

      _____

   k. Was provider willing to make concessions on charges?

      (1) NO (2) YES

   l. Dates of visits to non-DCCT clinic:

      First Visit: MONTH DAY YEAR Final Visit: MONTH DAY YEAR

      If you are unable to provide the final visit date, update this form with CoC if and when the patient stops seeing this provider.

   n. Reimbursement arrangements to patient for travel to local clinic:

      _____

DIABETES CONTROL AND COMPLICATIONS TRIAL
Details of Pregnancy and Outcome

This form is to be completed at the termination of each pregnancy occurring during the DCCT. The original of this form is to be sent to the Coordinating Center in the special Morbidity/Mortality Classification Committee mailings and a copy kept in the clinic files. The sources needed to complete this form will include the patient, obstetrical notes/interview, delivery notes, neonatal notes and/or interview with the neonatologist in charge of the infant.

A. IDENTIFYING INFORMATION

1. Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. Date Form Completed: __ __/__ __/__ __ (Month Day Year)
5. Specify date of occurence or recognition of outcome: __ __/__ __/__ __ (Month Day Year)
   Or if date uncertain (1)
6. Specify date DCCT clinic learned of outcome: __ __/__ __/__ __

B. PRIOR PREGNANCY HISTORY:

(Enter number, use leading zeros.)

1. How many prior pregnancies have you had, including live births, miscarriages, abortions, and stillbirths? __ __
2. How many pregnancies resulted in induced abortion? __ __
3. How many pregnancies resulted in miscarrage? __ __
4. How many pregnancies resulted in stillbirths? __ __
5. How many pregnancies resulted in live births? __ __
6. How many neonatal deaths occurred? __ __
7. How many children are still living? __ __
8. How many pregnancies delivered preterm (< 37 weeks)? __ __
9. How many pregnancies delivered postterm (> 42 weeks)? __ __

C. EVENTS DURING THIS CURRENT PREGNANCY

1. Indicate all the drugs taken during this pregnancy:

Aspirin	(1)	Lithium	(1)
Marijuana	(1)	Isotretinoin (Accutane)	(1)
Cocaine	(1)	Tetracycline	(1)
Methadone/heroin	(1)	Estrogens/Progestins (including oral contraceptives)	(1)
Anticoagulants	(1)		
Antiepileptics	(1)		

Other: _____ (1)

2. Have you had any infection or illness during this pregnancy? No (1) Yes (2) Unknown (3)

If yes, specify type of infection or illness:

a) _____ Week __ __

b) _____ Week __ __

3. Did preterm labor occur? No (1) Yes (2)

If yes:
a) At what week of gestation? ___ ___

b) What medications were used to stop labor? ___ ___
(Check all that apply.)

Ritodrine	(1)
Magnesium	(1)
Terbutaline	(1)
Other _____	(1)

c) Was therapy successful in stopping labor? No (1) Yes (2)

4. Did preeclampsia/eclampsia occur during pregnancy?

	No	Yes	Week of Onset
a) Preeclampsia	(1)	(2)	___ ___
If yes, answer b) and c), always answer d)			
b) Check criteria used:			
1. Protein (> 0.5 g)	(1)	(2)	___ ___
2. Hypertension (≥ 140 or ≥ 90)	(1)	(2)	___ ___
3. Edema	(1)	(2)	___ ___
4. Hyperreflexia	(1)	(2)	___ ___
5. Change in renal function	(1)	(2)	___ ___
6. Cerebral symptoms (lethargy, headache)	(1)	(2)	___ ___
7. Other:_____	(1)	(2)	___ ___

c) Treatment

	No	Yes	Week Of Onset
1. Delivery	(1)	(2)	___ ___
2. $MgSO_4$	(1)	(2)	___ __
3. Antihypertensive Rx	(1)	(2)	___ ___
4. Other Specify _____	(1)	(2)	___ ___
d) Eclampsia	(1)	(2)	___ ___

5. Did any of the following other maternal complications occur during this pregnancy? No (1) Yes (2)

If yes, check complications:			Week of Onset
a) Spotting	(1)	(2)	___ ___
b) Bleeding	(1)	(2)	___ ___
c) Fever	(1)	(2)	___ ___
d) Amniotic fluid leakage	(1)	(2)	___ ___
e) Placental abruption	(1)	(2)	___ ___
f) Anemia (HCT <= 30%)	(1)	(2)	___ ___
g) Thrombophlebitis	(1)	(2)	___ ___
h) Hydramnios	(1)	(2)	___ ___
i) Pulmonary Embolism	(1)	(2)	___ ___
j) D & C	(1)	(2)	___ ___
k) Placenta Previa	(1)	(2)	___ ___
l) Premature rupture of membranes	(1)	(2)	___ ___

Patient ID _____

D. PREGNANCY TERMINATION (Go to Section E if pregnancy resulted in birth)

1. Date of termination __ __/__ __/__ __ (Month/Day/Year)

2. Gestational age __ __ Weeks

3. Date of start of last menstrual period (LMP) __ __/__ __/__ __ (Month/Day/Year)

4. Reason for termination (check one)

a) Ectopic pregnancy (1)

b) Spontaneous abortion (2)

Induced abortion

c) (i) non-medical (3)

c) (ii) medical (4)

specify: _____

_____

d) Intrauterine Death (5)

E. DELIVERY INFORMATION

1. Date of birth __ __/__ __/__ __ (Month/Day/Year)

2. Date of start of LMP __ __/__ __/__ __ (Month/Day/Year)

3. Gestational age (Weeks)

By dates from LMP __ __

By ultrasound __ __

4. Type of Delivery (check one)

a) Spontaneous vaginal (1)

b) Induced at term (2)

c) Induced at preterm (3)

d) C/S without labor (Cesarean section) (4)

e) C/S after labor trial (5)

5. If induced, specify why _____

_____

6. If C/S, specify indication

	No	Yes
a) Repeat	(1)	(2)
b) Failure of progression	(1)	(2)
c) Cephalo/pelvic disproportion	(1)	(2)
d) Fetal distress	(1)	(2)
e) Preeclampsia	(1)	(2)
f) Eclampsia	(1)	(2)
g) Obstetrician election	(1)	(2)
h) Patient choice	(1)	(2)
i) Other Specify _____	(1)	(2)

7. Postpartum Infection (requiring antibiotics prior to discharge) or other illness

(Check all that apply)

		No	Yes
a)	Endometritis	(1)	(2)
b)	Other pelvic infection	(1)	(2)
c)	Urinary infection	(1)	(2)
d)	Wound infection	(1)	(2)
e)	Pulmonary infection	(1)	(2)
f)	Chorioamnionitis during labor	(1)	(2)
g)	Other maternal illness	(1)	(2)

Specify: _____

_____

F. INFANT INFORMATION

1. Number of infants (If more than one infant, complete additional sections F, G and H for each infant.

One (1) Two (2) Three (3) > Three (4)

2. Infants gender

Male (1)
Female (2)
Ambiguous (3)

On Nursery Admission:

3. Length (cm) ___ ___.___

4. Birthweight (grams) ___ ___ ___ ___

5. Head Circumference (cm) ___ ___.___

6. Chest Circumference (cm) ___ ___.___

7. APGAR Scores

a) 1 minute ___ ___

b) 5 minute ___ ___

8. Birth place was outside the study center facilities? No (1) Yes (2)

9. Highest Level of Care Required

Well Baby Nursery (1)
Other for < 12 hours (2)
Other for >= 12 hours (3)

10. Lowest venous glucose value during first 6 hours of life ___ ___ ___ mg/dl

11. Father's age at time of birth (If unknown enter 99) ___ ___

12. Is father IDDM? No (1) Yes (2) Unknown (3)

G. NEONATAL COURSE (72 hours after birth)

1. Neonatal Complications

		No	Yes
a)	Hypoglycemia (< 40 mg/dl)	(1)	(2)
b)	Respiratory Distress	(1)	(2)
c)	Bilirubin	(1)	(2)

If yes, give highest measured level: (mg/dl) ___ ___.___

Indicate infants age when drawn (hrs) ___ ___

d) Hypocalcemia (calcium < 7.0 mg/dl) (1) (2)

e) Most abnormal state of consciousness

Normal (1)
Hyperalert (2)
Lethargic (3)
Comatose (4)
Unknown (5)

f) Other (list): (1) (2)

_____

_____

_____

Patient ID _____

g) Birth Trauma (1) (2)

1) ERB's paralysis (1) (2)

h) Proven infection (1) (2)

1) Specify site _____

	No	Yes
i) Death	(1)	(2)

2) Date of Death __ __/__ __/__ __
Month Day Year

3) Cause of Death_____

4) ICDA CODE_____

H. NEWBORN EXAMINATION FOR CONGENITAL MALFORMATION

Date of examination (within 3 days of birth):

__ __/__ __/__ __
Month Day Year

	No	Yes
1. Are any congenital malformations present?	(1)	(2)

If yes, specify:

_____

_____

_____

Name of person completing this form:

_____

Certification No.

__ __ - __ __

Control and Complications Trial

(Fold here)

FAMILY STUDIES

April 28, 1990
DCCT Form 108.1

FORM 1: PARENTS AND SIBLINGS OF DCCT PATIENT

A. IDENTIFYING INFORMATION

1. Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. Form Date: ____/__ __/__ __ (Month / Day / Year)

(Fold here)

Please provide information for members of immediate family of the immediate family of the DCCT patient, listing the patient as a "child" below. Does the DCCT patient have diabetic offspring? (Y N) If yes, please complete Form 2, showing the DCCT patient as father or mother.

NAME	CODE	SEX	SAME BIOLOG-ICAL PARENTS?	DATE OF BIRTH Mo/Day/Yr	LIVING? No(1) Yes(2)	CURRENT AGE OR AGE AT DEATH Years	DIABETIC? No(1)Yes(2)	AGE DIABETES DIAGNOSED? Years	USE INSULIN? No(1)Yes(2)	DAYTIME PHONE NO. (w/AREA CODE) (Or unknown)
FATHER:	FA	M	X							
MOTHER:	MO	F	X							
DCCT PATIENT:	PT									
OLDEST SIBLING:	S1									
NEXT SIBLING:	S2									
NEXT SIBLING:	S3									

Name of person completing this form: _____

Certification No. __ __ - __ __

(Fold here)

FORM 2; SPOUSE/OFFSPRING OF DCCT PT (DO NOT USE IF NO AFFECTED CHILDREN)

A. IDENTIFYING INFORMATION

1. Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. Form Date: ____/__ __/__ __ (Month / Day / Year)

(Fold here)

Please provide information for spouse and offspring of the DCCT patient, listing the patient as a parent. For father or mother, as appropriate, indicate PT (patient), and WI (wife) or HU (husband) for other parent.

NAME	CODE	SEX	SAME BIOLOG-ICAL PARENTS?	DATE OF BIRTH Mo/Day/Yr	LIVING? No(1) Yes(2)	CURRENT AGE OR AGE AT DEATH Years	DIABETIC? No(1)Yes(2)	IF DIABETIC: AGE DIABETES DIAGNOSED? Years	IF DIABETIC: USE INSULIN? No(1)Yes(2)	IF DIABETIC: DAYTIME PHONE NO. (w/AREA CODE) (Or unknown)
FATHER:		M	X							
MOTHER:		F	X							
OLDEST CHILD:	C1									
NEXT CHILD:	C2									
NEXT CHILD	C3									
NEXT CHILD:	C4									

Name of person completing this form: _____ Certification No. __ __ - __ __

(Fold here)

Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Catecholamine Specimen Mailing List

This mailing list is used whenever the DCCT clinic ships a container of specimens to the Central Biochemistry Laboratory (CBL) for analysis of catecholamine content. A series of five (5) samples should be included. Four copies of this form are to be distributed as follows:

(1) ORIGINAL -- Complete and place inside insulated shipping containers with specimens

Mail to: DCCT Central Biochemistry Laboratory
ATTN: L275, Mayo 626-3645
University of Minnesota Hospital and Clinic
420 Delaware Street
Minneapolis, MN 55455

(2) COPY -- Send separately to the address above.

(3) COPY -- Send to the Coordinating Center in the weekly forms mailing.

(4) COPY -- Retain in clinic files.

Clinic Number: __ __

Specimens Shipped on: __ __ / __ __ / __ __ (Month / Day / Year)

Specimens Collected From: __ __ / __ __ / __ __ (Month / Day / Year) through __ __ / __ __ / __ __ (Month / Day / Year)

PLASMA FOR CATECHOLAMINES

PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE SPECIMENS DRAWN Month Day Year	PATIENT'S AGE	COMMENTS (Indicate if less than 5 samples are included.)
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	_____
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	_____
__ __ __ __ __	__ __ __	__ __/__ __/__ __	__ __	_____

DIABETES CONTROL AND COMPLICATIONS TRIAL

Report of Local Laboratory Standards for Nerve-Conduction Values

Instructions:

Use this form to report the "normal reference values" your laboratory uses to evaluate EMG test results. "Normal reference values" are defined as values such that any more extreme test result would be interpreted as unequivocal evidence of abnormal function.

Return this form to the Coordinating Center in the addressed pre-stamped envelope.

A. IDENTIFYING INFORMATION

1. Clinic Number: |__|__|
2. Today's date: |__ __|__ __|__ __|
3. Name of person filling out form:

_____

4. Certification number: __ __ __ __

B. SUMMARY OF NORMAL REFERENCE VALUES

1. Median nerve motor conduction:

Wrist-abd. poll. brev. muscle

a) Latency (msec) |__|__|.|__|
b) Amplitude (mV) |__|__|.|__|

F-wave (wrist)

c) Latency (msec) |__|__|.|__|

Elbow-wrist

d) Conduction velocity (m/sec) |__|__|.|__|
e) Amplitude (mV) |__|__|.|__|

2. Median nerve sensory conduction:

Digit II-wrist

a) Conduction velocity (m/sec) |__|__|.|__|
b) Amplitude (uV) |__|__|.|__|

3. Peroneal nerve motor conduction:

Ankle-ext. dig. brev.

a) Latency (msec) |__|__|.|__|
b) Amplitude (mV) |__|__|.|__|

Below cap. fib.-ankle

c) Conduction velocity (m/sec) |__|__|.|__|
d) Amplitude (mV) |__|__|.|__|

F-wave (ankle)

e) Latency (msec) |__|__|.|__|

4. Sural sensory conduction:

Calf-lateral malleolus

a) Conduction velocity (m/sec) |__|__|.|__|
b) Amplitude (uV) |__|__|.|__|

DIABETES CONTROL AND COMPLICATIONS TRIAL

POSTURAL STUDY CATECHOLAMINE ANALYSIS RESULTS

Assays will be performed by Ada Simon, Ph.D., Cardiovascular Division, Biochemical Research Lab, University of Minnesota. Results will be reported to Jean Bucksa at the Central Biochemical Laboratory who in turn will complete this form for transmittal to the Central ANS Coding Unit (CACU) for interpretation. The CACU will provide the Coordinating Center with an interpretation of the results.

Dr. Pfeifer's address:

Michael Pfeifer, M.D.
Diabetes Research and Analysis Assoc., Inc.
101 Prosperous Place, Suite 361
Lexington, Kentucky 40509

---

1. Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient Initials: __ __ __
4. Patient Age: __ __

MONTH/ DAY/ YEAR

5. Collection Date: __ __/__ __/__ __
6. Arrival Date: __ __/__ __/__ __
7. Analysis Date: __ __/__ __/__ __
8. Forwarded to CACU: __ __/__ __/__ __

SAMPLE	COLLECTION TIMES	NOREPINEPHRINE (pg/ml)
1. RR Variation-Pre	_____	__ __ __ __
2. Postural-Pre	_____	__ __ __ __
3. Postural + 2 min	_____	__ __ __ __
4. Postural + 5 min	_____	__ __ __ __
5. Postural + 10 min	_____	__ __ __ __

COMMENTS: _____

_____

_____

Signature: _____

Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL

Weight Gain Questionnaire

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number ___ ___
2. Patient ID Number ___ ___ ___ ___ ___
3. Patient's Initials ___ ___ ___
4. Date ___ ___ ___ ___ ___ ___
   Month Day Year
5. Treatment Group: Experimental (1)
   Standard (2)

B. VOLUNTEER INFORMATION

1. a) Did you ever weigh more than you do now? No (1) Yes (2)

   If NO, skip to question 2.

   b) If YES, what was your highest weight? (Women do not count pregnancy weight.) ___ ___ ___ lbs. or ___ ___ . ___ kgs.

   c) Did this weight occur while in the DCCT? No (1) Yes (2)

2. Excluding the year your diabetes was diagnosed, what is your lowest adult weight (since age 18)? ___ ___ ___ lbs. or ___ ___ . ___ kgs.

3. a) At what age did you weigh this? ___ ___ yrs.

   b) In what year did you weigh this? 19 ___ ___

4. Have you ever been told by any member of your DCCT Clinic that you need to lose weight? No (1) Yes (2)

   If YES, by whom? (Check all that apply.)

   - nurse (1)
   - dietitian (1)
   - psychologist (1)
   - physician (1)
   - behavioral scientist (1)
   - other (1)

5. With whom do you live (Check all that apply.)

   - no one (1)
   - spouse/significant other (1)
   - child/children (1)
   - roommate (1)
   - siblings (1)
   - mother (1)
   - father (1)
   - other (1)

FOR THE FOLLOWING, USE THE PICTURES ON THE LAST PAGE OF THIS FORM

	PICTURE LETTER	NOT APPLICABLE OR UNKNOWN
6. Please choose the picture that best resembles your current weight.	___	
7. Please choose the picture that best resembles your biological mother's weight (best describes her weight for most of her adult life).	___	(1)
8. Please choose the picture that best resembles your biological father's weight (best describes his weight for most of his adult life).	___	(1)

9. *How many biological siblings do you have?* (If none, record 00 and go to Question 12.) __ __

   Don't know (1)

10. For each sibling, list the picture letter which best corresponds to their weight, and check for Male or Female.

		Male	Female			Male	Female
Sibling #1	___	(1)	(2)	Sibling # 7	___	(1)	(2)
Sibling #2	___	(1)	(2)	Sibling # 8	___	(1)	(2)
Sibling #3	___	(1)	(2)	Sibling # 9	___	(1)	(2)
Sibling #4	___	(1)	(2)	Sibling #10	___	(1)	(2)
Sibling #5	___	(1)	(2)	Sibling #11	___	(1)	(2)
Sibling #6	___	(1)	(2)	Sibling #12	___	(1)	(2)

	No	Yes
11. Do you have a twin?	(1)	(2)
If YES, does he/she have diabetes?	(1)	(2)
Which sibling # is your twin? ___		

	NOT APPLICABLE
12. Which picture best resembles the current weight of your spouse or significant other? ___	(1)

	No	Yes
13. Was your diabetes diagnosed after age 18?	(1)	(2)

If no, go to question 17

14. What was your weight six months before your diabetes was diagnosed? __ __ __ lbs.
    or __ __ . __ kgs.

    Don't remember (1)

15. Using the pictures, what picture best resembles your weight 6 months before your diabetes was diagnosed? PICTURE LETTER ___

FOR THE FOLLOWING TIME FRAMES PLEASE INDICATE HOW MUCH EFFORT YOU DID/DO PUT INTO CONTROLLING YOUR WEIGHT

16. a) Before your diabetes was diagnosed, were you trying to:

gain weight?	(1)
lose weight?	(2)
stay the same?	(3)

    b) How much effort did you put into this?

none	(1)
a little effort	(2)
some effort	(3)
a lot of effort	(4)
enormous effort	(5)
don't remember	(6)

17. a) After your diabetes was diagnosed, but before entering the DCCT, were you trying to:

gain weight?	(1)
lose weight?	(2)
stay the same?	(3)

    b) How much effort did you put into this?

none	(1)
a little effort	(2)
some effort	(3)
a lot of effort	(4)
enormous effort	(5)
don't remember	(6)

18. a) Since joining the DCCT, have you been trying to:

gain weight?	(1)
lose weight?	(2)
stay the same?	(3)

    b) How much effort do you put into this?

none	(1)
a little effort	(2)
some effort	(3)
a lot of effort	(4)
enormous effort	(5)

19. Since you have been in the DCCT, in what type(s) of diet(s) have you received instructions?
(Check all that apply.)

ADA exchange diet	(1)
point system	(1)
menus	(1)
equivalent calories	(1)
TAG (Total Available Glucose)	(1)
gram carbohydrate/carbohydrate counting	(1)
don't remember	(1)
other	(1)

specify: _____

20. In general how well do you understand your dietary recommendations?
(Check the description that best applies.)

not at all	(1)
very little	(2)
a little	(3)
fairly well	(4)
very well	(5)

21. How often do you follow your dietary recommendations?

never	(1)
rarely (1-20% of the time)	(2)
sometimes (21-40% of the time)	(3)
often (41-60% of the time)	(4)
very often (61-80% of the time)	(5)
almost always (81-100% of the time)	(6)

22. In general, how much emphasis has the DCCT staff placed on weight management?
(Check the one that best applies.)

none	(1)
a small amount	(2)
a moderate amount	(3)
a good amount	(4)
a great amount	(5)

23. a) Since joining the DCCT, have you had any major life events which affected your weight by at least 10 lbs.?
(See 23b below for events)

No	Yes
(1)	(2)

b) If yes, please check all items and whether weight was gained or lost or item does not apply.

	DOES NOT APPLY	GAIN	LOSS
job change	(1)	(2)	(3)
marriage	(1)	(2)	(3)
divorce	(1)	(2)	(3)
pregnancy	(1)	(2)	(3)
smoking cessation	(1)	(2)	(3)
death in family	(1)	(2)	(3)
other	(1)	(2)	(3)

specify: _____

24. In general, how much emphasis has the DCCT DIETITIAN placed on portion control (estimating correct portions)?

none	(1)
a small amount	(2)
a moderate amount	(3)
a good amount	(4)
a great amount	(5)

25. How often do YOU emphasize portion control?

not at all	(1)
a small amount	(2)
a moderate amount	(3)
a good amount	(4)
a great amount	(5)

LISTED BELOW ARE SOME SITUATIONS WHEN YOU MIGHT NOT FOLLOW YOUR REGULAR FOOD PATTERN. USING THE SCALE A-E, INDICATE HOW OFTEN THESE SITUATIONS APPLY TO YOU. WRITE THE MATCHING LETTER ONLY; FILL IN ONE LETTER FOR EACH BLANK.

A	B	C	D	E
Almost Never or 1 time/mo	2-3 times per month	1-3 times per week	4-5 times per week	Daily

Example: If you usually stick to your meal plan when eating out, you might answer in the following manner:

I might not follow my regular food plan because:

I am eating away from home. A

26. I might not follow my regular food plan because:

I am still hungry.	___
I feel like my blood sugar is low.	___
I crave a food I should not eat.	___
It is a special occasion.	___
I am worried, tired, or under stress.	___
I am too busy to follow a diet.	___
I do not understand all or part of my diet.	___
I am "burned out"; tired of following a diet.	___
My work is especially hectic.	___
Other:	___

specify: _____

27. How often do you discuss weight control with the dietitian? (Check the one that best applies.)

More than once per month	(1)
Monthly	(2)
Every 2 Months	(3)
Every 3 Months	(4)
Every 6 Months	(5)
Once a year	(6)
Never	(7)

28. If you receive ongoing counseling for weight control, who provides the counseling? (Check all that apply.)

DCCT dietitian	(1)
DCCT nurse	(1)
DCCT physician	(1)
DCCT psychologist	(1)
Other:	(1)

specify (including non-DCCT personnel:

_____

Not Applicable, I do not receive follow-up for weight control (1)

29. If you eat at least one meal per day with family, or significant others, how often do they help you with your meal plan?

not at all	(1)
every now and then (less than once a week)	(2)
often (more than once a week)	(3)
most times (almost every day)	(4)
not applicable (do not eat meals with friends or significant others)	(5)

30. Were you taught the amounts and types of sugar-containing foods or glucose replacement (tabs, gel) to take for low blood sugar?

No	Yes	Don't Remember
(1)	(2)	(3)

31. When treating low blood sugar, how often do you think you eat more than you should?

never	(1)
rarely (1-20% of the time)	(2)
sometimes (21-40% of the time)	(3)
often (41 to 60% of the time)	(4)
very often (61 to 80% of the time)	(5)
almost always (81 to 100% of the time)	(6)

32. If you overeat to treat low blood sugar, describe the situations that apply; list the matching answer by each situation.

A	B	C	D	E	F
Never	Rarely (1-20% of time)	Sometimes (21-40% of time)	Often (41-60% of time)	Very Often (61-80% of time)	Almost Always (81-100% of time)

I overeat to treat low blood sugar because:

I am afraid that my blood sugar will not respond. __
I eat extra out of habit. __
A family member pressures me to overeat. __
I feel very hungry. __
I have had episodes of hypoglycemia that scared me and I want to avoid future reactions. __
It's a chance to eat something sweet, but I have trouble controlling the amount. __
I feel a loss of self-control when I have symptoms of hypoglycemia, and I eat until the symptoms go away or until I start to feel better.
Other __

specify: _____

33. How often do you walk briskly or do another form of more intense physical activity for more than 20 minutes? (Check number of times per week, and fill in number of months per year.)

never	(1)	
less than 1 time per week	(2)	___ months per year
1-3 times per week	(3)	___ months per year
4-6 times per week	(4)	___ months per year
7 times per week (daily)	(5)	___ months per year
more than 8 times per week	(6)	___ months per year

34. What percent of the time do you eat extra food when doing more intense physical activity? Circle one:

A	B	C	D	E	F
Never	Rarely (1-20% of time)	Sometimes (21-40% of time)	Often (41-60% of time)	Very Often (61-80% of time)	Almost Always (81-100% of time)

35. What percent of the time do you modify your insulin when doing more intense physical activity? Circle one:

A	B	C	D	E	F
Never	Rarely (1-20% of time)	Sometimes (21-40% of time)	Often (41-60% of time)	Very Often (61-80% of time)	Almost Always (81-100% of time)

36. How do you feel about your current weight? (Check the one that best applies.)

Very satisfied	(1)
Somewhat satisfied	(2)
Somewhat dissatisfied	(3)
Very dissatisfied	(4)

37. How often does your weight affect your daily activities?

Never	(1)
Rarely (1-20% of the time)	(2)
Sometimes (21-40% of the time)	(3)
Often (41 to 60% of the time)	(4)
Very often (61 to 80% of the time)	(5)
Almost always (81 to 100% of the time)	(6)

38. How great a threat do you feel your weight is to your health?

No threat	(1)
Somewhat of a threat	(2)
Very much a threat	(3)

39. Please rate your current motivation to lose weight:

Do not want to lose weight	(1)
Low	(2)
Moderate	(3)
High	(4)

40. How much do you want to weigh?

lbs. __ __ __

or kgs. __ __.__

41. BELOW IS A LIST OF THINGS PEOPLE MIGHT DO OR SAY TO SOMEONE WHO IS TRYING TO IMPROVE HIS OR HER EATING HABITS. PLEASE READ AND GIVE AN ANSWER TO EVERY QUESTION. PLEASE RATE EACH QUESTION TWICE. UNDER HOUSEHOLD, RATE HOW OFTEN ANYONE LIVING IN YOUR HOUSEHOLD HAS SAID OR DONE THE ITEM DESCRIBED, DURING THE PAST THREE MONTHS.UNDER FRIENDS/CO-WORKERS, RATE HOW OFTEN YOUR FRIENDS, ACQUAINTANCES OR CO-WORKERS, NOT LIVING IN YOUR HOUSEHOLD, HAVE SAID OR DONE THE ITEM DESCRIBED, DURING THE LAST THREE MONTHS.

PLEASE WRITE ONE NUMBER FROM THE FOLLOWING RATING SCALE:

never	= 1
rarely (1-20% of the time)	= 2
sometimes (21-40% of the time)	= 3
often (41-60% of the time)	= 4
very often (61-80% of the time)	= 5
almost always (81-100% of the time)	= 6

EXAMPLE: Made fun of food I eat:

household 2
friends/co-workers 5

This would be the answer if people in your household rarely make fun of the foods you eat but your friends very often make fun of the foods you eat.

a) Encouraged me not to eat "unhealthy foods" (cake, chips) when I am tempted to do so.

household __
friends/co-workers __

b) Asked me how I'm doing with my meal plan.

household __
friends/co-workers __

c) Reminded me to eat my meal plan.

household __
friends/co-workers __

d) Complimented me on following my meal plan when there are foods present that I'm trying not to eat.

household __
friends/co-workers __

e) Commented if I went off my meal plan.

household __
friends/co-workers __

f) Ate foods in front of me that I'm trying not to eat.

household __
friends/co-workers __

g) Refused to eat the same foods I eat.

household __
friends/co-workers __

h) Brought home foods I'm trying not to eat.

household __
friends/co-workers __

i) Got angry when I encourage them to eat the foods I eat.

household __
friends/co-workers __

j) Offered me food I'm trying not to eat.

household __
friends/co-workers __

42. Using the following rating scale, please indicate how often you may have used the following strategies to control or lose weight, since joining the DCCT.

1	2	3	4	5
Never	Rarely	Sometimes	Often	Very Often

a) Eat less and decrease your insulin __

b) Eat the same as always and decrease your insulin __

c) Increase your activity __

d) Other, specify: _____ __

_____

43. If you feel you are overweight, check the FOUR most important items in terms of how much you think each contributes to your weight:

don't feel I am overweight	( )
heredity	( )
low level of physical activity	( )
eating too frequently	( )
eating larger amounts of food than necessary	( )
eating wrong kinds of food	( )
eating to prevent reactions	( )
over treating reactions	( )
insulin therapy	( )
glandular or metabolic disorder	( )
other	( )

specify: _____

44. BELOW IS A LIST OF THINGS PEOPLE MIGHT DO WHILE TRYING TO CHANGE THEIR EATING HABITS. WHETHER YOU ARE TRYING TO CHANGE YOUR EATING HABITS OR NOT, PLEASE RATE HOW CONFIDENT YOU ARE THAT YOU COULD REALLY MOTIVATE YOURSELF TO DO THINGS LIKE THESE CONSISTENTLY, FOR AT LEAST SIX MONTHS.

Please circle one for each question.

EXAMPLE:

A) Eat unsalted, unbuttered popcorn.

I know I cannot		Maybe I can		I know I can	Does not apply
1	2	3	[4]	5	6

This would be your answer if you thought you could do this, a stronger answer than 3 (maybe), but not as strong as 5 (I know I can).

a) Stick to your meal plan when you feel depressed, tired, bored or tense.

I know I cannot		Maybe I can		I know I can	Does not apply
1	2	3	4	5	6

b) Stick to your meal plan when there are "problem" foods readily available at a party.

I know I cannot		Maybe I can		I know I can	Does not apply
1	2	3	4	5	6

c) Stick to your meal plan when the only snack close by is from a vending machine where both inappropriate and appropriate snacks are available.

I know I cannot		Maybe I can		I know I can	Does not apply
1	2	3	4	5	6

d) Stick to your meal plan when dining with friends or co-workers.

I know I cannot		Maybe I can		I know I can	Does not apply
1	2	3	4	5	6

e) Stick to your meal plan when you are alone and there is no one to watch you.

I know I cannot		Maybe I can		I know I can	Does not apply
1	2	3	4	5	6

45. a) How often do you feel overwhelmed by the demands of managing your diabetes?

never	(1)
rarely (1-20% of the time)	(2)
sometimes (21-40% of the time)	(3)
often (41-60% of the time)	(4)
very often (61-80% of the time)	(5)
almost always (81-100% of the time)	(6)

b) If you feel this way Sometimes, Often, Very Often or Almost Always does this make you less able to follow your meal plan? No (1) Yes (2)

46. a) During the past 12 months, have you consumed an average of at least one alcoholic beverage per week? No (1) Yes (2)

b) How many 12-ounce bottles of beer (excluding "light" beer) have you consumed during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL CHARACTERIZE A TYPICAL WEEK.) __ __ Bottles

c) How many 12-ounce bottles of "light" beer have you consumed during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL CHARACTERIZE A TYPICAL WEEK.) __ __ Bottles

d) How many 4-ounce glasses of wine have you consumed during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) __ __ Glasses

e) How many 1 1/2-ounce shots of straight hard liquor and 1 1/2-ounce mixed drinks have you consumed during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) __ __ Shots

FOR PATIENTS IN EXPERIMENTAL THERAPY ONLY

47. In general, how much emphasis has been placed on the DCCT HbAlc goal (6.05) by DCCT Staff? (Check the one that best applies.)

none	(1)
a small amount	(2)
a moderate amount	(3)
a good amount	(4)
a great amount	(5)

48. How often does your weight or weight gain affect your ability to achieve the DCCT HbAlc goal (6.05)? (Check the one that best applies.)

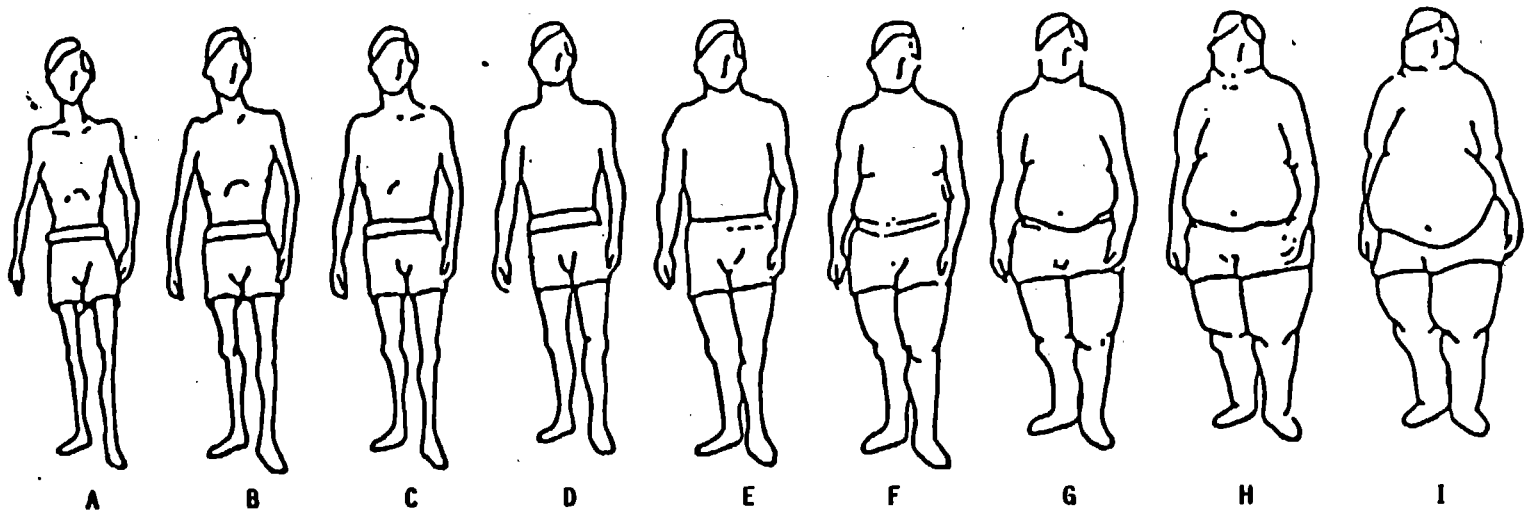
never	(1)
rarely (1-20% of the time)	(2)
sometimes (21-40% of the time)	(3)
often (41-60% of the time)	(4)
very often (61-80% of the time)	(5)
almost always (81-100% of the time)	(6)

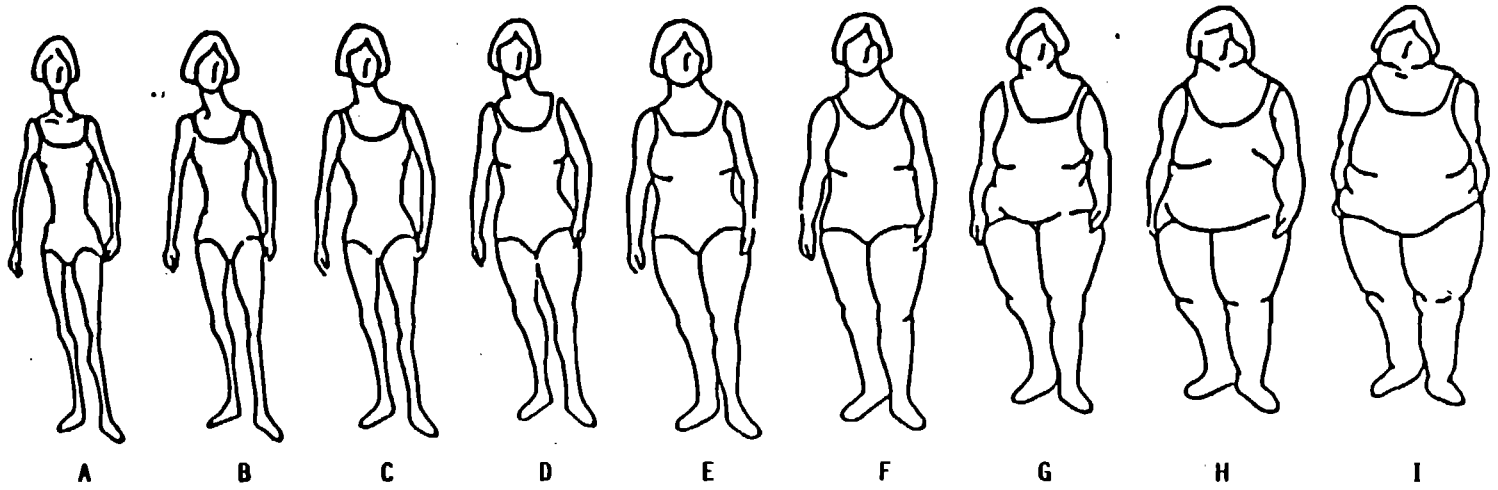
49. How often does your weight or weight gain affect your motivation to achieve the DCCT HbAlc goal (6.05)? (Check the one that best applies.)

never	(1)
rarely (1-20% of the time)	(2)
sometimes (21-40% of the time)	(3)
often (41-60% of the time)	(4)
very often (61-80% of the time)	(5)
almost always (81-100% of the time)	(6)

PLEASE TAKE A MOMENT TO REVIEW YOUR ANSWERS.

THANK YOU FOR YOUR TIME AND PARTICIPATION IN THIS STUDY





Danish Adoption Register from Stunkard, Albert J., Sorensen, Thorkald, and Schulsinger, Finis, "Use of the Danish Adoption Register for the Study of Obesity and Thinness", Genetics of Neurological and Psychiatric Disorders edited by Seymour S. Kety, Lewis P. Rowland, Richard L. Sidman, and Steven W. Matthysse, Raven Press, New York © 1983.

DCCT Diabetes Control and Complications Trial

DIABETES CONTROL AND COMPLICATIONS TRIAL
Family Study Checklist for Relatives with Diabetes

This checklist is to be completed by a DCCT staff person during the phone call to the relative of a DCCT volunteer. It is a guideline to be used to obtain information from relatives of DCCT patients on their status regarding complications of diabetes. The DCCT Relative Number should be the same as the number used for this person on DCCT Form 108.1. (i.e., DCCT Patient ID plus Relative Code: FA, MO, S1, S2, etc.) If a date or time is asked for and the month or number of months is unknown, use 00. Complete the entire checklist for each person called, regardless of the information you learn. Send in to the CoC when have completed all of your calls.

A. IDENTIFYING INFORMATION

1. Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. DCCT Relative Code: __ __
5. DCCT Relative Initials: __ __ __
6. DCCT Relative Birthdate: __ __/__ __/__ __ (Month/ Day /Year)
7. If DCCT Relative is less than 13 years old, who supplied information? MO (1) FA (2)
8. Gender: Male (1) Female (2)
9. Date of this contact: __ __/__ __/__ __ (Month/ Day /Year)

B. DIABETES HISTORY (brief):

1. What date was diabetes diagnosed: __ __/__ __ (Mo/Yr) Unknown (3)
2. Have you ever taken oral drugs for diabetes? NO (1) YES (2)
   a. If yes, are you currently taking oral drugs? (1) (2)
   b. If no, how long ago did you stop taking oral agents? __ __/__ __ (Mo/Yr) Unknown (3)
3. Are you currently taking insulin? (1) (2)
4. When did you begin permanent use of insulin: __ __/__ __ (Mo/Yr) Unknown (3)
5. What is your current total daily dose of insulin: __ __ units
6. Are you currently taking oral drugs and insulin? NO (1) YES (2)
7. If yes to #3 or #6, what is your current regimen of insulin (answer one):

   ≤ 2 shots (1) Pump (3)
   MDI (2) Other (4)

   Specify: _____
8. Have you ever been hospitalized for DKA? NO (1) YES (2) UNKNOWN (3)

C. EYE COMPLICATIONS

Have you ever been told by a health care professional that you have or had:

1. Any diabetes related eye problems? NO (1) YES (2) UNKNOWN (3)

   If yes, specify: _____

   Have you ever had:

2. Laser treatment? NO (1) YES (2) UNKNOWN (3)
3. Impairment of vision? (1) (2) (3)
4. Cataracts? (1) (2) (3)
5. Detached retina? (1) (2) (3)

D. KIDNEY COMPLICATIONS

Have you ever been told by a health care professional that you have or had:

	NO	YES	UNKNOWN
1. Diabetic kidney problems?	(1)	(2)	(3)
2. Protein or Albumin in the urine?	(1)	(2)	(3)
Have you ever had:			
3. Kidney transplant?	(1)	(2)	(3)
4. Kidney dialysis?	(1)	(2)	(2)

E. CARDIOVASCULAR COMPLICATIONS

Have you ever been told by a health care professional that you have or had:

	NO	YES	UNKNOWN
1. Any problems with heart or blood vessels?	(1)	(2)	(3)
If yes, specify: _____			
2. Abnormal EKG?	(1)	(2)	(3)
Have you ever had:			
3. Heart pains or angina?	(1)	(2)	(3)
4. Heart attack?	(1)	(2)	(3)
5. Coronary bypass surgery?	(1)	(2)	(2)
6. Stroke?	(1)	(2)	(3)
7. High blood pressure?	(1)	(2)	(3)
8. Drug treatment for high blood pressure?	(1)	(2)	(3)
a) If yes, are you currently receiving drug treatment?	(1)	(2)	(3)

F. PERIPHERAL VASCULAR COMPLICATIONS

Have you ever been told by a health care professional that you have or had:

	NO	YES	UNKNOWN
1. Any trouble with circulation in legs?	(1)	(2)	(3)
2. Foot ulcers:	(1)	(2)	(3)
3. Gangrene?	(1)	(2)	(3)
Have you ever had:			
4. Non-traumatic amputation?	(1)	(2)	(3)

G. OTHER MAJOR MEDICAL DISEASES

	NO	YES	UNKNOWN
1. Do you have any serious medical problems not mentioned yet?	(1)	(2)	(3)

Specify: _____

2. List any that might make participation difficult or unlikely, e.g., cancer:

_____

_____

_____

****
* CONTINUE TO NEXT PAGE *
****

H. WILLINGNESS TO PARTICIPATE

Explain that the next step is to schedule an appointment for the clinical assessments and discuss what time commitment would be necessary. Reiterate general information about the examination. Determine where is the nearest DCCT center to this person.

1. How far do you live from the nearest DCCT Center?

   _____ miles

2. Would you have transportation problems getting to a DCCT center? NO (1) YES (2)

   Specify: _____

3. Would you have to take vacation or sick time at work or time off from school to come to the center? (1) (2)

   If yes, is this a problem? (1) (2) UNKNOWN (3)

ANSWER IF THE PERSON HAS CHILDREN:

4. Would you have trouble getting someone to care for your children while you come to the center? (1) (2)

   Specify: _____

5. Will you agree to come to the DCCT clinic located in _____ for the examinations? NO (1) YES (2) UNCERTAIN (3)

6. What times are most convenient for you to come to the center?

   _____

   _____

   _____

7. What times will it be impossible for you to come to the center?

   _____

   _____

TO BE ANSWERED BY DCCT STAFF

8. Are you able to satisfy all restrictions in order to schedule the examinations for this person? NO (1) YES (2) UNCERTAIN (3)

   If not, specify: _____

   _____

   _____

Name of person completing this form: Certification No.

_____ __ __ - __ __

DIABETES CONTROL AND COMPLICATIONS TRIAL
Body Composition Measurements

A. IDENTIFYING INFORMATION

1. Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. Date Form Completed: __ __/__ __/__ __ (Month / Day / Year)
5. Visit number (nearest quarterly visit): __ __

B. MEASUREMENTS:

Measurements are taken twice and recorded. If the two measures are not within 0.5 cm (5.0 mm) of each other, two additional measurements are taken and all four measures are recorded.

1. Waist Circumference (cm) -- Natural

	NO	YES
Is lipohypertropy present?	(1)	(2)
Is lipoatrophy present?	(1)	(2)

a. First measurement: ___ ___ ___.___
b. Second measurement: ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 0.5 cm.

c. Third measurement: ___ ___ ___.___
d. Fourth measurement: ___ ___ ___.___

2. Iliac Waist Circumference (cm)

	NO	YES
Is lipohypertropy present?	(1)	(2)
Is lipoatrophy present?	(1)	(2)

a. First measurement: ___ ___ ___.___
b. Second measurement: ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 0.5 cm.

c. Third measurement: ___ ___ ___.___
d. Fourth measurement: ___ ___ ___.___

3. Hip Circumference (cm)

	NO	YES
Is lipohypertropy present?	(1)	(2)
Is lipoatrophy present?	(1)	(2)

a. First measurement: ___ ___ ___.___
b. Second measurement: ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 0.5 cm.

c. Third measurement: ___ ___ ___.___
d. Fourth measurement: ___ ___ ___.___

C. STATURE

1. Weight (kg)

a. First measurement: ___ ___ ___ ___.___

b. Second measurement: ___ ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 0.2 kilograms (200 gm).

c. Third measurement: ___ ___ ___ ___.___

d. Fourth measurement: ___ ___ ___ ___.___

2. Height (cm)

a. First measurement: ___ ___ ___.___

b. Second measurement: ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 1.0 cm (10.0 mm)

c. Third measurement: ___ ___ ___.___

d. Fourth measurement: ___ ___ ___.___

D. BIOELECTRIC IMPEDANCE ANALYSIS

Determine resistance and reactance, in ohms, at one electrode placement then move the electrodes attachments to another placement until ipsilateral and contralateral measurements are completed.

Record (c) and (d) if the first two resistance measurements are not within 2 ohms or the reactance measurements are not within 1 ohm.

	Resistance	Reactance
1. Right Arm to Right Leg		
a) first measurement	___ ___ ___	___ ___
b) second measurement	___ ___ ___	___ ___
If necessary,		
c) third measurement	___ ___ ___	___ ___
d) fourth measurement	___ ___ ___	___ ___
2. Right Arm to Left Leg		
a) first measurement	___ ___ ___	___ ___
b) second measurement	___ ___ ___	___ ___
If necessary,		
c) third measurement	___ ___ ___	___ ___
d) fourth measurement	___ ___ ___	___ ___
3. Left Arm to Left Leg		
a) first measurement	___ ___ ___	___ ___
b) second measurement	___ ___ ___	___ ___
If necessary,		
c) third measurement	___ ___ ___	___ ___
d) fourth measurement	___ ___ ___	___ ___
4. Left Arm to Right Leg		
a) first measurement	___ ___ ___	___ ___
b) second measurement	___ ___ ___	___ ___
If necessary,		
c) third measurement	___ ___ ___	___ ___
d) fourth measurement	___ ___ ___	___ ___

Name of person completing this form: _____

Certification No. ___ ___ - ___ ___

DIABETES CONTROL AND COMPLICATIONS TRIAL

Cost Project Questionnaire

Clinic No. __ __ Date of Completion: __ __/__ __/__ __

Person Completing Form:_____ Certifcation Number: __ __ - _ __

INSTRUCTIONS FOR COMPLETING THE COST PROJECT QUESTIONNAIRE

The purpose of this questionnaire is to collect cost data associated with the DCCT standard and experimental treatments. Cost-effectiveness and cost-benefit studies will be performed if the null hypothesis of no treatment group differences is rejected, i.e., if experimental treatment is shown to prevent or delay the development of retinopathy. Costs to be measured include the costs of the treatments and the costs of the adverse side effects of the treatments, and the costs associated with the medical management of complications. Costs related to the experiment itself, that is, costs related to data collection and surveillance of complications, will not be measured because they are not costs of treatment and would not be expected to differ for experimental and standard treatment group subjects.

A small working group has been meeting since February 1991 to define the general structure of the project and to outline the data needed to determine the costs specific to the standard and experimental treatment groups and the costs common to both. The group has reviewed existing data including national cost data, results of the DCCT treatment survey and data routinely reported to the Coordinating Center such as insulin dose, frequency of injections, frequency of blood glucose monitoring, and alerts. A questionnaire has been drafted to collect the necessary data that were not already available from existing sources.

One questionnaire should be submitted by each clinic. At each clinic, a copy of the questionnaire should be distributed to each member of the treatment team because the individual items are to be completed by the persons with the best knowledge of those items. For example, the dietitian should complete all questions related to dietary management, the behavioral scientist should complete all questions related to his/her interactions with the patients, and so on for all team members. The questionnaire should be discussed as soon as possible at a subsequent meeting of the full treatment team to ensure that everyone understands his/her role and to ensure these there is uniform understanding of the questions. Over the next 4 to 6 weeks each team member should then complete as many questions on the questionnaire as are relevant to him/her. In completing the questionnaire, special attention should be paid to "big ticket" cost items - that is - hospitalization and hospital days. To measure these, medical records should be reviewed and hospital days counted. Team members should also count and time various activities to refine their estimates. It is anticipated that team members will need to question patients about participant costs. The results of the questionnaires completed by individual team members will need to be compiled. Each center will need to discuss the results of the individual questionnaires at a team meeting to reconcile differences so that a single fully completed questionnaire can be submitted to the Coordinating Center by May 1, 1992.

Each clinic should work independently to complete the questionnaire. Information provided in the questionnaire should accurately reflect standard and experimental treatment as delivered at that clinic. There are no right or wrong answers to any of the questions. Your assistance in this is greatly appreciated.

IF YOU HAVE ANY QUESTIONS, YOU SHOULD CONTACT BILL HERMAN, M.D. AT (404) 488-5024

SEND COMPLETED QUESTIONNAIRE IN A SEPARATE MAILING TO THE COORDINATING CENTER ADDRESSED TO DOUGLAS ARNOLD.

I. STANDARD TREATMENT GROUP

A. INSULIN

1. During their participation in the DCCT, about what percent of standard patients were ever prescribed jet injectors? ___%
2. For standard patients prescribed jet injectors, what % of all doses are now administered by jet injector? ___%
3. During their participation in the DCCT, about what % of standard patients were ever prescribed insulin pens? ___%
4. For standard patients prescribed insulin pens, what % of all doses are now administered by insulin pens? ___%
5. What is the average frequency of pen needle changes? every ___ doses

B. GLUCAGON, ETC.

1. On average, how many glucagon kits are distribted per standard patient per year? ___.__ kits
2. On average, how many 6 tablet boxes of glucose tablets are distributed per standard patient per year? ___ boxes
3. On average, how many tubes of glucose gel are distributed per standard patient per year? ___ tubes

C. DIET

For standard patients, the MOO calls for the reinforcement of the dietary program every six months.

1. Every 6 months, how many minutes of dietitian time are required per standard patient (includes preparation time and time spent with the patient, including time at the annual visit, does not include time spent with the diet history)? ___ min.
2. What % of standard patients per year require additional dietary counseling for achievement of study goals? ___%
   a. What is the average number of additional visits with the dietitian to achieve study goals per standard patient not achieving study goals per year? ___ visits
   b. What is the average time per visit? ___ min.
   c. What is the average number of phone calls with the dietitian needed to achieve study goals per standard patient not achieving study goals per year? ___ calls
   d. What is the average time per call? ___ min.

D. SELF-MONITORING

1. Approximately what % of standard patients now use meters for blood glucose monitoring? ___%
2. On average, how many times per quarter do standard patients now test urine ketones? ___ times

E. CLINIC VISITS AND EDUCATION

1. Approxmiately how many educational materials are distributed per standard patient per year? ___ handouts ___ videos

F. QUARTERLY VISITS FOR STANDARD PATIENTS

(Includes amount of time spent on direct patient care including history, physical exam, review of monitoring results, education, goal setting, and clinical record keeping - does not include: time spent scheduling, dietitian time, time spent preparing forms and tubes, blood drawing, or time spent completing Form 021.7, sections A and C through H)

Minutes per quarterly visit per patient:

1. Physician: ___ min.
2. Nurse: ___ min.
3. Behavioral Scientist: ___ min.
4. Other (specify): _____ ___ min.

G. ANNUAL VISITS FOR STANDARD PATIENTS

(Includes amount of time spent on direct patient care including history, physical exam, review of monitoring results, education, goal setting, and clinical record keeping - does not include: time spent scheduling, dietitian time, time spent preparing forms and tubes, blood drawing, or time spent completing Form 003.3, sections A and G through L)

Minutes per annual visit per patient:

1. Physician: __ __ min.
2. Nurse: __ __ min.
3. Behavioral Scientist: __ __ min.
4. Other (specify):

_____ __ __ min.

H. LABORATORY

1. Plasma glucose:

a. What % of standard patients currently have plasma glucose levels done at local labs? __ __ __%

b. For patients having blood glucose levels done at local labs, how many times per year are they performed? __ __ times

I. ALERTS, ETC.

1. For standard patients with glycosylated hemoglobin alerts:

a. What is the average number of followup visits related to an alert (per alert) (do not count Quarterly or Annual Visits)? (Enter NA if not applicable, e.g.-no experience with glycosylated hemoglobin alerts) __ __ visits

b. What is the average staff time per visit?

1) For physician: __ __ min.
2) For nurse: __ __ min.
3) For dietitian: __ __ min.
4) For behavioral scientist: __ __ min.

c. Describe the frequency and time spent on calls related to a glycosylated hemoglobin alert (per alert) (includes no answer, busy, etc.)

	# of calls per alert:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

2. For standard patients who develop hypertension:

a. What is the average number of followup visits in the first year after the alert (do not count Quarterly or Annual Visits)? (Enter NA if not applicable, e.g. - no experience with standard patients developing hypertension) __ __ visits

b. What is the average staff time per visit?

1) For Physician: __ __ min.
2) For Nurse: __ __ min.
3) For Dietitian: __ __ min.
4) For Behavioral Scientist: __ __ min.
5) Other (specify):

_____ __ __ min.

c. Describe the frequency and time spent on calls related to hypertension in the first year after the alert (includes no answer, busy, etc.):

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

3. For standard patients who develop persistent hypercholesterolemia:

   a. What is the average number of followup visits related to an alert (per alert) (do not count Quarterly or Annual Visits)? (Enter NA if not applicable, e.g.- no experience with standard patients developing hypercholesterolemia): __ __ visits

   b. What is the average staff time per visit?

      1) For Physician: __ __ min.

      2) For Nurse: __ __ min.

      3) For Dietitian: __ __ min.

      4) For Behavioral Scientist: __ __ min.

      5) Other (specify): _____ __ __ min.

   c. Describe the frequency and time spent on calls related to a hypercholesterolemia alert (per alert) (includes no answer, busy, etc.):

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify): _____	__ __ calls	__ __ min.

4. For standard patients who develop severe hypoglycemia requiring assistance by another person:

   a. What is the average number of followup visits per episode? (Enter NA if not applicable, e.g.-no experience with standard patients developing severe hypoglycemia) __ __ visits

   b. What is the average staff time per visit?

      1) For Physician: __ __ min.

      2) For Nurse: __ __ min.

      3) For Dietitian: __ __ min.

      4) For Behavioral Scientist: __ __ min.

      5) Other (specify): _____ __ __ min.

   c. Describe the frequency and time spent on calls related to severe hypoglycemia per episode: (includes no answer, busy, etc.)

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify): _____	__ __ calls	__ __ min.

5. For standard patients who develop ketoacidosis:

   a. What is the average number of followup visits per episode? (Enter NA if not applicable, e.g.-no experience with standard patients developing keto-acidosis __ __ visits

   b. What is the average staff time per visit?

      1) For Physician: __ __ min.

      2) For Nurse: __ __ min.

      3) For Dietitian: __ __ min.

      4) For Behavioral Scientist: __ __ min.

      5) Other (specify): _____ __ __ min.

   c. Describe the frequency and time spent on calls related to ketoacidosis per episode: (includes no answer, busy, etc.)

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify): _____	__ __ calls	__ __ min.

6. For standard patients with eye alerts:

   a. What is the average number of ophthalmology follow-up visits per alert (excluding normally scheduled annual visits) (Enter NA if not applicable, e.g.-no experience with standard patients developing eye alerts) __ __ visits

   b. What is the average ophthalmologist time per visit? __ __ min.

   c. Describe the frequency and amount of time spent on calls related to an eye alert (per alert) (includes no no answer, busy, etc.):

	# of calls per alert:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Behavioral Scientist:	__ __ calls	__ __ min.
4) Other (specify): _____	__ __ calls	__ __ min.

7. For standard patients with renal alerts:

   a. What is the average number of follow-up visits in the first year after the alert (do not count Quarterly or Annual Visits) (Enter NA if not applicable, e.g.-no experience with standard patients developing renal alerts) __ __ visits

   b. What is the average staff time per visit?

   1) For Physician: __ __ min.

   2) For Nurse: __ __ min.

   3) For Dietitian: __ __ min.

   4) For Behavioral Scientist: __ __ min.

   5) Other (specify): _____ __ __ min.

   c. Describe the frequency and time spent on calls related to a renal alert in the first year after the alert: (includes no answer, busy, etc.)

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify): _____	__ __ calls	__ __ min.

8. For standard patients with neurobehavioral alerts:

   a. What is the average number of followup visits per alert? (Enter NA if not applicable, e.g.-no experience with standard patients developing neurobehavioral alerts) __ __ visits

   b. What is the average staff time per visit?

   1) For Physician: __ __ min.

   2) For Nurse: __ __ min.

   3) For Behavioral Scientist: __ __ min.

   4) Other (specify): _____ __ __ min.

   c. Describe the frequency and time spent on calls related to a neurobehavioral alert (per alert): (includes no answer, busy, etc.)

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify): _____	__ __ calls	__ __ min.

9. In the past year, what % of standard patients required additional counseling for weight management? __ __ __ %

For standard patients who required additional counseling for weight management:

a. What is the average number of follow-up visits per year? __ __ visits

b. What is the average staff time per visit?

1) For Physician: __ __ min.

2) For Nurse: __ __ min.

3) For Dietitian: __ __ min.

4) For Behavioral Scientist: __ __ min.

5) Other (specify):

_____ __ __ min.

c. Describe the frequency and time spent on calls related to weight management per year: (includes no answer, busy, etc.)

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

J. DEVIATIONS FOR PREGNANCY OR PURPOSELY PURSUING CONCEPTION

In-Patient Initiation of Experimental Treatment:

1. At your clinic (over the past 2 years) what % of pregnant standard patients were admitted to hospital for initiation of experimental treatment? __ __ __ %

2. What was the average length of hospitalization (days per patient)? __ __ days

3. At your clinic (over the past 2 years) what % of nonpregnant patients pursuing conception were admitted to hopsital for initiation of experimental treatment? __ __ __ %

4. What was the average length of hospitalization (days per patient)? __ __ days

K. TELEPHONE CALLS TO STANDARD PATIENTS
(for medical management, illness and intercurrent events not related to alerts or scheduling)

For each of the following providers, what is the average number of calls per standard patient per year and the average time per call?

	# of calls per year:	Time per call:
1. Physician:	__ __ calls	__ __ min.
2. Nurse:	__ __ calls	__ __ min.
3. Dietitian:	__ __ calls	__ __ min.
4. Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

L. LETTERS FOR STANDARD PATIENTS
(individual correspondence to patients, referring physicians, insurance companies, licensing agencies, etc. <u>does</u> include lab results--<u>does not</u> include newsletters)

1. In the past year, how many letters were written for each standard patient? __ __ letters

2. What percent of letters were prepared by the following providers, and what is the average time per letter?

Prepared by:	% of letters	Time per letter:
a. Physician:	__ __ __ %	__ __ min.
b. Nurse:	__ __ __ %	__ __ min.
c. Dietitian:	__ __ __ %	__ __ min.
d. Secretary:	__ __ __ %	__ __ min.
e. Clerk:	__ __ __ %	__ __ min.
f. Other (specify):		
_____	__ __ __ %	__ __ min.

M. PARTICIPANT COSTS FOR STANDARD PATIENTS
(Question standard patients directly about participant costs)

1. How much time does the patient spend "doing" standard treatment each day (includes time spent monitoring and taking injections)?

   Minutes per day: __ __ min.

2. Hypoglycemia: (Enter NA if not applicable, e.g.-no standard patients hospitalized for hypoglycemia in past 2 years)

   a. For standard patients who were hospitalized for hypoglycemia in the past 2 yrs, what is the average number of ICU days per hypoglycemia hospitalization? __ __ days

   b. What is the average number of floor days per hypoglycemia hospitalization? __ __ days

   c. Over the past 2 yrs, what is the average number of days lost from school/work related to hypoglycemia per standard patient per year? __ __ days

   d. During the entire study period, how many standard patients have been hospitalized at your clinic for elective evaluation of hypoglycemia/loss of consciousness? N = __ __

   e. What was the average length of stay per patient hospitalized? __ __ days

3. Ketoacidosis: (Enter NA if not applicable, e.g.-no standard patients hospitalized for ketacisosis in past 2 years)

   a. For standard patients who were hospitalized for DKA in the past 2 years, what is the average number of ICU days per ketoacidosis hospitalization? __ __ days

   b. What is the average number of floor days per ketoacidosis hospitalization? __ __ days

   c. Over the past 2 years, what is the average number of days lost from school/work related to ketoacidosis per standard patient per year? __ __ days

4. Other Medical Care:

   a. What % of standard patients currently see physicians outside of the DCCT? __ __ __ %

   b. For standard patients who currently see physicians outside of the DCCT, what was the average number of visits in the past year? __ __ visits

II. EXPERIMENTAL TREATMENT GROUP

A. CSII

1. Inpatient Initiation of CSII Treatment for patients randomized at your clinic:

   a. At the time of randomization, what was the average length of hospitalization for the initiation of CSII treatment? __ __ days

   b. How much staff time was spent per admission?

      1) DCCT Physician: __ __ hours

      2) DCCT Nurse: __ __ hours

      3) DCCT Dietitian: __ __ hours

      4) DCCT Behavioral Scientist: __ __ hours

      5) Pump Representative: __ __ hours

      6) Other (specify): _____ __ __ hours

   c. On average, how many local laboratory plasma glucose levels were done during the admission?

      # of glucose levels per admission: __ __

   d. On average, how many times was SMBG done during the admission?

      # of times per inpatient day: __ __

   e. At the time of initiation of CSII treatment at randomization, how many educational materials were used or distributed per patient?

      1) # of audio tapes per patient: __ __

      2) # of video tapes per patient: __ __

      3) # of handouts per patient: __ __

2. Intensive Post-Hospitalization Outpatient CSII Follow-up for patients randomized at your clinic (This refers to the period of time lasting approximately 6 months after the inpatient initiation of CSII therapy at randomization)

   a. What was the average duration of intensive follow-up?

      # of weeks per patient: __ __ weeks

   b. What was the average number of visits per CSII patient per month? __ __ visits

   c. What was the average amount of staff time spent during these visits?

      # of Minutes Per Visit:

      1) Physician: __ __ min.

      2) Nurse: __ __ min.

      3) Dietitian: __ __ min.

      4) Behavioral Scientist: __ __ min.

      5) Pump Representative: __ __ min.

      6) Other (specify):

      _____ __ __ min.

   d. During this period, about how many phone contacts were made per patient per week during normal business hours? __ __ calls

   e. What % of calls were made by the following providers, and what was the average time per call?

	% of calls made by:	Avg. time per call:
1) Physician:	__ __ __ %	__ __ min.
2) Nurse:	__ __ __ %	__ __ min.
3) Dietitian:	__ __ __ %	__ __ min.
4) Behavioral Scientist:	__ __ __ %	__ __ min.
5) Other (specify):		
_____	__ __ __ %	__ __ min.

   f. During this period, about how many phone contacts were made per patient per week outside of normal business hours? __ __ calls

   g. What % of calls were made by the following providers, and what was the average time per call?

	% of calls made by:	Avg. time per call:
1) Physician:	__ __ __ %	__ __ min.
2) Nurse:	__ __ __ %	__ __ min.
3) Dietitian:	__ __ __ %	__ __ min.
4) Behavioral Scientist:	__ __ __ %	__ __ min.
5) Other (specify):		
_____	__ __ __ %	__ __ min.

3. Current Initiation of CSII Treatment at your clinic:

   a. In the past 2 years, what % of experimental patients changing from MDI to CSII were hospitalized? __ __ __ %

   b. For patients who were hospitalized, what was the average length of hospitalization? __ __ days

   c. How much staff time was spent per admission?

      1) DCCT Physician: __ __ hours

      2) DCCT Nurse: __ __ hours

      3) DCCT Dietitian: __ __ hours

      4) DCCT Behavioral Scientist: __ __ hours

      5) Pump Representative: __ __ hours

      6) Other (specify):

      _____ __ __ hours

   d. On average, how many local laboratory plasma glucose levels were done during the admission?

      # of glucose levels per admission: __ __

   e. On average, how many times was SMBG done during the admission?

      # of times per inpatient day: __ __

f. At the time of initiation of CSII treatment for patients changing from MDI, how many educational materials were used or distributed per patient?

1) # of audio tapes per patient: __ __

2) # of video tapes per patient: __ __

3) # of handouts per patient: __ __

4. Current Intensive Post-Initiation Outpatient CSII follow-up at your clinic:

a. In the past 2 years, what was the average duration of intensive followup for patients changing from MDI to CSII?

# of weeks per patient: __ __ weeks

b. What was the average # of visits per CSII patient per month? __ __ visits

c. What was the average amount of staff time spent during these visits?

# of Minutes Per Visit:

1) Physician: __ __ min.

2) Nurse: __ __ min.

3) Dietitian: __ __ min.

4) Behavioral Scientist: __ __ min.

5) Pump Representative: __ __ min.

6) Other (specify): _____ __ __ min.

d. During this period, about how many phone contacts were made per patient per week during normal business hrs? __ __ calls

e. What % of calls were made by the following providers, and what was the average time per call?

	% of calls made by:	Avg. time per call:
1) Physician:	__ __ __ %	__ __ min.
2) Nurse:	__ __ __ %	__ __ min.
3) Dietitian:	__ __ __ %	__ __ min.
4) Behavioral Scientist:	__ __ __ %	__ __ min.
5) Other (specify): _____	__ __ __ %	__ __ min.

f. During this period, about how many phone contacts were made per patient per week outside of normal business hours? __ __ calls

g. What % of calls were made by the following providers, and what was the average time per call?

	% of calls made by:	Avg. time per call:
1) Physician:	__ __ __ %	__ __ min.
2) Nurse:	__ __ __ %	__ __ min.
3) Dietitian:	__ __ __ %	__ __ min.
4) Behavioral Scientist:	__ __ __ %	__ __ min.
5) Other (specify): _____	__ __ __ %	__ __ min.

5. Current CSII Treatment

a. On average, how often do CSII patients change syringes? every __ __ days

b. What types of tubing/needles are used?

% of patients who use:

1) soft-sets: __ __ __ %

2) sub Q sets: __ __ __ %

3) polyfin sets: __ __ __ %

4) other (_____): __ __ __ %

c. On average, how often do CSII pts. change the tubing/needle? every __ __ days

d. What percent of CSII patients use site covers in addition to those provided with the tubing/needles? __ __ __%

e. What types of site covers are used?

% of patients who use:

1) op site: __ __ __ %

2) no skin: __ __ __ %

3) tegaderm: __ __ __ %

4) bioclusive: __ __ __ %

5) other (_____): __ __ __ %

f. How do CSII patients prepare their sites?

% of patients who use:

1) alcohol: __ __ __ %

2) betadine: __ __ __ %

3) hexachlorophene: __ __ __ %

4) betadine ointment: __ __ __ %

5) bard wipes: __ __ __ %

6) other (_____): __ __ __ %

g. On average, how many shower packs do CSII patients use per month? __ __ packs

h. On average, how many pump cases do CSII patients use per year? __ __ cases

B. MDI

1. Inpatient Initiation of MDI Treatment for patients randomized at your clinic:

a. At randomization, what was the average length of hospitalization for the initiation of MDI treatment? __ __ days

b. How much staff time was spent per admission?

1) DCCT Physician: __ __ hours

2) DCCT Nurse: __ __ hours

3) DCCT Dietitian: __ __ hours

4) DCCT Behavioral Scientist: __ __ hours

5) Other (specify):

_____ __ __ hours

c. On average, how many local laboratory plasma glucose levels were done during the admission?

# of glucose levels per admission: __ __

d. On average, how many times was SMBG done during the admission?

# of times per inpatient day: __ __

e. At the time of initiation of MDI treatment at randomization, how many educational materials were used or distributed per patient?

1) # of audio tapes per patient: __ __

2) # of video tapes per patient: __ __

3) # handouts per patient: __ __

2. Intensive Post-Hospitalization Outpatient MDI Followup for patients randomized at your clinic - (This refers to the period of time after the inpatient initiation of MDI therapy at randomization):

a. What was the average duration of intensive followup?

# of weeks per patient: __ __ weeks

b. What was the average number of visits per MDI patient per month? __ __ visits

c. What was the average amount of staff time spent during these visits?

# of minutes per visit

1) Physician: __ __ min.

2) Nurse: __ __ min.

3) Dietitian: __ __ min.

4) Behavioral Scientist: __ __ min.

5) Other (specify): _____ __ __ mins.

d. During this period, about how many phone contacts were made per patient per week during normal business hours? __ __ calls

e. What were the percent of calls made by the following, and the average time per call?

	% of calls made by:	Avg. time per call:
1) Physician:	__ __ __ %	__ __ min.
2) Nurse:	__ __ __ %	__ __ min.
3) Dietitian:	__ __ __ %	__ __ min.
4) Behavioral Scientist:	__ __ __ %	__ __ min.
5) Other (specify):		
_____	__ __ __ %	__ __ min.

f. During this period, about how many phone contacts were made per patient per week outside of normal business hours? __ __ calls

g. What % of calls were made by the following providers, and what was the average time per call?

	% of calls made by:	Avg. time per call:
1) Physician:	__ __ __ %	__ __ min.
2) Nurse:	__ __ __ %	__ __ min.
3) Dietitian:	__ __ __ %	__ __ min.
4) Behavioral Scientist:	__ __ __ %	__ __ min.
5) Other (specify): _____	__ __ __ %	__ __ min.

3. Current Initiation of MDI at your clinic:

a. In the past 2 years, what % of experimental patients changing from CSII to MDI were hospitalized? __ __ __ %

b. For patients who were hospitalized, what was the average length of hospitalization? __ __ __ %

c. How much staff time was spent per admission?

1) DCCT Physician: __ __ hours

2) DCCT Nurse: __ __ hours

3) DCCT Dietitian: __ __ hours

4) DCCT Behavioral Scientist: __ __ hours

5) Other (specify): _____ __ __ hours

4. Current Intensive Post-Initiation Outpatient MDI Follow-up at Your Clinic

a. In the past 2 years, what is the average duration of intensive followup for patients changing from CSII to MDI?

# of weeks per patient: __ __ weeks

b. What is the average number of visits per MDI patient per month? __ __ visits

c. What is the average amount of staff time spent during these visits?

# of minutes per visit

1) Physician: __ __ min.

2) Nurse: __ __ min.

3) Dietitian: __ __ min.

4) Behavioral Scientist: __ __ min.

5) Other (specify): _____ __ __ min.

d. About how many phone contacts are made per patient per weekduring normal business hours? __ __ calls

e. What is the percent of calls made by the following, and the average time per call?

	% of calls made by:	Avg. time per call:
1. Physician:	__ __ __ %	__ __ min.
2. Nurse:	__ __ __ %	__ __ min.
3. Dietitian:	__ __ __ %	__ __ min.
4. Behavioral Scientist:	__ __ __ %	__ __ min.
5) Other (specify): _____	__ __ __ %	__ __ min.

f. About how many phone contacts are made per patient per week outside of normal business hours? __ __ calls

g. What % of calls are made by the following providers, and what is the average time per call?

	% of calls made by:	Avg. time per call:
1) Physician:	__ __ __ %	__ __ min.
2) Nurse:	__ __ __ %	__ __ min.
3) Dietitian:	__ __ __ %	__ __ min.
4) Behavioral Scientist:	__ __ __ %	__ __ min.
5) Other (specify): _____	__ __ __ %	__ __ min.

5. Current MDI Treatment

a. On average, what % of MDI patients are now using indwelling catheters or buttons ___ ___ ___ %

b. About how often do these patients change their catheters or buttons? every ___ ___ days

c. About what % of MDI patients were ever prescribed jet injectors? ___ ___ ___ %

d. For MDI patients prescribed jet injectors, what % of all MDI doses are now administered by jet injector? ___ ___ ___%

e. About what % of MDI patients were ever prescribed insulin pens? ___ ___ ___ %

f. For MDI patients prescribed insulin pens, what % of all MDI doses are now administered by pen? ___ ___ ___%

g. On average, what is the frequency of pen needle changes? every ___ ___ doses

C. ROUTINE OUTPATIENT EXPERIMENTAL TREATMENT (applicable to both CSII and MDI patients)

1. Glucagon, etc.

a. On average, how many glucagon kits are distributed per experimental patient per year? ___ ___.___ kits

b. On average, how many 6 tablet boxes of glucose tablets are distributed per experimental patient per year? ___ ___ ___ boxes

c. On average, how many tubes of glucose gel are distributed per experimental patient per year? ___ ___ tubes

2. Diet

a. In the reinforcement of dietary program for experimental patients:

1) What is the average frequency of dietitian visits per experimental patient per year? ___ ___ times

2) How many minutes of dietitian time are required per visit (includes preparation time and time spent with the patient, including time at the annual visit, does not include time spent with the diet history)? ___ ___ min.

b. What % of experimental patients require additional dietary counseling for achievement of study goals? ___ ___ ___ %

1) What is the average number of additional visits with the dietitian to achieve study goals per experimental patient not achieving study goals per year? ___ ___ visits

2) What is the average time per visit? ___ ___ visits

3) What is the average number of phone calls with the dietitian needed to achieve study goals per patient not achieving study goals per year? ___ ___ calls

4) What is the average time per call? ___ ___ min.

3. Self-Monitoring

a. On average, how many times per quarter do experimental patients now test urine ketones? ___ ___ times

4. Clinic Visits and Education

a. About how many educational materials are distributed per experimental patient per year? ___ ___ handouts

___ ___ videos

D. MONTHLY VISITS FOR EXPERIMENTAL PATIENTS

(Includes time spent on history, review of monitoring results, education, goal setting, and clinical record keeping - does not include: time spent scheduling, dietitian time, time spent preparing forms and tubes, blood drawing)

Minutes per monthly visit per patient:

1. Physician: __ __ min.
2. Nurse: __ __ min.
3. Behavioral Scientist: __ __ min.
4. Other(specify): _____ __ __ min.

E. QUARTERLY VISITS FOR EXPERIMENTAL PATIENTS

(Includes time spent on history, physical exam, review of monitoring results, education, goal setting, and clinical record keeping - does not include: time spent scheduling, dietitian time, time spent preparing forms and tubes, blood drawing, or time spent completing Form 021.7 sections A and C through H)

Minutes per quarterly visit per patient:

1. Physician: __ __ min.
2. Nurse: __ __ min.
3. Behavioral Scientist: __ __ min.
4. Other(specify): _____ __ __ min.

F. ANNUAL VISITS FOR EXPERIMENTAL PATIENTS

(Includes time spent on history, physical exam, review of monitoring results, education, goal setting, and clinical record keeping - does not include: time spent scheduling, dietitian time, time spent preparing forms and tubes, blood drawing, or time spent completing Form 003.3 sections A and G through L)

Minutes per annual visit per patient:

1. Physician: __ __ min.
2. Nurse: __ __ min.
3. Behavioral Scientist: __ __ min.
4. Other(specify): _____ __ __ min.

G. LABORATORY

1. Plasma glucose:

a. What % of experimental patients currently have plasma glucose levels done at local labs? __ __ __ %

b. For patients having plasma glucose levels done at local labs, how many times per year are they performed? __ __ times

H. ALERTS, ETC.

1. For experimental patients who develop hypertension:

a. What is the average number of followup visits in the first year after the alert (do not count Monthly, Quarterly or Visits)? (Enter NA if not applicable, e.g.-no experience with experimental patients developing hypertension) __ __ visits

b. What is the average staff time per visit?

1) For Physician: __ __ min.
2) For Nurse: __ __ min.
3) For Dietitian: __ __ min.
4) For Behavioral Scientist: __ __ min.
5) Other(specify): _____ __ __ min.

c. Describe the frequency and time spent on calls related to hypertension in the first year after the alert (includes no answer, busy, etc.)

	# of calls	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify): _____	__ __ calls	__ __ min.

2. For experimental patients who develop persistent hypercholesterolemia:

   a. What is the average number of followup visits related to an alert (per alert) (do not count Monthly, Quarterly or Annual Visits)? (Enter NA if not applicable, e.g.-no experience w/experimental patients developing hypercholesterolemia) __ __ visits

   b. What is the average staff time per visit?

      1) For Physician: __ __ min.

      2) For Nurse: __ __ min.

      3) For Dietitian: __ __ min.

      4) For Behavioral Scientist: __ __ min.

      5) Other (specify): _____ __ __ min.

   c. Describe the frequency and time spent on calls related to a hypercholesterolemia alert (per alert) - (includes no answer, busy, etc.):

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

3. For experimental patients who develop severe hypoglycemia requiring assistance by another person:

   a. What is the average number of followup visits per episode? (Enter NA if not applicable, e.g.-no experience with experimental patients developing severe hypoglycemia) __ __ visits

   b. What is the average staff time per visit?

      1) For Physician: __ __ min.

      2) For Nurse: __ __ min.

      3) For Dietitian: __ __ min.

      4) For Behavioral Scientist: __ __ min.

      5) Other (specify): _____ __ __ min.

   c. Describe the frequency and time spent on calls related to severe hypoglycemia per episode: (includes no answer, busy, etc.)

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

4. For experimental patients who develop ketoacidosis:

   a. What is the average number of followup visits per episode? (Enter NA if not applicable, e.g.-no experience with experimental patients developing ketoacidosis) __ __ visits

   b. What is the average staff time per visit?

      1) For Physician: __ __ min.

      2) For Nurse: __ __ min.

      3) For Dietitian: __ __ min.

      4) For Behavioral Scientist: __ __ min.

      5) Other (specify): _____ __ __ min.

   c. Describe the frequency and time spent on calls related to ketoacidosis per episode: (includes no answer, busy, etc.)

	# of calls:	Time per call:
1. Physician:	__ __ calls	__ __ min.
2. Nurse:	__ __ calls	__ __ min.
3. Dietitian:	__ __ calls	__ __ min.
4. Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

5. For experimental patients with eye alerts:

   a. What is the average number of ophthalmology follow-up visits per alert (excluding normally scheduled annual visits?) (Enter NA if not applicable, e.g.-no experience with experimental patients developing eye alerts) __ __ visits

   b. What is the average ophthalmologist time per visit? __ __ min.

   c. Describe the frequency and amount of time spent on calls related to an eye alert (per alert) - (includes no answer, busy, etc.)

	# of calls per alert:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Behavioral Scientist:	__ __ calls	__ __ min.
4) Other (specify):		
_____	__ __ calls	__ __ min.

6. For experimental patients with renal alerts:

   a. What is the average number of followup visits in the first year after the alert (*do not count* Monthly, Quarterly or Annual Visits)-(Enter NA if not applicable, e.g. -no experience with experimental patients developing renal alerts) __ __ visits

   b. What is the average staff time per visit?

1) For Physician:	__ __ min.
2) For Nurse:	__ __ min.
3) For Dietitian:	__ __ min.
4) For Behavioral Scientist:	__ __ min.
5) Other (specify): _____	__ __ min.

   c. Describe the frequency and time spent on calls related to renal alerts in the first year after the alert (includes no answer, busy, etc.)

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

7. For experimental patients with neurobehavioral alerts:

   a. What is the average number of followup visits per alert? (Enter NA if not applicable, e.g.- no experience with experimental patients developing neurobehavioral alerts) __ __ visits

   b. What is the average staff time per alert?

1) For Physician:	__ __ min.
2) For Nurse:	__ __ min.
3) For Behavioral Scientist:	__ __ min.
4) Other (specify): _____	__ __ min

   c. Describe the frequency and time spent on calls related to a neurobehavioral alert (per alert): (includes no answer, busy, etc.)

	# of calls:	per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

8. In the past year, what % of experimental patients required additional counseling for weight management? __ __ __ %

For experimental patients who required additional counseling for weight management:

a. What is the average number of follow-up visits per year? __ __ visits

b. What is the average staff time per visit?

1) For Physician: __ __ min.

2) For Nurse: __ __ min.

3) For Dietitian: __ __ min.

4) For Behavioral Scientist: __ __ min.

5) Other (specify):

_____ __ __ min.

c. Describe the frequency and time spent on calls related to weight management per year: (includes no answer, busy, etc.)

	# of calls:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

I. TELEPHONE CALLS TO EXPERIMENTAL PATIENTS (for medical management, illness and intercurrent events not related to alerts or scheduling)

For each of the following providers, what is the average number of calls per experimental patient per year and the average time per call?

	# of calls per year:	Time per call:
1) Physician:	__ __ calls	__ __ min.
2) Nurse:	__ __ calls	__ __ min.
3) Dietitian:	__ __ calls	__ __ min.
4) Behavioral Scientist:	__ __ calls	__ __ min.
5) Other (specify):		
_____	__ __ calls	__ __ min.

J. LETTERS FOR EXPERIMENTAL PATIENTS (individual correspondence to patients, referring physicians, insurance companies, licensing agencies, etc., does include lab results, does not include newsletters)

1. In the past year, how many letters were written for each experimental patient? __ __ letters

2. What percent of letters are prepared by the following providers, and what is the average time per letter?

a. Physician:	__ __ __ %	__ __ min.
b. Nurse:	__ __ __ %	__ __ min.
c. Dietitian	__ __ __ %	__ __ min.
d. Secretary:	__ __ __ %	__ __ min.
e. Clerk:	__ __ __ %	__ __ min.
f. Other (specify):		
_____	__ __ __ %	__ __ min.

K. HOSPITALIZATION

1. In the past 2 years, what % of experimental patients required rehospitalization for adjustment of doses and education? ___ ___ ___ %

   For such patients:

   a. What was the average number of hospital days per rehospitalization? ___ ___ days

   b. How much staff time was spent per admission?

      1) DCCT Physician: ___ ___ hours

      2) DCCT Nurse: ___ ___ hours

      3) DCCT Dietitian: ___ ___ hours

      4) DCCT Behavioral Scientist: ___ ___ hours

      5) Other (specify):

      _____ ___ ___ hours

L. PARTICIPANT COSTS
(Question Experimental patients directly about participant costs)

1. How much time does the patient spend "doing" experimental treatment (includes time spent monitoring and taking insulin)?

   a. Minutes per CSII patient per day: ___ ___ min.

   b. Minutes per MDI patient per day: ___ ___ min.

2. Hypoglycemia: (Enter NA if not applicable, e.g.-*no experimental patients hospitalized for hypoglycemia in past 2 years*)

   a. For experimental patients who were hospitalized with hypoglycemia in the past 2 years, what was the average number of ICU days per hypoglycemia hospitalization? ___ ___ days

   b. What is the average number of floor days per hypoglycemia hospitalization? ___ ___ days

   c. Over the past 2 years, what is the average number of days lost from school/work related to hypoglycemia per experimental patient per year? ___ ___ days

   d. During the entire study period, how many experimental patients have been hospitalized at your clinic for elective evaluation of hypoglycemia/loss of consciousness? N = ___ ___

   e. What was the average length of stay per patient hospitalized? ___ ___ days

3. Ketoacidosis: (Enter NA if not applicable, e.g.-no experimental patients hospitalized for ketoacidosis in past 2 years)

   a. For experimental patients who were hospitalized for DKA in the past 2 years, what was the average number of ICU days per ketoacidosis hospitalization? ___ ___ days

   b. What is the average number of floor days per ketoacidosis hospitalization? ___ ___ days

   c. Over the past 2 years, what is the average number of days lost from school/work related to ketoacidosis per experimental patient per year? ___ ___ days

4. Other Medical Care:

   a. What % of experimental patients currently see physicians outside of the DCCT? ___ ___ ___ %

   b. For experimental patients who currently see physicians outside of the DCCT, what was the average number of visits in the past year? ___ ___ visits

III. STANDARD AND EXPERIMENTAL TREATMENT GROUPS

A. TREATMENT TEAM MEETINGS

1. What is the average number of treatment team meetings per year? __ __
2. What is the average duration of meeting? __ __ __ min.
3. How much time is devoted to standard patients per meeting? __ __ min.
4. How much time is devoted to experimental patients per meeting? __ __ min.
5. What is the attendance of team meetings during the past year (indicate vacant positions by NA)?
   - a. Physician 1: __ __ __ % of meetings
   - b. Physician 2: __ __ __ % of meetings
   - c. Physician 3: __ __ __ % of meetings
   - d. Physician 4: __ __ __ % of meetings
   - e. Trial Coordinator: __ __ __ % of meetings
   - f. Research Nurse 1: __ __ __ % of meetings
   - g. Research Nurse 2: __ __ __ % of meetings
   - h. Research Assistant 1: __ __ __ % of meetings
   - i. Research Assistant 2: __ __ __ % of meetings
   - j. Secretary 1: __ __ __ % of meetings
   - k. Secretary 2: __ __ __ % of meetings
   - l. Dietitian 1: __ __ __ % of meetings
   - m. Dietitian 2: __ __ __ % of meetings
   - n. Behavioral Scientist 1: __ __ __ % of meetings
   - o. Behavioral Scientist 2: __ __ __ % of meetings

   Other (specify):

   - p. _____ __ __ __ % of meetings
   - q. _____ __ __ __ % of meetings

B. ON-CALL TREATMENT TEAM (after hours and weekends)

1. How many hours per week is a physician available to take calls (outside of normal business hours)? (7 days - 40 hours = 128 hours) __ __ __ hours
2. How many hours per week is a nurse available to take calls (outside of normal business hours)? (7 days - 40 hours = 128 hours) __ __ __ hours
3. Currently, what is the average number of experimental patient calls per month? __ __ calls
   - a. What percentage of calls are taken by the nurse: __ __ __ %
   - b. What is the average duration of a nurse call? __ __ min.
   - c. What percentage of calls are taken by the physician? __ __ __ %
   - d. What is the average duration of a physician call? __ __ min.
4. Currently, what is the average number of standard patient calls per month? __ __ calls
   - a. What percentage of calls are taken by the nurse: __ __ __ %
   - b. What is the average duration of a nurse call? __ __ min.
   - c. What percentage of calls are taken by the physician? __ __ __ %
   - d. What is the average duration of a physician call? __ __ min.

C. ADHERENCE ACTIVITIES

1. In a typical year, what was the number of adherence activities?

   a. For standard patients: __ __ activities

   b. For experimental patients: __ __ activities

2. What was the duration of a typical activity (in hours)?

   a. For standard patients: __ hours

   b. For experimental patients: __ hours

3. How much time was spent planning a typical activity (in hours)?

   a. For standard patients

      Number of hours spent:

      1) Physician: __ __ hours

      2) Nurse: __ __ hours

      3) Behavioral Scientist: __ __ hours

      4) Dietitian: __ __ hours

      5) Research Assistant: __ __ hours

      6) Secretary: __ __ hours

   b. For experimental patients

      Number of hours spent:

      1) Physician: __ __ hours

      2) Nurse: __ __ hours

      3) Behavioral Scientist: __ __ hours

      4) Dietitian: __ __ hours

      5) Research Assistant: __ __ hours

      6) Secretary: __ __ hours

4. What was the average cost per patient (and significant other) of a typical activity (includes cost of refreshments, materials, supplies, meeting space, etc.)

   a. Cost per standard patient: $__ __

   b. Cost per experimental patient: $__ __

5. Typically, what percent of the adherence activities are educational (as opposed to social):

   a. For standard patients: __ __ __%

   b. For experimental patients: __ __ __%

6. # of staff members attending activity:

   a. For standard patients:

      1) Physician: N = __

      2) Nurse: N = __

      3) Behavioral Scientist: N = __

      4) Dietitian: N = __

      5) Research Assistant: N = __

      6) Secretary: N = __

      7) Other (specify):

      _____ N = __

   b. For experimental patients:

      1) Physician: N = __

      2) Nurse: N = __

      3) Behavioral Scientist: N = __

      4) Dietitian: N = __

      5) Research Assistant: N = __

      6) Secretary: N = __

      7) Other (specify):

      _____ N = __

7. How much time was spent preparing and/or distributing newsletters, anniversary letters, holiday cards, birthday cards, etc. last year:

   a. Physician: __ __ hours

   b. Nurse: __ __ hours

   c. Behavioral Scientist: __ __ hours

   d. Dietitian: __ __ hours

   e. Research Assistant: __ __ hours

   f. Secretary: __ __ hours

D. PARTICIPANT COSTS
(Question patients directly about participant costs)

1. On average, what is the one-way travel time to clinic (excluding patients who fly)? __ __ __ min.

2. On average, what is the one-way travel distance to the clinic (excluding patients who fly)? __ __ __ miles

3. What is the cost of parking per visit at clinic (regardless of who pays)? $__ __.__ __

4. What percent of patients require child care for clinic visits (regardless of who pays)? __ __ __ %

5. What is the cost of child care per visit at clinic for those requiring child care (regardless of who pays)? $__ __

6. How much time is lost from work per patient per monthly visit? __.__ hours

7. What % of patients take this time as unpaid leave? __ __ __ %

8. How much time is lost from work per patient per quarterly visit? __.__ hours

9. What % of patients take this time as unpaid leave? __ __ __ %

E. SCHEDULING COSTS

1. What is the average amount of time required to schedule a medical management visit (e.g., a monthly, quarterly or annual visit (includes time spent coordinating with team, calling, and rescheduling):

	Monthly	Quarterly	Annual
# of minutes per completed visit:	__ __	__ __	__ __

2. What % of scheduling is done by:

a. Nurse:	__ __ __	__ __ __	__ __ __
b. Secretary:	__ __ __	__ __ __	__ __ __
c. Clerk:	__ __ __	__ __ __	__ __ __
d. Other (specify):			
_____	__ __ __	__ __ __	__ __ __

F. ADDITIONAL COSTS

How much other interdisciplinary time is spent solving patient related problems not already noted (e.g. - time spent talking at the water cooler)?

Minutes per patient per month:

1. Standard patients:

   a. Physician: __ __ min.

   b. Nurse: __ __ min.

   c. Behavioral scientist: __ __ min.

   d. Dietitian: __ __ min.

   e. Research Assistant: __ __ min.

2. Experimental patients:

   a. Physician: __ __ min.

   b. Nurse: __ __ min.

   c. Behavioral scientist: __ __ min.

   d. Dietitian: __ __ min.

   e. Research Assistant: __ __ min.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Lipoprotein Ancillary Study Specimen Mailing List

This mailing list is used whenever the DCCT clinic ships a container of specimens to the Central Biochemistry Laboratory (CBL) for analysis of lipoproteins as part of Dr. John Brunzell's ancillary study. A series of five (5) 1 ml and one (1) 3 ml samples should be included. Four copies of this form are to be distributed as follows:

(1) ORIGINAL -- Complete and send with the specimens

Mail to: DCCT Central Biochemistry Laboratory
ATTN: L275, Mayo 626-3645
University of Minnesota Hospital and Clinic
420 Delaware Street
Minneapolis, MN 55455

(2) COPY -- Send to the address above with the original.

(3) COPY -- Send to the Coordinating Center in the weekly forms mailing.

(4) COPY -- Retain in clinic files.

Clinic Number: __ __

Specimens Shipped on: __ __ | __ __ | __ __
Month | Day | Year

Specimens Collected From: __ __ | __ __ | __ __ through __ __ | __ __ | __ __
Month | Day | Year | Month | Day | Year

PLASMA FOR LIPOPROTEIN ANALYSIS

PATIENT ID NUMBER	PATIENT'S INITIALS F M L	DATE SPECIMENS DRAWN Month Day Year	COMMENTS (Indicate if less than 6 samples are included.)
__ __ __ __ __	__ __ __	__ __/__ __/__ __	_____
__ __ __ __ __	__ __ __	__ __/__ __/__ __	_____
__ __ __ __ __	__ __ __	__ __/__ __/__ __	_____

Diabetes Control and Complications Trial

VALIDATION STUDY

DIABETES CONTROL AND COMPLICATIONS TRIAL
Body Composition Measurements

A. IDENTIFYING INFORMATION

1. Clinic Number: __ __
2. Patient ID Number: __ __ __ __ __
3. Patient's Initials: __ __ __
4. Date Form Completed: __ __/__ __/__ __ (Month/Day/Year)
5. Visit number (nearest quarterly visit): __ __

B. MEASUREMENTS:

Measurements are taken twice and recorded. If the two measures are not within 0.5 cm (5.0 mm) of each other, two additional measurements are taken and all four measures are recorded.

1. Waist Circumference (cm) -- Natural

	NO	YES
Is lipohypertropy present?	(1)	(2)
Is lipoatrophy present?	(1)	(2)

a. First measurement: ___ ___ ___.___

b. Second measurement: ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 0.5 cm.

c. Third measurement: ___ ___ ___.___

d. Fourth measurement: ___ ___ ___.___

2. Iliac Waist Circumference (cm)

	NO	YES
Is lipohypertropy present?	(1)	(2)
Is lipoatrophy present?	(1)	(2)

a. First measurement: ___ ___ ___.___

b. Second measurement: ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 0.5 cm.

c. Third measurement: ___ ___ ___.___

d. Fourth measurement: ___ ___ ___.___

3. Hip Circumference (cm)

	NO	YES
Is lipohypertropy present?	(1)	(2)
Is lipoatrophy present?	(1)	(2)

a. First measurement: ___ ___ ___.___

b. Second measurement: ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 0.5 cm.

c. Third measurement: ___ ___ ___.___

d. Fourth measurement: ___ ___ ___.___

C. STATURE

1. Weight (kg)

a. First measurement: ___ ___ ___ ___.___

b. Second measurement: ___ ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 0.2 kilograms (200 gm).

c. Third measurement: ___ ___ ___ ___.___

d. Fourth measurement: ___ ___ ___ ___.___

2. Height (cm)

a. First measurement: ___ ___ ___.___

b. Second measurement: ___ ___ ___.___

Record (c) and (d) only if first 2 measurements are not within 1.0 cm (10.0 mm)

c. Third measurement: ___ ___ ___.___

d. Fourth measurement: ___ ___ ___.___

D. BIOELECTRIC IMPEDANCE ANALYSIS

Determine resistance and reactance, in ohms, at one electrode placement then move the electrodes attachments to another placement until ipsilateral and contralateral measurements are completed.

Record (c) and (d) if the first two resistance measurements are not within 2 ohms or the reactance measurements are not within 1 ohm.

	BIA #1 Resist	BIA #1 React	BIA #2 Resist	BIA #2 React
1. BS Pre (BIA #1) ___ ___ ___				
2. Right Arm to Right Leg				
a) first measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
b) second measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
If necessary,				
c) third measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
d) fourth measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
3. Right Arm to Left Leg				
a) first measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
b) second measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
If necessary,				
c) third measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
d) fourth measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
4. Left Arm to Left Leg				
a) first measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
b) second measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
If necessary,				
c) third measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
d) fourth measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
5. Left Arm to Right Leg				
a) first measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
b) second measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
If necessary,				
c) third measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
d) fourth measurement	___ ___ ___	___ ___	___ ___ ___	___ ___
6. BS PP (BIA #2) ___ ___ ___				

Name of person completing this form: _____

Certification No. ___ ___ - ___ ___

Diabetes
Control and
Complications
Trial

July 17, 1992
DCCT Form 125.1
Page 1 of 1

DIABETES CONTROL AND COMPLICATIONS TRIAL

Community Comparison Project
HEMOGLOBIN REPORTING LOG

INSTRUCTIONS:

RESULTS: Separate sheets will be completed by Terry Spennetta, representing WESDR and Jean Bucksa of the DCCT. Laboratory results will be returned to Duke Owen on a weekly basis. Samples will be run in duplicate with the average value reported. WESDR samples will be analyzed via ISOLAB for HbA1 content, the CBL will use the DIAMAT to measure HbA1c content.

SAMPLES: Dr. Santiago will ship copies of this form, having completed the "Sample Number", "Date Drawn" and "Date Shipped" columns, and a split sample duplicate on wet ice to each of the labs for 150 non-DCCT samples. He will send an additional copy of the partially completed Form 125 to Duke Owen at the CoC. Shipments will be made on Mondays and Wednesdays.

Jean Bucksa
DCCT Central Biochemistry Laboratory
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612-626-3645

Terry Spennetta
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GWU Biostatistics Cente
6110 Executive Blvd., Suite 750
Rockville, Maryland 20852
301-881-9260

Laboratory
Klein - WESDR - HbA1 (1)
Bucksa - DCCT - HbA1c (2)

	Sample Number (001-150)	Date Drawn			Date Shipped			Date Analyzed			HbA1 (WESDR) or HbA1c (DCCT)	COMMENTS
		MO	DAY	YR	MO	DAY	YR	MO	DAY	YR		
Non-DCCT Sample											.	
Non-DCCT Sample											.	
Non-DCCT Sample											.	
Non-DCCT Sample											.	
Non-DCCT Sample											.	
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Non-DCCT Sample											.	
Non-DCCT Sample											.	
Non-DCCT Sample											.	

DIABETES CONTROL AND COMPLICATIONS TRIAL

HEALTH STATUS QUESTIONNAIRE

SF-36

INFORMATION TO BE SUPPLIED BY CLINIC COORDINATOR:

1. Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Today's date __ __ __ __ __ __ (Month Day Year)
5. Visit Number __ __

NOTE. While the RAND Corporation permits copying of the SF-36 questions, the graphic layout of the form used in the DCCT was copyrighted by another organization. We therefore present the questions below without reproducing the actual layout of the form.

Health Status Questionnaire
SF-36

The variables in the dataset that correspond to each question are shown in the data summary that follows these questions.

Information entered by clinic staff.

1. Clinic Number
2. Patient ID Number
3. Patient's Initials
4. Today's date
5. Visit Number

INSTRUCTIONS TO PATIENT:

This survey asks for your views about your health. This information will be summarized in your medical record and will help your doctors keep track of how you feel and how well you are able to do your usual activities.

Answer every question by circling the appropriate number. 1, 2, 3, ... If you are unsure about how to answer a question, please give the best ·answer you can and make a comment in the left margin.]

1. In general, would you say your health is:

Response categories: 1: Excellent, 2: Very Good, 3: Good, 4: Fair, 5: Poor

2. Compared to one year ago, how would you rate your health in general now?

Response categories:
1: Much better now than one year ago,
2: Somewhat better now than one year ago,
3: About the same,
4: Somewhat worse than one year ago,
5: Much worse now than one year ago

HEALTH AND DAILY ACTIVITIES

3. The following questions are about activities you might do during a typical day. Does your health limit you in these activities? If so, how much?

Response categories for all items, 3.a to 3.j:
1: Yes, Limited a Lot, 2: Yes, Limited a Little, 3: No, Not Limited at All

a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports

b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf

c. Lifting or carrying groceries

d. Climbing several flights of stairs

e. Climbing one flight of stairs

f. Bending, kneeling, or stooping

g. Walking more than a mile

h. Walking several blocks

i. Walking one block

j. Bathing and dressing yourself

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

Response categories for all items, 4.a to 4.d:

1: Yes, 2: No

a. Cut down on the amount of time you spent on work or other activities

b. Accomplished less than you would like

c. Were limited in the kind of work or other activities

d. Had difficulty performing the work or other activities (for example, it took extra effort)

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

Response categories for all items, 5.a to 5.c:

1: Yes, 2: No

a. Cut down on the amount of time you spent on work or other activities

b. Accomplished less than you would like

c. Didn't do work or other activities as carefully as usual.

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

Response categories: 1: Not at All, 2: Slightly, 3: Moderately, 4: Quite a bit; 5: Extremely

PAIN

7. How much bodily pain have you had during the past 4 weeks?

Response categories: 1: None, 2: Very Mild, 3: Mild, 4: Moderate; 5: Severe; 6: Very Severe

8. During the past 4 weeks, how much did pain interfere with your normal work (including work both outside the home and housework)?

Response categories: 1: Not at all, 2: A little bit, 3: Moderately, 4: Quite a bit; 5: Extremely

YOUR FEELINGS

9. These questions are about how you feel and how things have been with you during the past month. For each question, please indicate the one answer that comes closest to the way you have been feeling.

How much of the time during the past month ...

Response categories: 1: All of the Time, 2: Most of the Time, 3: A Good Bit of the Time, 4: Some of the Time, 5: A Little of the Time, 6: None of the Time.

a. did you feel full of pep?

b. have you been a very nervous person?

c. have you felt so down in the dumps nothing could cheer you up?

d. have you felt calm and peaceful?

e. did you have a lot of energy?

1. have you felt downhearted and blue?

g. did you feel worn out?

h. have you been a happy person?

j. did you feel tired?

j. has your health limited your social activities (like visiting with friends or close relatives)?

HEALTH IN GENERAL

10. Please choose the answer that best describes how true or false each of the following statements is for you.

Response categories: 1: Definitely True, 2: Mostly True, 3: Not Sure, 4: Mostly False, 5: Definitely False

a I seem to get sick a little easier than other people.

b. I am as healthy as anybody I know.

c. I expect my health to get worse.

d. My health is excellent.

Appendix B

DCCT TEACHING OBJECTIVES

Name: _____

DCCT #: _____

Group: _____

RESPONSIBILITY OF DIETITIAN

UPON COMPLETION OF TEACHING DIET AND NUTRITION THERAPY, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. Explain the role of diet in the management of diabetes.	_____
2. Explain the reason for regularly spaced, uniform meals.	_____
3. Describe the relationship between diet and insulin.	_____
4. Describe the effect of weight control on the management of diabetes.	_____
5. State the effect of simple carbohydrate on diabetic control.	_____
6. State the effect of complex carbohydrates, fats, and protein on diabetic control.	_____
7. Describe how to adjust his/her diet for increased activity (planned and unplanned), delayed meals, illness and the use of alcohol.	_____
8. Verbalize the correct selection of foods and amounts allowed at mealtime from individual diet prescription.	_____
9. Explain how to adjust diet for unusual situations (e.g., travel, changes in work schedules).	_____
10. Verbalize the selection of foods appropriate for school lunch menu, cafeteria or restaurant.	_____
11. Verbalize own diet plan.	_____

_____

HEALTH CARE PROVIDER

LOADING THE SYRINGE INTO PUMP	DATE ACHIEVED
1. Demonstrate proper filling of syringe.	_____
2. State the maximum amount which can be added to syringe.	_____
3. State the minimal amount which can be left in syringe before syringe change.	_____
4. Demonstrate accurate insulin preparation.	_____
5. Demonstrate filling syringe with only one day supply of insulin and rationale.	_____
6. Calculates correctly a one day supply of insulin to prepare in syringe.	_____
7. Calculates correctly basal and pulse dose amounts of insulin which should have infused over selected time periods to determine if the pump is infusing correctly.	_____
8. Demonstrates proper loading and securement of syringe.	_____
9. Verbalizes reasons to be aware of amount of insulin in syringe immediately before placing pump in the run mode each day.	_____

CARE AND USE OF SOFTWARE	
1. States proper maintenance and storage of adequate supplies for infusion pump.	_____
2. States correctly the ratio of air bubble content in infusion set to amount of insulin displaced.	_____
3. States where to acquire emergency supplies.	_____

SKIN PREPARATION	DATE ACHIEVED
1. States proper infusion sites for insertion of pump tubing.	_____
2. States proper frequency of syringe/tubing changes.	_____
3. Demonstrates aseptic technique during insertion of needle and cleansing of skin.	_____
4. States warning signs of local skin irritation, allergy, infection, intradermal insulin administration.	_____
5. States proper action to take in the event of local skin problems.	_____

NEEDLE INSERTION	
1. States proper angle of insertion.	_____
2. Demonstrates proper angle of insertion.	_____
3. States the effects of different sites on absorption of insulin.	_____
4. Demonstrates proper securement of infusion set.	_____
5. Demonstrates changing syringe without changing catheter tubing.	_____

INSULIN ADJUSTMENT/BLOOD GLUCOSE CONTROL	
1. States algorithms for routine days for control of blood glucose.	_____
2. States algorithms for sick days for control of blood glucose.	_____
3. States effect of basal/pre-meal bolus on glucose levels.	_____
4. States proper procedure for sudden elevations or drop in blood glucose values.	_____
5. States how various nutrients affect control using a continuous infusion pump.	_____
6. States appropriate procedure when meal is skipped or delayed.	_____

IDENTIFICATION - INSULIN PUMP	DATE ACHIEVED
1. States proper identification to place on pump.	_____

PUMP FAILURE/MALFUNCTION	
1. States importance of having accessible conventional equipment at home.	_____
2. States proper "trouble spots" to assess if pump malfunctions.	_____
3. States personnel to contact in case of trouble with infusion pump.	_____
4. States acceptable alternate insulin schedule to be used in case of pump failure.	_____

ACTIVITIES OF DAILY LIVING WITH CONTINUOUS INSULIN DELIVERY SYSTEM	
1. Verbalizes appropriate time periods of the pump without supplementation.	_____
2. States appropriate alternate insulin dose to be used in case of temporary discontinuance of infusion pump. (swimming, evening out)	_____
3. States appropriate precautions to take with temperature changes.	_____
4. States alternate pump settings for exercise, sexual relations, sleeping, etc.	_____
5. Verbalizes appropriate precautions to take when traveling.	_____
6. Demonstrates alternative methods to wearing pump with changes in attire.	_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

MULTIPLE DAILY INJECTIONS/PEN PUMP

AFTER COMPLETION OF THE STANDARD EDUCATIONAL OBJECTIVES AND FURTHER TEACHING SESSIONS, THE PERSON WHO IS TO BE ON MULTIPLE DAILY INJECTIONS WILL BE ABLE TO:	DATE ACHIEVED
1. State the purpose of MDI (multiple daily injections).	_____
2. State the purpose of a pre-meal dose.	_____
3. State the onset, peak, duration of action of regular insulin.	_____
4. State the onset, peak, duration of action of NPH, lente, or ultra-lente insulin.	_____
5. State the proper timing of a pre-meal dose.	_____
6. Prick finger to obtain an adequate amount of blood for home blood glucose monitoring.	_____
7. Demonstrates correct procedure for use of a reflectance meter.	_____
8. Demonstrates ability to visually interpret blood strips accurately.	_____
9. State the correct frequency and times for home blood glucose monitoring.	_____
10. State when urine should be tested for acetone.	_____
11. State the expected range of blood glucose pre-meal, 90-120 minutes after meals, and at 3 a.m.	_____
12. States correct algorithm for adjustment of insulin according to blood glucose level for a routine day.	_____
13. State correct algorithm for adjustment of insulin for treatment of sick days.	_____
14. State correct algorithm for adjustment of insulin for changes in diet and/or exercise.	_____
15. Measure a variety of dosages accurately.	_____
16. Demonstrate correct procedures for choosing and rotating sites.	_____

17. Demonstrate aseptic technique during cleansing of skin and insertion of needle. _____

18. State symptoms of local skin reaction, allergies or infection. _____

19. State correct intervention in the event of local skin problems. _____

20. State the effect on the absorption rate of insulin when different sites are used. _____

AFTER COMPLETION OF TEACHING SESSIONS ON MDI AND THE PEN PUMP, THE PERSON WILL BE ABLE TO:

1. State proper infusion sites for insertion of pump tubing. _____

2. Demonstrate correct filling of the insulin syringe and priming of the tubing. _____

3. Demonstrate correct procedure in assembling the pen pump. _____

4. State correct number of units left unused in the catheter after syringe is emptied. _____

5. State correct frequency of syringe and tubing changes. _____

6. Demonstrate aseptic technique during cleansing of skin and insertion of needle. _____

7. Demonstrate correct angle of insertion. _____

8. Demonstrate a correct and comfortable method of securing the infusion set. _____

9. Demonstrate how to activate the pen pump. _____

10. Discard the stainless steel mixing ball in the syringe if using only regular insulin while maintaining sterility. _____

11. Demonstrate attaching syringe to catheter without removing stainless steel mixing ball if two insulins are used. _____

12. Demonstrate knowledge of both the internal and external dosage know. _____

13. State correct number of clicks per unit of insulin needed. _____

14. States correct procedure for maintenance and storage of adequate supplies for pen pump. _____

15. States where to acquire emergency supplies. _____

16. States importance of keeping syringes at home in case of pump malfunction. _____

17. States appropriate personnel to contact in case of trouble with pen pump. _____

_____ 3-19

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING INSULIN ADMINISTRATION, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. Verbalize the type(s), concentration and dose of insulin used.	_____
2. Verbalize the onset, peak and duration of actions of insulin(s) used.	_____
3. Verbalize correct time(s) for insulin administration.	_____
4. Demonstrate accurate drawing up and injection of insulin.	_____
5. Verbalize proper injection sites and rotation pattern.	_____
6. Verbalize correct care of insulin syringe and needles.	_____
7. Verbalize proper storage of insulin.	_____
8. Verbalize why a daily insulin injection may never be omitted.	_____
9. Verbalize correct procedure to follow in case of insulin misadministration.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

DCCT EDUCATIONAL OBJECTIVES - INSULIN PUMP

After successfully completing the basic curriculum for the standard education of the diabetic patient, the following additional objectives should be accomplished by the patient/significant other who is to be placed on an insulin pump:

MECHANICS OF PUMP	DATE ACHIEVED
1. State the name/model insulin infusion pump.	_____
2. State the purpose of the basal infusion.	_____
3. Demonstrate basal setting adjustment.	_____
4. State the purpose of the pre-meal bolus.	_____
5. Demonstrate pre-meal bolus setting adjustment and administration.	_____
6. State proper timing of pre-meal bolus before meals.	_____
7. State purpose of supplemental dose.	_____
8. Demonstrate supplemental dose setting and activation.	_____
9. State alarms available on pump.	_____
10. Demonstrate alarm settings.	_____
11. State the purpose of priming of syringe.	_____
12. Demonstrate priming of tubing.	_____
13. Demonstrate on/off system.	_____
14. Demonstrate actions taken to properly clean and maintain pump.	_____
15. Demonstrate proper recharging procedure for pump batteries.	_____
16. State life-span of battery.	_____
17. State duration of fully charged battery.	_____

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING THE USE OF PROPER IDENTIFICATION, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. Verbalize the importance of wearing a medic alert tag.	_____
2. Verbalize the importance of carrying identification as a diabetic at all times.	_____
3. State where proper identification can be purchased.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING THE DEFINITION(S) OF DIABETES, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. State a simple working definition of diabetes.	_____
2. State three ways diabetes is controlled.	_____
3. State the role of food activity and medication in the treament of diabetes.	_____
4. Describe what happens in the body when insulin is deficient.	_____
5. State effect of physical activity on regulation of glucose.	_____
6. State effect of stress on regulation of glucose.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING URINE TESTING PROCEDURE, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. Demonstrate urine testing for sugar and acetone using testing materials correctly.	_____
2. Demonstrate accurate interpretation of results of sugar and acetone testing.	_____
3. Verbalize correct voided specimen to use for urine testing.	_____
4. Verbalize correct frequency of urine testing.	_____
5. Verbalize significance of sugar and acetone in urine in explaining symptoms.	_____
6. Verbalize when need to report test results to DCCT center.	_____
7. Verbalize frequency of urine testing when ill.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF THE TEACHING ON ILLNESS MANAGEMENT, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. Explain relationship between illness and ketoacidosis.	_____
2. List early signs of ketoacidosis.	_____
3. State when to notify the DCCT center.	_____
4. Describe and demonstrate how to modify the mealplan as it relates to: - total calories - type and amount of food and fluids - if nauseated or vomiting	_____
5. State when to test urine.	_____
6. State principles of general care during illness.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING INFORMATION RELATED TO HYPERGLYCEMIC AND HYPOGLYCEMIC REACTIONS, THE DIABETIC PATIENTS WILL BE ABLE TO:	DATE ACHIEVED
HYPOGLYCEMIA	
1. State the signs and symptoms of hypoglycemia.	_____
2. Verbalize and describe symptoms experienced.	_____
3. Define "insulin reaction".	_____
4. State situations conducive to causing low blood sugar.	_____
5. State ways to prevent low blood sugar reactions.	_____
6. State effect of prolonged or excessive physical activity.	_____
7. State ways to treat low blood sugar.	_____
8. State need to notify DCCT center of repetitive or severe reactions.	_____
HYPERGLYCEMIA	
1. State signs and symptoms of hyperglycemia.	_____
2. State possible causes of symptoms of hyperglycemia.	_____
3. State ways to prevent symptoms of hyperglycemia and ketoacidosis.	_____
4. State actions to take to treat symptoms of hyperglycemia.	_____
5. State when to contact DCCT for help.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING RELATED TO EXERCISE, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. State preferred times for exercise.	_____
2. State the benefits of an exercise program.	_____
3. Verbalize the effect of excessive or prolonged exercise as a cause of hypoglycemia.	_____
4. State appropriate snacks for exercise.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF DIABETES TEACHING, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. Discuss feelings related to own diagnosis of diabetes.	_____
2. Discuss how diabetes affects own lifestyle.	_____
3. Discuss how diabetes affects their family.	_____
4. Discuss how diabetes affects future plans.	_____
5. Discuss impact of diabetes on feelings of independence or dependence.	_____
6. Verbalize own confidence to manage diabetes.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING FOOT CARE/HYGIENE, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. Verbalize the value of good personal hygiene.	_____
2. Verbalize why there is a need for inspection and special care of the feet daily.	_____
3. Demonstrates correct way of washing and drying feet.	_____
4. Verbalize how to care for toenails, calluses, and corns.	_____
5. Verbalize when to see the podiatrist.	_____
6. State the rationale of the following foot care measures: - avoiding tight garments - protection from heat and cold - appropriate exercise program - keeping skin clean - applying lanolin as needed for dry skin	_____
7. Verbalize the effect of smoking on circulation of blood, especially to the legs and feet.	_____
8. State signs to check for in examination of the legs and feet.	_____
9. State four signs of infection.	_____
10. Verbalize what to do about alterations in skin condition.	_____
11. State three safety measures in preventing alterations in skin condition.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING THE USE OF GLUCAGON, THE DIABETIC PATIENT AND SIGNIFICANT OTHER WILL BE ABLE TO:	DATE ACHIEVED
1. Verbalize and describe signs and symptoms that occur with an insulin reaction.	_____
2. Verbalize and define a severe insulin reaction.	_____
3. Verbalize the different treatment for mild and severe reactions.	_____
4. State indications for use of glucagon.	_____
5. Demonstrate proper storage and mixing of glucagon.	_____
6. Demonstrate ability to give injection by patient and significant other.	_____
7. Explore what could have been done to prevent this severe reaction from occurring.	_____
8. State importance of notifying DCCT center of any severe reaction.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING HEALTH CARE NEEDS, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. Verbalize how to contact DCCT center or emergency facilities in case of illness.	_____
2. Verbalize health care and research reasons for regular visits to DCCT center.	_____

_____

HEALTH CARE PROVIDER

Name: _____

DCCT #: _____

Group: _____

UPON COMPLETION OF TEACHING SELF BLOOD GLUCOSE MONITORING, THE DIABETIC PATIENT WILL BE ABLE TO:	DATE ACHIEVED
1. Demonstrate the proper use of an autolet/monojector/ autoclix/hemalet.	_____
2. Demonstrate the proper technique for obtaining a drop of blood for a blood sugar test.	_____
3. Demonstrate the proper procedure for use of Chemstrip bG/Dextrostix.	_____
4. Verbalizes appropriate time intervals for testing blood sugars.	_____
5. Demonstrates proper use/care of the Accu-Chek/ Glucometer.	_____
6. Demonstrates the ability to accurately visualize Chemstrip bG's.	_____
7. Verbalizes the importance of recording blood sugars.	_____
8. Verbalizes when it is appropriate to also test urine for ketones.	_____
9. Verbalizes when it is appropriate to contact the DCCT center.	_____

_____

HEALTH CARE PROVIDER

NOTE. Forms 3.4 and 122 are missing from the archived MOOP. For completeness, copies for these forms have been added to this copy of the MOOP.

(Handwritten annotations on forms were not present on original copies.)

Form 3.4: Close-Out Medical History and Physical Examination
Used only in the close-out period, December 1992 - April 1993

Purpose: Collect final updates on physical characteristics, lifestyle, diabetes management, adherence to the assigned treatment regimen, medical history since the last clinic visit, and family medical history.

Collection Schedule: Once per patient during the close-out period.

Data Set Name: F0034

Structure: One record per patient evaluated during close-out.

Size: 1423 observations of 501 variables.

DIABETES CONTROL AND COMPLICATIONS TRIAL

Close-Out Medical History and Physical Examination

This form is to be completed during the close-out clinic visit. The visit number that you should use is the next quarterly visit number in the patient's sequence of scheduled visits. At the time of the visit, data will be collected on this form to document modifications of therapy and to update information on the status of patients on deviations from assigned treatment and transfers to inactive status. Also there are questions that are used to update information that was collected at screening.

Unless otherwise indicated, questions on this form refer to the patient's experience since the last completed quarterly clinic visit (i.e., approximately the last 90 days).

If in completing this evaluation it is found that the patient has experienced an intercurrent event, complete the Notification of Intercurrent Event (DCCT Form 020) and, if applicable, the Notification of Hypoglycemic Intercurrent Event (DCCT Form 083) and Further Details of Hypoglycemic Event (DCCT Form 92.2).

Send the original of this form to the Coordinating Center in the weekly forms mailing, retaining a copy in the clinic's files.

A. IDENTIFYING INFORMATION

1. DCCT Clinic Number __ __
2. Patient ID Number __ __ __ __ __
3. Patient's Initials __ __ __
4. Date of Visit __ __ / __ __ / __ __ (Month / Day / Year)
5. Was it necessary to reschedule the patient for this visit for any reason? No (1) Yes (2)

   How many times? __ __
6. What is the follow-up visit number? __ __
7. Enter the date of the LAST COMPLETED quarterly visit. Unless otherwise specified, all questions on this form refer to the patient's experience since this date.

   __ __ / __ __ / __ __ (Month / Day / Year)

B. DEMOGRAPHIC AND GENERAL INFORMATION

1. Birthdate __ __ / __ __ / __ __ (Month / Day / Year)
2. Gender Male (1) Female (2)

3a) Marital status of patient: (CHECK ONLY ONE)

- Never married (1)
- Married or remarried (2)
- Separated (3)
- Divorced (4)
- Widowed (5)

b) If married, how many times? ___

c) If married, remarried, separated, divorced or widowed, when did marital status last change? __ __ / __ __ (Month / Year)

4. Occupation of patient and household providers:

(CHECK ONLY ONE BOX FOR EACH PERSON DESCRIBED. SEE CHAPTER 6 OF THE MANUAL OF OPERATIONS. IF THE PATIENT IS MARRIED, INDICATE THE OCCUPATION OF HIS/HER SPOUSE. IF NOT MARRIED AND IF LIVING WITH PARENT(S), INDICATE OCCUPATION(S) OF PARENT(S). IF LIVING WITH GUARDIAN OR FRIEND WHO PROVIDES ECONOMIC SUPPORT TO THE PATIENT'S HOUSEHOLD, INDICATE OCCUPATION OF GUARDIAN/FRIEND. ALWAYS INDICATE OCCUPATION OF PATIENT. IF ANY OF THESE ARE RETIRED OR CURRENTLY UNEMPLOYED, CHECK CATEGORY CORRESPONDING TO THE TYPE OF OCCUPATION WHICH THE INDIVIDUAL DID OR COULD DO; ALSO CHECK THE CORRESPONDING BOX MARKED "UNEMPLOYED OR RETIRED.")

	Patient	Spouse	Mother	Father	Guardian/ Friend
a) Professional, technical or similar worker	(01)	(01)	(01)	(01)	(01)
Manager, offical, or proprietor	(02)	(02)	(02)	(02)	(02)
Craftsman, foreman, or similar worker	(03)	(03)	(03)	(03)	(03)
Clerical or similar worker	(04)	(04)	(04)	(04)	(04)
Sales Worker	(05)	(05)	(05)	(05)	(05)
Operative or similar worker	(06)	(06)	(06)	(06)	(06)
Service worker	(07)	(07)	(07)	(07)	(07)
Laborer	(08)	(08)	(08)	(08)	(08)
Farmer	(09)	(09)	(09)	(09)	(09)
Homemaker	(10)	(10)	(10)	(10)	(10)
Student	(11)	(11)	(11)	(11)	(11)
Other or unknown	(12)	(12)	(12)	(12)	(12)
b) Unemployed or retired	(1)	(1)	(1)	(1)	(1)
c) Check here if the answer to either (a) or (b) above represents a change in the occupation category during the past year	(1)	(1)	(1)	(1)	(1)

5. Education of patient and household providers. (CHECK HIGHEST LEVEL COMPLETED BY EACH PERSON FOR WHOM OCCUPATION IS GIVEN IN QUESTION B.4.)

	Patient	Spouse	Mother	Father	Guardian/ Friend
Graduate School	(1)	(1)	(1)	(1)	(1)
College graduate	(2)	(2)	(2)	(2)	(2)
Some college or trade school	(3)	(3)	(3)	(3)	(3)
Secondary school graduate	(4)	(4)	(4)	(4)	(4)
Some secondary school	(5)	(5)	(5)	(5)	(5)
Elementary school	(6)	(6)	(6)	(6)	(6)
None	(7)	(7)	(7)	(7)	(7)
Unknown	(8)	(8)	(8)	(8)	(8)

6. Has the patient been a full-time or part-time student during the past year? No (1) Yes (2)

Proceed to Section C. _____

7. Note current level in school:

a) If in elementary or secondary school, grade: __ __

b) If in trade school, year: __

c) If in college, year: __

d) If in graduate school, year: __

8. Has the patient ceased attending school during the past year for ANY reason other than graduation (e.g., dropped out, expelled, moved to a new city, could no longer afford school)? No (1) Yes (2)

If YES, explain: _____

_____

_____

C. SMOKING STATUS

1. During the past 12 months, has the patient ever smoked cigarettes or cigarillos? No (1) Yes (2)

Proceed to Question C.5 _____

2. Does the patient currently smoke cigarettes or cigarillos? No (1) Yes (2)

Proceed to Question C.4 _____

3. How long has it been since the patient quit smoking cigarettes or cigarillos? months __ __

4. During the period in the past 12 months when the patient smoked cigarettes or cigarillos, on the average, how many cigarettes and cigarillos a day did he/she smoke? __ __ cigarettes or cigarillos per day

5. During the past 12 months, has the patient ever smoked pipes or cigars? — No (1) Yes (2)

   Proceed to Question C.9

6. Does the patient currently smoke pipes or cigars? — No (1) Yes (2)

   Proceed to Question C.8

7. How long has it been since the patient quit smoking pipes and cigars? — months __ __

8. During the period in the past 12 months when the patient smoked pipes or cigars, on the average, how many pipefuls and cigars per week did the patient smoke? — pipefuls or cigars per week __ __

9a. During the past 12 months has the patient lived in a residance where there were individuals who smoked? — No (1) Yes (2)

b. During the past 12 months has the patient worked in an environment where co-workers smoked? — No (1) Yes (2)

D. DRINKING STATUS

1. During the past 12 months, has the patient consumed an average of at least one alcoholic beverage per week? — No (1) Yes (2)

   Proceed to Section E

2. How many 12-ounce bottles of beer (excluding "light" beer) did the patient consume during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL CHARACTERIZE A TYPICAL WEEK.) — (A) Bottles __ __

3. How many 12-ounce bottles of "light" beer did the patient consume during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) — (B) Bottles __ __

4. How many 4-ounce glasses of wine did the patient consume during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) — (C) Glasses __ __

5. How many 1 1/2-ounce shots of straight hard liquor and 1 1/2-ounce mixed drinks did the patient consume during the past 7 days? (IF THE PAST 7 DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.) — (D) __ __

6. Does the total amount of alcohol consumed by the patient in the past 7 days (OR IN A TYPICAL WEEK) exceed 560 grams? — No (1) Yes (2)

   Use this table if necessary:

   Amount X Grams

   (A) _____ X 13 = _____

   (B) _____ X 10 = _____

   (C) _____ X 12 = _____

   (D) _____ X 15 = _____

   TOTAL GRAMS OF ALCOHOL _____

E. EXERCISE AND ACTIVITY

1. Which of the following best describes the patient's level of activity on the job, at school or, for homemakers, in homemaking?

   Sedentary (such as office work with occasional inter-office walking, etc.; e.g., secretary) (1)

   Moderate activity (requires considerable, but not constant, lifting, walking, bending, pulling, etc.; e.g., homemaker with family and without domestic assistance, policeman, student taking physical education course) (2)

   Strenuous activity (requires almost constant lifting, bending, pulling, scrubbing, etc.; e.g., furniture mover, heavy domestic work) (3)

2. During the past seven days, how many hours and minutes did the patient spend in the following types of leisure time activities? (IF THE PAST SEVEN DAYS WERE ATYPICAL, CHARACTERIZE A TYPICAL WEEK.)

Light activity (Examples: billiards, bowling, ballroom dancing, golf with power cart, non-competitive volleyball)	Hours	Minutes
Moderate activity (This level is marked by modest increases in heart rate and breathing. Most healthy individuals find these activities comfortable and can continue them for a few hours without undue fatigue. Examples: leisure cycling (5.5 mph), frisbee playing, horseback riding, sailing, table tennis, croquet, golf without power cart)	Hours	Minutes
Hard activity (When exercising at this intensity, most people will likely perspire. Most untrained people could not exercise at this intensity without taking frequent rest periods. Examples: cycling (9.4 mph), half-court basketball, water skiing, downhill skiing, karate or judo, doubles tennis, roller skating, gymnastics)	Hours	Minutes
Very hard activity (Includes strenuous sports involving a lot of movement or running. Only a well-trained individual can perform at this intensity for extended periods of time. Examples: racing cycling, football, full-court basketball, rapid marching, squash, continuous, moderate to fast swimming, rope jumping, cross country running, singles tennis, field hockey)	Hours	Minutes

F. FAMILY MEDICAL HISTORY

1. Number of persons living in the patient's household: (INCLUDE THE PATIENT) __ __

2. Is there a family history of diseases of the following types? (Consider parents, grandparents, siblings, children)

	Parents			Grandparents			Siblings				Children			
	Yes	No	Un-known	Yes	No	Un-known	Yes	No	Un-known	Not Applic-able	Yes	No	Un-known	Not Applic-able
a) Hypertension	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
b) Myocardial infarction	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
(i) If YES, before age 40?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
(ii) If YES to (i), in a diabetic person?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
c) Autoimmune endocrine disease	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
d) Serious eye disease or blindness	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
(i) If YES, due to diabetes?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
e) Renal disease	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
(i) If YES, due to diabetes?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
f) Psychiatric disorders	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
g) Neurologic disease	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
(i) If YES, due to diabetes?	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
h) Hyperlipidemia	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
i) IDDM	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)
j) NIDDM	(1)	(2)	(3)	(1)	(2)	(3)	(1)	(2)	(3)	(4)	(1)	(2)	(3)	(4)

G. DIABETES MANAGEMENT

Answer Section G for all patients except where specified. Do not complete this section at the randomization visit. When completing this section, refer to the previous day's insulin dosage only. However, if in your judgement the previous day's dosage was atypical of the patient's regimen, use another recent day that you would consider typical.

1. Specify types of insulins used by this patient: (CHECK ALL THOSE THAT APPLY)

Human regular	(1)	Pork Regular	(1)
Human Semilente	(1)	Pork Semilente	(1)
Human NPH	(1)	Pork NPH	(1)
Human Lente	(1)	Pork Lente	(1)
Human Ultralente	(1)	Pork 70/30	(1)
Human 70/30	(1)		

Beef/pork Regular	(1)
Beef/pork Semilente	(1)
Beef/pork NPH	(1)
Beef/pork Lente	(1)
Beef/pork Ultralente	(1)

2. To what group was this patient randomized?

Standard (1) Experimental (2)

3. a) What insulin regimen is currently being used by this patient?

Insulin infusion pump	(1)
three or more daily injections	(2)
one or two daily injections	(3)
other:	(4)

(describe the regimen in Question Number 5)

b) Is this the regimen prescribed by the DCCT clinic? No (1) Yes (2)

4. Please summarize this patient's usual insulin regimen here. (Refer to the previous day's insulin dosage only. However, if the previous day's dosage was atypical, use the most recent day that you would consider typical. Round off to the nearest whole unit.)

Total number of units per day: __ __ __

Number of Units Used	Breakfast	Lunch	Supper	Bedtime	Other
Regular	__ __	__ __	__ __	__ __	__ __
Semilente	__ __	__ __	__ __	__ __	__ __
NPH	__ __	__ __	__ __	__ __	__ __
Lente	__ __	__ __	__ __	__ __	__ __
Ultralente	__ __	__ __	__ __	__ __	__ __
70/30	__ __	__ __	__ __	__ __	__ __

NOTE: When filling out this table, consider all insulin given between breakfast and lunch as part of the lunch dose. All insulin between lunch and supper is part of the supper dose. All insulin between supper and bedtime snack is part of the snack dose. If a patient gives a prescribed mealtime dose which happened to be zero on the day recorded, record "0" in the appropriate space. If no dose was prescribed for a given time of day, leave the space blank. If a patient is on a pump, do not record basal here. Meal insulin only refers to bolus doses. Capture basal in number 6 following.

5. If the insulin regimen used by this patient on a typical day cannot accurately be recorded on the table (question 4) please leave the table blank and describe the regimen here:

Answer if #4 is blank: No Yes
I am describing the insulin regimen here: (1) (2)

If yes, specify:

_____

_____

6. COMPLETE ONLY FOR PATIENTS USING AN INSULIN INFUSION PUMP

Total number of UNITS BASAL insulin infused per day: __ __

Total number of different BASAL RATES used per day: __ __

Has the patient had any technical problems with the insulin infusion pump?

No	Yes
(1)	(2)

If YES, specify: _____

_____

7. COMPLETE THIS QUESTION ONLY FOR PATIENTS CURRENTLY ON ONE OR TWO DAILY INJECTIONS:

a) Have you prescribed a change in the insulin regimen or dose since the last visit?

No	Yes
(1)	(2)

If YES, please indicate the reason.

	No	Yes
Symptomatic polyuria/polydipsia/nocturia	(1)	(2)
Unacceptable degree of hypoglycemia	(1)	(2)
Recurrrent ketonuria	(1)	(2)
Hemoglobin A1c above the action limit	(1)	(2)
Pregnancy	(1)	(2)
Other:	(1)	(2)

Specify _____

b) How is this patient monitoring his/her diabetes?

	No	Yes	Uncertain
Self blood glucose monitoring	(1)	(2)	(3)
Urine glucose monitoring	(1)	(2)	(3)

8. COMPLETE THIS QUESTION FOR PATIENTS IN BOTH GROUPS:

Do you suspect that this patient's reported glucose (urine and/or blood) monitoring results are inaccurate or fictitious?

No	Yes	Not Sure
(1)	(2)	(3)

Explain: _____

_____

H. DEVIATIONS FROM ASSIGNED TREATMENT

1. Since the last visit, has the patient been on a "deviation from treatment" (as defined in Section 12.5 of the Protocol) at any time? No (1) Yes (2)

   a. If yes, is the patient currently on deviation from treatment? No (1) Yes (2)

      (i) If NO, enter date of termination of deviation: __ __ Month __ __ Day __ __ Year

      (ii) If this is a new (started since last QV) deviation: enter date of DCCT Form 022, Notification of Deviation from Assigned Treatment: __ __ Month __ __ Day __ __ Year

I. TRANSFER TO INACTIVE STATUS

1. Since the last visit, has the patient been on inactive status at any time? (as defined in Section 12.7 of the Protocol) No (1) Yes (2)

   a. If yes, is the patient currently on transfer to inactive status? No (1) Yes (2)

      (i) If NO, enter date of return to active status: __ __ Month __ __ Day __ __ Year

      (ii) If this is a new transfer to inactive status, enter date of DCCT Form 016, Application for Transfer to Inactive Status: __ __ Month __ __ Day __ __ Year

J. MODIFICATIONS OF FOLLOW-UP SCHEDULE FOR ENDPOINT ASSESSMENTS

(See Manual of Operations Chapter 11)

1. Since the last visit, has the patient been on a modified follow-up schedule at any time? No (1) Yes (2)

   If YES, indicate which assessments:

   _____

   _____

2. Is the patient currently on a modified follow-up schedule? No (1) Yes (2)

K. MODIFICATIONS OF THERAPY FOR PATIENTS RANDOMIZED TO THE STANDARD GROUP ONLY

1. Since the last visit, has the patient been on a modified therapy at any time? No (1) Yes (2)

Proceed to Question L.1 _____

a) Since the last visit, has this patient used glucose monitoring at greater frequency than specified in the Protocol (urine testing 4x/day or self blood glucose monitoring once per day) at your direction? No (1) Yes (2)

IF YES, record frequency: SBGM __/day

UGM __/day

b) Since the last visit has this patient used more than two injections of insulin per day or used an insulin pump to achieve first or second priority standard treatment group goals at your direction at any time?

(NOTE: PERMISSION OF THE TREATMENT COMMITTEE IS REQUIRED PRIOR TO INSTITUTING THIS MODIFICATION OF THERAPY) No (1) Yes (2)

Proceed to question d) _____

If this modification was started since the last visit:

(i) Enter date permission was received from the Treatment Committee to institute the regimen in this patient __ __ Month __ __ Day __ __ Year

(ii) Enter date that new regimen was started __ __ Month __ __ Day __ __ Year

c) Is the patient currently using more than two injections per day or an insulin pump to achieve first or second priority treatment goals for the standard treatment group? No (1) Yes (2)

If NO, enter date of return to one or two injections of insulin per day __ __ Month __ __ Day __ __ Year

If this patient is using more than two injections per day or an insulin pump for reasons other than instructed by you to achieve first and second priority goal for the Standard Group, this represents a deviation from assigned treatment, and should be recorded in Section H and on Form 022.

d) Other modification; specify: No (1) Yes (2)

_____

_____

FOR PATIENTS RANDOMIZED TO THE EXPERIMENTAL GROUP ONLY

2. Since the last visit, has the patient been on a modified treatment protocol? No (1) Yes (2)

Proceed to Question L.1 _____

a) Since the last visit, have you instituted a planned out-patient visit schedule on a less frequent basis than the required monthly visit schedule? No (1) Yes (2)

b) Have you instructed this patient to perform self blood glucose monitoring on a less frequent daily schedule than the required minimum of four times a day, including three pre-prandial and one bedtime sample? No (1) Yes (2)

If yes, record frequency __ / day

c) Have you instructed this patient to use less stringent goals of therapy? No (1) Yes (2)

(i) Specify the new goals:

HbAlc (range) __ __.__ to __ __.__

Blood glucose (range):

Preprandial __ __ __ to __ __ __

Postprandial __ __ __ to __ __ __

3:00 a.m. __ __ __ to __ __ __

(ii) Specify the reason and situation for modification of goals of therapy in this patient:

_____

_____

_____

(iii) Specify the date that the new goal(s) became effective: __ __ Month __ __ Day __ __ Year

(iv) Are the stated goals in effect at present? No (1) Yes (2)

If NO, enter the date that the patient returned to the goals of the experimental treatment group set forth in the Protocol: __ __ / __ __ / __ __ (Month / Day / Year)

d) Other modification; specify: No (1) Yes (2)

_____

_____

L. DIABETES MONITORING - ANSWER FOR PATIENTS CURRENTLY ON 3 OR MORE INJECTIONS OR PUMP

1. Summarize the patient's performance of glucose monitoring. Use the patient's "Daily Diabetes Monitoring Record" to do this. The "number should have done" is the number of tests you instructed the patient to do. Record performance of these prescribed tests only; do not record extra tests performed.

	BLOOD	
Testing Required by Protocol	Number Actually Done	Number Should Have Done
Before breakfast	__ __ __	__ __ __
Before lunch	__ __ __	__ __ __
Before dinner	__ __ __	__ __ __
Bedtime	__ __ __	__ __ __
3:00 a.m.	__ __ __	__ __ __

2. Is the patient performing more self blood glucose monitoring than prescribed? No (1) Yes (2) Uncertain (3)

M. DIABETES MONITORING - ANSWER FOR PATIENTS CURRENTLY ON ONE OR TWO INJECTIONS

1. Summarize the patient's performance of glucose monitoring. Use the patient's "Daily Diabetes Monitoring Record" to do this. The "number should have done" is the number of tests you instructed the patient to do. Record performance of these prescribed tests only; do not record extra tests performed.

	URINE		BLOOD	
Testing Required by Protocol	Number Actually Done	Number Should Have Done	Number Actually Done	Number Should Have Done
Before breakfast	__ __ __	__ __ __	__ __ __	__ __ __
Before lunch	__ __ __	__ __ __	__ __ __	__ __ __
Before dinner	__ __ __	__ __ __	__ __ __	__ __ __
Bedtime	__ __ __	__ __ __	__ __ __	__ __ __

2. Is the patient performing more glucose monitoring (urine or blood) than prescribed? No (1) Yes (2) Uncertain (3)

N. INDICATIONS OF NON-ADHERENCE TO TREATMENT PROTOCOL

1. Answer a) - i) for all patients.

a) How often has the patient claimed to have followed the meal plan?

Not applicable	(0)
Never followed meal plan	(1)
Very infrequently (less than 10% of the time)	(2)
Infrequently (10-44% of the time)	(3)
About half the time (45-55% of the time)	(4)
Most of the time (56-90% of the time)	(5)
Almost all of the time (more than 90% of the time)	(6)
Always followed meal plan	(7)

	No	Yes	Uncertain
b) Has the patient followed a pattern of eating suggestive of an eating disorder (e.g., history of bulimia, vomiting, anorexia)?	(1)	(2)	(3)
c) (i) How many illnesses (intercurrent events or not) has the patient experienced? (If none, enter 00 and proceed to 1.d)	__		
(ii) During how many of these illnesses has the patient been known to have failed to adjust the insulin dose as prescribed?	__		
d) Has the patient used a type of insulin which has not been prescribed?	(1)	(2)	(3)
e) Has the patient been rotating the site of injection (or, in pump patients, the site of infusion)?	(1)	(2)	(3)
f) Has the patient completed less than all seven of the capillary blood collections required for the Profilset?	(1)	(2)	(3)
g) (i) How many intercurrent events (as defined in Chapter 10 of the Manual of Operations) has the patient experienced? (If none, enter 00)	__		
(ii) How many of these intercurrent events has the patient failed to report in the appropriate time window? (If none, enter 00)	__		
h) Has the patient failed to bring in his/her daily record?	(1)	(2)	(3)
i) Does the patient perform self blood glucose monitoring? (If no or uncertain, proceed to Question N.2)	(1)	(2)	(3)
If yes: (i) Has the patient been using self blood glucose monitoring to adjust his/her insulin dosage?	(1)	(2)	(3)
(ii) Does the patient perform self blood glucose monitoring more than once per day?	(1)	(2)	(3)

2. ANSWER (a) - (f) FOR PATIENTS RANDOMIZED TO THE STANDARD TREATMENT GROUP

On how many days has the patient . . .

a) taken more than the prescribed units of insulin (excluding sick days)? __ __

b) taken extra injections of insulin? __ __

c) taken fewer injections of insulin? __ __

d) failed to take his/her prescribed insulin dose? __ __

e) failed to perform and record at least two urine tests or one blood glucose test a day? __ __

f)(i) been ill? __ __

(ii) failed to test and record urine acetone during an illness? __ __

3. ANSWER (a) - (d) FOR PATIENTS RANDOMIZED TO THE EXPERIMENTAL TREATMENT GROUP

a) On how many days has the patient not followed the prescribed algorithm for insulin delivery? __ __

b) How many times has the patient failed to do the prescribed 3:00 a.m. blood tests? __ __

c) How many times has the patient failed to promptly report a low 3:00 a.m. blood glucose to the clinic? __ __

d) How many times has the patient failed to monitor urine acetone when blood glucose was >240 mg/dl or during an illness? __ __

4. ANSWER (a) - (c) FOR PATIENTS RANDOMIZED TO THE EXPERIMENTAL TREATMENT GROUP AND USING INSULIN INFUSION PUMPS

a) How many times has the patient failed to follow instructions for changing batteries? __ __

b) How many times has the patient failed to follow instructions for changing catheters? __ __

c) How many times has the patient failed to follow instructions for changing syringes? __ __

O. DIABETES CONTROL - ANSWER FOR ALL PATIENTS

1. Symptoms of hyperglycemia (Std pts priority I goals)

a) How many nights in the past week did the patient wake up ONCE to urinate? __

b) How many nights in the past week did the patient wake up TWO OR MORE times to urinate? __

c) On the average, how many 8 ounce glasses of fluid did the patient drink per day? __ __

d) How many times did the patient experience DKA? __ __
(As defined in Chapter 10 of the Manual of Operations)

If the patient has had DKA, complete the Notification of Intercurrent Event (Form 020) if it has not previously been completed for this event.

e) Did the patient experience other symptoms of hyperglycemia? No (1) Yes (2)

If YES, specify: _____

_____

2. How many days has the patient had moderate or large ketonuria? __ __
(If none, enter 00 and proceed to Question O.3.)

How many of these were . . .

a) explained by change in routine? __ __

b) due to illness? __ __

c) due to medical equipment failure? __ __

d) spontaneous or unexplained? __ __

3. a) Is the patient female? No (1) Yes (2)

Proceed to Question 0.4 _____|

b)(i) Has the patient had any vaginal itching or discharge? No (1) Yes (2)

Proceed to Question 0.3.c _____|

(ii) Was the patient treated for this? No (1) Yes (2)

(iii) Specify treatment: _____

_____

c)(i) Does the patient menstruate? No (1) Yes (2)

Proceed to Question 0.4 _____|

(ii) Enter date of start of last menstrual period:

__ __ __ __ __
Month Day Year

d)(i) Was the last menstrual period more than five weeks ago? No (1) Yes (2)

Proceed to Question 0.4 _____|

(ii) Was a pregnancy test performed? No (1) Yes (2)

If no, why not? _____

_____

If yes, did the test indicate pregnancy? No (1) Yes (2)

Complete the Notification of Intercurrent Event (Form 020) if it has not previously been completed for this pregnancy. _____|

4. Symptoms of hypoglycemia since last QV

a) Number of hospitalizations for hypoglycemia. (Hospitalization implies overnight admission to the hospital; an emergency ward visit that did not result in hospitalization does not apply.) __ __

If the patient has been hospitalized for hypoglycemia, complete Notification of Intercurrent Event (Form 020), the Notification of Hypoglycemic Intercurrent Event (Form 083), and Further Details (Form 092) if not previously completed for this hospitalization.

If any hospitalizations, give specific reasons:

_____

_____

b) How many times did the patient experience hypoglycemia of such severity that the patient . . .

(i) lost consciousness without seizure __ __

(ii) lost consciousness with seizure __ __

c) How many times did the patient experience hypoglycemia of such severity . . .

(i) that the patient required professional medical assistance, including placement of an IV or an intravenous injection of glucose? __ __

(ii) as to require the assistance of another person, such as the administration of glucagon, but did not require any of the assistance described in (i)? __ __

(iii) as to require the assistance of another person but did not require any of the help described in (i) or (ii)? __ __

d) Complete only if severe hypoglycemia which the patient could not treat himself/herself has occurred:

(i) How many times has the patient received glucagon? __ __

(ii) How many times has the patient received IV glucose to treat hypoglycemia? __ __

(iii) Did any episodes result in injury to the patient or others? No (1) Yes (2)

If YES, specify: _____

_____

If the patient has experienced severe hypoglycemia which he/she could not treat himself/herself, please complete Notification of Intercurrent Event (Form 020), Notification of Hypoglycemic Intercurrent Event (Form 083) and Further Details (Form 092) for for any episodes for which this has not previously been done.

e) Does the patient have a history of recurrent (more than one) hypoglycemic episodes resulting in cerebral impairment (e.g., coma, severe confusion, seizure, loss of consciousness) of such severity that he/she was unable to help himself/herself before the development of warning symptoms of hypoglycemia (e.g., adrenergic symptoms or sweating)? No (1) Yes (2)

f) Does the patient have a history of recurrent (more than one) hypoglycemic episodes resulting in cerebral impairment (e.g., confusion, lethargy, bizarre behavior, etc.) that the patient recognized and was able to treat himself/herself, but occurred before the development of warning symptoms of hypoglycemia (.e.g, adrenergic symptoms or sweating)? No (1) Yes (2)

g) How many times in the past seven days did the patient experience hypoglycemia which was mild enough for the patient to treat himself/herself? __ __

h) If the patient has experienced hypoglycemia in the past seven days which was mild enough for the patient to treat himself/herself, answer Items (i) through (iii) below. Otherwise, skip to Section P.

(i) Did mild hypoglycemia occur:

While the patient was awake (1)

While the patient was asleep (2)

Both (3)

(ii) What was the usual reason for the mild hypoglycemia? (CHECK ALL THAT APPLY)

Missed meal or snack (1)

Decreased food intake at meal or snack (1)

Increased exercise level (1)

Too much insulin taken (1)

Lack of early warning signs of low blood glucose (1)

Other; specify: _____ (1)

_____

Unexplained (1)

(iii) What symptoms does the patient have with mild hypoglycemia? (CHECK ALL THAT APPLY)

Adrenergic warning symptoms (1)

Diaphoresis (sweating) (1)

Altered mental status (1)

Other (1)

None (1)

P. DIABETES RELATED COMPLICATIONS AND/OR CATEGORY 3 INTERCURRENT EVENTS

If the patient has been hospitalized (overnight) to treat any of the following diabetes-related complications or Category 3 events, the Notification of Intercurrent Event (Form 020) must be completed for each hospitalization (see Chapter 10 of the Manual of Operations).

If no hospitalization occurred, Category 3 Intercurrent Events are reported on this form only; Form 20 is not required.

1. OPHTHALMIC

	Right Eye	Left Eye
a) Has the patient had blurred or reduced vision?	No (1) Yes (2)	No (1) Yes (2)
If YES, explain: _____		
b) Has the patient experienced floaters or flashing lights?	No (1) Yes (2)	No (1) Yes (2)
c) Has the patient had any other eye problems?	No (1) Yes (2)	No (1) Yes (2)
If YES, specify: _____		
d) Will the patient be sent to the ophthalmologist for a special visit?		No (1) Yes (2)

2. NEUROLOGIC

Has the patient had any of the following?

a) Paresthesias (pain or numbness) in hands or feet	No (1) Yes (2)
(i) If the patient has pain, is he/she taking medication for the pain?	No (1) Yes (2)
(ii) What is the medication? _____	
b) Unexplained muscle weakness	(1) (2)
c) Vomiting or bloating after meals	(1) (2)
d) Bouts of persistent or recurrent diarrhea	(1) (2)
e) Bouts of urinary retention	(1) (2)
f) Dizziness or lightheadedness (not associated with hypoglycemia)	(1) (2)
g) Fainting (not associated with hypoglycemia)	(1) (2)
h) Seizure (not due to hypoglycemia)	(1) (2)

If YES, complete the Notification of Intercurrent Events (Form 020) if it has not already been completed for this condition. _

i) Impotence	No (1)	Yes (2)	Not Applicable (3)
j) Has the patient developed symptoms compatible with a focal neuropathy (described as sudden onset, asymmetrical and self-limited, i.e., cranial mononeuropathy, proximal motor neuropathy, truncal neuropathy)?			No (1) Yes (2)
k) Other neurologic problem ?			No (1) Yes (2)
If YES, specify: _____			
l) Will the patient be sent to the neurologist for a special visit?			No (1) Yes (2)

3. RENAL

Has the patient had any of the following?

	No	Yes
a) Edema (of renal etiology only)	(1)	(2)
b) Other renal problem	(1)	(2)

If YES, specify: _____

4. VASCULAR

Has the patient had any of the following?

	No	Yes
a) Shortness of breath	(1)	(2)
b) Symptoms of congestive heart disease	(1)	(2)
c) Other symptoms suggestive of a suspected non-acute MI (as defined MOO Chapter 10)	(1)	(2)
d) Symptoms suggestive of transient ischemic attack(s) (As defined in Chapter 10 of the Manual of Operations)	(1)	(2)
e) Other vascular problem	(1)	(2)

If Yes to c) complete the Notification of Intercurrent Events (Form 020) if it has not already been completed for this condition.

If YES, specify: _____

5. INFECTIONS

Has the patient had any of the following?
(As defined in Chapter 10 of the Manual of Operations)

	No	Yes
a) Urinary tract infection (e.g., cystitis, pyelonephritis, perinephric abscess)	(1)	(2)
b) Upper or lower respiratory tract infection	(1)	(2)
c) Gastroenteritis with fever	(1)	(2)
d) Cutaneous (non-infusion site) or mucocutaneous (e.g., Candida vulvo-vaginitis, furunculosis, dental abscess) infection	(1)	(2)

If YES, specify: _____

	No	Yes
e) Post-operative or deep wound infection	(1)	(2)
f) Gangrene	(1)	(2)
g) Other infections not specifically defined in the Manual of Operations (i.e., mononucleosis, epididymitis, measles, chicken pox)	(1)	(2)

If YES, specify: _____

ANSWER THE FOLLOWING ONLY FOR PATIENTS WHO USE AN INDWELLING NEEDLE OR CATHETER FOR INSULIN ADMINISTRATION.

	No	Yes
h) Has the patient had infection at the insertion site (e.g., >1.5 cm erythema and purulence)?	(1)	(2)

Complete the Notification of Intercurrent Event (Form 020).

6. MINOR OUTPATIENT SURGERY OR INCIDENTAL TRAUMA (e.g., simple fracture, uncomplicated laceration).

	No	Yes
	(1)	(2)

If YES, specify: _____

7. INTERCURRENT ENDOCRINE EVENT

	No	Yes
(e.g., hypothyroidism, Grave's disease, Cushing's disease)	(1)	(2)

If YES, specify: _____

_____

8. ADVERSE PSYCHOSOCIAL REACTION

	No	Yes
	(1)	(2)

If YES, specify: _____

_____

9. OTHER

	No	Yes
a) Has the patient experienced any other medical problems or difficulties in carrying out the diabetes treatment regimen (includes imprisonment)?	(1)	(2)

If YES, explain: _____

_____

Q. REVIEW OF SYSTEMS

1. SKIN

a) Does the patient have a history of any of the following?	No	Yes
Eruptive xanthoma	(1)	(2)
Xanthelasma	(1)	(2)
Necrobiosis	(1)	(2)
Shin spot (diabetic dermopathy)	(1)	(2)
b) Other significant skin condition?	(1)	(2)

If YES, specify: _____

_____

2. PSYCHIATRIC

a) Does the patient have a history of any of the following?	No	Yes
(i) Nervousness or anxiety	(1)	(2)
(ii) Unreasonable fears	(1)	(2)
(iii) Eating disturbance	(1)	(2)
(iv) Affective disorder	(1)	(2)
(v) Suicide attempt	(1)	(2)
(vi) Criminal conduct	(1)	(2)
(vii) Psychiatric hospitalization or outpatient psychiatric treatment which included the use of tranquilizers such as phenothiazines	(1)	(2)
b) Other significant psychiatric condition?	(1)	(2)

If YES, specify: _____

_____

3. FEMALE/REPRODUCTIVE
(SKIP TO QUESTION Q.4 IF THE PATIENT IS MALE)

a) Does the patient have a history of any of the following?	No	Yes
(i) Nodules in breast	(1)	(2)
(ii) Breast cancer	(1)	(2)
(iii) Breast discharge	(1)	(2)
(iv) Irregular menses	(1)	(2)
(v) Dysmenorrhea	(1)	(2)
(vi) Vaginitis	(1)	(2)
b) Other significant gynecologic condition?	(1)	(2)

If YES, specify: _____

_____

c) Has the patient ever used oral contraceptives? No (1) Yes (2)

If YES, (i) specify type of drug and use duration:

_____

_____

(ii) Is the patient currently using oral contraceptives? No (1) Yes (2)

d) Does the patient use any other form of birth control? No (1) Yes (2)

If YES, specify: _____

_____

e) Has the patient experienced any difficulties with sexual function? No (1) Yes (2)

4. CHEST PAIN ON EFFORT

a) Have you ever had any pain or discomfort in your chest? No (1) Yes (2)

(i) If "NO" have you ever had any pressure or heaviness in your chest? (1) (2)

If "NO" proceed to Section 5, Claudication.

b) Do you get this pain when you walk uphill or hurry? No (1) Yes (2) N/A (3)

c) Do you get this pain when you walk at an ordinary pace on a level surface? No (1) Yes (2)

d) When you get this pain, what do you do?

Stop (1)
Slow down (2)
Continue at the same pace (3)

e) What happens to it if you stand still?

Relieved (1)
Not relieved (2)

f) How soon does the pain go away when you stand still?

10 minutes or less (1)
More than 10 minutes (2)

g) Please show where the pain was (record all areas mentioned):

	No	Yes
(i) Sternum upper or middle	(1)	(2)
(ii) Sternum (low)	(1)	(2)
(iii) Left anterior chest	(1)	(2)
(iv) Left arm	(1)	(2)
(v) Other, specify _____	(1)	(2)

5. CLAUDICATION

a) Do you get pain in either leg on walking? No (1) Yes (2)

If "NO" proceed to Section R, MEDICATIONS.

b) Does this pain ever begin when you are standing still or sitting? (1) (2)

c) In what part of your leg do you feel it?

_____

(i) Pain includes calf/calves (1) (2)

d) Do you get it if you walk uphill or hurry? No (1) Yes (2) N/A (3)

e) Do you get it if you walk at an ordinary pace on the level? No (1) Yes (2)

f) Does the pain ever disappear while you are walking? (1) (2)

g) What do you do if you get this pain when you are walking?

Stop (1)
Slow down (2)
Continue at the same pace (3)

h) What happens to it if you stand still?

Relieved (1)
Not relieved (2)

i) How soon?

10 minutes or less (1)
More than 10 minutes (2)

R. MEDICATIONS

1. On the average, how many aspirin-containing tablets or other prostaglandin inhibitors does the patient use each month? (IF NONE, ENTER 000) ___ ___ ___

2. Has the patient used or is he/she currently using any prescription drug on a regular basis other than insulin? No (1) Yes (2) _____

   Specify: _____

3. Has the patient used any over-the-counter drugs? No (1) Yes (2) _____

   Specify: _____

4. Does the patient use vitamin supplements on a regular basis? No (1) Yes (2) _____

   Specify: _____

S. PHYSICAL EXAMINATION (A COMPLETE PHYSICAL EXAMINATION SHOULD BE DONE.)

1. Date of last physical examination — Month __ Day __ Year __

2. Current weight (kg) (To convert pounds to kilograms, multiply by 0.454.) ___.__

3. Change in weight since previous exam (kg) (CIRCLE + OR -) + - ___.__

4. What is the patient's desired weight (kg)? ___.__

5. Is the patient less than 18 years old? No (1) Yes (2)
   IF NO, skip to Question S.7.

6. Has patient failed to maintain normal growth and development (see Manual of Operations Chapter for definition)? No (1) Yes (2)

7. Current height (cm) (To convert inches to centimeters, multiply by 2.54.) ___.__

8. Pulse (bpm) ___

9. Sitting blood pressure (RIGHT ARM)

   a) Systolic (mm Hg) ___

   b) Diastolic (mm Hg) ___

   c) Has hypertension been previously documented and has the Notification of Intercurrent Form been completed and sent to the Coordinating Center? No (1) Yes (2)

   SKIP TO QUESTION S.10 _____

   d) Is the current systolic or diastolic blood pressure so high as to be above the normal range as stated in Chapter 10 of the Manual of Operations i.e., ≥ 140 systolic or ≥ 90 diastolic? No (1) Yes (2)

   IF YES, PATIENT SHOULD RETURN ON ANOTHER DAY WITHIN ONE MONTH FOR A SECOND DETERMINATION OF BLOOD PRESSURE. COMPLETE ITEMS e) THROUGH g) AT THAT TIME.

   e) Date of second sitting blood pressure determination — Month __ Day __ Year __

   f) Sitting blood pressure:

   Systolic (mm Hg) ___

   Diastolic (mm Hg) ___

   g) Does the systolic or diastolic blood pressure indicate hypertension as defined in the MOO, Chapter 10 i.e, ≥ 140 systolic or ≥ 90 diastolic? No (1) Yes (2)

   Complete the Notification of Intercurrent Event (DCCT Form 020). _____

10. General Examination

   a) Examine the patient for abnormalities of the following sites.

	Normal	Abnormal	Not Done
Ears, Nose and Throat	(1)	(2)	
Thyroid	(1)	(2)	
Lungs	(1)	(2)	
Breasts	(1)	(2)	
Abdomen	(1)	(2)	
i) Hepatomegaly	Absent (1)	Present (2)	
ii) If present, how large (span)?		__ __ cm	
Lymphatic system	(1)	(2)	
Rectum	(1)	(2)	(3)
Pelvis	(1)	(2)	(3)
Genitalia	(1)	(2)	

11. Cardiovascular Examination

a) Examine the patient for the following cardiac abnormalities.

Rhythm	Regular (1)	Irregular (2)
Venous Pressure	Normal (1)	Abnormal (2)
Cardiomegaly	Absent (1)	Present (2)
S3 Gallop	(1)	(2)
S4 Gallop	(1)	(2)
Systolic Ejection Murmur	(1)	(2)
Diastolic Murmur	(1)	(2)
Other Murmur:	(1)	(2)
If PRESENT, specify: _____		
Rub	(1)	(2)
Other Cardiac Abnormality:	(1)	(2)
If PRESENT, specify: _____		

12. Peripheral Pulse Examination

a) Indicate the grade of the peripheral pulses using the following scale for the right and left pulse.

	RIGHT SIDE			LEFT SIDE		
	Normal (1)	Diminished (2)	Absent (3)	Normal (1)	Diminished (2)	Absent (3)
Carotid						
Brachial	(1)	(2)	(3)	(1)	(2)	(3)
Radial	(1)	(2)	(3)	(1)	(2)	(3)
Femoral	(1)	(2)	(3)	(1)	(2)	(3)
Popliteal	(1)	(2)	(3)	(1)	(2)	(3)
Posterior Tibial	(1)	(2)	(3)	(1)	(2)	(3)
Dorsalis Pedis	(1)	(2)	(3)	(1)	(2)	(3)

b) Indicate the presence or absence of bruits.

	RIGHT		LEFT	
	Absent	Present	Absent	Present
Femoral	(1)	(2)	(1)	(2)
Carotid	(1)	(2)	(1)	(2)
Other:	(1)	(2)	(1)	(2)

If PRESENT, specify: _____

13. Extremities and Skin Examinations

	RIGHT SIDE		LEFT SIDE	
	Absent	Present	Absent	Present
Ulceration	(1)	(2)	(1)	(2)
Skin discoloration	(1)	(2)	(1)	(2)
Gangrene	(1)	(2)	(1)	(2)
Charcot joint	(1)	(2)	(1)	(2)
Deformity	(1)	(2)	(1)	(2)

If PRESENT, specify: _____

_____

14. Injection sites (INCLUDING CATHETER SITES):

	Absent	Present
a) Lipoatrophy	(1)	(2)
b) Lipohypertrophy	(1)	(2)
c) Inflammation	(1)	(2)

15. Feet:

	Absent	Present
a) Ulcers	(1)	(2)
b) Infection	(1)	(2)
c) Abnormal toenails	(1)	(2)

16. Were any other abnormalities noted on physical examination? No (1) Yes (2)

Specify: _____

_____

T. BLOOD GLUCOSE PROFILE, HEMOGLOBIN A1c, LIPID AND RENAL STUDIES

1. Will the Profilset be mailed to the Central Biochemistry Laboratory? No (1) Yes (2)

2. Why not? (CHECK ALL THAT APPLY THEN SKIP TO QUESTION T.9)

Kit damaged after collection	(1)
Patient forgot to do collection	(1)
Patient lost kit	(1)
Patient refused to do collection	(1)
Other or unknown	(1)

3. On what date were the collections performed? Month __ Day __ Year __

4. On what date will the Profilset be mailed? Month __ Day __ Year __

5. What accession number will be used on the Profilset? BGP1 thru BGP7 - _ _ _ _ _ _ _

6. a. Was this profilset supposed to have been quality-controlled? No (1) Yes (2)

(i) If yes, which stick number did the patient duplicate? (If not done, answer 0) ____ stick

(ii) Was this the correct stick number? No (1) Yes (2)

If the patient is randomized to the Experimental Treatment Group, answer Questions T.7 and T.8; otherwise, proceed to Question T.9.

7. Did the patient perform self blood glucose monitoring on the day he/she obtained the Profilset specimens? No (1) Yes (2)

Proceed to Question T.9

8. Using the patient's "Daily Diabetes Monitoring Record", specify the results of the self blood glucose monitoring performed on that day:

Prebreakfast	__ __ __	mg/dl
90 min. p.c.	__ __ __	mg/dl
Prelunch	__ __ __	mg/dl
90 min. p.c.	__ __ __	mg/dl
Presupper	__ __ __	mg/dl
90 min. p.c.	__ __ __	mg/dl
Bedtime	__ __ __	mg/dl

9. The quarterly blood sample is to be taken for HbA1c measurement.

a) HbA1c accession number: H - __ __ __ __ __ __

b) Date specimen collected: __ __ __ __ __ __ (Month Day Year)

10. Will lipid specimens be mailed to the Central Biochemistry Laboratory for annual visit? No (1) Yes (2)

Proceed to Question T.13 _____

11. On what date will the specimens be drawn? __ __ __ __ __ __ (Month Day Year)

12. What accession number will be used? L - __ __ __ __ __ __

13. Will renal studies specimens be mailed to the Central Biochemistry Laboratory for annual visit? No (1) Yes (2)

Process to end of form and sign _____

14. On what date will the specimens be collected? __ __ __ __ __ __ (Month Day Year)

15. What accession number will be used? S and U - __ __ __ __ __ __

Name of person responsible for information on this form: _____

Certification Number __ __ - __ __

REMINDER: The Notification of Intercurrent Event (DCCT Form 020) must be completed if the patient has experienced any of the intercurrent events Category 1 or Category 2 listed in Chapter 10 of the DCCT Manual of Operations For hypoglycemia episodes, complete the Notification of Hypoglycemic Intercurrent Event (DCCT Form 083) and Further Details of Hypoglycemic Event (Form 092) as well.

Form 122: Patient Experience Questionnaire

Purpose: To evaluate patients' attitudes regarding the conduct of the trial and various aspects of their participation in it.

Collection Schedule: Close-out only.

Data Set Name: F1221

Structure: One record per patient (not obtained from every subject).

Size: 1393 observations of 88 variables.

Known Anomalies: None.

Diabetes Control and Complications Trial

CLOSE-OUT

DIABETES CONTROL AND COMPLICATIONS TRIAL
PATIENT EXPERIENCE QUESTIONNAIRE

DIRECTIONS: The purpose of this questionnaire is to assess how various aspects of the DCCT have influenced your participation in the Trial and your willingness to carry out all the requirements. That is, we want you to tell us what factors were important in your decision to come in to the clinic repeatedly for diabetes management and testing for data collection. If you were seen at more than one DCCT clinic during your participation in the trial, please answer the following questions for your current clinic.

We hope you feel free to be perfectly frank about your involvement with the study. We have made arrangements so that your responses to this questionnaire will be private. After you have completed the questionnaire, please insert it in the attached addressed and stamped envelope. Your local DCCT staff will not see your answers. Seal the envelope and return the sealed envelope to the staff.

A. IDENTIFYING INFORMATION

1. Clinic Number ___ ___
2. Patient ID Number ___ ___ ___ ___ ___
3. Patient's Initials ___ ___ ___
4. Date of Completion ___ ___ ___ ___ ___ FSASDATE
   Month Day Year

B. PATIENT EXPERIENCE

1. OVERALL

OVERALL, WHAT EFFECT DID THE DIABETES CONTROL AND COMPLICATIONS TRIAL HAVE ON YOUR LIFE? PLEASE CIRCLE ONE ANSWER.

	BAD EFFECT			NO	GOOD EFFECT			
LBB1	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
	1	2	3	4	5	6	7	8

2. ABOUT THE STAFF

a) TO WHAT EXTENT DID THE FOLLOWING STAFF NEGATIVELY OR POSITIVELY INFLUENCE YOUR DECISION TO CONTINUE PARTICIPATION IN THE STUDY. PLEASE CIRCLE AN ANSWER FOR EACH STAFF MEMBER LISTED. IF YOU HAVE MORE THAN ONE PERSON IN EACH CATEGORY, AND THEY HAD DIFFERING EFFECTS, PICK THE MOST EXTREME.

	TEMPTED ME TO LEAVE THE DCCT			NO	HELPED ME TO STAY WITH THE DCCT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB2A1 1) Your mental health professional(s)	1	2	3	4	5	6	7	8
LBB2A2 2) Your dietitian(s)	1	2	3	4	5	6	7	8
LBB2A3 3) Your nurse(s)	1	2	3	4	5	6	7	8
LBB2A4 4) Your doctor(s)	1	2	3	4	5	6	7	8

b) RANK THE FOLLOWING STAFF ACCORDING TO THE DEGREE TO WHICH EACH MOST INFLUENCED YOUR PARTICIPATION, WITH THE NUMBER ONE BEING THE ONE WHO MOTIVATED YOU THE MOST TO STAY AND NUMBER 4 THE STAFF PERSON WHO INFLUENCED YOU TO PARTICIPATE THE LEAST OR MADE YOU CONSIDER DROPPING OUT. USE EACH NUMBER ONLY ONCE.

LBB2B1 1) Your dietitian(s) ___

LBB2B2 2) Your nurse(s) ___

LBB2B3 3) Your mental health professional(s) ___

LBB2B4 4) Your doctor(s) ___

c) DID YOU EXPERIENCE STAFF CHANGES DURING THE STUDY (I.E., STAFF MEMBER LEFT THE TEAM?) NO (1) YES (2) IF NO, GO TO QUESTION 3.

LBB2C IF YES, WHAT EFFECT DID THE CHANGE HAVE ON YOUR PARTICIPATION? (IF YOU EXPERIENCED MORE THAN ONE CHANGE, ANSWER ACCORDING TO THE STAFF CHANGE THAT HAD THE MOST EFFECT - POSITIVE OR NEGATIVE). CIRCLE AN ANSWER FOR EACH STAFF MEMBER LISTED.

	LESSENED MY PARTICIPATION			NO	IMPROVED MY PARTICIPATION			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB2C1 1) Nurse	1	2	3	4	5	6	7	8
LBB2C2 2) Dietitian	1	2	3	4	5	6	7	8
LBB2C3 3) Doctor	1	2	3	4	5	6	7	8
LBB2C4 4) Mental health professional	1	2	3	4	5	6	7	8

3. CLINIC VISITS

WHAT EFFECT DID THE FOLLOWING ASPECTS OF YOUR CLINIC VISITS HAVE ON YOUR PARTICIPATION? CIRCLE ONE ANSWER FOR EACH ASPECT OF YOUR CLINIC.

	BAD EFFECT			NO	GOOD EFFECT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB3A a) Scheduling of clinic visits	1	2	3	4	5	6	7	8
LBB3B b) Amount of time you needed to be absent from work, home or school	1	2	3	4	5	6	7	8
LBB3C c) Distance to the clinic	1	2	3	4	5	6	7	8
LBB3D d) Convenience of parking	1	2	3	4	5	6	7	8
LBB3E e) Waiting time	1	2	3	4	5	6	7	8
LBB3F f) Child care concerns	1	2	3	4	5	6	7	8
LBB3G g) Need for transportation help	1	2	3	4	5	6	7	8

Patient

4. COMMUNICATION

WHAT EFFECT DID EACH OF THE FOLLOWING ASPECTS OF COMMUNICATION HAVE ON YOUR PARTICIPATION? CIRCLE ONE ANSWER FOR EACH QUESTION ABOUT COMMUNICATION.

	BAD EFFECT			NO	GOOD EFFECT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB4A a) Too many phone calls from the clinic	1	2	3	4	5	6	7	8
LBB4B b) Too few phone calls from the clinic	1	2	3	4	5	6	7	8
LBB4C c) Too long phone calls from the clinic	1	2	3	4	5	6	7	8
LBB4D d) Too short phone calls from the clinic	1	2	3	4	5	6	7	8
LBB4E e) Availability of staff to take calls	1	2	3	4	5	6	7	8
LBB4F f) Flexibility/convenience of phone calls from the clinic	1	2	3	4	5	6	7	8
LBB4G g) Responses to my questions/health care needs (including referrals to other specialists)	1	2	3	4	5	6	7	8

5. STUDY REQUIREMENTS

WHAT EFFECT DID THE FOLLOWING STUDY REQUIREMENTS HAVE ON YOUR PARTICIPATION?

	BAD EFFECT			NO	GOOD EFFECT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB5A a) Your treatment group assignment (Standard or Experimental)	1	2	3	4	5	6	7	8
LBB5B b) Not knowing test results some treatment change or more frequent visits needed	1	2	3	4	5	6	7	8
LBB5C c) Number of clinic visits	1	2	3	4	5	6	7	8
LBB5D d) Number of added studies/procedures after enrollment in the study	1	2	3	4	5	6	7	8
LBB5E e) Number of insulin injections	1	2	3	4	5	6	7	8
LBB5F f) Need to use pump to reach glucose targets	1	2	3	4	5	6	7	8
LBB5G g) Amount of daytime glucose testing	1	2	3	4	5	6	7	8
LBB5H h) 3am glucose testing	1	2	3	4	5	6	7	8
LBB5I i) Amount of record keeping that you are required to do	1	2	3	4	5	6	7	8

DURING THE DCCT YOU HAVE BEEN ASKED TO COMPLETE A GREAT MANY TESTS. THE DCCT HAS HAD A SUCCESSFUL RECORD IN ACHIEVING A HIGH RATE OF COMPLETION. IT IS POSSIBLE THAT YOU HATED ALL THE TESTS BUT COMPLETED THEM ANYWAY. IN THE FOLLOWING SECTIONS (6, 7, 8) WE WANT YOU TO RATE EACH EXAM OR PROCEDURE AS TO ITS EFFECT ON YOUR PARTICIPATION IF YOU WERE TO START THE DCCT OVER.

6. TESTS

WHAT EFFECT DID THE FOLLOWING BLOOD AND URINE TESTS HAVE ON YOUR PARTICIPATION?

	BAD EFFECT			NO	GOOD EFFECT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB6A a) Non-fasting blood tests	1	2	3	4	5	6	7	8
LBB6B b) Fasting blood tests	1	2	3	4	5	6	7	8
LBB6C c) Blood glucose profile sets (Quarterly Visits)	1	2	3	4	5	6	7	8
LBB6D d) 4-hour urine collection (annually)	1	2	3	4	5	6	7	8

7. EXAMS/PROCEDURES

WHAT EFFECT DID THE FOLLOWING EXAMS AND PROCEDURES HAVE ON YOUR PARTICIPATION?

	BAD EFFECT			NO	GOOD EFFECT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB7A a) History & physical exam (Quarterly Visits)	1	2	3	4	5	6	7	8
LBB7B b) Blood pressure measurements	1	2	3	4	5	6	7	8
LBB7C c) Eye photos	1	2	3	4	5	6	7	8
LBB7D d) Eye exams	1	2	3	4	5	6	7	8
LBB7E e) Neurological exams	1	2	3	4	5	6	7	8
LBB7F f) Nerve Conduction (Electromyelogram)	1	2	3	4	5	6	7	8
LBB7G g) ANS tests (Autonomic Nervous System)	1	2	3	4	5	6	7	8
LBB7H h) EKGs (Electrocardiogram)	1	2	3	4	5	6	7	8
LBB7I i) Neurobehavioral tests	1	2	3	4	5	6	7	8
LBB7J j) Psychological Symptoms Forms	1	2	3	4	5	6	7	8
LBB7K k) Quality of Life questionnaires	1	2	3	4	5	6	7	8
LBB7L l) Diet histories (in clinic)	1	2	3	4	5	6	7	8
LBB7M m) Fluroescein angiograms	1	2	3	4	5	6	7	8

8. OTHER TESTS AND PROCEDURES

WHAT EFFECT DID THE FOLLOWING TESTS AND PROCEDURES HAVE ON YOUR PARTICIPATION?

	BAD EFFECT			NO	GOOD EFFECT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB8A a) 24-hr urine collection	1	2	3	4	5	6	7	8
LBB8B b) GFR Study (Glomerular Filtration Rate)	1	2	3	4	5	6	7	8
LBB8C c) Body measurements	1	2	3	4	5	6	7	8
LBB8D d) BIA (Bioelectrical Impedance Analysis)	1	2	3	4	5	6	7	8
LBB8E e) Genetic/Family Studies	1	2	3	4	5	6	7	8
LBB8F f) Skin biopsies (if performed)	1	2	3	4	5	6	7	8

9. OTHER SERVICES

WHAT EFFECT DID THESE OTHER SERVICES PROVIDED BY YOUR CLINIC HAVE ON YOUR PARTICIPATION IN THE STUDY?

	BAD EFFECT			NO	GOOD EFFECT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB9A a) Education programs	1	2	3	4	5	6	7	8
LBB9B b) Social events	1	2	3	4	5	6	7	8
LBB9C c) Newsletters	1	2	3	4	5	6	7	8
LBB9D d) Gifts and other incentives	1	2	3	4	5	6	7	8
LBB9E e) Other communication (letters, cards)	1	2	3	4	5	6	7	8
LBB9F f) Meals	1	2	3	4	5	6	7	8

10. SUPPORT

WHAT EFFECT DID OTHERS HAVE ON YOUR PARTICIPATION IN THE STUDY?

	BAD EFFECT			NO	GOOD EFFECT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB10A a) Spouse/significant other	1	2	3	4	5	6	7	8
LBB10B b) Children	1	2	3	4	5	6	7	8
LBB10C c) Parents	1	2	3	4	5	6	7	8
LBB10D d) Friends	1	2	3	4	5	6	7	8
LBB10E e) Employers	1	2	3	4	5	6	7	8
LBB10F f) Other study participants	1	2	3	4	5	6	7	8
LBB10G g) Other individuals with diabetes	1	2	3	4	5	6	7	8

	NEGATIVE EFFECT			NO	POSITIVE EFFECT			
	EXTREMELY	MODERATELY	SLIGHTLY	EFFECT	SLIGHTLY	MODERATELY	EXTREMELY	N/A
LBB11 11. WHAT EFFECT DID FREE DIABETES MECIAL CARE HAVE ON YOUR PARTICIPATION?	1	2	3	4	5	6	7	8
LBB12 12. WHAT EFFECT DID FREE DIABETES SUPPLIES HAVE ON YOUR PARTICIPATION?	1	2	3	4	5	6	7	8

	NO	YES	NOT SURE
LBB13 13. IF YOU HAD TO DO IT ALL OVER WOULD YOU ENROLL IN THE DCCT?	(1)	(2)	(3)

Comments: _____

_____

LBB14
14. WHAT WAS YOUR MOST IMPORTANT REASON FOR CONTINUING IN THE STUDY? INDICATE THE SINGLE MOST IMPORTANT REASON.

Receiving free care	(1)	Physician	(7)
Receiving free supplies	(2)	Other DCCT staff	(8)
Improved diabetes care	(3)	Emotional bond with staff	(9)
Family encouragement	(4)	Interest in answering the research questions	(10)
Trial Coordinator	(5)		
Nurse	(6)	Interest in helping others to learn more about diabetes	(11)
		Other: _____	(12)

15. LIFE DECISIONS:

WE ARE INTERESTED IN KNOWING TO WHAT EXTENT YOU CONSIDERED YOUR PARTICIPATION IN THE STUDY WHEN MAKING DECISION ABOUT EVENTS IN YOUR LIFE.

THE FACT THAT I WAS/AM A DCCT PARTICIPANT WAS AN IMPORTANT CONSIDERATION WHEN I HAD TO MAKE DECISIONS ABOUT:

	Strongly Disagree	Disagree	Had No Relationship	Agree	Strongly Agree	N/A
LBB15A a) Changing jobs	1	2	3	4	5	6
LBB15B b) Going to school	1	2	3	4	5	6
LBB15C c) Change in residence	1	2	3	4	5	6
LBB15D d) Change in marital status	1	2	3	4	5	6
LBB15E e) Having a baby	1	2	3	4	5	6
LBB15F f) Health insurance	1	2	3	4	5	6