MDRD Clinical Center Manual of Operations
Chapter 2
Study Coordinators' Chapter

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1. The Role of the Study Coordinator

1.1 Job Description

The Study Coordinator is part of the multidisciplinary team involved in the MDRD Study. The Study Coordinator position is a full time position. Each Clinical Center must interview and hire a Study Coordinator. It is suggested that the person hired have a health care background. Previous research experience, computer background, and experience with renal patients is helpful but not necessary.

1.2 Overall Responsibilities

Working with the Principal Investigator, the Study Coordinator guarantees that the MDRD Study Protocol is followed at the Clinical Center. The Study Coordinator is under the supervision of the Principal Investigator and works in cooperation with the Principal Investigator and other members of the MDRD Study team to achieve the goals of the study. By studying the Protocol and attending training sessions, he or she becomes thoroughly familiar with the Protocol and guides the study team to make sure that the Protocol is adhered to consistently at each center. The study teams at the clinical centers will consist of Principal Investigators, additional physicians and co-investigators, dietitians, MDRD Technicians, study coordinators, key entry persons and secretaries.

The Study Coordinator implements and oversees the local operation of the MDRD Study. This includes setting up and managing the clinic, coordinating patient care activities, and serving as a liaison between the study team and other clinic personnel involved in the study.

The Study Coordinator serves the MDRD Study as a data manager. Data management duties include obtaining and documenting data for the study; seeing that data are properly entered and transmitted, communicating with the Data Coordinating Center (DCC) to make sure that data are correct and up to date; and seeing that any queries or problems that arise with data collection are resolved.

The Study Coordinator must guarantee the accuracy of the data reported on MDRD forms. This includes, for example, 1) making sure the units for any lab measure match the units on the form, 2) making sure that data from local lab reports which go on the form are seen rather than accepted over the telephone, 3) making sure that if a data decision is made during key entry, the paper form reflects exactly what was entered into the database, 4) making sure all out-of-range data and data corrections are properly processed using Forms 24 and 25, and 5) following all other procedures which have been outlined for forms completion. The MDRD study is only as good as the data that are recorded.

The Study Coordinator, in conjunction with the rest of the study team, manages the patient's health and progress throughout the study, assists in managing patient problems and assists in maintaining patient compliance, as described in Section 12.1 of this chapter.

The Study Coordinator serves as a backup to the key entry person in that person's absence. Specially certified Study Coordinators might also serve as backup for MDRD Technicians or dietitians. Each of these areas of responsibility is discussed in greater detail elsewhere: key entry in Computer Chapter 5 or the Key Entry Chapter 10, and laboratory work in MDRD Technician Chapter 3, and nutrition in Dietitians' Chapter 1.

2. Training and Certification

2.1 Introduction

All MDRD Study Coordinators are certified at the Data Coordinating Center to guarantee uniformity of procedures. Coordinators are expected to be thoroughly familiar with the MDRD Study Protocol and Manual of Operations. Certification can be accomplished in two ways: by attendance at the overall week-long certification session prior to enrollment of the Phase III patients (for all initial Study Coordinators) or by a two-day certification visit to the Data Coordinating Center (for new Coordinators required when an original Coordinator leaves). During Phase III, two-day certification sessions to train replacement personnel will be held no more frequently than quarterly. All Study Coordinators serve as back-ups for key entry persons and will fill in during times in which one key entry person has left and a second has not yet been certified. Study Coordinators are certified in five aspects of their positions: Forms Completion, Data Entry, Data Transmission, Error Correction, and Electronic Mail. Each Key Entry person must also be certified in these five tasks. If any Clinical Center has an MDRD Technician or Dietitian who will be a back up to the Study Coordinator, that person must also be certified in these five tasks. Other MDRD Technicians and Dietitians will be certified in Forms Completion only. Any MDRD staff member may use the electronic Mail system to send and receive messages. Only certified personnel may complete forms* enter or transmit data, and respond to queries.

Each Clinical Center's computer should be in place prior to the Study Coordinator's training. All Study Coordinators should know how to use their center's PC to log into the Cleveland Clinic VAX and must send a simple mail message to the DCC prior to their training. This is to guarantee that

each center's computer is set up so that when the Study Coordinator returns from training, he or she can begin working on the data related aspects of the job.

2.2 Certification Requirements

In order to be certified and receive a Study Coordinator Certification Number, all five requirements must be met. There is no partial certification. Details for each of the five certification requirements are given below.

2.2.1 Forms Completion

All study personnel will be trained and certified in how to complete the paper forms and how to make corrections on these. Additionally, Study Coordinators will be trained in when to complete each paper form and how to send batches of paper forms to the DCC. To be certified, the person must attain a score of 70 percent or greater on the (open book) Study Coordinator Forms Completion Quiz. This quiz will be developed at the DCC and tested on the other central personnel for ambiguities before it is administered to the Study Coordinators. Notes, manuals and protocols can be used during this quiz. Because the quiz is designed to be uncomplicated and is open book, it is anticipated that most people will have excellent scores.

If anyone should score less than 70 percent at training, they may bring their quiz home with them and write out an explanation of the correct answer for the items they missed. When this explanation is given to the DCC staff and reviewed, they will be certified.

*NOTE: The Chart Review Form 01 can be completed by any member of the team, certified or not.

2.2.2 Data Entry

Each Study Coordinator must know how to open a Datalex batch, enter data, verify data, close a batch, and export a file for later data transmission. To be certified, the person will be given a completed form which they must enter in Datalex on the PC. DCC staff members will check to see if the form was properly entered. Any Study Coordinator who has trouble with this procedure at first may try again as many times as necessary until it is successfully completed.

2.2.3 Data Transmission

Each Study Coordinator must know how to transmit a data file created by Datalex. The file must be transmitted from the PC to the Cleveland Clinic VAX, where it is loaded into the MDRD Scientific Information Retrieval (SIR) database. To be certified, the Study Coordinator must transmit the data file which they created in "Data Entry" above. A member of the certification team will inspect files on the VAX and make sure that the form was properly transmitted. Any Study Coordinator who has trouble with this procedure at first may try again as many times as necessary until it is successfully completed. Note that data transmission will usually be done automatically at night.

2.2.4 Error Correction

After a data form is entered and transmitted, it may be rejected by the MDRD SIR database due to an inconsistency. When this happens, or when an unusual discrepancy is found in a center's data, a query is generated at the Data Coordinating Center and electronically transmitted to the appropriate Clinical Center. Clinical Center personnel read the query, interpret the discrepancy, and respond to the query in the manner specified in the Computer Chapter 5 of this Manual of Operations.

To be certified, the Study Coordinator must read a query which is written on their VAX account (MDRDSMITH, for example) and respond to it properly. A member of the certification team will later check the VAX query database to make sure the query response was done correctly. Any Study Coordinator who has trouble with Error Correction during the Certification process may try again as many times as necessary until he or she can complete it.

2.2.5 Electronic Mail Files

At training, the reading and sending of mail messages will be reviewed. It is assumed that everyone will know how to perform these simple procedures. The instructions are in Computer Chapter 5 of this Volume of the Manual of Operations. However, the Study Coordinator will also need to be able to EXTRACT mail from the Mail utility, moving it to the VAX directory. The Study Coordinator should so be able to move (download) a file from the VAX directory to the PC for storage or editing. Similarily, the study coordinator should be able to upload a message created on a word processor on the PC to the VAX. This message could then be distributed over electronic mail. Thus, Study Coordinators will learn how to EXTRACT a mail file, print it, DOWNLOAD this file from the VAX to their PC, print the file from the PC, and UPLOAD a file from their PC to the VAX and send an electronic mail message.

To be certified, the Study Coordinator must extract a message which the DCC has placed on his or her VAX account's mail utility, print it from the VAX, download it to the PC, and print it from the PC. A member of the DCC Certification team will check the PC directory to see if the file has been successfully downloaded. Any Study Coordinator who has trouble manipulating mail files during the Certification process may try again as many times as necessary until he or she can complete it.

2.2.6 Certification Numbers

When all five Certification Criteria have been met, the Study Coordinator will be considered certified. Certified Coordinators will be provided with certification numbers which will be entered in appropriate locations on patient data forms, i.e., where the form specifies "Certification number of person completing this form."

2.2.7 Recertification

The Study Coordinators will meet at least annually during Phase III. After two years of Phase III (mid-way through the four year study), the Study Coordinators'meeting will include a review of some study procedures and an abbreviated re-certification process. All Study Coordinators will attend this meeting, and the recertification will help assure standardization of procedures. As with certification, any person who initially has trouble with any aspect of the re-certification may keep trying until he or she does this correctly.

3. Setting Up the Clinical Center

3.1 Space Management

It is recognized that each Clinical Center's space set up will vary, as will the amount of space available. The more organized and efficient the use of space, the more smoothly this study will run. One of the Study Coordinator's initial tasks is to work with the Principal Investigator to survey the available space and assess how it can be used to meet the study's needs. This is a list of minimal space needs:

3.1.1 Patient Care

There must be adequate space to see the patient. At regular visits there should be space for the clinician, the patient and at least one other person at any given time. The space should be well lit, and temperature controlled. There should be room available to write and display materials, and to examine the patient. During GFR visits, the space must be very comfortable, with a reclining chair or bed and a restroom nearby. Likewise, a quiet and comfortable location should be available for measurement of blood pressure. Many Clinical Centers may have use of an outpatient area, clinic room, hospital room or Clinical Research Center space. The Study Coordinator should make sure that the space the patient is being seen in is consistent with that Clinical Center's policies for patient care areas.

3.1.2 Office space

There should be adequate office space for all members of the study team. The team may share space or have individual office areas. It is the responsibility of the Principal Investigator and the Study Coordinator to discuss this with the other study team members. The layout of office space will differ among Clinical Centers. In general, office space should be well lit and

temperature controlled. There should be enough total room available to house the two MDRD computers, as well as desks and supplies for the dietitians, secretary/key entry person, Study Coordinator and MDRD Technician. In addition, room must be available for patient records for at least 60 patients, plus storage for excess patient records and all supplies and special low protein foods, as specified in the Dietitians' Chapter 1 of this Manual.

3.1.3 Supplies:

The Study Coordinator is responsible for making sure that all necessary supplies are available prior to initiation of Phase III. Requirements and availability will vary at each center. Below is a suggested list of necessary supplies.

a. Desks:

   All members of the study team will need the use of desk space. The Study Coordinator should meet with all team members including the Principal Investigator to discuss the available number of desks.

b. Computer terminals:

   The MDRD study team will need two microcomputers. One of these will be used primarily by the dietitian for the CBORD Professional Diet Analyzer; the second will be used primarily for key entry and responses to data queries. The Study Coordinator should make sure that these are purchased and set up before Phase III training. Since the Study Coordinator serves as a back-up for the key entry person, and is also a data manager, it is essential that he or she become familiar with the computer as soon as possible. Refer to the Computer Chapter 5 of this Manual for more information.

c. File cabinets:

The Study Coordinator works with the PI to obtain file cabinets which can be locked for security. He or she will need to make sure that there is enough cabinet space available to store the following:

3.1.4 Forms

a. Blank forms

The Clinical Center should keep about 100 copies of each blank data form in stock. Forms should be filed in a system that the Study Coordinator has organized, and should be easily available to the other team members. The system should be such that it is readily apparent when a center is running low on a given form. Due to the large number of forms and instructional material, it is preferable to have one four drawer file cabinet available for blank forms. Other items to be filed here will include informed consents, patient handbooks and other educational items.

b. Completed Forms

Copies of completed forms from each patient visit accumulate too rapidly to be kept in the patient's chart. The Study Coordinator should set up a file system to keep copies of all completed MDRD forms. Due to the large number of patients in the study and rapid accumulation of forms, it is advisable to have one four drawer file cabinet available to hold completed copies of forms. In addition, the Study Coordinator may want to use other files for record keeping and informational purposes.

3.1.5. Miscellaneous office supplies

The Study Coordinator and other team members may choose to keep other supplies to help the study run smoothly. These would be items such as locally ordered appointment cards, business cards, or stamper pads; centrally supplied MDRD stationary; and usual office supplies.

3.1.6. Supplies for other team members

The dietitians, MDRD technician and key entry person will have certain supply area space requirements. The Study Coordinator is not solely responsible for other team member's supplies, but she should be aware of what supplies are needed, how and where they are stored. She should assist them in obtaining and storing whatever supplies are needed. It is especially important that the Study Coordinator be familiar with what is used by the key entry person since she will serve as that person's back-up.

3.1.7 Equipment/Supply List For Sample Handling/Processing

The following list of items will be needed for local Clinical Center sample handling/processing functions. Please note that these items are in addition to the normal clinical equipment such as needles and gauze. Some of these items can be borrowed when needed, instead of purchasing them.

a. Swinging-Bucket refrigerated centrifuge capable of 2200 XG, or approximately 3000 RPM in a standard size centrifuge. Calculate the RPM required for your particular centrifuge with the formula contained in the MDRD Technician's Chapter 3 of this Manual. Check your calculation with the Central Amino Acid Lab if you are uncertain. This centrifuge is needed for amino acid samples, and it can be used for Biochemistry samples, if convenient.

b. Microcentrifuge for spinning micro centrifuge tubes (for Amino Acids-if required by Central Amino Acid Lab). Talk to your laboratory personnel regarding what is available.

c. Refrigerator space for blood and urine specimens.**

d. Refrigerator space for ketoacids, separate from specimens.**

e. Graduated cylinders (1000 ml or 2000 ml) for measuring urine volumes. One of the cylinders should be designated "Radioactive use Only" for measuring GFR sample volumes. Do not contaminate Biochemistry 24 hour urine samples with radioactivity.

f. 10 ml volumetric pipet, class "A", for diluting QC samples every four months.

g. 1 ml SMI pipet for processing amino acid samples. (-If required by Central Amino Acid Lab.)

h. Waterproof pen or marker for labeling specimens.

i. Labels or label tape.

j. Freezer for storing amino acid samples at -70 degrees centrigrade, if it is anticipated that samples will not always be sent off the same day that they are prepared.

3.1.8 Equipment for Blood Pressure Measurement

An appropriate mercury sphygmomanometer (as specified by the MDRD Quality Control Committee).

** Do not store ketoacids or food products in the same refrigerator with Blood or Urine specimens.

3.2 RECORD KEEPING

3.2.1 Introduction

The Study Coordinator, as data manager, organizes and maintains the MDRD records. This is especially important since the Study Coordinator assumes operational responsibility for the integrity for the MDRD data. Each Study Coordinator will organize records differently, but he or she should work with the other team members in accommodating their needs. The Study Coordinator must become thoroughly familiar with where and how records are kept, and must have easy access to all records when necessary, including dietary ones.

3.2.2 Patient Charts

Each patient should have his or her own record which is easily identifiable. The Study Coordinator updates and maintains these records. Each Clinical Center should develop a record system that suits its purposes. Some suggestions for pertinent information for the chart are:

a. Initial history and health profile
b. Progress notes
c. Laboratory reports from local and central labs
d. Copies of the informed consent and economic information forms
e. Information on contact persons who will know how to reach the patient.
f. Flow sheets with all the pertinent monthly data collected on the patient.

The dietitian and MDRD Technician will need to keep records on the patient as well. Depending on local preference, these record files may be combined or maintained separately. The Study Coordinator should have access to all records since he or she serves as the Data Manager.

3.2.3 Copies of completed Forms:

Once a patient form is completed, the original is sent to the Data Coordinating Center, and a copy is kept at the Clinical Center. For certain forms, an additional copy must be sent to the Nutrition Coordinating Center or a Central Laboratory. The Study Coordinator organizes and maintains a system for filing these completed forms. The Study Coordinator must have easy access to these files. Data forms will be printed on NCR paper, so minimal photocopying will be required.

3.2.4 Miscellaneous records:

The Study Coordinator and other team members may choose to keep other types of study records. These will serve to monitor and account for MDRD activities for areas important to that Clinical Center. Again, it is stressed that if team members keep records of certain activities, the Study Coordinator should keep track of these records. Some activities for which it is helpful to keep logs include:

a. Quality Control Procedures
b. Data Transmission Reports
c. Queries and Responses
d. Mailings of form orders and receipts of forms
e. Receipts of computer software updates
f. Special Low Protein Diet Products
g. Keto Acids (pills, pckets, flavors) and other drugs
h. Electronic Mail
i. Correspondence
j. Supplies
k. Meeting agendas and minutes

3.3 Liaison Personnel

Prior to the beginning of Phase III patient enrollment, the Study Coordinator should contact and meet with all Clinical Center liaison personnel. Development of a positive working relationship with these people will help the study to run smoothly. Each liaison person should be familiar with the MDRD Study objectives and protocol, and have written copies of the procedures pertinent to their role. People from the departments listed below are those who will have some involvement with the study.

3.3.1 Special Funds

There will be a person in the accounting department at each center who administers the grant funds. It is advisable for the Study Coordinator to meet with these people, and become familiar with their institutional policies for the handling of grants. This is especially important when supplies need to be purchased.

3.3.2 Billing/Accounting

At every Clinical Center, the Study Coordinator should make certain that the billing department has a system for handling charges that are generated through patient visits. The Study Coordinator may need to meet with the billing representative prior to the initiation of the study: however, the billing representatives should deal directly with HCFA if any questions or issues arise. The Study Coordinator should not serve as an intermediary between HCFA and the Hospital billing office. Both the billing representative and Study Coordinator should be familiar with the HCFA procedures for handling charges. For more detailed information on billing, refer to the Billing Chapter 7 of this Manual of Operations.

3.3.3 Pharmacy

The Study Coordinator will need to meet with the Pharmacy Representative and organize a system for storing and dispensing the MDRD supplements. The Study Coordinator should make sure that the Pharmacy has a written copy of the MDRD pharmacy procedures, and that the pharmacist knows what is needed to store supplements (i.e., amount of shelf space and refrigerator or freezer space) and a list of contacts at the central Drug Distribution Center. The Study Coordinator must be sure that the pharmacist has the prescription form. For more information on Pharmacy procedures, refer to Chapter 6 of the Manual of Operations.

3.3.4 Nuclear Medicine/Radiation Safety

The Study Coordinator, the Principal Investigator, and the MDRD Technician should meet with personnel from Nuclear Medicine and Radiation Safety. It is imperative that the Study Coordinator be thoroughly familiar with radiation safety procedures at the Clinical Center. He or she should also understand how the Nuclear Medicine department and MDRD Technician carry out the protocol for doing GFR's. This is especially important since GFR's are the primary outcome variable, and require strict protocol adherence. (In some centers, the Study Coordinator will serve as the Backup MDRD technician.) Personnel in the Nuclear Medicine Department must have a copy of the MDRD GFR procedures from Chapter 3 of this Manual as well as the list of contact people at the central GFR lab. Refer to the Clinical Center MDRD Technicians' Chapter 3 of this Manual for more information on GFR's.

3.3.5 Local Laboratory

The Principal Investigator, MDRD Technician and Study Coordinator should meet with representatives from the local laboratory. The local lab representatives need to be familiar with MDRD local laboratory quality control requirements, although the MDRD personnel will be ones completing Form 21, Local Quality Control Form, and Form 22, CAP Quality Control Form. They should also have a list of contact persons at the Central Biochemistry Lab. It should be made clear that the MDRD Technician will need use of a local lab centrifuge if there is no proper centrifuge in the MDRD area. Refer to chapter 3 for more information on local lab procedures.

3.3.6 EKG Lab

The Study Coordinator and Principal Investigator should decide who will be performing the EKGs, Cardiology personnel or the MDRD Technician, and they should determine whose electrocardiogram machine will be used. The Study Coordinator is responsible for making sure all EKGs are performed when required.

3.3.7 Referring Physicians

It is important to stay in contact with the patient's referring physician, if there is one. The Study Coordinator should work with the Principal Investigator in providing referring physicians with updates on the patient. Specifics should be resolved locally.

3.3.8 Clinical Research Center (CRC)

If activities (e.g. GFR's) are taking place in a Clinical Centers' CRC, the P.I., Study Coordinator, and MDRD Technician should meet with the CRC staff to review the Protocol and delineate specific activities which will be ongoing in the CRC.

4. Clinic Management

Since the Study Coordinator oversees the overall operation of the protocol, he or she will need to coordinate and manage the clinic in an organized fashion.

4.1 Scheduling of activities

The Study Coordinator is the person responsible for scheduling all MDRD activities. Since there will be many patients at each Clinical Center, it is important to organize the workload so that it is evenly distributed over the course of the week, and that data are accurate and timely.

4.1.1 Scheduling the Patient Visits

During the enrollment period, patients should be scheduled for Baseline 0 visits at a rate of about three per month, assuming a sample size of 60 patients enrolled over a 21 month period. Try not to have more than two B0 visits in a week. This is to avoid too many patients coming in for any type of visit during any given week in the future. Once a patient has been entered into Baseline, the DCC generates a Baseline visit schedule. The schedule has a target date for each visit, along with a suggested time window. If a Baseline visit cannot be held during the suggested time window, it may be rescheduled later, outside the window. However, the patient must complete all Baseline visits within five months in order to be randomized.

Once the patient has entered Follow-Up, a new schedule two is generated. During Follow-Up, the time window is $\pm$ two weeks. If a Follow Up visit cannot be held during the Follow-Up window, it is a missed visit. If a visit is delayed until the next month's window, it is the next month's visit. A missed F4 visit is never made up during the F5 window.

If patients are entered into the study at the rate of three per month, then during the remainder of the study, patients should be able to stick to the visit windows and allow for an even weekly distribution of visits. (Given a population of 60 patients per center, a reasonable goal would be to not have more than 20 patient visits per week.) When scheduling the visits in a given week, the Study Coordinator must take into consideration:

a. Coordination of activities among each team member.

b. Obtaining the data in a timely fashion. Since data must be transmitted within two working days of the visit, there must be time following each patient visit to complete forms and compile data. The Study Coordinator should work with other team members to set up a weekly visit schedule which accommodates this.

Example #1: Alternating Visit Days

If the clinical center were to see 12 patients in a given week, an example of patient visits and work could be scheduled as follows:

Monday - Six patients visits; two with GFR's

Tuesday - All team members work on their forms and charting; by Tuesday afternoon the Study Coordinator gets all the data and checks it over. (At some centers local lab data may arrive a day or two later.)

Wednesday - Six patient visits; one with GFR. Meanwhile the key entry person is entering and transmitting Monday's data.

Thursday - Finish up Wednesday's data.

Friday - The Key Entry tech enters Wednesday's data, other team members do paperwork, and all have a meeting, etc.

Example #2: Visits in the Morning

The clinical center may choose to hold a few patient visits every day, and spend the afternoons doing data compiling and paper work.

A tentative system should be organized prior to initiation of the study and revised as experience is gained. Whatever system is in place for organizing and scheduling patient visits, the Study Coordinator will need to assess these factors:

a. Each patient's own schedule, and his or her windows for visits.
b. Team members' schedules.
c. Availability of clinic space at any given time. The sooner that a system for patient visits is established, the more smoothly the trial will run.

4.1.2 Scheduling the QWB Interviews

The QWB Interview is administered to patients over the phone at their homes around the times of the B3, F6, F12 (and every six months thereafter) visit. Therefore, the times for those interviews should be scheduled at the B2, F5, F11 (and every six months thereafter) visits. The Study Coordinator should ask the patient for an appropriate time slot, confirm the patient phone number and notify the DCC QWB interviewer.

4.2. Coordination of Functions Between the Study Team Members

It is the Study Coordinator's responsibility to notify the other team members of the MDRD activities. He or she serves as a liaison in communication, problem solving and scheduling. The Study Coordinator notifies the other team members of patient visits and pertinent meetings. The Coordinator should work with them to design a system which allows each team member to see the patient at different times, without conflict. Team meetings should be held weekly, and the Study Coordinator should work with the MDRD Study team in scheduling these.

5. Data Management

The Study Coordinator has operational responsibility for the integrity of the data. Therefore an accurate system for compiling the data must be organized. Once a patient visit has occurred, each team member has one working day to complete his or her forms. By the end of that day, the Study Coordinator should have all forms in hand and checked for forms completion procedures and accuracy of data items. By the next day, the data should be given to the key entry person who has one day to enter it. Therefore, within 24 hours of when the data is given to be entered, the Study Coordinator should check to make sure that it has been entered. The Study Coordinator and Key Entry person may want to set up a check system to monitor this procedure.

Other forms to be completed, such as flow charts that the clinical center is keeping, should be filled out within a week of the patient visit to avoid backlog of work. Since there should be weekly meetings of the clinical center team, the Study Coordinator may want to compile data to be presented at a weekly meeting.

When the key entry person is not available, the Study Coordinator will enter data. The data must be entered in a timely fashion even when the key entry person is away from the office.

The Study Coordinator oversees data transmission by making sure that all the data are accurate prior to being transmitted. Once data are transmitted, the key entry person notifies the Study Coordinator. Keeping a log book of the response messages indicating successful transmission is recommended. The forms are then given to the Study Coordinator to see that the NCR paper copies are sent or filed.

If a query is generated, the Study Coordinator needs to respond to it or review it before the key entry person responds to it. (It is preferable to keep a paper record of queries.) When the key entry person is absent, the Study Coordinator is responsible for data transmission. The data must be transmitted in a timely fashion. For more information on data transmission, refer to the Computer Chapter 5 of the Manual of Operations.

6. Patient Management

6.1 Preparation for Patient Visits

The Study Coordinator is responsible for ensuring that the patient is reminded prior to every scheduled monthly visit. He or she may call the patient, designate another person to do so, or send a reminder card. Reminder calls should occur two to four days prior to the visit so the patient has time to begin a 24 hour urine collection or to get an HCG RIA pregnancy test done if needed. The pregnancy test may be performed at any appropriate lab if the patient or the Study Coordinator obtains written results for the clinical center file. Results of pregnancy tests should be kept in the MDRD files.

Patients should be reminded to fast and abstain from taking the designated drugs if necessary. Study visits occur within designated time intervals, and it is essential no visit be missed because the patient forgot the appointment. Reminder cards will probably be sufficient once a patient has become familiar with study visits.

Prior to the patient visit the Study Coordinator should assemble the necessary forms for that particular visit. Either the Study Coordinator or dietitian will assemble the necessary nutrition forms. A schedule for required forms may be found in the forms manual, and in the appendix to this chapter. It is important to review the forms before the visit to assure all the required information can be obtained at the time of the visit and that all appropriate team members will be present for the visit.

The Study Coordinator should determine which laboratory tests will be required at the visit. Laboratory tests will be performed both centrally and locally at Baseline visits 0 and 3, and at every other visit during Follow-up (2,4,6, etc.). Some items are measured locally and other items are measured centrally. A schedule for the required tests for Baseline and Follow-Up may be found in Sections 6 and 9 of the MDRD Protocol and in the appendix to this chapter. Urine collection containers, 4 liter jugs with 250 ml. of 5% acetic acid, should be given to the patient at every visit for the next visit.

During the Follow-up period, the Study Coordinator will be responsible for seeing that the patient receives his or her medications. It is recommended that the dietitian give the medication to the patients, since the dietitian will be instructing the patients regarding, for example, how to take the keto acid supplements. The medications include the MDRD Multi-vites, iron, calcium carbonate, and keto acid supplements, and will be supplied in cooperation with the local pharmacy. (The local pharmacy will obtain the multi-vites and the keto acids from the central pharmacy.) Compliance with Study medications will be determined by monthly pill counts. The Study Coordinator is responsible for making sure the pills are counted. It is recommended that this task be performed by the pharmacist or as a second choice, by the key entry person, since the Study Coordinator and the Dietitian will be busy with the patient during the visit.

7. Screening

7.1 Purpose

The purpose of the screening period is to identify patients eligible for enrollment into the study. Patients may be screened at any time during the 21-month recruitment period ending in September 1990; however, they must be entered into Baseline within two months of the date of the measurement of the serum creatinine that is used for the determination of eligibility, and the last day a patient may enter Baseline is September 30, 1990. Screening is divided into two parts: chart review and the patient visit. The Study Coordinator will assist the Recruitment Coordinator and other members of the center in doing chart reviews. For further details on this aspect of recruitment, see the Recruitment Coordinators' chapter.

7.2 Eligibility for a Screening Visit

Each patient who meets the following criteria should be evaluated:

1. Age 18-70 years
2. Most recent serum creatinine during the past one year within the limits below:
   a. 1.4 - 7.0 mg/dl (men)
   b. 1.2 - 7.0 mg/dl (women)
3. Not taking insulin
4. Not a kidney transplant recipient. A Form 1 should be completed for all patients who are evaluated. Eligibility and exclusion criteria are listed in the Protocol and on Form 1. Each patient eligible by chart review should be invited for screening visit. A Form 02 should be completed to document those eligible for the screening visit who decline to attend the visit.

7.3 Screening Visit

Prior to a screening visit, the Study Coordinator should make sure that the Principal Investigator will be available at the time of the screening visit to discuss the study, and that the dietitian will be available to do the anthropometric measurements. The patient should have an opportunity to meet all members of the Study team during screening. It should be determined prior to the patient's visit if any lab work (such as albumin or creatinine) is required to determine eligibility. The Volunteer's Information Handbook, the Primary Informed Consent and any other relevant study material should be available. Patients may come back for extra "informed consent visits" until they thoroughly understand the consent form and agree or decline to enter the Study. The Baseline 0 "Physical Exam" may be done anytime from the screening visit to the Baseline 0 Visit.

After the visit the Study Coordinator should complete the Screening Form (#03) to determine eligibility for entrance into Baseline. Before patients can enter Baseline, they must be determined eligible on the basis of all criteria defined in the Screening Form, and they must have signed the Primary Informed Consent Form. (Note that this form may include consent for Study F.) The Study Coordinator must photocopy this consent form and send a photocopy to the Data Coordinating Center. The original informed consent form should be kept in a secure location at the Clinical Center. The informed consent forms away from other study forms in a secure manner, since they include the patients' names. Patients found to be ineligible to enter Baseline may be rescreened at a later date. Patients eligible to enter Baseline who do not enter Baseline become part of Study G.

7.4 Scheduling the Baseline 0 Visit

The Study Coordinator should schedule the initial Baseline 0 (B-0) visit, the Demographic and Baseline Exam Visit, when all members of the Study team will be available. The patient should be aware that this will be a long visit as it will include measurement of the GFR, collection of demographic data, nutritional assessment, and in most cases, a physical exam. The patient should be given "Instructions for Collection of a 24 Hour Urine" and "Instructions for Preparation for a GFR". If the patient is a menstruating female, she must be instructed to have a pregnancy test (qualitative serum HCG RIA) within 72 hours of the GFR measurement. The GFR may be scheduled on a different day than the rest of the B-0 visit, but it is recommended that the B-0 GFR should be within 15 days of the B-0 visit. (Note that Baseline diet is assigned on the basis of the B-0 GFR.) Before the Baseline Visit, the patient should be given a 4-liter container with 250 ml. of 5% acetic acid added for a 24-hour urine collection. The patient should be instructed to bring the 24 hour urine collection to the Baseline 0 visit. The urine may be collected within 15 days prior to the visit. The urine should be refrigerated and must arrive at the Central Biochemistry Laboratory within one week of collection. The patient should be given instructions for the time and location of the visit and the telephone number to contact members of the study team with any questions.

The Baseline 0 visit must be scheduled within two months of the date of the measurement of the serum creatinine that is used for determination of eligibility. This time limit must be strictly adhered to, since a patient could become ineligible over time. If more than two calendar months have

elapsed since the date of the screening visit, the patient cannot have a Baseline 0 visit. If, on a day after the two month period has ended, the Clinical Center staff wishes to enter a person into Baseline, a new screening visit must be held and the patient can have a Baseline 0 Visit at a later date.

If a Clinical Center overlooks this requirement and a B0 visit is held more than two months from a screening visit, the Data Coordinating Center will send a notice to the Clinical Center saying that this visit violated the Protocol and is not an official Baseline 0 visit. Any data (including GFR information) gathered at this visit will not go into the MDRD data base. If the patient is going to continue, the patient must have a new screening visit followed by a new Baseline 0 Visit within two months of that screening visit.

8. Baseline

The Baseline Period is three months long. During the first month patients will undergo assessment of GFR, urinary protein excretion, usual protein intake on an unmodified diet, dietary history, nutritional status, medical history, physical examination and laboratory evaluation. During the second and third months, patients will be prescribed a defined diet and dietary protein intake, compliance with study procedures will be monitored, and urinary protein excretion will be assessed. At the end of the three month Baseline Period, assessment of GFR, urinary protein excretion, and dietary protein intake will be repeated. Target dates are given for all Baseline visits and missed visits should be made up as soon as possible. It is hoped that most patients will complete Baseline in the target time of three months. However, the maximum interval from Baseline 0 GFR to Baseline 3 GFR cannot exceed 5 months. If this limit is exceeded, the patient is excluded. The Baseline period could be repeated after a one month delay followed by a new screening visit, if enrollment of Phase III patients is still in progress.

At the Baseline 0 visit, a Form 04, the Demographic and Baseline Exam Form is completed. Fasting blood tests, 24-hour urine collection, measurement of GFR, physical exam and nutritional assessments are performed/obtained. This visit must be coordinated with the physician, dietitian and GFR technician and is a long visit.

GFR measurements will be performed at the B-0 and B-3 visits, but may be scheduled on a separate day within 2 weeks of either scheduled visit date. The patient needs to be fasting for these visits and if the patient is a menstruating female, a qualitative serum HCG-RIA must be obtained within 72 hours of the scheduled GFR measurement. During the GFR, the

dietitian may be able to complete aspects of the nutritional assessments. This generally becomes easier on subsequent visits as the patient's anxiety concerning the GFR test decreases. A Form 16 must be completed each time a GFR measurement is done. A patient who does not have both Baseline GFRs cannot be randomized (See Protocol).

A physical exam will be performed by the physician at the Baseline 0 visit. This may be done at the Screening visit or sometime between the screening visit and the Baseline 0 Visit if it is more convenient. At the remainder of the Baseline visits, the patient will have blood pressure and pulse measured and be assessed for the presence of edema. Blood pressure will be measured as described in the Protocol.

Laboratory tests will be obtained at the B-0 and B-3 visits. Required laboratory tests for each Baseline visit are listed in the Protocol and in Appendix 1 of this chapter. Note that some are local and some are Central. The Study Coordinator or GFR technician should complete a Form 17, Central Laboratory Mailing Form, to send with the samples to the Central Biochemistry Lab or a Form 19, Amino Acid Mailing Form, to send with the samples to the Central Amino Acid Laboratory. (See Chapter 3 of the Manual of Operations for sample handling and mailing instructions.) Local laboratory tests should be reported to the Data Coordinating Center on Form 06, Local Laboratory Measurement Form.

A 24-hour urine collection is required within $\pm$ 15 days of the target date of each of the four Baseline visits. The urine should be refrigerated and must arrive at the Central Biochemistry Laboratory within one week of collection. This is to be mixed and measured, and an aliquot sent by the Clinical Center to the Central Laboratory. The patient may not measure the urine or mail the aliquot. The MDRD Technician or Study Coordinator will complete Form 17, Central

Laboratory Mailing Form, to send with each aliquot. (See Chapter 3 of the Manual of Operations for sample handling and mailing instructions). It is important to ascertain whether the urine collection is accurate and complete (i.e., if the patient remembered to discard the first urine sample and collected all of the urine for 24 hours). Otherwise, the urine should not be sent to the Central Laboratory, and the patient should collect another urine if it is still possible to do so during Baseline. The patient should be given a 4 liter container with 250 ml. of 5% acetic acid at each visit for the next visit. Results from three urines are required for randomization. All four urines should be collected, both because the Protocol includes four urines and because this way, if one is unmeasurable, three results will still be available. When a patient does not have at least three 24-hour urines by the end of Baseline, that patient cannot be randomized unless these are completed within the five-month time limit (see Protocol).

Three social science questionnaires will be given to the patient during Baseline. The Symptom Checklist (SCL-90-R, Form 28) will be given at the Baseline 3 visit. The Study Coordinator will review the form with the patient and complete the cover page of Form 28, Symptom Checklist Form. The patient should complete the checklist at the visit. The Quality of Well Being Interview Form 27, will also be done around the time of the Baseline 3 visit. The Patient Symptom Form 26 will be done at each monthly visit.

An EKG is required Baseline 2 visit. The Study Coordinator should complete Form 18, ECG Mailing Form, and mail the original 8 x 11 inch EKG (no strips) with an extra copy of the EKG and two copies of the form to the Data Coordinating Center. A second copy of the original EKG should be kept in the patient's chart.

The Economic Information Form 29 will be completed at each patient's Baseline 0 Visit. For all patients entering Baseline, Form 07, Renal Diagnosis Form, should be completed at or before the Visit 1. This form is to be completed by the physician and the Study Coordinator.

There is an extra visit with the dietitian (Baseline 0-A) between the Baseline 0 and Baseline 1 visit. The computer schedule from the Data Coordinating Center will not be available before these visits, so the Study Coordinator should set the date for this visit at two weeks after the Baseline 0 visit. The dietitian will schedule the 3-day diet diary between visits B0 and B0A. There is also an extra visit with the dietitian (Baseline 1-A) between the Baseline 1 and Baseline 2 visits.

At the conclusion of the Baseline period, which must occur within five months of the Baseline 0 visit, the Study Coordinator should complete Form 08, Secondary Screening/Baseline Dropout Form to determine the patient's eligibility for randomization. A final Baseline 3 report will be sent by the Data Coordinating Center with the final status of the patient with regards to the GFR, body weight, creatinine, urinary protein excretion, estimated protein intake and albumin. The results of both these reports must affirm that the patient is eligible in order for the Study Coordinator to call to the DCC to randomize the patient.

All Baselines should be completed in three months. If a patient's compliance is such that he or she cannot complete the Baseline Period within five months, he or she is excluded due to poor or doubtful compliance (see Protocol). However, all Baselines should be completed in three months.

9. Randomization

The study team should work together to decide whether a given patient will be randomized, considering the likelihood of the patient reaching a stop point or becoming lost to follow-up. Patients who are likely to be in the study less than a year should not be randomized. Only patients judged to be motivated should be randomized. When a patient's Secondary Informed Consent has been signed and all eligibility criteria have been reviewed, the Study Coordinator can call the Data Coordinating Center for a random blood pressure and diet assignment. This must occur within 6 weeks of the Baseline 3 visit. Although the Study Coordinator has the primary responsibility for getting the randomization assignment, the Principal Investigator or designated Co-Investigator may make a randomization phone call if the Study Coordinator is not available. Randomization calls may be made Monday through Friday, from 8:00 A.M. to 4:30 P.M. Eastern Time only.

During the phone call the Study Coordinator will complete Form 09, the Clinical Center Randomization Form, and the Data Coordinating Center Staff person will complete Form 37, the Data Coordinating Center Form for Randomization into Studies A and B. Once the patient has been randomized, the Study Coordinator should inform the study team of the patient's diet and blood pressure assignment. The dietitian will require approximately two weeks in order to prepare for the first Follow-up Visit when the patient will be instructed in his or her follow-up diet. This visit should be scheduled with the patient within four to six weeks of the Baseline 3 visit.

Randomization to a dietary intervention will mark the patient's official and irrevocable entry into the Study, and all evaluation studies will be conducted whether or not the patient adheres to the assigned dietary or blood pressure regimen. If a patient later decides, despite the teams best efforts, that he or she will not follow his or her MDRD diet or blood pressure assignment, it is still very important for that patient to attend visits and provide laboratory data, especially GFR data.

10. Follow-Up

The follow-up period will last for a maximum of 45 months, depending on the date the patient is enrolled during the recruitment period and the date the patient is randomized. (The Data Coordinating Center will generate a customized follow-up appointment schedule for each patient.)

The Study Coordinator must keep close track of patient visits during follow-up as different measurements and activities occur at different visits. Follow-up visits must be scheduled within ± 15 days of the scheduled target date.

At each visit the Study Coordinator will complete a Form 05, Monthly Visit Form. The patient will be seen by the physician, dietitian and Study Coordinator at each visit and the MDRD Technician at every fourth visit (plus the F2 visit). Each monthly visit will require a 24 hour urine collection, a limited physical exam, a pill count, and nutritional counselling and assessment. The 24-hour urine collection must be collected within ± 15 days of the scheduled visit, should be refrigerated and must arrive at the Central Lab <u>within one week</u> of collection. All urine will be sent from the Clinical Center to the Central Laboratory for measurements after the sample has been mixed, measured and an aliquot obtained at the Clinical Center. <u>Patients may not mail urines themselves.</u> The Study Coordinator or GFR technician should complete Form 17, Laboratory Measurement Form, and enclose an extra copy of the form with the aliquot to be sent to the Central Lab.

Laboratory tests will be obtained at every other monthly visit (F-2, F-4, F-6, F-8 etc.). The patient will have fasting blood work every four months and at the time of the GFR measurements (F-2, F-4, F-8, F-12, etc.) A schedule of laboratory tests to be performed locally and centrally is found in the Protocol and in Appendix 2 of this Manual. For each sample to be sent to the Central Laboratories, the Study Coordinator or the GFR technician should complete Forms 17 or 19 as appropriate and enclose extra copies of the form with the specimens. Samples for amino acid determinations will be obtained every four months for patients on Diet K and every eight months for all other patients. These samples require special preparation and handling and Chapter 3 in the Manual of Operations should be reviewed prior to the visit. When Central Lab Quality Control is being carried out in conjunction with the analysis of a patient's specimen, the QC ID Matching Form should be completed.

GFR determinations will be obtained every 4 months with an additional measurement at the F2 visit. The window for the GFR determination is $\pm$ 1 month of the target date. At the time of each GFR, the GFR technician will complete Form 16, GFR Determination Worksheet.

Social science questionnaires will be given to the patient during Follow-up. The Symptom Checklist SCL-90-R (Form 28) is a self administered questionnaire which the Study Coordinator should review with the patient. The patient will complete the form and the Study Coordinator will complete the cover page. The Quality of Well-Being Form, Form 27, will be administered to the patient by a phone interview from the Data Coordinating Center every six months at F6, F12, and the SCL 90-R every four months at F4, F8, F12, and so on. The Patient Symptom Form 26 will be completed by the patient at each monthly visit.

An EKG will be obtained every six months at visits F-5, F-11 etc. The Study Coordinator will complete Form 18, the EKG Mailing Form, and send the original 8" x 11" EKG (no strips) and an extra copy of the EKG and the Mailing form to the Data Coordinating Center. The Annual Follow-Up Information Form 13 and the Economic Information Form 29 will be completed annually at the F12, F24, and F36 visits.

Please refer to Chapter 1 in the Manual of Operations for the dietitian's role during Follow-up.

11. Enhancing Compliance

11.1 Patient Management

The Study Coordinator can help to enhance compliance primarily by building a good rapport with the patient and his/her family. The Study Coordinator, as part of the study team, is involved with the health management and education of the patient. He or she assists in assessing the patient's knowledge level about his or her disease and the study procedures, and in conjunction with the study team educates the patient appropriately. The Study Coordinator also troubleshoots problems and provides support for the patient and family as necessary. Consideration of all the family members is important to the study. Each member affects and is affected by the patient's illness and involvement with the study.

11.2 Clinic Management

Compliance is also enhanced if the clinic runs smoothly. Keeping the environment safe and clean is important. Time management is essential. Patients should not be kept waiting excessively long. In between patient visits, reminder calls or cards are essential. Not only do they reinforce study procedures, they are a good way to maintain contact with the patient and deal with problems.

12. Intercurrent Illness, Action Items and Stop Points

The Study Coordinator should review any patient illness with the Principal Investigator at each monthly visit to determine if the criteria for intercurrent illness as defined in the Protocol is met (Section 10 pp. 10.1-10.3) and record the information on Form 05, the Monthly Visit Form. An intercurrent illness is defined as a short-term or long-term illness which might affect renal function or nutritional status or which might be an important outcome measure for the study. Whenever possible and consistent with good medical care, the physician and dietitian will attempt to keep the patient on his or her prescribed Study diet.

If a short-term illness is identified, Form 10, Unscheduled Medical Attention Form, should be completed and the patient should not be scheduled for any follow-up visits or measurements until after the illness. If the patient is no longer within the acceptable time window, he or she should be scheduled for the next routine monthly visit. Stop points should not be declared during a short term illness. If a long-term illness is identified, Form 10, Unscheduled Medical Attention Form, should be completed, and the patient should continue with follow-up visits and measurements as scheduled. Stop points are declared if they arise during a long-term illness.

The Study Coordinator should promptly review the data collected at each visit for possible action items and stop points. Action items are events that occur during follow-up which prompt a change in the diet or vitamin prescription or in the frequency of measurements. These events are changes in the GFR, physical exam, serum measurements or diet records (low vitamin A intake). A detailed description of action items with the action to be taken is found in the Protocol, Section 10.

If an Action Item occurs the Study Coordinator should notify the Principal Investigator and the Dietitian. The Data Coordinating Center should be notified if they have not already informed the Clinical Center that they have detected the action item. If an action item is identified by the Data Coordinating Center, the Clinical Center will be notified immediately using electronic mail. When the Study Coordinator receives an electronic mail message that a patient has reached an action item, she should acknowledge the mail message and notify the Principal Investigator and the Dietitian. The Action Item Response Form 23 should be completed.

At the time that a stop point is declared, the Clinical Management Committee must be notified. The Study Coordinator should complete a Form 11, Stop Point Form, and an additional battery of blood tests should be obtained. The tests to be included are the tests included at an F4 visit. In addition a GFR measurement should be obtained within one month except in case of a GFR stop point or Initiation-of-Dialysis or Transplantation Stop Point.

After reaching a stop point, patients are to be followed to determine the occurrence of important outcome measures even though they may no longer be on a study diet according to Protocol. Follow-up after stop points is as stated in the Protocol, Section 13, and the Abbreviated Follow-Up Form is completed every four months.

13. Patient Transfer, Lost to Follow-up and Death

13.1 Transfer

If a study patient moves to another U.S. geographic area served by a different Clinical Center, the patient should be reassigned to the care of the new center, in the same treatment group to which he or she was randomized. New consent must be obtained. The Study Coordinator should contact the Data Coordinating Center and complete a Form 30, Patient Transfer Form. The former center should supply the new center with the patient's relevant information.

If the patient should move to an area not served by another Clinical Center, every effort will be made to maintain the treatment regimens specified in the Protocol, and to document the subsequent clinical course and renal function. This will include trying to get patients back for visits and lab tests when feasible. It is very important to get Follow-up GFR measurements.

13.2 Lost to Follow-up

A patient might be considered lost to routine follow-up when he or she misses four or more consecutive monthly visits without rescheduling them and it has been determined that the patient will no longer be a part of the MDRD Study. However, once randomized, a patient can take a few months off and then come back to the study, or can go off his or her diet or blood pressure regimen and still keep having visits. Alternatively a patient may desire to withdraw and be lost to follow-up, as provided in the consent form; and this wish must be respected. However, once a patient has been randomized, any information is preferred to no information. The monthly visit form Form #05 must continue to be completed, with the "visit not held" item specified. When a patient misses four consecutive follow-up visits, Form #14 should be completed to specify why.

13.3 Patient Deaths

In the event of a patient death the Study Coordinator should notify the Data Coordinating Center immediately with a telephone call or by electronic mail and subsequently document this by submission of a Form 15, Death Notification Form. Copies of death certificates and autopsy reports should be forwarded to the Data Coordinating Center when the become available. After this is done, no further information or forms are required.

14. Additional Studies

14.1 Study F

Patients enrolled in Baseline who drop out during Baseline or who complete Baseline but are not eligible for randomization should be followed every four months as part of Study F. Informed consent to continue as part of Study F may not be required, or it may be part of the Baseline Informed Consent Form. Patients in Study F may be re-screened and re-enter Baseline one month after exclusion from randomization if Phase III enrollment is still going on. The Study Coordinator is responsible for keeping track of these Study F patients and either obtaining the required data over the phone from the patient or his physician, or preferable by scheduling visits. The Data Coordinating Center will generate a Study F appointment schedule. The first data collection should occur four months after the patient's Baseline 0 visit, or eight months after B0 if the four-month date has passed. The purpose of the Study F is to determine vital status, the occurrence of dialysis or transplantation, and to collect minimal laboratory data (serum albumin and creatinine, which are analyzed at the Central Biochemistry Laboratory). The Study Coordinator should complete Study F and G Abbreviated Follow-up Form 47 at the time of each Study F data collection.

14.2. Study G

Patients eligible for Baseline who do not enter Baseline because they will not consent should be followed annually from the date of the final screening visit. The Study Coordinator is responsible for keeping track of the Study G patients and collecting the Study G data, preferably by telephone. The purpose of Study G is to determine vital status, the occurrence of dialysis or transplantation, and to collect minimal laboratory data (serum albumin and creatinine, which are analyzed at the Central Biochemistry Laboratory). The Study Coordinator should complete the Study F and G Abbreviated Follow-up Form 47 at the time of each Study G data collection.

14.3 Study C

Patients in Study A who reach a GFR stop point and no other stop points are eligible for Study C. Study C is designed to compare the effects of Diet M or L (whichever the patient was randomized to) to those of Diet K. Study C enrollment is reported on Form 31. The specific aim of the Study is to compare the rate of decline of GFR in the same patient during treatment with two different study diets. The patient must sign a separate consent form which must be treated in the same manner as previous consent forms. The Study Coordinator will schedule patient visits and measurements exactly as described in the Protocol for patients in Study B randomized to Diet K. The patients' previous blood pressure goal will not change. Patient data will be recorded on standard MDRD Study forms as for patients in Study B randomized to Diet K.

Sometimes, when a Study A patient reaches a GFR Stop Point, the Study Team may be more interested in modifying the blood pressure control regimen rather than the diet. Of course, in these cases, the patient should not enroll in Study C.

15. Site Visits

Clinical Centers may expect annual Site Visits. The Site Visit Team will usually consist of personnel from NIH, the MDRD External Monitoring Committee, HCFA, the Nutrition Coordinating Center, and the Data Coordinating Center. The Chairman of the Steering Committee may also be present.

The Site Visit Team will schedule the visit with the Principal Investigator and suggest an agenda. The Principal Investigator and Study Coordinator may need to revise the order of the agenda due to local constraints. They will also need to make sure everyone called for is available at their scheduled time, such as the institutional support personnel, the MDRD Study Team and personnel from billing, the radioisotope lab, the pharmacy, and the local biochemistry lab. The Study Coordinator must also arrange for escorting personnel to lead the members of the Site Visit Team to Study sites at labs or offices in other buildings.

The Study Coordinator should help the MDRD Clinical Center Staff prepare for the Site Visit. The NCC and DCC will give advance notice of outstanding issues to the greatest extent possible. HCFA may also give advance notice of outstanding issues which should be discussed with the billing people.

The Data Coordinating Center staff person will be looking to the Study Coordinator to help resolve a variety of issues, such as frequencies of missed visits, missing forms, missing data, missing Informed Consent Forms, and missing responses to queries. Data from the database will be compared to data on lab reports from the local labs to check consistency. The DCC will try to make sure that all paper forms in the DCC files are also in the MDRD Computer database, and that all the forms in the MDRD database have been received at the DCC. Any discrepancies will be resolved at the site visit. The Study

Coordinator should make sure that he or she and the Data Coordinating Center staff person have adequate time to work on these issues together.

The Study Coordinator should work with the other personnel to make sure that all materials are especially well-organized and accessible should the team need to see any item. The Site Visit team may ask the Clinical Center to prepare a short summary of each patient enrolled thus far, including information on visits, diagnoses, and special problems. Early in the study when there are fewer patients, the team may ask that the Clinical Center Staff give a short oral review of each patient's experience. The Study Coordinator should work with the PI and dietitian in preparing this. She should also work with the PI in preparing any handouts, overheads, or slides the local team feels are necessary.

The DCC will bring along reports of the Clinical Center's laboratory procedural performance provided by the Central GFR Lab, the Central Biochemistry Iab Staff, and the Drug Distribution Center. The Study Coordinator should work with the MDRD Technician in preparing for any discussion related to laboratory procedures.

The Site Visit will include time for the Clinical Center staff to raise study issues and problems for consideration by the Site Visit Team. It may be helpful if relevant issues to be discussed are raised beforehand at the local weekly meeting.

At the end of the Site Visit, there will be an executive session of the Site Visit Team followed by feedback to the Principal Investigator. A written report will follow about a month later.

16. Close Out

Patients will have their final visits during the last two months of the Study, as described in the Protocol. During this time period, Close Out Form 43 and close out for Study F, G, and Stop Point Patients Form 45 should be completed for every patient who was enrolled in Baseline plus every Study G patient.

Post Close Out Visits will be held for patients in studies A, B, and C approximately 10 weeks after the Close out Visit, and the Post Close Out Form 44 will be completed.

APPENDICES

TABLE 9.2.
FREQUENCY AND LOCATION OF BASELINE LABORATORY TESTING FOR PHASE III

	Baseline Consent	Month #		Follow-Up Consent	
TESTS	0+	1	2	3++	
Glucose	L			L	R
Sodium	L			L	
Chloride	L			L	
Potassium	L			L	
Bicarbonate	L			L	A
CBC	L			L	
WBC					
Hgb					
Hct					N
Iron	L			L	
Magnesium	L			L	
Phosphorus	C			C	
Calcium	L			L	D
SUN	C			C	
Creatinine	C			C	
					O
Albumin	C			C	
Transferrin	C			C	
LDH				C	
SGOT				C	M
Bilirubin				C	
Uric Acid				C	
Standard Lipid Profile	C			C	
Total, HDL, LDL Cholesterol, Triglycerides					I
Complete Lipid Profile				C	
HDL2, HDL3, Apo-lipoproteins A1 and B					Z
Hemoglobin A_{1c}				C	
					A
Amino Acids				C	
Plasma "After Thought"				C	
24 Hr Urine					T
pH	C	C	C	C	
Protein	C	C	C	C	
Urea Nitrogen	C	C	C	C	
Creatinine	C	C	C	C	I
Phosphorus	C	C	C	C	
Sodium	C	C	C	C	
Potassium	C	C	C	C	
"After Thought"				C	O
GFR	C			C	
Electrocardiogram			C		
					N

L = Local Laboratory Determination C = Central Laboratory Determination

+ = 8-Hour Fasting Measurement ++ = 12-Hour Fasting Measurement

TABLE 12.1 FREQUENCY AND LOCATION OF FOLLOW-UP LABORATORY TESTING FOR PHASE III

TESTS		Month #																						
		1	2+	3	4+	5	6	7	8+	9	10	11	12+	13	14	15	16+	17	18	19	20+	21	22	23	24+,[1]
Glucose	R		L		L		L		L		L		L		L		L		L		L		L		L
Sodium			L		L		L		L		L		L		L		L		L		L		L		L
Chloride			L		L		L		L		L		L		L		L		L		L		L		L
Potassium			L		L		L		L		L		L		L		L		L		L		L		L
Bicarbonate	A		L		L		L		L		L		L		L		L		L		L		L		L
CBC			L		L		L		L		L		L		L		L		L		L		L		L
WBC																									
Hgb																									
Hct	N																								
Iron					L				L				L				L				L				L
Magnesium					L				L				L				L				L				L
Phosphorus	D		C		C		C		C		C		C		C		C		C		C		C		C
Calcium			L		L		L		L		L		L		L		L		L		L		L		L
SUN			C		C		L		C		L		C		L		C		L		C		L		C
Creatinine	O		C		C		L		C		L		C		L		C		L		C		L		C
Albumin			C		C		C		C		C		C		C		C		C		C		C		C
Transferrin			C		C		C		C		C		C		C		C		C		C		C		C
LDH	M								C								C								C
SGOT									C								C								C
Bilirubin									C								C								C
Uric Acid									C								C								C
Standard Lipid Profile Total, HDL, LDL Cholesterol, Triglycerides	I				C				C				C				C				C				C
Complete Lipid Profile HDL2, HDL3, Apo-liproteins A1 and B	Z												C												C
Hemoglobin A_{1c}	A				C				C				C				C				C				C
Amino Acids									C								C								C
Alloisoleucine*					C				C				C				C				C				C
Plasma "After Thought"	T												C												C
24 Hr Urine																									
pH		C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Protein		C	C	C	C	C	C	C	C				C				C				C				C
Urea Nitrogen	I	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Creatinine		C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Phosphorus		C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Sodium		C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
Potassium	O	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
"After Thought"													C												C
GFR			C		C				C				C				C				C				C
Electrocardiogram	N					C						C						C						C	

*Diet K

[1]Follow-up beyond two years will follow a similar pattern.

+Fasting Measurements (12 hour fast, except for F2 which requires an 8 hour fast.)

L = Local Laboratory Determination C = Central Laboratory Determination

Modification of Diet in Renal Disease Study

SCHEDULE FOR FORMS COMPLETION

	FORM #	SCREENING	BASELINE 0	1	2	3	RANDOMIZATION	FOLLOW UP 01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	1	X																													
	2		X																												
	3			X																											
	4		X																												
	5			X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	6		X			X			X		X		X		X		X		X		X		X		X		X		X		X
	7			X																											
	8		----------			X																										
	9						X												X												
	13																		X												X
	16		X			X			X		X				X				X				X				X				X
	17		X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	18				X							X						X						X						X	
	19					X					X				X				X				X				X				X
	26		X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	27					X							X						X						X						X
	28					X					X				X				X				X				X				X
	29		X																X												X
C																															
E	32		X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
N	33		X			X			X		X		X		X		X		X		X		X		X		X		X		X
T	35				X							X						X						X						X	
R	36					X					X				X				X				X				X				X
A	37						X																								
L																															
	42		X			X			X		X				X				X				X				X				X
	46	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	48			X													X												X		

CHAPTER 2: APPENDIX 4

Modification of Diet in Renal Disease Study

UNSCHEDULED FORMS

Form #

10 Unscheduled Medical Attention
11 Stop Point Form
12 Abbreviated Follow-up Form (Study F, stop point - every four months)
14 Multiple Missed Visits Form
15 Death Notification Form
20 Local Lab QC Form - 1 form per month
46 Local Blood Pressure QC Form - every fourth month
21 CAP QC Form - every 4 months
22 QC ID Matching Form - 2 times per year per center
23 Action Item Response Form - Monthly for any patient who reached action item.
24 Out of Range Data Form
25 Data Change Form
30 Patient Transfer Form
31 Study C Assignment Form
34 Central Lab Quality Control Form - every 4 months
39 Peer Group Range Form - every 4 months by central lab
40 Stop Point Review Form
41 Death Review Form
47 Studies F and G Form every 4 months or annually

M D R D
VISIT TYPES AND NUMBERS

		VIST	VISN
1.	**Screening** if patient screened multiple times use 2.0, 3.0, etc...	S	1.0
2.	**Baseline** BOA Nutrition record data	B	0.0 0.5 1.0 2.0 3.0
	if BP or albumin repeated for eligibility 3.9 (Forms 17, 33, or 46)		
3.	**Follow-Up** F1A Nutrition data	F	1.0 1.5
	F2A Nutrition data		2.0 2.5 3.0 4.0 . . . 48.0
	If required protocol procedures are done between visits in response to action items.....		##.1
4.	**Post Stop point** at the time of a stop, blood work similar to an F4 visit & GFR should be done. No form 5.	P	1.0 (Forms 6, 17, 33, 16)
5.	**Abbreviated FU**	A	4.0 8.0 12.0 . . . 48.0
	Procedures for patients done after a stoppoint is reached. The schedule is every 4th month (so original appointment schedule is accurate) so no 'off' (F5, F11) visits should occur.		
6.	**Study F & G**	X	4.0 6.0 12.0 . . . 48.0
7.	**Close Out** Details will follow.	C	
8.	**Post Close-Out** Details will follow.	Z	

Preparing for your GFR

Name:
Physician:
Appointment Date:
Appointment Time:
(You must fast for 12 hours prior to the appointment time.)

A. This appointment is for a special kidney function test to determine how well your kidneys are working. This test will measure your GFR (Glomerular Filtration Rate). Please allow six hours for the test. It may require less time, but you should allow enough time in order to prevent feeling rushed.

If you are a menstruating woman, you will be asked to come in for a blood test called a B-HCG before your GFR appointment. This test will verify that you are not pregnant and that you can have your GFR measured.

B. There are three important things to remember the day before your test:

1. Drink an extra quart (four cups) of fluid to make sure that you have enough water in your body. This extra fluid should be consumed during the course of the day, not all at once. Your study team can provide suggestions on how to do this.
2. If you have any symptoms of an acute illness such as a cold or the flu, or if you have received any radiation such as an X-ray or another test, call your study team. Your GFR may need to be rescheduled.
3. When planning your evening meal, remember that at the GFR test visits, you must fast for 12 hours before the test begins. Except for drinking water and taking the medications your doctor has told you to take, do not eat or drink anything for 12 hours before your GFR test.

C. The morning of your GFR test:

1. Only take the morning medications that your doctor has told you to take.
2. As usual, bring all your study medications and supplements to the visit with you, and bring in the jug or jugs containing your 24-hour urine.
3. Eat nothing and drink only water. You should drink a ten-ounce glass of water one hour before your arrival at your Clinical Center.
4. You will be asked to provide a fresh urine sample a few minutes after arriving at the clinic. It will be easier for you if you try not to urinate during the time right before your appointment.
5. If your trip to your Clinical Center is long (over an hour), you may want to bring along a bottle of water that you can drink during the drive, about an hour before your GFR appointment.

How to collect your 24-hour urine

1. First, get out your urine collection jug and make sure it has some liquid preservative in it. Label the jug (in the space marked "beginning time") with the time and date of the beginning of your 24-hour time period. Then, empty your bladder completely but **do not save this urine.** You will save all the urine after this one.

2. During the next 24 hours, save all of your urine in this jug. It is very important that you save any and all urine you pass during these 24 hours. This includes any urine passed when you wake during the night or when you have bowel movements. Be sure to urinate before you swim or take a shower . The accuracy of your urine test results depends on the collection of **all of your urine** during the 24-hour time period.

3. Make sure the jar is tightly closed after each time you add urine to it. Store the jar in a safe place, out of the reach of children. If any of the liquid preservative or urine spill on your clothing or skin, immediately rinse with plenty of water.

4. After 24 hours, empty your bladder, even if you do not feel you need to. This is the last urine you will save in the jug. Write the time you take this last sample in the space marked "ending time" on the jug.

5. Check again to make sure the jar is tightly closed, and bring it to your Clinical Center as soon as possible.

Note: Women may find it easier to collect their urine by urinating into a special container called a "hat" and then pouring the urine from the "hat" into the jug. Your Clinical Center staff can provide you with this special container.

Appendix 8

VISIT WINDOWS

General Rules and how To Correct Forms Outside the Window

The purpose of this section is to describe what will happen when a Follow-up visit is held outside the window. During Baseline, we have recommended visit windows, but as you know, the main thing is to make sure a patient finishes Baseline before the five month limit is up. During Follow Up we have absolute visit windows of +/- 15 days which are defined in the Protocol and listed on your patient's Follow Up appointment schedule. (There is also a +/- 15 day range defined for blood and urine and a +/- 30 day range defined for GFR and EKG.)

Remember to double check at the beginning of every visit to make sure you are in the time window for the visit you are trying to conduct. Whatever window you're in, that's the visit you're having, even if you missed the previous visit. Although, ideally there would be no missed visits, we do expect that there will be some missed visits along the way.

Now, IF YOU ACCIDENTALLY HOLD A VISIT OUTSIDE ITS WINDOW and complete forms as if the visit was held, here is the relatively complex sequence of events which need to be followed.

First, you will be queried on any forms that designate an improper visit number. Say the window for F4.0 was from January 1 to January 31 with a target date of January 15. Say you held a visit on February 4, mistakenly thought it was an F4.0, and filed a Form 5 (visit form), a Form 16 (GFR form), and a Form 17 for urine and blood all labelled F4.0. The database knows the visit windows. The form 5 would be rejected, as would the form 17, since the visit was outside the window and more than 15 days from the target date. The form 16 would go in the database, since the F4.0 GFR can be held within +/- 30 days from the target date.

Since there are no days in a year that do not fall in a target range, a decision needs to be made by the clinical center on how to handle the data. Basically, there are two options:

1. Identify the mistaken visit as missed (as if the visit never occurred) and use some of the data from the mistaken visit for the next visit. This would be done by revising the forms/data from the mistaken visit as if the visit number were what it should have actually been given the date of the visit (I.E. F5.0 in this example). This would also mean that the patient may not need to come in again for the next visit (F5.0) except to possible complete some procedures that were not done.
2. Identify the mistaken visit as missed (as if the visit never occurred) and hold an entirely new F5.0 visit.

Regardless of which option you choose, the data sent for the incorrect visit number (i.e. F4.0) must be modified to reflect that the visit was missed. For missed visits, the only forms we expect in the database are forms that have an appropriate question as to whether the visit/procedure was done. These forms include the following forms: monthly exam (5), GFR Worksheet (16), biochemistry mailing (17), EKG mailing (18), amino acid mailing (19), abbrev follow-up (12), and study F & G (47). (Refer to your forms manual page 2.5.5). Also, any forms not in the above listing that may have been sent to the DCC or central labs will need to be deleted for the mistakenly held visit.

If your center chooses to hold the next scheduled visit - Choice #2, (and effectively, ignore the mistakenly held visit), no further action would be needed after you have modified the original set of forms to indicate that the visit was missed (in this example, the F4.0 forms indicate a missed visit and then sometime during the F5.0 window, you would hold the F5.0 Visit as usual).

If your center chooses to convert the F4.0 Visit to be the F5.0 Visit and not call the patient back for another exam until the F6 window - Choice # 1, the previous data/forms identified as F4.0 would need to be modified to reflect a visit number of 5.0 or whatever the case may be. A word of

caution here; we cannot make a blanket change to all the forms completed for the mistakenly held F4.0 Visit to indicate F5, because some of the procedures required at F4.0 are not required at F5.0 and vice versa. In this example, the following procedures were required at F4: Monthly Exam (5), Patient Symptom (26), SCL90 (28), Blood Pressure (46), Pill Count (73 - if on Diet K), Local Labs (6), Central Blood/Urine (17), Amino Acids (19) and GFR (16). At F5.0, there is no local or central lab blood done, no amino acid, and no GFR. But there should be an EKG done. In terms of forms, this means that for the F4.0-F5.0 example, the Form 5, 26, 46, and 73 need modified to indicate VISN=5.0 (since they were originally held in the F 5.0 window). The Form 6 is deleted. Item 6A and all of item 7 on the Form 17 is modified to reflect that the blood should not have been drawn (it may be easier to inform the DCC to delete the Form 17 and resend a revised one). There would be no Form 19 for F-5.0 (only the original Form 19 would remain (from F4.0) that was modified to reflect that no amino acid was done as noted in the steps to indicate that the visit was missed). Since the GFR that would have been done at F4.0 is stiff within its window--recall that GFR's have a +/- 30 day window; the Form 16 would be able to remain in the database as F4.0's GFR--therefore, no change required here. The same holds for the Form 28; the SCL90 is given a 30 day window and therefore can remain as F 4.0. (see paragraph below describing windows for procedures that are not explicitly defined in the Protocol). The patient would need to be called in to have an EKG done in this example. But keep in mind that with the 30 day window around EKG's, it would be possible to obtain it at the F6.0 Visit (if held on the early side of the target window), but it is important that the EKG Forms still be identified as F5.0 since this was when it was required by Protocol.

As you can see, this is no easy task. Rather than modifying forms that were inappropriately sent, we must ask that you tell us to delete all the data for the mistakenly held visit and that you complete and transmit a new set of forms for the visit (i.e. F5.0).

When you do receive a query on the topic of visits held outside the allowable window, keep in mind that there are different problems that may have occurred. There may have simple been a typo in the VISN, VIST, or date

of visit field or it may be that the visit was actually held outside the window. If it is outside the window, when responding to the query, please indicate that the forms for the visit (i.e. 4.0) should be deleted and that you will send a new set of data. The DCC will then delete the original set of data and your center can keyenter the new set of data for the missed visit (i.e. 4.0) and, if applicable, can keyenter data for the next visit as described above.

This scenario applies to other visits and other forms, but I hope the example we gave will help you.

HERE ARE SOME MORE RULES FOR VISIT WINDOWS THAT WILL BE ADDED TO THE MANUAL OF OPERATIONS. Every monthly form done for a visit needs to be in range for the visit (+/-15 DAYS). Other Forms that are completed infrequently (not monthly) will have a window of +/- 30 days unless otherwise stated in the protocol. The exception here is the central blood samples--although collected every other month, the protocol specifies +/- 15 days.

Allowable Windows By Form Number

B = Baseline window, apply when applicable
F = Study F windows, apply when applicable

FORM #	WINDOWS
1	------
2	------
3	------
4	Within 62 days of most recent creatinine on Form 3
5	+/- 15 days; B
6	+/- 15 days; B
7	------
8	------
9	------
10	------
11	------
12	+/- 15 days
13	+/- 15 days; F
14	------
15	------
16	+/- 30 days; B

Allowable Windows By Form Number
(continued)

B = Baseline window, apply when applicable
F = Study F windows, apply when applicable

FORM #	WINDOWS
17	+/- 15 days; B, F
18	+/- 30 days; B
19	+/- 15 days; B
20	------
21	------
22	------
23	+/- 15 days
24	------
25	------
26	+/- 15 days; B
27	+/- 35 days; B
28	+/- 30 days; B
29	+/- 30 days; B
30	------
31	------
32	+/- 15 days; B
33	+/- 15 days; B, F
34	------
35	+/- 30 days; B
36	+/- 15 days; B
37	------
38	------
39	------
40	------
41	------
42	+/- 30 days; B
46	+/- 15 days; B
47	+/- 30 days
48	+/- 30 days; B
49	------
50	------
51	------
62*	+/- 30 days; B
64*	+/- 30 days; B
65	+/- 30 days; B
66	------
71	+/- 30 days
72	+/- 30 days
73	+/- 15 days
74	+/- 30 days; B
76	+/- 15 days for regular follow-up visits
77	+/- 15 days; B
78	------
79	+/- 15 days

* Form 62 = 24 Hour Recall
Form 64 = 3 Day Recall

PLEASE NOTE:
If you realize that a SAMPLE you just sent to the ONE OF THE CENTRAL LABS is not going to be used, it would be helpful if you would let the LAB know by a mail message. Then, if they have not yet analyzed it, they will know that they do not have to. Also, for samples that will be used but were originally misidentified, please inform the labs for their record keeping and filing (i.e. urine originally identified for f4.0 may be switched to be associated with f5.0)

If you have any questions on any of this, call the DCC. But the best way to deal with it is by prevention - pay attention to the visit windows and remember that if a patient must miss a visit, then he or she simply missed that visit unless it can be rescheduled within the visit window. Just move on to the next visit.

A FEW MORE NOTES:

Just keep in mind that whatever is required for a certain visit number must be reflected in the database with the correct visit number on the appropriate forms.

THERE ARE SEVERAL RULES INVOLVED HERE:
monthly visit allowable ranges (see your appointment schedules);
what procedures are required at what visit (refer to schedule of patient events in the protocol, section 23) ;
some procedures have different ranges than other procedures (usually based on frequency - refer to "Allowable Windows By Form Number" table in MOP);
rules for completing a subset of forms when a visit is "missed". (See page 2.5.5 in MOP, Volume II)

Also, keep in mind that the query needs to be responded to and if applicable, central labs need to be informed that they do not need to assay a particular sample or that a visit number may be different than what their sample and forms indicate. (This is important because they get this information separately from what goes in the database. Therefore, even though the database will get updated, the labs will not readily know this and their data will therefore reject from the database and that would

result in the reports generated from their results being delayed.)

FOR STUDY F MISSED VISITS:
If a Study F Visit is not held, 1) be sure to enter a date of visit that is within the window (such as the target date) and 2) a Form 17 does NOT need to be completed indicating that no Study F blood was drawn (unlike the routine Follow-Up Visits).

APPENDIX 9

TEMPORARY TRANSFER PATIENTS

A "temporary" transfer patient can be defined as a patient who is "assigned" and followed by one Clinical Center, but due to factors such as extended vacations near another MDRD Clinical Center, arrangements can be made for the patient to be seen at another Center.

1. The "original" CC makes the arrangements with the "destination" CC and the Patient.

2. The "destination" CC holds the visits for a specified amount of time.

3. The "destination" CC completes appropriate forms given the type of visit(s) being held.
   a. Forms are identified with the patients "original" ID number, "original" namecode, and "original" CC number.
   b. The certification number at the end of the forms are completed using the "destination" certification numbers.

4. The "destination" CC keyenters the data

5. Any Reports that are generated from the data sent to the DCC from the "destination" CC are sent to the "originating" CC. It is up to the "originating" CC to get these reports to the "destination" CC (via Federal Express, FAX, Electronic Mail, etc.)

6. The only exception to item 5 is that any Queries generated from the data sent from the "destination" CC gets sent to the "destination" CC.

Keep in mind that these "temporary" transfers differ from a "permanent" Transfer in not changing the patients ID number.

APPENDIX 10

RE-ENTERING PATIENTS INTO SCREENING OR BASELINE

A patient that is considered for the MDRD Study and becomes ineligible for follow-up at some point may be re-studied if there is agreement by the study team at the clinical center that the patient may now be eligible due to changing medical conditions and/or attitudes. This can occur at two points: screening or baseline.

RESCREENING PATIENTS

If the screening form 3 indicates that the patient is not eligible or he's eligible and not willing to consent, and if the MDRD study team believes that conditions and/or attitudes may have sufficiently changed to make the patient eligible, he may be rescreened by

a. completing another form 3 identified as a Screening Visit number 2.0, and maintaining the original ID/namecode.
   -the creatinine chart should only be updated with more recent creatinines, do not repeat the chart from the 1st screening visit.

b. if eligible, the study will proceed as usual with a Baseline number 0.0 visit; if ineligible, transmit the Form 3 for VISN=2. The patient may again be considered for the study at a later date (which would be Screening Visit number 3).

RESTARTING BASELINE

When a patient restarts Baseline, a new ID number is assigned via Form 1. However, before any forms are transmitted to the DCC, the Chart Review (Form 1) and Screening Visit Form (Form 3) must be filled out and eligibility must be determined. If the patient is not eligible at this point, he/she will remain in Study F under the original ID number with no new data being transmitted to the DCC. If eligible, transmit the Form 1 and 3 and proceed with the Baseline visit according to the options listed on the follwing page. Once it has been determined that a patient should be re-entered into Baseline, there are several options on how to proceed:

1. USUAL REENTRY:
   Complete Form 1
   Hold all visits starting with Screening Visit 1.0
   Perform all procedures
   (as if this is the first time the patient is going through the study)

2. PARTIALLY STREAMLINED REENTRY:
   Complete Form 1
   Hold all visits starting with Screening Visit 1.0
   option: at dietitians discretion, the B-0A visit may be omitted
   Perform all procedures
   option: The (original) B-3.0 GFR can be used for the B-0.0 GFR

3. STREAMLINED REENTRY:
   Complete Form 1
   For patients who have completed all of Baseline:
   Hold all visits except a Screening Visit 1.0 and a B-0.0 visit
   option: at dietitians discretion, the B-0A visit may be omitted
   Perform all procedures except B-0.0 procedures

   FOR ANY PATIENT RESTARTING BASELINE, DO NOT FORGET TO COMPLETE A FORM 8 TO INDICATE THAT THE ORIGINAL ID HAS DROPPED FROM BASELINE.

USUAL RE-ENTRY INTO BASELINE

1. Assign a new ID Number.
   -complete a form 1 using the new ID/namecode combination and indicate the original ID number in item 10a and 10b.
   -obtain additional screening (if required) and baseline informed consents

2. Screening Visit
   -hold the screening visit and complete form 3 and 46 (and form 51 if necessary). Anthropometrics and blood pressure need to be re-measured since eligibility is being rechecked.

(make sure the creatinine chart on the back of form 3 is completed using all creatinines from the past 3 years and any new ones done during the first baseline period.)

3. Hold the B-0.0 Visit
   a) within 2 months of the newest creatinine (as with any B-0 visit) and
   b) at least 1 month after the last baseline visit from the patients first baseline period
   c) complete all B-0.0 procedures

4. Continue through the Baseline Period

PARTIALLY STREAMLINED RE-ENTRY INTO BASELINE

1. Assign a new ID Number.
   -complete a form 1 using the new ID/namecode combination and indicate the original ID number in item 10a and 10b.
   -obtain additional screening (if required) and baseline informed consents

2. Screening Visit
   -hold the screening visit and complete form 3 and 46 (and form 51 if necessary). Anthropometrics and blood pressure need to be re-measured since eligibility is being rechecked.
   (make sure the creatinine chart on the back of form 3 is completed using all creatinines from the past 3 years and any new ones done during the first baseline period.)

3. Hold the B-0.0 Visit
   a) within 2 months of the newest creatinine (as with any B-0 visit) and
   b) at least 1 month after the last baseline visit from the patients 1st baseline period
   c) complete all B-0.0 procedures except the B-0.0 GFR

4. Inform the DCC via electronic mail that you will be using the original B-3.0 GFR for the second Baseline Period B-0.0 GFR (being sure to specify both the original and new ID/namecode)
   -The new B-0.0 visit must be held within 2 months of the date of the previous B-3.0 GFR.
   -a B-0.0 GFR report will be generated for the new ID.

NOTE: The B-0.0 blood and urine must still be collected using this option

5. At the dietitians discretion, the B-0A visit may or may not be held. The B0A visit may be considered optional for any patients who previously completed Baseline and are reentering Baseline within two months from their previous visit. To facilitate this process, the dietitian should assess before the B0 visit whether the patient's skills would be compromised if the B0A visit is not held. Patients whom the dietitian determines should not miss the visit or those who are reentering Baseline more than 2 months after the last visit should follow the usual visit schedule and attend the B0A visit (per 12/89 EMC Protocol changes document).

   Food Record:
   Regardless of whether a special (B-0A) visit is held or not, a new "B-0A" food record is required. The food record normally documented at the B0A visit may be documented at the B0 Visit. Instructions and the food record are to be mailed prior to the appropriate visit.
   The clinical center will then mail the B-0A record to the NCC as usual. (The food record still should be identified as B0A, not B0.)
   The B0-A 24-hour recall does not need to be completed of there is no B-0A visit. It will be copied to the "new" B-0A recall upon notification of your intentions to the DCC via electronic mail.

STREAMLINED RE-ENTRY INTO BASELINE
Effective 3/19/90

1. The Clinical center must initiate the process with
   a) a Form 8 dropping the "original" ID (if not already done)
   b) a form 1 (noting item 10a and 10b),

c) a mail message to the DCC (attention Kathy Fatica) indicating that they want the Baseline Visit # 3.0 data to be used for the new ID number patients' Baseline Visit # 0.0.

The following steps will then occur.

SCREENING:

2. Form 3/51

The DCC will then create a new version of the Form 3/51 replacing

a. the original ID/Namecode with the new ID/Namecode,

b. visn remains as 1.0 and the date remains the same

c. will replace the most recent creatinine with the B-0 creatinine from Form 33 (item 12).

3. Form 46

The DCC will also copy the original Form 46 using the new ID/Namecode and maintaining the Screening date and visn=1.0.

The clinical center may want to create these paper forms for their files, but they do not need to keyenter them since the DCC will copy this information into the database under the new ID number.

B-0 VISIT:

4. The DCC does the following:

creates the B-3 data for the "original" ID will be substituted for the B-0 data for the "new" ID that is reentering Baseline.

a. Form 4:

The "original" B-0 Form 4 will be copied to the "new" ID with the following revisions: ID, date of visit will be the date of the "original" B-3 visit

b. Form 16/42

The "original" B-3 GFR forms will be copied to be "new" B-0 with the following revisions: ID and visn (the original date of GFR will be maintained).

c. Form 46

The "original" B-3 MAP Form revisions to ID and visn

d. Form 17/32,33
The "original" B-3 Blood and Urine Form revisions to ID, visn

e. Form 62
The B-0 24-hour recall will be copied to the new ID with visn remaining as B-0.

The clinical center may want to create these paper forms for their files, but they do not need to keyenter them since the DCC will copy this information into the database under the new ID number.

f. Modified Reports reflecting the "copied" B-0 GFR, Blood, and Urine will be generated under the "new" Id number.

B-0A VISIT:

3. At the dieticians discretion, the B-0A visit may or may not be held regardless of whether the B-3.0 data is used for B-0.0 or not. "The B0A visit may be considered optional for any patients who previously completed Baseline and are reentering Baseline within two months from their previous B3 visit. To facilitate this process, the dietitian should assess before the B0 Visit whether the patient's skills would be compromised if the B0A Visit is not held. Patients whom the dietitian determines should not miss the visit or those who are reentering Baseline more than 2 months after the last B3 visit should follow the usual visit schedule and attend the B0A Visit." (per 12/89 EMC protocol changes document)

Food Record:
Regardless of whether a special (B-0A) visit is held or not, a new "B-0A" food record is required. The food record normally documented at the B0A visit may be documented at the B0 visit if it is held or the B1 visit if no B0 visit is being held. Instructions and the Food Record are to be mailed prior to the appropriate visit.
The clinical center will then mail the B0A record to the NCC as usual. (The Food Record still should be identified as B0A, not B0 or B1.) (The DCC will not be copying this data, a new record will be transmitted by the NCC)

24-Hour Recall:

The B-0A 24-hour recall does not need to be completed if there is no B-0A visit. It will be copied to the "new" B-0A recall upon notification of your intentions to the DCC via electronic mail.

Anthropometry (Form 65)

The B0A Anthropometry will not be repeated; the original B-2.0 anthropometry data will be copied by the DCC and revised with the "new" ID/namecode, visn= 0.5, and the "original" date of visit will be maintained.

The clinical center may want to create this paper form for their files, but they do not need to keyenter it since the DCC will copy this information into the database under the new ID number.

B-2 DATA:

4. Form 18/35

The B-2.0 EKG will not be repeated; the data will be copied by the DCC and revised with the "new" ID number and will maintain the "original" date of visit as well as visit type and visit number being B-2.0.

An EKG report will be regenerated under the new ID number.

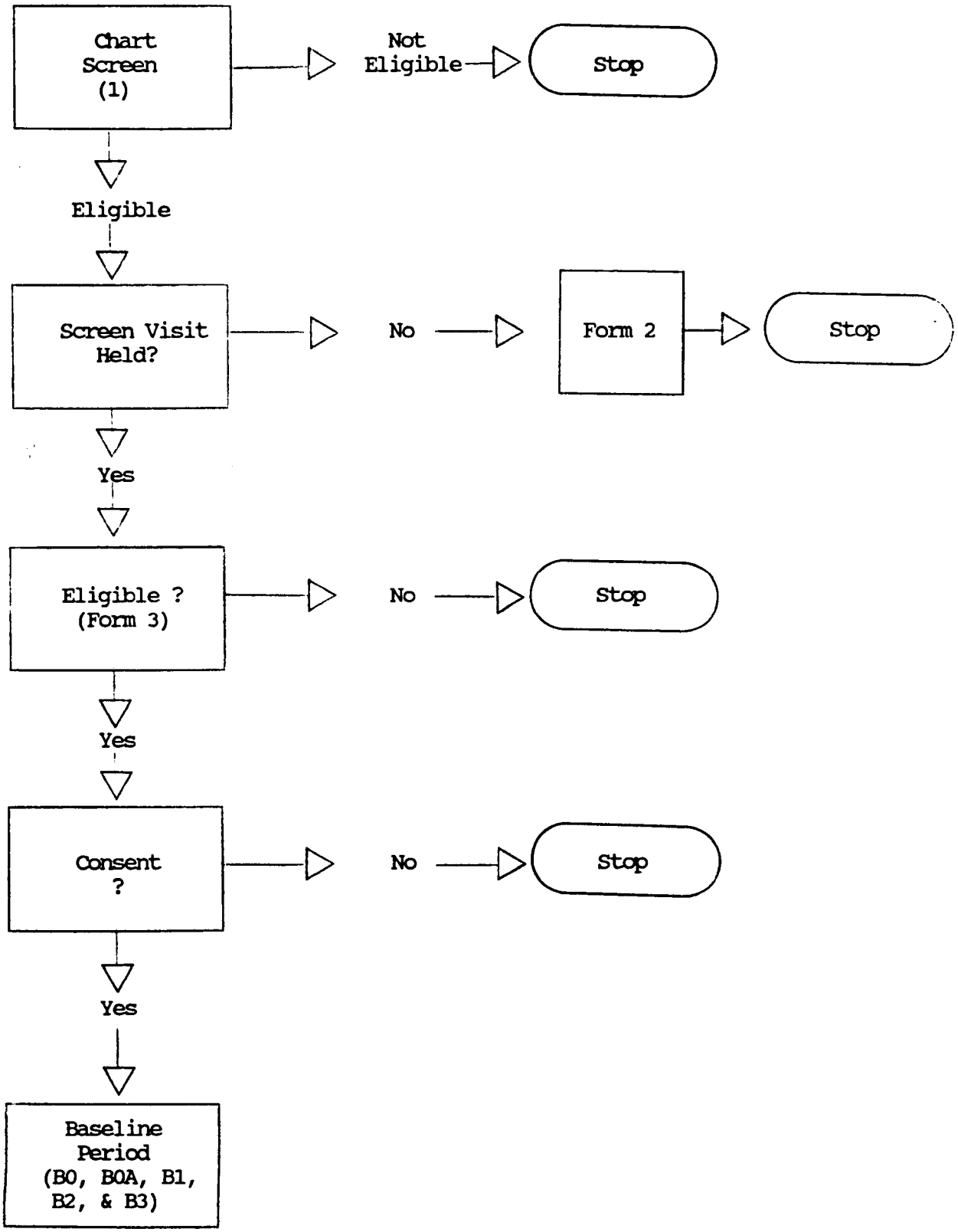
The clinical center may want to create this paper form for their files, but they do not need to keyenter it since the DCC will copy this information into the database under the new ID number.

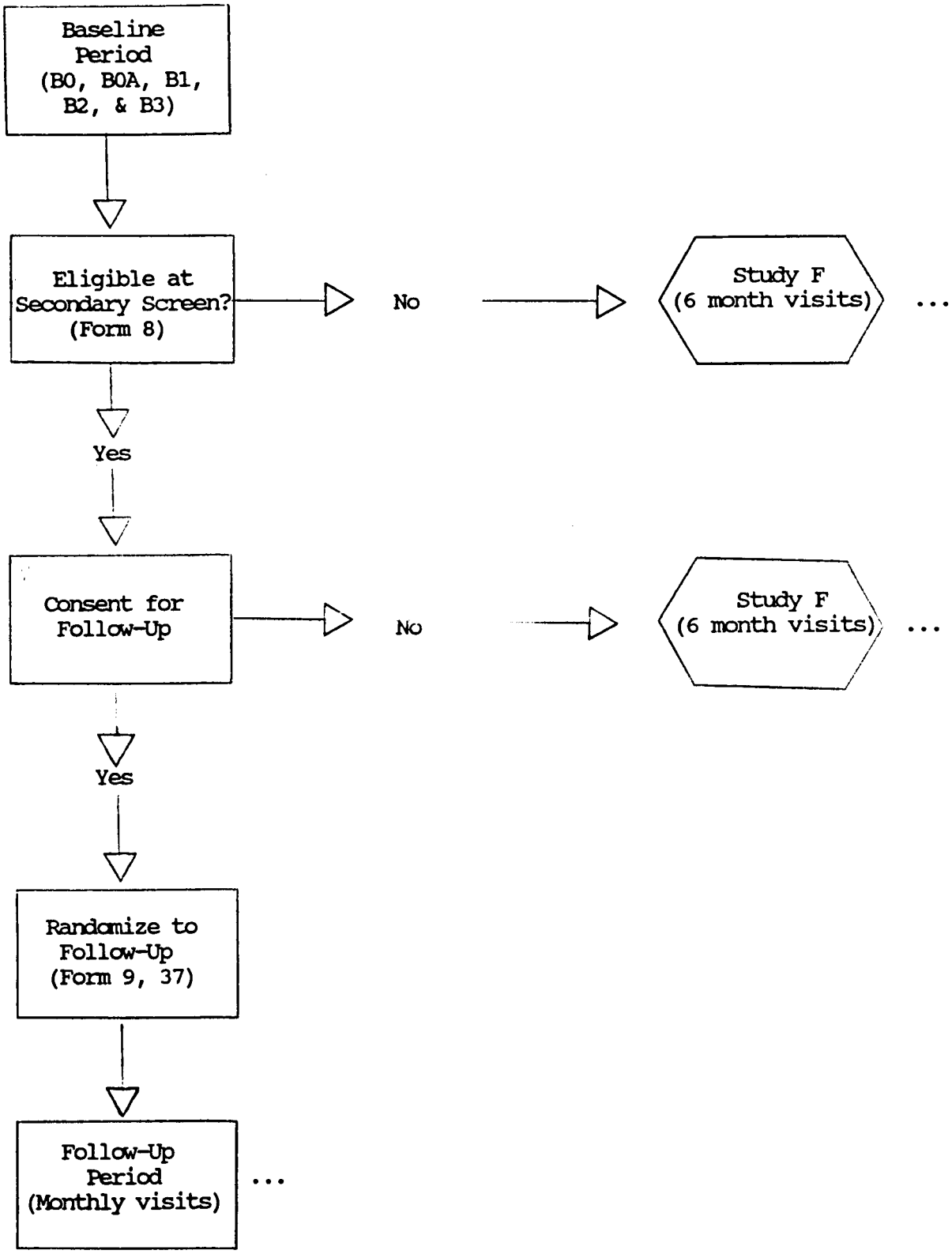
It is strongly recommended that the B-0 visit be held if there is not a complete set of data from the B-3.0 visit.

Not more than 2 months can elapse from the prior B-3 to the time that reentry is initiated. Recall that the "original" B-3 date of visit will now become the "new" B-0 Date of Visit and the maximum of 5 months from B-0 to the (new) B-3 visit will still be in effect. In terms of reentering the Baseline period in general, you will recall that before a patient can re-enter, one month or more needs to elapse from the time of "original" Baseline 3.0 visit to the "new" Baseline 1.0 visit (refer to Protocol page 9.10).

APPENDIX 11

MDRD Patient Flow From Chart Review to Follow-Up




Baseline Period (B0, B0A, B1, B2, & B3)
Eligible at Secondary Screen? (Form 8)
No
Study F (6 month visits)
...
Yes
Consent for Follow-Up
No
Study F (6 month visits)
...
Yes
Randomize to Follow-Up (Form 9, 37)
Follow-Up Period (Monthly visits)
...