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1. BACKGROUND

Chronic prostatitis is a disabling condition affecting an untold number of men of all ages and ethnic origins. As early as 1980, the National Ambulatory Care Survey reported 20 office visits/1,000 men/year for symptoms compatible with prostatitis (1). Although by one estimate, 50% of men will suffer from symptoms of prostatitis at some point in their lives, most symptomatic men do not have bacterial prostatitis, for which the treatment and management is usually successful (2). Therefore, as noted by Krieger *et al.* (3), the most common syndromes for men with chronic prostatitis are *idiopathic* (abacterial prostatitis). Depending on the status of the expressed prostatic secretions (EPS), these patients with chronic abacterial prostatitis are classified further as a) nonbacterial prostatitis if the EPS is purulent (leukocyte count elevated) or b) prostatodynia if the EPS is not purulent. To date there is no standardized method of diagnosis and treatment of this condition. As noted recently by Nickel and Sorensen (4), the problems and frustrations found in clinical trials investigating therapies for nonbacterial prostatitis are that

> "our definition of the syndromes is unclear, the etiology is obscure, the relevance of the only objective finding we have (leukocytosis) is unknown, symptoms are highly variable, the natural history of the disease has not been adequately studied and the numbers in most clinical trials, including ours, are small".

They concluded that "since the symptoms are paramount in these patients, evaluation of response can only be achieved by using reproducible and validated symptom evaluation instruments".

Recognizing the importance of addressing problems in the diagnosis and treatment of prostatitis, a National Institute of Diabetes, Digestive and Kidney (NIDDK) Diseases Workshop on Chronic Prostatitis (5) was held in Bethesda, MD on December 7-8, 1995, from which the new consensus working definition and classification of prostatitis syndromes (NIDDK reference standard) for research studies on these diseases and disorders was summarized as follows:

1. *Acute bacterial prostatitis* is an acute infection of the prostate.
2. *Chronic bacterial prostatitis* is a recurrent infection of the prostate.
3. *Chronic nonbacterial prostatitis/chronic pelvic pain syndrome* (CPPS), where there is no demonstrable infection. Subgroups of this class are:
   - 3.1 *Inflammatory chronic pelvic pain syndrome*, where white cells are found in the semen, expressed prostatic secretions (EPS), or voided bladder urine-3 (VB-3).
   - 3.2 *Non-inflammatory chronic pelvic pain syndrome*, where white cells are NOT found in the semen, EPS, and VB-3.
4. *Asymptomatic inflammatory prostatitis* (AIP), where there are no subjective symptoms but white blood cells are found in prostate secretions or in prostate tissue during an evaluation for other disorders.

Patients in Categories 1-3 are characterized by chronic pain; however, unlike patients in Category 1 & 2, patients with Category 3 prostatitis do not have any detectable infection of the prostate as determined by conventional microbiological techniques. Abnormalities in the EPS are the primary objective features of Category 3 prostatitis and chronic pain is the primary subjective symptom. The majority of patients with chronic prostatitis are Type 3 (3).

The occurrence and persistence of pain as a primary presenting symptom is an important aspect of both diagnosis and outcome evaluation. In the recent review article in *Pain* by Egan and Krieger (6), they note that Achronic abacterial prostatitis is remarkably similar to chronic pain syndromes@, and accordingly they make the case for therapy based on multidisciplinary approaches to pain management, rather than the traditional >organ system= approach. Many therapies have been tried for chronic prostatitis, with a primary focus on improving bladder outlet resistance. However, the general consensus among clinical urology research investigators conducting therapy trials involving chronic prostatitis patients is well reflected in the recent summary of Nickel and Sorensen (4) that

> "more research and larger clinical studies in the nonbacterial chronic prostatitis syndromes are urgently required."

In response to these growing concerns about the diagnosis and treatment of Chronic Prostatitis, the NIDDK funded the Chronic Prostatitis Clinical Research Network (CPCRN), comprised of six (6) Clinical Research Centers (CRCs) and a Data Coordinating Center (DCC), effective October 1, 1997. The primary research questions to be addressed by the CPCRN will encompass the diagnosis, etiology, natural history and prognosis, and the development of treatment strategies focused on Chronic Abacterial Prostatitis - Chronic Pelvic Pain Syndrome (CPPS). In support of these broad research goals, the CPCRN formed Working Groups to coordinate the development of a longitudinal Chronic Prostatitis Cohort (CPC) Study, the development and validation of a symptom severity index for CPPS, as well as other laboratory and clinical outcome measures. Ultimately, the goals of the CPCRN are to conduct well-controlled, multicenter epidemiological studies and therapeutic trials aimed at providing definitive answers to the unresolved questions of diagnosis and treatment of CPPS.

2 SPECIFIC AIMS

The goal of the Chronic Prostatitis Cohort (CPC) Study is to assemble and follow a cohort of patients with Chronic Pelvic Pain Syndrome (CPPS). The specific aims are to

i) define the condition Chronic Prostatitis (CP) or Chronic Pelvic Pain Syndrome (CPPS);
ii) develop techniques to aid in the diagnosis of CP;
iii) characterize the patient with CP;
iv) study the natural history and prognosis of patients with CP;
v) set the stage to conduct epidemiological studies to address etiologic hypotheses;
vi) set the stage to begin clinical trials and offer effective therapy for CP.

To implement this CPC Study, a centralized, standardized registry containing data on patients at baseline screening and longitudinal follow-up will include demographic and diagnostic information, patient medical history, symptoms, and treatments and their outcomes. In addition, serum and prostatic fluid specimens will be stored in specimen banks for future use by qualified investigators.

3 CPC STUDY ORGANIZATION

The CPC Study organization includes 6 Clinical Research Centers, a Data Coordinating Center, a Steering Committee, NIDDK Project Staff, and several working subcommittees. The responsibilities of each component are described below.

3.1 CLINICAL RESEARCH CENTERS

The responsibilities of each Clinical Center include:

1. Recruiting and following patients throughout the course of the five-year study.
2. Confirming eligibility of each patient based on the study criteria identified in the protocol.
3. Adhering to study protocol in the implementation of procedures and the acquisition of data.
4. Collecting data of high quality.
5. Collaborating with other study investigators in the development of the manual of procedures, acquisition of high quality data, and the analysis and publication of study results.

3.1.1 BASIC SCIENCE STUDIES

Clinical centers will conduct basic science research projects in support of the overall goals of the CPCRN. These studies will be conducted in parallel to the CPC Study. As preliminary data from basic science projects are analyzed, opportunities to expand the most promising investigations to more of the clinical centers will be explored. Based on these results, targeted studies addressing etiologic, diagnostic and prognostic issues will be proposed utilizing the CPC Study and appropriately selected control groups.

3.2 DATA COORDINATING CENTER

The Data Coordinating Center will provide administrative, biostatistical, epidemiological and data management leadership for the CPC Study in the design/conduct of collaborative research programs. Additional responsibilities include:

1. Preparation of the study protocol, manual of procedures, and case report forms, based on collaboration with the Steering Committee and NIDDK Project Scientists.
2. Provision of overall leadership in the biostatistical and epidemiological study designs for etiologic, diagnostic, natural history and prognostic studies.
3. Collaboration with other study investigators in the development and testing of data questionnaires and study procedures.
4. Development of data and specimen tracking procedures.
5. Provision of an efficient data management system, utilizing the client-server model.
6. Development of validation protocols to study objective laboratory-based findings.
7. Training of Clinical Research Center staff and monitoring clinic performance in overall study procedures.
8. Coordination of Steering Committee and External Advisory Committee meetings.
9. Preparation of detailed reports regarding patient recruitment and retention, data collection activities, and interim results to the External Advisory Committee.

10. Collaboration with study investigators in the analysis and publication of study results.

3.3 STEERING COMMITTEE

The Steering Committee is the primary governing body of the CPC Study. Steering Committee members include the NIDDK Project Scientists, and the principal investigators from each of the Clinical Research Centers and the Data Coordinating Center. Although other study investigators will often attend meetings, all major scientific decisions will be made by the Steering Committee (one vote for each member). The primary responsibilities of the Steering Committee include:

1. Identifying the specific aims of the study.
2. Determining study eligibility criteria.
3. Developing the study plan.
4. Developing the study protocol and manual of procedures, and participating in forms development.
5. Overseeing standardized implementation of the study protocol.
6. Establishing subcommittees, as needed.
7. Reviewing and approving all publications based on any data collected for the CPC Study.
8. Monitoring overall study quality control.
9. Approving outside study investigators for access to data and stored specimens for their own epidemiological and clinical studies.
10. Establishing the time line for the study.
11. Establishing the goals and the agenda for Steering Committee meetings.

3.3.1 PUBLICATIONS, PRESENTATIONS & ANCILLARY STUDIES COMMITTEE (PP&AS)

This committee was formed to expedite review process for publications, presentations and ancillary studies. It will include the following CPCRN members: John Kusek (NIH), Dick Landis (DCC), Tony Schaeffer (Chairman), and a principal investigator who will serve on the committee on a rotating basis for six month intervals. The immediate goal is to consider the impact of proposed ancillary studies on the CPC Study and to develop a policy for integration of such studies within the CPC. This group will also serve as the Committee on Access to CPC Study Data and Patient Specimens.

3.4 NIDDK PROJECT SCIENTIST

The NIDDK Project Scientist's primary responsibility is to provide scientific support in all aspects of the CPC Study, including protocol development, quality control, interim data monitoring, final data analysis and interpretation, preparation of publications, and performance monitoring.

3.5 WORKING SUBCOMMITTEES

The Steering Committee establishes working subcommittees as needed to carry out various tasks to achieve the specific aims. Subcommittees established thus far, include Committee on the CPC Protocol, Committee on Symptom Index Development, Laboratory Measures Committee, and Basic Science Projects Committee.

3.6 PROJECT COLLABORATORS

3.6.1 CLINICAL CENTER INVESTIGATORS

***** Clinical Center Principal Investigators:

1. *****Schaeffer, Anthony J., M.D. (Chairman of the Steering Committee)
   Northwestern University
   Department of Urology
   Chicago, IL

   Nadler, Robert, M.D.
   Northwestern University
   Department of Urology
   Chicago, IL

2. *O'Leary, Michael P., M.D., M.P.H.
   Brigham and Women=s Hospital
   Department of Surgery
   Boston, Massachusetts

   McNaughton Collins, Mary, M.D., M.P.H.
   Massachusetts General Hospital
   Division of General Medicine
   Boston, Massachusetts

3. *Nickel, Curtis J., M.D.
   Queen=s University
   Department of Urology
   Kingston, Ontario, Canada

   Jarvi, Keith, M.D.
   Toronto General Hospital
   Toronto, Ontario, Canada

4. *Pontari, Michel A., M.D.
Temple University Hospital
Department of Urology
Philadelphia, PA

Ruggieri, Michael R., Ph.D.
Temple University
School of Medicine
Philadelphia, PA

5. Litwin, Mark S., M.D., M.P.H.
University of California at Los Angeles
Department of Urology
Los Angeles, CA

Shoskes, Daniel, M.D.
Harbor-UCLA Medical Centre
Department of Surgery
Torrance, CA

6. *Alexander, Richard B., M.D.
University of Maryland
Division of Urology
Baltimore, MD

3.6.2 DATA COORDINATING CENTER INVESTIGATORS

***** Principal Investigator

Landis, J. Richard, Ph.D.
University of Pennsylvania
Center for Clinical Epidemiology and Biostatistics
Philadelphia, PA

Propert, Kathleen J., Sc.D.
University of Pennsylvania
Center for Clinical Epidemiology and Biostatistics
Philadelphia, PA

Feldman, Harold I., M.D., M.S.
University of Pennsylvania
Center for Clinical Epidemiology and Biostatistics
Philadelphia, PA

Farrar, John T., M.D.
University of Pennsylvania

Center for Clinical Epidemiology and Biostatistics
Philadelphia, PA

3.6.3 NIDDK PROJECT SCIENTISTS

Kusek, John W., Ph.D.
NIH/NIDDK
Bethesda, MD

Nyberg, Leroy, M.D., Ph.D.
NIH/NIDDK
Bethesda, MD

3.6.4 EXTERNAL ADVISORY COMMITTEE

*Chairman of the EAC

*Krieger, John N., M.D., Chairman
VA Puget Sound Health Care System
Section of Urology 112 UR
Seattle, WA

Anderson, Rodney U., M.D.
Stanford University Medical Center
Department of Urology
Stanford, CA

Berger, Richard E., M.D.
University of Washington
Seattle, WA

Roerhborn, Claus, M.D.
University of Texas Southwestern Medical Center
Department of Urology
Dallas, TX

Bergstahl, Eric, M.S.
Mayo Clinic
Section of Biostatistics
Rochester, MN

Tornetta, Steve
Conshohocken, PA

4. GENERAL POLICY

4.1 CHANGING THE PROTOCOL

The objectives of the CPC Study are most likely to be achieved if the protocol does not require alteration during the study. Any changes in the protocol will result in some degree of heterogeneity of the data, which complicates the analyses and may compromise the scientific integrity of the study. However, occasions may arise in which protocol changes are necessary. Therefore, changes in the protocol will be considered only if they are required to ensure patient safety or will significantly enhance the scientific validity of the study (7).

4.1.1 INITIATING A PROTOCOL CHANGE

Any member of the CPC Study may request a change to any portion of the study protocol. The member wishing to change the protocol should present the proposed change(s) in writing t either the Chair of the Steering Committee or the Principal Investigator of the Data Coordinating Center (DCC), who will then contact the other. The DCC Principal Investigator and the Chair of the Steering Committee will then jointly decide on the appropriate mechanism (letter, conference call, meeting) to handle the proposal depending on the implications of the proposed change. Proposed changes with only a minor impact on the current course of the CPC study can be properly handled through a letter to each member of the Steering Committee. Proposed changes with a greater impact on the course of the CPC Study will be presented to the Steering Committee via conference call or formal meeting to allow all members to benefit from the scientific debate generated in these discussions. Proposed changes can be implemented only after the Steering Committee reaches a majority vote and the NIDDK Project Officer approves of the proposed changes. Once a proposed change has been approved, the DCC will coordinate all activities required to implement the change.

4.1.1a Protocol Amendments

Over the course of the CPC study, it may be necessary to make amendments to the study protocol. Protocol amendments must be jointly agreed upon by the CPCRN Steering Committee. The DCC will be responsible for implementing the protocol amendments. A document will be created to address protocol changes. Each amendment will be listed and it's location in the protocol clearly delineated in this document. Prior to revising the protocol, the amendments will be approved by the principal investigator. Major protocol amendments will results in a new edition of the protocol. Minor protocol amendments will be referred to as protocol updates. Each edition or update will have an effective date. The amendment document and revised protocol will be distributed by the DCC to all clinical centers, as soon as possible. It is the responsibility of each clinical center to submit protocol changes to their IRB for approval

4.2 PUBLICATIONS AND PRESENTATIONS

4.2.1 INTRODUCTION

The policy of the CPC Study concerning publications and presentations is designed to achieve five objectives:

i. To assure timely publication of the results of the CPC Study to the appropriate professional audiences,

ii. To avoid premature publication of results that might compromise the performance of the study (such as by publication of trend results before such trends become statistically convincing) or that might compromise the ability to publish the results in high quality peer reviewed journals (as by premature release to the lay press),

iii. To maintain high standards of quality of all material published by the CPC Study,

iv. To guard against duplicate publication of results by assuring absence of overlap of materials prepared by various writing committees, and

v. To assure equitable attribution of credit to all of the professionals participating in the CPC Study.

To accomplish these ends, it is the policy of the CPC Study that preparation of all publications or presentations, other than materials prepared for local publicity purposes, must be assigned by the Steering Committee to specifically appointed writing committees, and that all such materials must be reviewed and approved by the Publications, Presentations, & Ancillary Studies (PP&AS) Committee before lication.

4.2.2 SCOPE OF POLICY AND EXCEPTION FOR LOCAL PUBLICITY MATERIALS

All material to be presented orally or submitted for publication or dissemination by individuals associated with the CPC Study and dealing with any aspect of the CPC Study must receive prior review and approval by the PP&AS Committee with the following exception:

> Material prepared for publicity purposes either nationally or within the recruitment region of a CPC Clinical Center, or presented orally or as handouts or posters to professional audiences solely for the purpose of informing the profession of the CPC Study and its objectives, need not be reviewed by the PP&AS Committee. Such material must be limited to a background discussion of the disease Chronic Prostatitis and a description of the CPC Study organization, objectives, and entrance criteria, and to results of the study that have previously been presented to a scientific body or published in a scientific journal. It must not influence discussion of any previously unpresented or unpublished CPC Study

outcomes or results, and must not itself result in publication of an abstract or other citable professional reference.

4.2.3 SOURCE OF SUGGESTIONS FOR PUBLICATIONS OF THE CPC STUDY

All participants in the CPC Study are invited to suggest topics appropriate for presentation as abstracts, peer reviewed papers, or chapters and reviews from the CPC Study. Such suggestions should be made to the Chair of the PP&AS Committee, who will review the request to be certain that there is no overlap with materials previously assigned to other writing committees. The Chair of the PP&AS Committee will forward copies to the Chair of the Steering Committee. Where such overlap exists, the Chair of the PP&AS Committee may make recommendations to the Steering Committee that the suggestion be referred to an existing writing committee, that additional participants be added to existing writing committees, or make other suggestions to resolve the overlap. However, final decision in this matter rests with the PP&AS Committee Chair.

It is the policy of the CPC Study to encourage non-physician professionals to prepare scientific presentations for their own professional meetings and to prepare scientific papers for their own professional journals in addition to participating in the preparation of papers for medical journals. Since the subject matter of these reports and papers may overlap with material being prepared by writing committees for medical journals, it is the policy of the CPC Study that under these circumstances, rather than forming a new writing committee, such non-physician professionals should be added to the existing writing committee concerned with related matters, specifically for the purposes of preparing such reports. The authors of these presentations and reports will be the members of the writing committee, with first author being the individual added to the committee for this purpose, using the appropriate authorship style described in section 4.2.6.

4.2.4 ASSIGNMENT OF WRITING COMMITTEES

The Chair of the PP&AS Committee, upon receipt of a recommendation for preparation of a topic for publication, will submit a proposal to the Steering Committee for approval of the publication effort. Appointments of writing committee chairmanships will be made in an equitable fashion to all professionals in a fashion that recognizes the special contributions of each member of the CPC Study to its performance.

Upon appointment of the Chair of a new writing committee, the Chair of the PP&AS Committee will notify the CPCRN of the new writing committee, soliciting indications of interest to be on that committee. If more individuals express interest than is practical to assign to a committee, the PP&AS Committee Chair will make the final assignments of the members of the committee. In all cases, writing committees dealing with an issue that requires analysis of data by the DCC will have a member of the DCC assigned to it.

From time to time it may be expedient for the chairmanship of a writing committee to be reassigned to another member of that committee, or for members to be dropped from or added to

a writing committee. The Chair of the PP&AS Committee is authorized to make such changes with the consensus of the members of the writing and PP&AS committees, or on his own authority where there is clear cause.

4.2.5 CLASSES OF REPORTS OF THE CPC STUDY

There are four classes of reports of the CPC Study:

A. Reports of the major outcomes of the Study. It is assumed that there will generally be only one or two such overall reports derived from each phase of the Study. Generally these reports will be prepared by the Steering Committee serving as the writing committee, with the Chair of the Steering Committee as the Chair of this committee.

B. Reports addressing in detail one aspect of the CPC Study, but in which the data are derived from the entire study.

C. Reports of data derived from a subset of centers by members of the CPC Study, (e.g., substudies or ancillary studies), or originally conceived analyses of data from the entire CPC Study (original analyses).

D. Reports of investigations initiated outside of the CPC Study, but using data or samples collected by the CPC Study. The investigators may be CPC or other investigators, but the source of the ideas and the funding for the study will have been derived outside of the CPC Study itself.

4.2.6 AUTHORSHIP POLICY

The authorship policy of the CPC Study must achieve two somewhat conflicting goals. First, it is recognized that the findings of the study, especially the findings reported in Type A and B reports, are derived from the efforts of the entire CPC professional staff. Thus, all reports, of whatever type, must give recognition to all participants of the CPC Study, and reports of Types A and B must give primary recognition to the entire study professional staff. On the other hand, it is recognized that the preparation of a manuscript places special demands on the assigned writing committee. Further, recognition of special effort and achievement is important in the professional careers of the study staff, and specific listing as an author is a significant motivating factor that will help assure prompt completion of writing assignments and timely publication of the results of the CPC Study. The CPC authorship policy attempts to recognize each of these goals. The authors of CPC publications will be listed as detailed below for each type of publication. The order of authorship will be determined by the Steering Committee after receiving recommendations from the PP&AS.

All publications and presentations:

Abstracts: by members of the writing committee, listed according to the Steering Committee's recommendations "and the CPC Study"[1], presented by XXXX. (This will usually be the Chair of the writing committee).

Papers: by members of the writing committee, listed according to the Steering Committee's recommendations "and the CPC Study"[1]

- The CPC participant box, Table 4.1, must be included in Type A papers.
- The CPC participant box will be included in all papers if this can be arranged with the publisher. Otherwise it will be referenced in one of the Type A papers. It will not be practical to publish the entire list of participants in abstracts.
- The participant box will be included in all Type C papers if this can be arranged with the publisher. Otherwise it will be referenced in one of the Type A paper.
- In Type D papers, the list of participants will be referenced in all cases. It will not be practical to publish the entire list of participants in abstracts.

4.2.7 LISTING OF PROFESSIONAL PARTICIPANTS IN THE CPC PARTICIPANT BOX

The CPC Study participant box will list all professionals that have participated in the CPC Study for a minimum of one year. The participants for each participating center will be listed together, with the center Principal Investigator listed first, and identified as "P.I." followed by the other center staff listed alphabetically. Each participant will be listed only by his/her professional and academic degrees, not by the specific position which he/she held in the study. The centers will be listed in the following order:

Chair of the Steering Committee
Clinical Centers
DCC
NIH/NIDDK

Prior to the publication of any papers from the CPC Study, each center will be asked to confirm and approve the listing of the personnel from that center in the CPC Participant Box.

Table 4.1

CPC Study Group

Northwestern University

Anthony J. Schaeffer, MD (PI)
Charles L. Bennett, MD, PhD
Wade Bushman, MD, PhD
Elizabeth A. Calhoun, PhD
James L. Duncan, PhD
Alisa Erika Koch, MD
Robert B. Nadler, MD

Brigham and Women's Hospital

Michael P. O'Leary, MD, MPH (PI)
Mary McNaughton Collins, MD, MPH
Debra Rhodes, MD
Judith Spolarich-Kroll, BA

Queen's University

J. Curtis Nickel, MD (PI)
Marc W. Mittelman, PhD
Joseph Downey, MSc

University of Toronto

Keith Jarvi, MD

Temple Unviersity

Michel A. Pontari, MD (PI)
Michael R. Ruggieri, PhD
Linda Kish

University of California at Los Angeles

Mark S. Litwin, MD, MPH (PI)
Daniel Shoskes, MD
Yining Xie

University of Maryland

Richard B. Alexander, MD
Sathibalan Ponniah, PhD
E. Bronwyn Byron

University of Pennsylvania School of Medicine

J. Richard Landis, PhD (PI)
Kathleen J. Propert, ScD
John T. Farrar, MD
Harold I. Feldman, MD, MS
Denise Cifelli, BS
Stephen Durborow, BS
Rikki R. Godshall, BA
Carman D. Gonzalez, BBA
Randy W. Hilderbrand, BS
Edwin G. Hoch, MS
Michael Kallan, MS
Alex Makarov
Louise M. Meri, MSS
Elizabeth J. Phillips, BS

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

John W. Kusek, PhD (Project Officer)
Leroy Nyberg, MD, PhD

4.2.8 ACKNOWLEDGMENT OF SUPPORT AND REPRINT ADDRESSES

Acknowledgment of grant support is to be used in all papers reporting results of the CPC Study. In the case of ancillary studies, additional sources of support should be cited as appropriate.

The CPC Study is supported by the Division of Kidney, Urologic and Hematologic Diseases of the National Institute of Diabetes and Digestive and Kidney Diseases, NIH, through cooperative agreements.

The following information regarding reprint requests should be included in all papers prepared for the CPC Study. The DCC will maintain an inventory of all CPCtudies and will address all requests for reprints.

Requests for reprints should be addressed to:

University of Pennsylvania School of Medicine
Center for Clinical Epidemiology and Biostatistics
The CPC Study Data Coordinating Center
501 Blockley Hall
423 Guardian Drive
Philadelphia, PA 19104 - 6021

4.2.9 SCHEDULE FOR COMPLETION OF WRITING ASSIGNMENTS

At the time that a writing committee is constituted by the Chair of the Steering Committee, the PP&AS Committee will establish a timetable for the completion of the writing assignment that takes into account deadlines for the publication, the amount of time that will be required for data analysis, the other commitments of the DCC, and the priority of the publication. The Chair of the writing committee will provide the Chair of the PP&AS Committee a general outline of the proposed publication within 30 days of receiving its assignment, to permit establishment of an appropriate timetable. Where overlaps of materials to be covered by different writing committees are detected, the Chair of the PP&AS Committee will attempt to resolve these informally with the chairs of the involved writing committees. In the event that this effort at mediation fails, the issue will be resolved by the Chair of the Steering Committee.

4.2.10 REVIEW OF ABSTRACTS AND PRESENTATIONS BY THE PP&AS COMMITTEE

To expedite review of abstracts, oral presentations, and any other material for which there is an explicit deadline for submission, the following procedure will be used:

i. The writing committee wanting to submit an abstract, give a talk, or submit other material for which there is an explicit submission deadline must contact the Chair of the PP&AS Committee 14 days prior to the submission deadline. In the event that the Chair is unavailable, a designee may be contacted. The Chair will name a subcommittee of three (3) members of the PP&AS Committee to review the submitted materials and will inform the writing committee and the PP&AS subcommittee of their appointment. The submitted material must be mailed by the submitter directly to the PP&AS members so as to reach them no fewer than seven (7) days prior to the deadline for submission.

ii. The members of the PP&AS subcommittee will review the submitted material and notify the Chair of the PP&AS Committee solely, in writing, of their approval or disapproval. If there is unanimous approval, the PP&AS Committee Chair will inform the submitter that

he/she has CPC Study approval for the submission. In the event of a split vote for approval, the issue will be submitted to the Steering Committee for resolution.

iii. All materials submitted for approval in this fashion will be distributed by overnight mail, together with notice of the disposition, to all members of the PP&AS Committee. All approved materials will also be forwarded to the NIDDK Project Officer, and for record-keeping purposes to the DCC, and will be distributed to the entire membership of the Steering Committee at the next meeting of that Committee as an appendix to the report of the PP&AS Committee.

iv. In the case of abstracts or other similar written material, the entire material to be submitted must be sent by the submitter for review by the PP&AS Committee.

v. In the case of an oral presentation, an outline of the talk and a copy of any slides to be presented must be submitted for review to the PP&AS Committee in accordance with the above rules at least seven (7) days prior to the scheduled oral or poster presentation.

4.2.11 REVIEW OF PAPERS BY THE PP&AS COMMITTEE

All materials for which there is no explicit deadline, and all full papers that may result in a citable scientific reference, whether or not there is a deadline for submission, must be submitted to the Chair of the PP&AS Committee for formal review by the entire Steering Committee. If there is a deadline for submission of a formal paper, it is the responsibility of the submitter to be certain that it is submitted to the PP&AS Committee Chair, at least 30 days prior to the deadline, to permit such review. This review will be conducted as follows:

i. The PP&AS Committee Chair will appoint a panel of three primary reviewers. The Chair will distribute the material to all members of the PP&AS Committee and to the Principal Investigator of each center participating in the CPC Study. The three members of the review panel will each prepare and send to the Chair a written critique of the submitted material for distribution to the entire PP&AS Committee. The P.I'.s of the various clinical centers will be given a deadline by which any comments or critiques from their center must be received by the PP&AS Committee Chair. This mechanism will assure that each professional participating in the CPC Study will have an opportunity to review all materials that will be submitted for publication bearing his/her name as a participant and co-author.

ii. The PP&AS Committee Chair will schedule a meeting of the Committee (generally by conference call) to discuss review of papers. The reviews of the panel members and any comments received from the clinical center PI's will be distributed to the committee.

iii. While discussion of the submitted papers and other materials will be led by the three appointed reviewers, all members of the Steering Committee will be invited to participate and all will vote on final disposition.

iv. In keeping with medical editorial traditions, there are three possible dispositions: approval of the material as submitted (possibly with some recommendations for revision that do not

require re-review), non-acceptance of the material as submitted but with recommendations to the authors for revisions and resubmission, and disapproval of the material.

v. The PP&AS Committee Chair will be responsible for communicating the decision of the Committee to the authors, with a summary of suggestions for revision, if any.

vi. If there is a recommendation for approval or final disapproval of submitted material, or if there is a recommendation for revision which is contested by the author(s), the PP&AS Committee Chair will report this outcome in writing to the Steering Committee for final action. In the case of a dispute between the PP&AS Committee and the author(s), the PP&AS Committee Chair will provide a copy of the submitted material and a summary critique to the Steering Committee, and the chair of the writing committee will be given an opportunity to submit a rebuttal.

vii. The authority to grant final approval for a formal scientific paper of the CPC Studrests with the Steering Committee. In the event that a delay until the next Steering Committee meeting would be disadvantageous, the Steering Committee will meet via a phone conference and vote for approval. All materials submitted for approval in this fashion will be forwarded, together with notice of disposition, to the Chair of the Steering Committee.

viii. In the event that editors of a scientific journal to which an approved CPC scientific manuscript is submitted suggest or require revisions of the manuscript, the revised manuscript must be reviewed again by the PP&AS Committee prior to resubmission in the same manner as described above. The PP&AS Chair should attempt to appoint the same reviewers that read the paper initially to review the revision, and every effort will be made to expedite such repeat reviews. The authors should include the journal reviewers comments and suggested revisions with their resubmission to the PP&AS Committee.

4.2.12 CRITERIA FOR REVIEW OF MATERIALS BY THE PP&AS COMMITTEE

All materials submitted to the PP&AS Committee will be reviewed for acceptability on two grounds:

i. Materials will be evaluated for scientific accuracy, quality, importance, and style. The intent is to assure that all approved CPC materials reflect well on the CPC Study.

ii. Materials will be reviewed to assure appropriateness of the content. The material will be reviewed to assure that it does not divulge prematurely additional outcomes or findings of the CPC Study or compromise the eventual publication of CPC findings in high quality peer reviewed journals. In this latter regard, it must be remembered that publication of reports of more than 400 words are generally taken to constitute prior publication of a body of material and will generally preclude subsequent publication of the material in a peer reviewed journal.

4.2.13 MAINTENANCE OF RECORDS OF PUBLICATIONS AND PRESENTATIONS

The DCC will maintain a record of all official publications and presentations of the CPC, as well as papers in progress, separated into the following categories:

i. Peer reviewed papers accepted and published in professional journals
ii. Invited editorials, reviews, chapters, and books
iii. Abstracts published in citable journals
iv. Other presentations at regional or national meetings which do not result in a citable abstract

This listing will be updated at least every six months and will be distributed to the P.I. of each center participating in the CPC Study, together with reprints or copies of any papers, chapters, or abstracts accepted for publication since the last update. This is intended to facilitate the updating of curricula vitae and the timely submission of reports to any research offices within the participating centers.

4.3 ANCILLARY STUDIES

Any ancillary study must be undertaken with careful consideration of its impact on the objectives of the CPC. Ancillary studies which complement the objectives may enhance the value of the CPC and may promote the continued interest of the investigators. However, to protect the integrity of the major study, a proposal to conduct an ancillary study must be reviewed by the PP&AS Committee before its initiation. All ancillary studies also will be reviewed for potential impact on the overall CPC Study.

4.3.1 DEFINITION OF AN ANCILLARY STUDY

An ancillary study is defined as research or data collection involving CPC Study patients using any technique, medication, procedure, questionnaire or observation other than those set forth in the CPC Protocol. The investigator responsible for the conduct of an ancillary study must be a member of the CPC Study Group.

4.3.2 REASON FOR REQUIREMENT OF APPROVAL

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

- cause a deviation from the Protocol;
- complicate interpretation of the study results;
- adversely affect patient cooperation;
- jeopardize the public image of the study;
- create a significant diversion of the study resources locally or at the Data Coordinating Center or any other CPC unit;

- in any way negatively influence the cooperative spirit of the collaborating investigators;
- otherwise compromise the scientific integrity of the study.

4.3.3 OUTLINE FOR SUBMISSION OF ANCILLARY STUDIES PROPOSALS

The proposal should include a brief description of the objectives, methods, significance of the study, plans for analysis and publications, and information regarding funding level and source. If a proposal is being submitted elsewhere for funding (e.g., a grant application), the source of funding should be identified and the application may be used as the basis for the request. Full details should be given concerning any procedures or tests to be carried out on a CPC Study patient, including any observations to be made or procedures to be conducted on patients outside of the clinic; any extra clinic visits required of the patient or any prolongation of the patient's usual clinic visits; any additional specimens (blood, urine, etc.) to be obtained or additional procedures to be done on specimens collected according to the CPC Protocol. The proposal should discuss the measures to be taken to ensure patient safety and confidentiality and an assessment by the investigator(s) of the potential impact of the ancillary study on the CPC Study. Prior approval by the appropriate Human Subjects Review Committee(s) must be demonstrated.

To assure that proposals for ancillary studies to be undertaken in conjunction with the main CPC Study protocol have adequate information to permit their evaluation, proposers must submit such proposals to the PP&AS Committee in the following format.

I. Study hypotheses.
   Specific outcome variables to be assessed.
II. Significance of the proposed ancillary study.
   Necessity of performing this ancillary study withi the context of the main study.
III. Affect of performance of this ancillary study on the main CPC Study. Specifically:
   a. Additions to the main CPC Study protocol. Identify and describe.
   b. Additional patient, staff, and/or DCC time required to complete this ancillary study.
IV. Cost of the ancillary study. Estimate should include costs of needed equipment, supplies, forms, statistical analysis, personnel time, and funding source.
V. Additional training of personnel required (if any).
VI. Data analysis and quality control.
   a. Information required from the main CPC database
   b. Specific additional measurements that will be made. Frequency?
   c. Assurance of data accuracy and precision.
   d. Sample size required to get meaningful answers. Assumptions made in the calculation of this estimate.
   e. Statistical methods used to analyze the resulting data.
VII. Precise protocol. Specify in detail.

4.3.4 PROCEDURES FOR OBTAINING ANCILLARY STUDY APPROVAL

The investigator should send his/her ancillary study proposal to the Chair of the PP&AS Committee, who will distribute it to all members of the PP&AS Committee. The proposal should be written in sufficient detail so that the PP&AS Committee can assess the study's scientific merit and potential impact on the CPC Study. Within 30 days of receiving the proposal, the Chair of the PP&AS Committee will summarize the questions and objections (if any) raised by members of the Committee and refer this summary to the applicant so that he/she may amplify, clarify, and/or withdraw his/her request. If not withdrawn, the members of the PP&AS Committee may re-review the request in light of the applicant's response(s) to the PP&AS original summary. The Chair will then prepare a statement of the Committee consensus. If the ancillary study requires access to the CPC Study patient specimens, the approval statement and all correspondence with the applicant will be forwarded to the Chair of the Committee on Access of CPC Study Data and Patient Specimens. Only if the Committee on Access of CPC Study Data and Specimens approves the release of the specimens will the proposal be forwarded to the Steering Committee for review. If access to study specimens is not requested, the approval statement of the PP&AS Committee and applicant correspondence will be forwarded directly to the Steering Committee. Each member should respond to the Chair of the PP&AS Committee within 30 days. No response will be considered approval. Approval or disapproval is based on majority opinion. Upon approval by the Steering Committee, ancillary studies will be forwarded to the NIDDK Project Officer for final authorization. The investigator may only proceed with the ancillary study once it has been authorized by the NIDDK.

In the event that the PP&AS Committee or the Committee on Access to Study Data and Patient Specimens, disapproves of a proposed ancillary project, the investigator can apply directly to the Steering Committee, whose decision may override that of the PP&AS Committee or Committee on Access to Study Data and Patients Specimens. If the Steering Committee also disapproves of the ancillary study, the proposed study can not be undertaken.

4.3.5 FUNDING OF ANCILLARY STUDIES

Funds are not available in the CPC Study for the conduct of ancillary studies. This includes funding for extra activities which may be required by the central units, particularly the DCC. An ancillary study proposal submitted for review must not only identify the amount of money needed to conduct the study, but also the sources where funds may be obtained. For example, an investigator may wish to submit a new research grant application, request support from foundations or drug companies, or seek other sources of support.

4.3.6 PUBLICATION OF ANCILLARY STUDY RESULTS

All reports, manuscripts or presentations using data derived from the ancillary study must be approved by the PP&AS Committee prior to publication or presentation according to the procedures set forth in section 4.2.

4.4 ACCESS TO CPC STUDY DATA AND PATIENT SPECIMENS

The primary goal of the CPC Study is to develop and maintain a centralized, standardized registry containing data on patients with symptomatology consistent with CP. In order to fully develop the longitudinal data and to provide sufficient time to pursue the research interests of the CPC Study investigators, study data and patient specimens will not be made available to external investigators until the current grant ends. At that time, all investigators, whether internal or external to the Study, must submit a proposal for approval to access CPC Study data and/or patient specimens. Applications for access to CPC Study data and/or patient specimens will be accepted for review on an annual basis.

4.4.1 PATIENT DATA

Investigators may request and receive access to an extensive registry of patient data including questionnaire and diagnostic information relevant to patient and family history, medication and treatment history, patient symptoms, voiding logs, clinical examinations, and laboratory and diagnostic results.

4.4.2 REQUESTING ACCESS TO STUDY DATA AND SPECIMENS

Investigators will be invited to apply for access to the CPC Study data and/or specimens. The Committee on Access to Study Data and Patient Specimens will work with the NIDDK to establish submission deadlines consistent with NIH RFA deadlines. Requests should be submitted to the PP&AS Chair as a proposal for an ancillary study following the guidelines described in Section 4.3.3: *Outline for Submission of Ancillary Studies Proposals.* The PP&AS Chair will evaluate the proposal and forward the request to the appropriate committee for review.

4.4.2.1 Requests for CPC Study Data

The PP&AS Chair will forward requests received for access to CPC Study data to the PP&AS Committee. The PP&AS Committee will consider the proposal as a request for Ancillary Study approval and will review the proposals for scientific merit and feasibility as outlined in Section 4.3: *Ancillary Studies*. If the PP&AS Committee grants approval to a proposal, the PP&AS Chair will forward the approved proposal, along with any comments from the PP&AS Committee to the Committee on Access to CPC Study Data and Patient Specimens for approval of the release of the CPC Study Data. The Committee on Access to CPC Study Data and Patient Specimens will have 30 days to review the proposals and submit their decision to the Chair of the Committee on Access to CPC Study Data and Specimens. The proposal will be presented at the next CPC Steering Committee meeting for general CPC Study approval. Upon Steering Committee approval, the proposal and all correspondence is forwarded for final review and approval by the NIDDK. In the event that the Steering Committee is no longer convening on a regular basis, the request will be forwarded directly to the NIDDK Project Officer after review by the Committee on Access to CPC Study Data and Patient Specimens. The investigator may only proceed with the ancillary study once it has been authorized by the NIDDK. The Chair of the PP&AS Committee will notify all applicants in writing of final approval or disapproval.

4.4.2.2 Requests for CPC Patient Specimens

Requests for CPC Patient Specimens will be reviewed on an annual basis. Proposals including requests for access to CPC Patient Specimens will be forwarded to the Chairperson. If the Chairperson approves the technical feasibility of the study, the proposal will be forwarded to the PP&AS Committee. The PP&AS Committee will consider the proposal as a request for Ancillary Study approval and will review the proposals for scientific merit and feasibility as outlined in Section 4.3: *Ancillary Studies*. If the PP&AS Committee grants approval to a proposal, the PP&AS Chair will forward the approved proposal, along with any comments from the PP&AS Committee to the Committee on Access to CPC Study Data and Patient Specimens for approval for the release of the study specimens. The Committee on Access to CPC Study Data and Patient Specimens will have 30 days to review the proposals and submit their decision to the Chair of the Committee. The proposal and any comments from the reviewing committees will be presented at the next CPC Steering Committee meeting for general CPC Study approval. Upon Steering Committee approval, the proposal and all correspondence is forwarded for final review and approval by the NIDDK. In the event that the Steering Committee is no longer convening on a regular basis, the request will be forwarded to the NIDDK Project Officer after review by the Committee on Access to CPC Study Data and Patient Specimens. The investigator may only proceed with the ancillary study once it has been authorized by the NIDDK. The Chair of the PP&AS Committee will notify all applicants in writing of final approval or disapproval.

4.5 HUMAN SUBJECT'S CONSIDERATIONS

4.5.1 INFORMED CONSENT

Each Clinical Center is responsible for ensuring that informed consent is obtained from each patient according to the guidelines of their local Institutional Review Board. The informed consent form, which must be written in clear, simple language, should describe, in detail, the screening process, the data collection and procedures schedule, and the length of follow-up. The informed consent form should also address the potential risks, benefits and costs due to the subject's participation in the study. Specifically, the following must be accomplished during the informed consent process:

- The patient must be informed that participation in the study is voluntary and refusal to participate will involve no penalty or loss of benefits.

- The patient must be informed of any alternative procedures.

- The patient must be made aware of his responsibilities throughout the screening phase and the entire follow-up period. The importance of continued follow-up should be stressed.

- An outline of safeguards to protect patient confidentiality must be included, as well as an indication of the patient's right to withdraw without penalty. This should be balanced with a discussion of the effect withdrawals have on the study, and the responsibility a patient has, within limits, to continue in the study if he decides to enroll.

- The consent form must include a statement of the policy of the local institution on compensation for study-related injuries, and information on any additional costs to the subject that may result from participation in the research.

- The patient must be informed of his right to have questions answered at any time, and whom to contact for answers or in the event of research-related injury.

- The patient must be informed that he will be notified of any changes in the protocol.

4.5.2 PATIENT CONFIDENTIALITY

Extensive efforts will be made to ensure that the patient's confidentiality is maintained. Each patient will be assigned a unique patient identification number. A log of the patient names and patient ID numbers will be maintained in a locked file cabinet at each Clinical Center. The staff at the Data Coordinating Center will not have access to this log. Only the patient ID number will be given to the Data Coordinating Center staff and entered into the CPC Study. Any communication between the Data Coordinating Center staff and the Clinical Center staff regarding patient data will occur via this patient ID number.

4.6 PERSONNEL ID NUMBERS

Each member of the clinical center staff involved in data collection for the CPC Study will be assigned a unique identification number. This number is used to identify the individual responsible for completing or reviewing a form. The identifier will contain 4 digits corresponding to the last four digits of the person's social security number.

5 PATIENT ENROLLMENT

5.1 PATIENT RECRUITMENT

The most important factor contributing to the success of the CPC Study is the successful recruitment and retention of men with chronic prostatitis. Each Clinical Center is responsible for recruiting 35 patients into the study each study year. An individual center may enroll more than 35 patients in any given year. This does not seem to be an overly optimistic projection of available numbers of patients. Enrollment data will be monitored by the DCC in order to continually assess enrollment rates. Because achievement of recruitment goals depends largely on the organizational structure of the individual clinics, each Clinical Center will be responsible for determining how best to recruit patients.

5.1.1 METHODS OF RECRUITMENT

Although most patients will be recruited for the CPC Study from the urology practice of the investigator, there are occasions when this is not sufficient or is not the sole source of patient recruitment. The following options are likely sources for patient enrollment:

Investigator=s own clinical practice.

Many potential patients can and will be identified simply by considering the current patient population in the urology practice. The success of this method depends largely on the number of patients in the population who are eligible and interested in the study. When considering this as the main source of potential study patients, investigators should not only evaluate how many patients will meet the study criteria, but also what percentage will be willing to participate in and comply with the study protocol.

Referral from the medical practice of other physicians.

It is likely that each Clinical Center will need to rely on the referral of chronic prostatitis patients from the medical practices of other urologists and internists to supplement enrollment from their own practice. In order to succeed, this method of recruitment requires the support of colleagues more than any other method. If potential referring physicians are not advocates of the study, or fear losing their patients to the study, the number of referrals will be minimal, and the method not reliable for recruiting patients.

Prostatitis Foundation home page on the world wide web.

The Prostatitis Foundation, which is supported by volunteers and donations, will announce the study on their home page which will refer interested patients and clinicians to the geographically appropriate investigator.

NIH sponsored press release one week prior to the launch of the study.

Approximately one week prior to the start of the CPC Study, the NIH will arrange a press release to introduce the study to the media and public.

NIH home page on the world wide web.

After the study has been officially introduced to the media and public, the CPC Study will be described on the NIH Home Page, NIDDK division, in the section AWhat=s New at NIDDK@, and/or ANIDDK Health information.@

Brochure for patients and clinicians.

Two separate brochures will be prepared and distributed by the DCC that will address the concerns of patients and clinicians. In the brochure entitled AInformation for Patients@, the CPC Study is described and the patient study requirements are listed. The brochure entitled AInformation for Clinicians@ describes more specifically the aims of the study, the type of data being collected, and the eventual transition from a cohort study to clinical trials. Clinical centers are encouraged to use these brochures. They should be stamped with the name and contact information of the study coordinator or physician=s office so that patients can contact researchers who can provide study and enrollment information. Also, these brochures may be used at health fairs and other educational and promotional events to advertise the CPC Study.

Patient Newsletter.

In an effort to keep patients interested in the study, the CPCRN will publish a newsletter every six months for distribution to enrolled patients and potential patients. The newsletter will include information regarding the status of the study, recent medical information and perhaps an interview with a study participant or investigator. Patients may withdraw from a study because they perceive that they are not getting anything in return for their efforts and the newsletter may reinforce commitment to the long range plans of the study for some patients.

5.2 PRE-SCREENING

The first contact with a potential participant will be considered a pre-screening contact and will include an introduction to the study, a review of the eligibility criteria, a description of tests and procedures involved, and a review of the follow-up contact schedule. The RC is responsible for evaluating the potential patient=s commitment to the study, including his stability within the geographic region. This should be done to ensure that he is willing and able to meet the demands of the follow-up phase of the study. It is suggested that the RC ask the following question: AAt this time, do you expect to be able to complete the follow-up phase for the CPC Study?@

Pre-screening may be conducted either over the phone or in the clinic. If the initial contact is by phone, the RC placing the call should identify him/herself and inform the potential patient how he was selected. The RC should provide information about the study, and answer questions. The potential patient should be given a copy of the informed consent, or if over the phone, a copy should be mailed or faxed. If he is willing, the RC should schedule a time to sign the informed consent and

begin the first screening contact visit. If necessary, the RC should schedule a follow-up call to allow the potential patient time to consider the study obligations.

Note: When scheduling the first screening visit, the patient should be informed that he should remain abstinent (without an ejaculation) for two days prior due to the FGTM test.

5.3 ADMINISTRATION OF INFORMED CONSENT

The informed consent must be the first form administered to all potential CPC Study participants. This form should be completed in a comfortable setting where the patient is able to make a free choice without pressure. Ample time should be given to allow the patient to thoroughly read and process the information alone. Inform the patient or parent/legal guardian of patients under 18 years of age, not to sign the Informed Consent until he has discussed the contents with the RC and all questions have been answered. The RC should familiarize the patient with the study and its requirements.

If the patient wishes to take the informed consent home before reaching a decision, then he may do so. At the subsequent visit, the RC should answer questions raised by the patient and review the patient=s responsibilities. The Informed Consent **must** be signed by the patient, or parent/legal guardian of patients under 18 years of age, and the Principal Investigator, in the presence of a third party (witness). A patient should not be asked to sign the consent statement if he has any doubts about enrolling or if the clinic staff believes he does not understand what his participation would involve. Under *no* circumstance is any study information to be collected or study procedures performed for the specific purpose of the CPC Study **before** the patient, or parent/legal guardian of patients under 18 years of age, has signed the informed consent form.

5.4 ASSIGNMENT OF PATIENT ID

Only after the patient has signed the Informed Consent will the patient be logged in the Patient Log and assigned a Patient ID. Each patient should be assigned the next available patient ID. Once a patient ID has been assigned, it should never, for any reason, be reassigned. See Patient Log (LOG), Section 7.4.2.7. The Patient Log form should be stored in a secure, locked filing cabinet.

The 5 digit patient ID is composed of three identifiers. The first digit indicates the protocol number. The second digit indicates the screening site. The last three digits are the sequential ordering of patients. Each Clinical Center will have a discrete range of ID numbers corresponding to the Clinical Center number. For example: ID# 1 3 0 0 8 describes protocol #1, at the University of MD, with patient ID # 008. Clinical centers are numbered as follows:

1 = Brigham and Women=s Hospital and Massachusetts General Hospital, Boston, MA
2 = Temple University Hospital, Philadelphia, PA
3 = University of Maryland Medical System, Baltimore, MD
4 = Northwestern Memorial Hospital, Chicago, IL
5 = Harbor - UCLA Medical Center, Los Angeles, CA
6 = Kingston General Hospital, Kingston, Ontario, Canada

Patient ID	Patient Initials	Patient Name
11001	JD	John Doe
11002	RS	Robert Smith
11003	MDC	Michael D. Cohen
11004	DW	Doug Weiss

Table 5.1 Patient Log example

5.5 PATIENT ELIGIBILITY

5.5.1 STUDY ELIGIBILITY CRITERIA

Every patient must meet the required criteria to be eligible to participate in the CPC Study. The *study eligibility criteria* consist of the following, and are contained in the Inclusion, Exclusion, and Deferral Checklists.

$ If the patient meets all of the inclusion criteria, then the patient proceeds to the Exclusion Checklist.
$ If the patient meets any of the exclusion criteria, then the patient is not eligible to participate in the CPC Study; if he passes the exclusion criteria, he can proceed to the Deferral Checklist.
$ If the patient meets any of the deferral criteria, the patient is temporarily deferred from enrolling into the CPC Study until such time that the new re-screening date is reached. The RC should flag this form for contact on the appropriate date. See Sections 5.5.1.3 and 5.5.2.

5.5.1.1 Inclusion Checklist:

The patient must meet the following criteria in order to be a candidate for the CPC Study**:**

$ The patient or parent/legal guardian must sign and date the Informed Consent;

- The patient must be a male;

- The patient must have had symptoms of discomfort or pain in the pelvic region for at least a three month period within the last six (6) months.

Note: Due to the nature of the study, pre-pubertal patients will not be enrolled in the study.

5.5.1.2 Exclusion Checklist:

If the patient meets any of the exclusion criteria, then he is precluded from participating in the CPC Study.

- Patients with history of prostate, bladder, or urethral cancer.

- Patients with inflammatory bowel disease (such as Crohn=s disease or ulcerative colitits, but not irritable bowel syndrome).

- Patients with history of pelvic radiation or systemic chemotherapy.

- Patients with history of intravesical chemotherapy.

- Patients treated with intravesical BCG.

- Patients with unilateral orchialgia without pelvic symptoms.

- Patients with active urethral stricture.

- Patients with neurological disease or disorder affecting the bladder.

- Patients with history of TURP, TUIP, TUIBN, TUMT, TUNA, balloon dilatation of the prostate, open prostatectomy, or any other prostate surgery or treatment such as cryotherapy or thermal therapy.

- Patients with a neurological impairment or psychiatric disorder preventing his understanding of consent and his ability to comply with the protocol.

Note: If a patient develops any of the exclusion criteria during the follow-up phase of the CPC Study, this will be reported in the IHC form. The patient will continue through the normal course of the study.

5.5.1.3 Deferral Checklist

If the patient meets any of the deferral criteria, he will be *temporarily* deferred from entering the study. The patient must be free of the condition, or off treatment for at least three months before he can enter the CPC Study. However, patients who have been diagnosed or treated for symptomatic genital herpes within the past 12 months will be deferred for 12months from date diagnosed, and until they have been symptom free for a 12-month period (asymptomatic for 12 months). See Table 5.2 Deferral/Re-entry Criteria.

Deferral Checklist	Re-entry Criteria (Patient deferred until...)
1. If the patient has been treated with antimicrobial (oral or parenteral) agents in the past three months, ***then***	treatment free for 3 months.
2. If the patient had a urinary tract infection with a urine culture value of >100,000 CFU/ml within the past three months, ***then***	condition absent for 3 months.
3. If the patient had any of the following sexually transmitted diseases (STDs) in the past three months, such as gonorrhea, chlamydia, mycoplasma, or trichomonas, but not including HIV/AIDS, ***then***	condition absent for 3 months.
4. If the patient had a prostate biopsy in the past three months, ***then***	3 months from date of procedure.
5. If the patient had experienced symptoms of acute or chronic epididymitis within the past 3 months, ***then***	condition absent for 3 months.
6. If the patient was diagnosed or treated for symptomatic genital herpes in the past 12 months, ***then***	12 months from date diagnosed, and until they have been symptom free for a 12-month period (asymptomatic for 12 months).

Table 5.2 Deferral/Re-entry Criteria

Unfortunately, patients can be poor historians and/or have a limited understanding of their health problems and associated treatments. It is, therefore, advisable to verify the responses to those questions which have been denoted Aas reported by the patient@ with their medical record, when possible. If there is a discrepancy, then the information in the patient=s medical record should be considered correct. For example, if the patient indicated that he has not taken any antimicrobials,

but his medical record clearly indicates that he was on an antimicrobial medication approximately 2 months ago, then the medical record should be considered correct and the patient deferred until he has been off the medication for 3 months.

Patients that are new at a center and for whom there is no medical record available, enrollment criteria will be based on the patient=s self-report. However, responses should be verified with the patient=s medical record whenever possible.

Note: If a patient develops any of the deferral criteria during the follow-up phase of the CPC Study, this will be reported in the IHC form. The patient will continue through the normal course of the study.

5.5.2 SCREENING AND RE-SCREENING REQUIREMENTS

Every potential participant must complete all of the screening phase requirements indicated in Chapter 6: *Visit Scheduling and Administration.* If a patient was previously deferred, he must be re-screened to confirm his current eligibility for the CPC Study. When a patient is re-screened, all screening forms and procedures must be re-done except for the Patient Log (LOG). A re-screened patient has already been assigned a patient ID during Screening Visit #1 and, therefore, should ***not*** be assigned a new ID number. Re-screened patients should retain their previously assigned ID number. A patient who was previously excluded, ***cannot*** be re-screened.

5.5.3 SCREENING FAILURES

A patient who does not complete the Screening Contact, for whatever reason, is considered a screening failure and will **not** be registered into the CPC Study Database. For example, a patient who completes, or partially completes, Screening Visit #1 and does not come back for Screening Visit #2 will be considered a screening failure. This does not include patients who have not had a laboratory test performed due to lab error or patient inability to complete a certain procedure despite efforts by the patient and PI. . All of the completed screening forms for patients who are considered screening failures, should be filed at the center in the CPC Patient File and should not be sent to the DCC.

Note: Patients must be able to provide **at least one** of the following samples: EPS, VB3 or semen sample, to be included in the study. If the patient is not able to provide at least one of these samples, then he will be considered a screening failure and must not be registered in the CPC Study database

5.6 PATIENT REGISTRATION

Only those patients who have completed the entire screening phase including forms and procedures, will be registered into the CPC Study Database. Patients who fall under the category of Screening Failure will **not** be registered into the CPC Study Database (see Section 5.5.3).

Once a patient has completed all of the required screening phase forms and procedures, is confirmed eligible by the Screening Confirmation (SCR) form, ***and*** is registered in the CPC Database, he then proceeds to the Follow-Up Phase of the CPC Study.

A patient may withdraw from the CPC Study at any time. Patients who withdraw and later request reinstatement into the study are permitted to do so. Such patients will resume the follow-up phase of the study at the point where they would be if there had been no interruption in their status. Data not acquired from the time of patient withdrawal to patient reinstatement will be considered missing data.

5.7 PATIENT TRANSFERS

It is possible for a CPC Study patient to transfer to another Clinical Center during the course of the study. It is preferred from a scientific, as well as operational point of view, that a patient complete the study at the same Clinical Center in which he was enrolled.

5.7.1 TRANSFER OF A PATIENT DURING THE SCREENING PHASE

It is strongly recommended that patients not be transferred during the screening process. However, if a patient indicates his desire to transfer to another Clinical Center during the screening phase, then he must be informed of the following:

$ Patient must either complete the screening phase at the originating center, **or**
$ Patient must suspend all further screening processes at the originating center and undergo the entire screening process from the beginning at the desired center.

5.7.2 TRANSFER OF A PATIENT DURING THE FOLLOW-UP PHASE

It is important that patients who have been registered at a particular Clinical Center retain their **original** patient ID and CPC Study File throughout the entire study. If a patient indicates his desire to transfer to another Clinical Center during the follow-up phase of the CPC Study, then the RC must adhere to the following guidelines:

$ The RC at the originating clinical center must complete the Patient Transfer (TRANS) form. This form will contain the patient=s ID, initials, next contact month and target date, and indicate the originating and receiving clinical centers.

$ The originating RC must provide the patient with contact information for the receiving clinical center, and instruct the patient that it is ***his*** responsibility to initiate contact with the receiving RC.

- The originating RC should notify the receiving RC and the DCC of the upcoming patient transfer via email or fax of the Patient Transfer form.

- The originating RC must send a copy of the patient=s CPC study records to the receiving clinical center.

- The receiving RC must create a new file for the patient=s CPC study records, and for all future follow-up contacts.

- Before any CPC Study forms and procedures are completed at the follow-up contact, the receiving RC must have the patient sign the receiving center=s Informed Consent.

- It will be the joint responsibility of both the originating and receiving RC=s to ensure the completeness and accuracy of the patient=s CPC Study records.

- The patient should request a transfer of his medical record from the originating center to the receiving center, following the originating center=s guidelines for transfer of medical records.

6 VISIT SCHEDULING AND ADMINISTRATION

6.1 SCREENING PHASE

The screening phase of the CPC Study is also known as Contact Month 0 of the study. Potential study participants must pass the study eligibility criteria (see Chapter 5: *Patient Enrollment, Section 5.5*) before undergoing the rest of the procedures for the screening phase. The screening phase is divided into two visits, Screening Visit #1 and Screening Visit #2. If it was not possible to obtain the required specimens during Visit #1, an additional visit may need to occur prior to the scheduled Visit #2, in order to obtain these specimens. Visits #1 and #2 must be scheduled at least one week apart and should be completed within a 2-3 week period. All screening criteria must be completed within 30 days of the initial visit in order for patients to remain eligible for study participation. Any clinic visit which takes place during the patient=s screening phase is referred to as a *screening visit*.

Screening phase procedures:

During the screening phase, each patient must provide the information needed to complete all data forms and laboratory procedures listed in Table 6.1. Details on how to complete all data forms are provided in Chapter 7: *Data and Administrative Forms*. Details on how to perform laboratory procedures and specimen handling procedures are provided in Chapter 8: *Laboratory Procedures.*

Order of data forms and laboratory tests:

The forms and procedures to be completed during the screening phase should be completed in an order which is agreeable to both the patient and the clinical center staff. However, the ideal order of these procedures, identified below, has been offered as a way to provide a balance of patient comfort and timeliness. Prior to obtaining a patient=s informed consent, potential study participants will be informed of all aspects of the study (including baseline screening procedures, follow-up procedures, assurance of patient confidentiality and any potential risks and benefits to the patient). The subsequent guidelines should be followed.

6.1.1 SCREENING VISIT #1

The first form to be completed is the Informed Consent, if not signed already. Prior to gathering information or performing procedures specifically for the CPC Study, the Informed Consent must be signed in ink and dated by the patient or parent/legal guardian of patients under 18 years of age, by the Principal Investigator, and witnessed and signed by one member of the clinical center staff.

After the Informed Consent is signed, the next group of forms to be completed, in order, are: Patient Assignment Log (LOG), Inclusion, Exclusion, and Deferral Checklists (INCL, EXCL, and DEF), and the Patient Contact Information (CONT). Once the patient has been assigned a Patient ID, and if the patient meets the eligibility criteria, he can proceed with the screening phase to the next form. A one-day Voiding Log (VOID) will be given to the patient during Screening Visit #1 to be returned

during Screening Visit #2. The RC is responsible for explaining the log and distributing instructions to the patient.

The Medical History (MED) form and the Prior Treatments (PRIOR) form both encompass data gathered on a patient=s medical history. These forms should be completed at the first screening visit.
The physical exam and the four-glass test must be performed by the physician at the first screening visit. In addition, the Physical Exam (EXAM) form should be completed during the exam. The Four-Glass Test Microscopy (FGTM) form and the Four-Glass Test Specimen Cultures (FGTSC) form should be completed as soon as the lab reports are available. The RC should remind the patient that he should remain abstinent (without an ejaculation) for two days prior to FGTM test. However, the sample may be collected even if the patient has not been abstinent.

Reminder to the RC, the four-glass test and semen sample cannot be done during the same visit. It is recommended that these two procedures be scheduled one week apart, however, a minimum of three days apart is acceptable, based on patient availability.

Note: If the patient is not willing to undergo the rectal exam that forms part of the physical exam, the patient will not be allowed to participate in the study.

The serum sample should be collected and stored during the first screening visit, and the Serum Sample (SERUM) form should be completed.

Screening Visit #1 close-out:
At the end of the first screening visit, the RC should instruct the patient to bring in all over-the-counter and prescribed medications that he is currently taking to his next screening visit. This will help the RC to complete the Concomitant Medications (CMED) form during Screening Visit #2.

The RC should remind the patient about the Voiding Log (VOID) which has to be completed and brought to the next screening visit.

The RC should explain to the patient that he must remain abstinent (without an ejaculation) for two days prior to Screening Visit #2, in order to provide the required semen sample.

The RC will schedule Screening Visit #2.

6.1.2 SCREENING VISIT #2

The RC will collect the Voiding Log (VOID) from the patient and will review it for completeness. The RC will collect all over-the-counter and prescribed medications that the patient is currently taking and will complete the Concomitant Medications (CMED) form.

The uroflow test and the urethral swab must be performed at Screening Visit #2. In addition, the Uroflow Study (URO) form must be completed after the test, and the Urethral Swab (SWAB) form should be completed as soon as the lab report is available.

The semen sample must be collected at Screening Visit #2. The Semen Sample (SEMEN) form should be completed as soon as the lab report is available. It is preferred that the patient be abstinent (without an ejaculation) for two days prior to providing this sample. However, the sample may be collected even if the patient has not been abstinent. If the patient says he is unable to provide the semen sample in the office, he will be given a sterile urine cup and will be asked to obtain the sample at home. Once the sample is obtained, it should be kept at room temperature for 30 minutes, then placed on ice, and brought to the clinic within one hour of obtaining the semen sample.

Note: A patient can refuse to provide a semen sample. However, the RC must inform the patient that in order to be eligible for the CPC Study at least one of the following: EPS, VB3 or a semen sample ***must*** be obtained. If none of these tests are obtained, the patient will be considered a screening failure and cannot be included in the study. See section 5.5.3

The Screening Confirmation (SCR) form must be signed and dated by the Research Coordinator and the Principal Investigator when the patient has completed the entire screening process to confirm the patient=s eligibility in the CPC Study.

Screening Visit #2 Close-out
The RC schedules the one-month Telephone Contact.

Table 6.1 Data and Administrative Forms for Screening Phase

SCREENING PHASE
Screening Visit #1: • Informed Consent • Inclusion Checklist (INCL) • Exclusion Checklist (EXCL) • Deferral Checklist (DEF) • Patient Contact Information (CONT) • Medical History (MED) • Prior Treatments (PRIOR) • Symptom Index (SXIND) • Physical Exam (EXAM) • Four Glass Test Microscopy (FGTM) • Four Glass Test Specimen Culture (FGTSC) • Serum Sample (SERUM) • Voiding Log (VOID), given to patient **Screening Visit #2:** • Collect Voiding Log (VOID) • Concomitant Medications (CMED) • Epidemiologic History (EPI) • Uroflow Study (URO) • Urethral Swab (SWAB) • Semen Sample (SEMEN) • Screening Confirmation (SCR) • Administrative Forms 1. Screening Contact Checklist (SCHK) 2. Data Processing Cover Sheet (DPCS) 3. Patient Contact Form (CONT), update if necessary

6.2 FOLLOW-UP PHASE

All eligible patients who have completed the screening phase will proceed to the Follow-Up Phase of the CPC Study. This study phase is comprised of three different types of contacts: Telephone Contact, Brief Clinic Contact, and Extensive Clinic Contact. The Telephone Contact, which may consist of a telephone interview conducted by the RC, takes place at months 1, 2 and 3 after the final screening visit and subsequently every 6 months, at months 9, 15, 21, 27, and 33. The Brief Clinic Contact and the Extensive Clinic Contact consist of patient visits to the clinic. The Brief Clinic Contact takes place at months 6, 18, and 30 after the final screening visit. The Extensive Clinic

Contact takes place at months 12, 24, and 36 after the final screening visit. It is anticipated that patients will be followed in the CPC Study for three years.

Note: Duration of follow-up for each patient will vary depending on the date the patient is registered into the CPC Study Database.

6.2.1 TELEPHONE CONTACTS

The first telephone contact should take place one month after the final screening visit and subsequently on month 2, 3, 9, 15, 21, 27, and 33 after the final screening visit. One week prior to the scheduled Telephone Contact, the RC should mail a copy of the Symptom Index (SXIND) to the patient, with a stamped self-addressed envelope, asking the patient to complete Symptom Index and return it to the clinic.

TELEPHONE CONTACT
Contact Months: 1, 2, 3, 9, 15, 21, 27, &33: • SXIND • Administrative Forms 1. Telephone Contact Checklist (TCHK) 2. Data Processing Cover Sheet (DPCS) 3. Patient Contact Information (CONT), update if necessary.

Table 6.2: Data and Administrative Forms for Telephone Contacts.

Forms requirements

Table 6.2 identifies the forms that should be completed for the Telephone Contacts. A new Patient Contact Information (CONT) form need only be completed if any of the patient=s information has changed since the last contact. The remaining forms must be completed for all patients undergoing a Telephone Contact.

Completion of data and administrative forms

Details on completing all data and administrative forms are provided in Chapter 7: *Data and Administrative Forms.*

Ideally, the telephone contact will consist of the RC reminding the patient that it is time for him to complete the Symptom Index (SXIND) and mail it to the clinic, if he has not already done so. In the event that the patient is not able to complete the Symptom Index himself, for whatever reason, the RC will interview the patient and the RC will complete the Symptom Index form.

Telephone Contact Close-out

The RC will schedule the next patient contact according to the Patient Follow-up Contact Schedule provided for each individual patient, and the RC will review all the forms. The RC will review all the forms

6.2.2 BRIEF CLINIC CONTACTS

Each patient will complete a series of Brief Clinic Contacts during the follow-up phase. These visits will occur at months 6, 18, and 30 after the final screening visit.

BRIEF CLINIC CONTACT
Contact Months: 6, 18, & 30: • Symptom Index (SXIND) • Interim Health Care (IHC) • Physical Exam (EXAM) • Four Glass Test Microscopy (FGTM) • Administrative Forms 1. Brief Clinic Contact Checklist (BCCHK) 2. Data Processing Cover Sheet (DPCS) 3. Patient Contact Information (CONT), update if necessary

Table 6.3: Data and Administrative Forms for Brief Clinic Contacts.

Forms requirements

Table 6.3 contains the list of forms and procedures that must be completed for each patient undergoing the Brief Clinic Contact. A new Patient Contact Information (CONT) form need only be completed if any of the patient=s information has changed since the last contact. The remaining forms must be completed for all patients undergoing a Brief Clinic Contact.

Completion of data and administrative forms and laboratory procedures.

Details on completing all required forms are provided in Chapter 7: *Data and Administrative Forms* and Chapter 8: *Laboratory Procedures.*

Brief Clinic Contact Close-out

The RC will schedule the next patient contact according to the Patient Follow-up Contact Schedule for each individual patient.

6.2.3 EXTENSIVE CLINIC CONTACTS

Each patient will complete a series of Extensive Clinic Contacts during the follow-up phase. These

will occur at months 12, 24, & 36 after the final screening visit.

EXTENSIVE CLINIC CONTACT
Contact Months: 12, 24, & 36: • Voiding Log (VOID) • Symptom Index (SXIND) • Interim Health Care (IHC) • Physical Exam (EXAM) • Four Glass Test Microscopy (FGTM) • Four Glass Test Specimen Culture (FGTSC) • Administrative Forms 1. Extensive Clinic Contact Checklist (ECCHK) 2. Data Processing Cover Sheet (DPCS) 3. Patient Contact Information (CONT), update if necessary

Table 6.4: Data and Administrative Forms for Extensive Clinic Contacts.

Forms requirements

Table 6.4 contains the list of forms that must be completed for Extensive Clinic Contacts. A new Patient Contact Information (CONT) form need only be completed if any of the patient=s information has changed since the last contact. The remaining forms must be completed for all patients undergoing an Extensive Clinic Contact.

Completion of laboratory procedures and data and administrative forms

The RC should mail a Voiding Log (VOID) to the patient=s mailing address prior to the visit, ensuring that the patient has ample time to complete the forms. At the beginning of the Extensive Clinic Contact, the RC should collect the completed Voiding Log (VOID).

Extensive clinic contact close-out

The RC will schedule the next patient contact according to the Patient Follow-up Contact Schedule provided for each individual patient. If the patient has forgotten to bring in his Voiding Log (VOID), the RC will remind the patient to mail the form to the clinic as soon as possible.

6.3 SCHEDULING OF CONTACTS

The RC will explain the three different types of follow-up contacts to the patient, the different forms and procedures required for each contact and the approximate length of time that should be allotted for each type of contact.

6.3.1 SCREENING VISITS

At the completion of Screening Visit #1, the RC should schedule the patient for Screening Visit #2. If it was not possible to obtain the required specimens during Visit #1, an additional visit may need to occur prior to scheduled Visit #2, in order to obtain these specimens. There must be a minimum of three days between these visits. All screening visits must be completed within 30 days from the date of the Inclusion (INCL) form to the date of the Screening Contact (SCR) form. However, it is best to schedule these visits as close together as possible.

At the end of the final screening visit, the RC will schedule the patient=s one-month follow-up Telephone Contact to take place in approximately 30 days. The RC should not wait to generate the Patient Follow-up Contact Schedule before scheduling the one-month Telephone Contact.

6.3.2 FOLLOW-UP CONTACTS

The clinical center will confirm that a patient is eligible for the Follow-up Phase of the CPC Study by signing the Screening Confirmation (SCR) form, and will generate the Patient Follow-up Contact Schedule from the CPC database. The Patient Follow-Up Contact Schedule will be generated for each individual patient according to the date of his final screening visit. This schedule indicates the sequence of follow-up contacts, target dates for each contact, and time windows in which the contact must be completed.

At the close of each contact, the RC will schedule the next contact, whether it is a telephone, brief clinic, or extensive clinic contact, by referencing the Patient Follow-up Contact Schedule.

Note: The RC should inform the patient that he should remain abstinent (without an ejaculation) for two days prior to each Brief and Extensive Clinic Contacts.

Determination of the Patient Follow-Up Contact Schedule

The target date for any follow-up contact is calculated by adding the correct number of days to the date of the patient=s final screening visit. The correct number of days is calculated by the number of months, based on a 30.4 day month, after the patient=s final screening visit in which the follow-up contact should occur.

The *time window* for any follow-up contact is the time frame in which the contact should be completed. The time window for all telephone contacts is defined as the interval of time starting 7

days before and ending 7 days after the target date of the contact. The time window for all clinic contacts is defined as the interval of time starting 14 days before and ending 14 days after the target date of the clinic visit. All dates are determined from the date of the final screening visit, without regard to whether they fall on a weekend or a holiday. (See Table 6.5)

Patient Follow-Up Contact Schedule

This schedule is generated to aid the RC in scheduling all follow-up contacts for patients. When the RC generates the Patient Follow-up Contact Schedule from the database, it should be placed in the patient=s study file. At the conclusion of a patient contact, the RC should refer to the schedule in order to schedule the next contact. The RC should document the completed contact date under the column titled AActual Contact Date@, and refer to the next line to determine the type and appropriate date of the next contact.

Scheduling contact dates within permissible time windows will be based on the patient=s pattern of adherence to scheduled contacts. When contact dates are adhered to, the contact should be scheduled as close as possible to the target date. Rescheduling of contacts should be discouraged. When rescheduling contacts, the next contact should be scheduled as early as possible within the permissible time window in order to increase the chances of rescheduled contacts falling within the window. If the RC or the patient is not sure when to schedule the next contact, it should be set as early as possible within the time window.

The RC should consult the Patient Follow-Up Contact Schedule whenever ***any*** appointment (non-study related) is scheduled for a study patient. Depending on the date of the appointment, the contact could qualify as one of the patient=s follow-up study contacts. The RC should adhere to the following guidelines to schedule future appointments or to determine whether one of the required follow-up contacts should be completed during an appointment.

If a patient has to reschedule a contact, the RC should attempt to reschedule the appointment within the remaining time window. If the contact cannot be planned within the time window, the contact should be scheduled and completed before the first possible date of the next contact window. If this is not possible, it will be considered a Amissed@ contact. (See 6.3.3 Missed Study Contacts.)

If a patient calls to schedule an appointment within the time window of a brief or extensive clinic contact, and the contact has not yet been completed, the brief or extensive clinic contact should be completed at that time. The original appointment for the brief or extensive clinic contact, therefore, need not be kept. A Sample Patient Follow-up Contact Schedule is shown below.

Patient Follow-Up Contact Schedule

Patient ID: 13086
Patient Initials: __ __ __
Final Screening Date: 05/31/98

The indicated contacts should be done within the time window specified and as close to the target date as possible.

	TIME WINDOW			
Type of Contact	**Target Date**	**First Possible Date**	**Last Possible Date**	**Actual Contact Date**
1 Month Phone	06/30/98	06/23/98	07/07/98	
2 Month Phone	07/31/98	07/24/98	08/07/98	
3 Month Phone	08/30/98	08/23/98	09/06/98	
6 Month Brief Clinic	11/27/98	11/13/98	12/11/98	
9 Month Phone	02/25/99	02/18/99	03/04/99	
12 Month Extensive Clinic	05/28/99	05/14/99	06/11/99	

Table 6.5: Sample Patient Follow-Up Contact Schedule

6.3.3 MISSED STUDY CONTACTS

If a follow-up contact cannot be completed within the time window allowed, the contact should be scheduled and completed before the window date of the next study contact. If the contact cannot be completed before the window date of the next contact, the contact must be considered missed, and a Missing Contact (MISS) form should be completed.

When a patient misses a follow-up contact, the RC should stress to the patient the importance of collecting follow-up data. When a patient misses multiple follow-up contacts, the PI may consider withdrawing the patient from the study. A patient will be considered lost to follow-up when he has missed six (6) consecutive months of contacts.

6.3.4 ADDITIONAL VISITS

Additional visits may be required for the patient=s normal medical care, however, data forms need not be completed. If there are any changes in the patient=s concomitant medications or treatments, this information must be recorded in the patient=s medical chart.

The RC need not complete data forms under the following circumstances:

$ A patient calls to schedule an appointment within the time window of a telephone/clinic contact and the required contact has already been completed in the window;

$ A patient calls to schedule a visit at a time in between study contact time windows, and the last contact by the patient was completed in its required time window;

$ A patient and RC have telephone contact outside of the patient=s required series of phone contacts.

Note: It is important to remember that if there is a change in CPC related symptoms, they will be recorded in the next contact on the Interim Health Care (IHC) form.

6.4 CONTACT REMINDERS

One week prior to any scheduled contact, the RC should mail to the patient a packet containing a reminder letter for the upcoming contact and any form(s) to be completed or referenced by the patient for that contact.

For the Telephone Contacts, the packet should include the following:

X A reminder letter of upcoming phone interview specifying the date and time the phone contact will be conducted;
X A copy of the Symptom Index (SXIND).
X A stamped, self-addressed envelope for the patient to return the SXIND to the clinic.

For the Brief Clinic Contacts the packet should include the following:

X A reminder letter of upcoming contact specifying the date and time the contact will be held.
X Due to the FGTM, the patient should remain abstinent (without an ejaculation) for two days prior to the visit.

For the Extensive Clinic Contacts, the packet should include the following:

X A reminder letter of upcoming contact specifying the date and time the contact will be held.
X Due to the FGTM, the patient should remain abstinent (without an ejaculation) for two days prior to the visit.
X Voiding Log (VOID).

The contact reminder packets provide the patient with instructions for preparing for the scheduled appointment. Examples of contact reminders are included in the Administrative Forms section of this manual. (See Appendix C.)

7 DATA AND ADMINISTRATIVE FORMS PROCEDURES

7.1 ACQUISITION OF FORMS FROM THE DCC

The forms are provided to the Clinical Centers in electronic format as PDF (portable document format) files. The Clinical Center is responsible for printing all administrative and data forms. The forms necessary for each contact are grouped together, in order to streamline the printing process.

7.2 GENERAL INSTRUCTIONS FOR THE COMPLETION OF DATA FORMS

7.2.1 GENERAL INSTRUCTIONS FOR ALL DATA FORMS

There are two types of forms being used for the CPC Study: Case Report Forms (which contain patient data), and Administrative Forms. Specific directions for completing each of the case report forms are provided in Section 7.3. The following items are instructions to be followed when completing any of the case report forms:

The RC should always verify the forms in a packet against the corresponding Contact Checklist to confirm that all forms are available before the patient arrives for the visit, or before a telephone contact is made. For any missing forms, the RC will be able to print a copy from the PDF file. The RC must be sure that the current version of all forms is used and printed. The DCC will notify RC's of revisions in forms.

All case report forms should be completed in ***black*** ink, as it is the most easily copied and will insure that photocopies of the original forms are legible. Pencil, blue ink or red ink are **not** to be used.

It is important that the RC completes the heading of the case report form ***before*** continuing with the form to insure easy identification in case of separated pages. There are two types of headings for the case report forms. Master headings are on the first page all CRF's and the abridged heading is found on subsequent pages of multiple page CRF's. The master heading contains the Patient ID, Patient Initials, Clinic Center, Contact Month, Date, and RC ID. The abridged heading contains the Patient ID, and Contact Month.

The RC ID is the last four digits of the SSN of the RC who has reviewed the forms. The RC is responsible for reviewing all of the forms completed for the CPC.

7.2.2 FORMS COMPLETION

On the left, under the CPC heading is a subheading which indicates by whom the form is to be completed: Patient Completed, Patient Interview Completed, Principal Investigator Completed, or Research Coordinator Completed. Descriptions of how these are to completed are found below.

7.2.2.1 Patient Completed Forms

Forms with the subheading "Patient Completed" are to be completed by the patient. The patient should be provided a quiet and comfortable place to sit which will allow him some privacy. The RC should be readily available in case of any questions. The RC should not hover over the patient as this may make the patient uncomfortable and want to rush through the form.

After the patient completes the form but before he leaves the clinic, the RC should review the form for completeness and legibility. If additional clarification or information is required it can be obtained efficiently while the patient is still present.

If the patient is uncomfortable about completing the forms by himself, or if the RC feels that the patient may have trouble reading the forms, the RC may interview the patient to complete the forms. The RC should ask, "*Would you like to complete these forms alone, or would you prefer for me to read them to you?"*. Since the patient may find some of the information on the forms to be sensitive, whenever possible, the patient should be encouraged to complete the forms alone.

Once the form is reviewed, the RC can provide the RC ID in the top right corner of the master heading of the form.

7.2.2.2 Patient Interview Completed Forms

These forms are not to be completed by the patient, but rather are designed to be administered to the patient by the RC. The forms are completed by interviewing the patient and asking specific questions found on the forms.

Interview Techniques
Before performing the interview, the RC should inform the patient that the interview will flow smoothly if the questions and responses are read in their entirety before the patient answers. If the patient needs clarification of any question, this can be done after the question has been read. Any text in ***bold italic*** print, in a shaded box or set off by a pointing hand (Λ) are instructions to the interviewer (RC) only and should not be read to the patient. A normal tone of conversation should be taken when addressing questions to the patient. Do not rush through the interview and keep interruptions to a minimum.

The RC is responsible for getting an appropriate answer from the patient if the patient's answer is unclear, incomplete, or irrelevant. If this occurs, the RC should use the "probing" technique

used by interviewers to refocus and redirect the patient's attention to the question. The interviewer should get the patient to elaborate or reconsider an incomplete or inappropriate answer without leading the patient or influencing the content of the answer (creating bias in their answer).

Rule #1: Keep it neutral. Be sure not to probe in a way that is leading or directive.

Rule #2: Use only probes similar to those on the list of standard probes provided in Appendix F.

Some questions addressed in the case report forms are personal and may be very sensitive issues for the patient. When a patient shows reluctance in answering a question, the interviewer should reassure the patient regarding the confidentiality of the response and explain the importance of the question. If the patient is still reluctant or refuses to answer, the issue should not be stressed as this may cause the patient to become alienated. The RC should make a note in the left margin of the form indicating that the patient refused to answer the question. Example: [PT. REF.]

The RC should review the form for completeness and legibility before terminating the interview, or before a patient leaves, in case additional information or clarification is required.

7.2.2.3 Research Coordinator Completed and Principal Investigator Completed

Forms indicated as Research Coordinator Completed should be completed *only* by the RC. Principal Investigator Completed forms should be completed by the PI or his designee. The PI's designee must be another physician. All forms that are to be completed by the RC or the PI should be completed during the contact unless awaiting a necessary lab report.

Upon the completion of all PI completed forms, the RC should review the form for completeness and legibility, and complete the RC ID in the upper right hand corner of the form. The PI should initial the form, for documentation.

7.2.3 REVIEW OF COMPLETED FORMS

The RC should review *all* forms for legibility, accuracy, and completeness *before* they are submitted to the DCC, preferably while the patient is still available to clarify questionable responses, or to provide missing information.

If the RC identifies an error while reviewing the forms, the error should be corrected on the current form by crossing out the error with a single line in **black** ink, and entering the correct information. Initial and date the change. Circle the correct answer for clarification, if necessary.

7.3 SPECIFIC DIRECTIONS FOR COMPLETING CASE REPORT FORMS

This section provides specific instructions on how to complete each case report form. The forms

are addressed in alphabetical order by form title. For each of the forms the following is provided: Purpose of the form, Who completes the form, When the form is to be completed, and Instructions. If you are unsure where to find specific information on how to fill the form, please contact the CPC Data Managers.

7.3.1 CONCOMITANT MEDICATIONS (CMED)

Purpose: To collect information on medications the patient is ***currently*** taking at screening which are ***not*** taken for treatment of prostatitis symptoms.

Who: Patient Interview Completed

When: Screening Contact - Visit #2

Instructions:
At the first screening visit, the RC will instruct the patient to bring in all of the over-the-counter and prescribed medications that he is currently taking to Screening Contact - Visit #2. The RC should ask the patient for what purpose he is taking the medication and document this information in the patient's chart. This will enable the RC to complete the Concomitant Medications (CMED) form during Screening Contact - Visit #2. If the patient fails to bring in the medications, the RC will ask the patient to recall his medications.

Q1-7: Refer to the Concomitant Medication Table (Appendix D) to classify the medications the patient is taking. If the patient has never heard of the medication classification and does not know if he is taking the medication, check "Unknown". If possible, refer to the current PDR or check with the physician about any medications.

Q8: Answer "yes" for any other form of medication that is not included in the reference list.

7.3.2 DEFERRAL CHECKLIST (DEF)

Purpose: To assess the patient's eligibility for the study according to the study deferral criteria.

Who: Research Coordinator Completed

When: Screening Contact - Visit #1

Instructions:

During pre-screening, the RC should review the deferral criteria with the patient, to prevent the patient from making an unnecessary trip to the clinic.

Q3: Patients should be free of these four specific sexually transmitted diseases which directly affect the normal function of the genitourinary system.

Q6: Patients should be deferred for **twelve months** after being diagnosed with or treated for symptomatic genital herpes. This is the only deferral criterion that is not three months.

Q7: **Eligibility Question:** If the patient is deferred, refer to Section 5.5: *Patient Eligibility* for the length of the deferral period. Record the approximate date that the patient will be eligible for re-screening.

7.3.3 EPIDEMIOLOGIC HISTORY (EPI)

Purpose: To collect background and demographic information, as well as sexual history.

Who: Patient Completed

When: Screening Contact - Visit #2

Instructions:

Q1: The year given for the date of birth must be four digits.

Q2: Ethnic origins are defined as follows:

Asian or Pacific Islander: A person having origins in any of the original peoples of the Far East, southeast Asia, the Indian subcontinent, or the Pacific islands. This area includes China, India, Japan, Korea, the Philippine Islands, and Samoa.

Black/African American (not Latino/Hispanic): A person having origins in any of the black racial groups of Africa.

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

Native American: A person having origins in any of the original peoples of North America who maintains cultural identification through tribal affiliation or community recognition.

White/Caucasian (not Latino/Hispanic): A person having origins in any of the peoples of Europe or the Middle East.

Multiracial: A person having origins from multiple ethnic backgrounds, including any combination of any of the above.

Other: A person not having any of the ethnic backgrounds mentioned above.

Q4: A partner can be someone of the same sex.

Q6a: This should be answered by patients who are U.S. citizens, due to the different economic scales in U.S. and Canada.

Q6b: This should be answered by patients who are Canadian citizens, due to the different economic scales in U.S. and Canada.

Q7a: This should be answered by patients who are U.S. citizens, due to the different health plans in U.S. and Canada.

HMO: Health Management Organization
POS: Point-of-Service
PPO: Preferred Provider Organization
Fee-for-service: Payment with reimbursement by insurance.
VA/CHAMPUS: Insurance for military personnel, or citizens who work for the military.
Self-pay: No insurance plan.

Q7b: This should be answered by patients who are Canadian citizens, due to the different health plans in U.S. and Canada. This question only asks for any ***additional*** insurance not already included in the patient's provincial medical plan (Canadian Health Care System).

Q8: Patient should indicate his ZIP/Postal Code. For US ZIP codes, five or nine digits is acceptable. All Canadian postal codes are six characters. No spaces or punctuation are necessary.

Q12: This includes any type of alcoholic beverage, such as beer, wine, wine coolers, or liquor.

Q14: Patient should indicate *anything* that he feels triggers his symptoms.

Q20a-f: If patient has *not* had a partner within the past 3 months, then N/A (not applicable) should be marked.

7.3.4 EXCLUSION CHECKLIST (EXCL)

Purpose: To assess the patient's eligibility for the study according to the study exclusion criteria.

Who: Research Coordinator Completed

When: Screening Contact - Visit #1

Instructions:

This form is to be completed after the consent and inclusion forms have been administered and before any other forms or procedures are undertaken. All questions should be verified by

reviewing patient's medical records.

Q2: Irritable bowel disease is not an exclusion criteria.

Q7: A urethral stricture is judged to be active if the patient has had a urethral dilatation in the last six months.

Q11: **Eligibility Question:** If the patient is found to be ineligible, then the RC should immediately stop the screening process. The patient may not be entered into the CPC Study.

7.3.5 FOUR GLASS TEST MICROSCOPY (FGTM)

Purpose: To collect microscopy information on the four samples taken during the Four Glass Test, including the Voided Bladder(VB)1, VB2, EPS sample, and the VB3.

Who: Research Coordinator Completed

When: Screening Contact - Visit #1; Contact Months: 6, 12, 18, 24, 30, and 36

Instructions:

The four glass test should be performed at the first screening visit. The patient should remain abstinent for 48 hours prior to the four glass test.

The semen sample must not be taken the same day as a four glass test. Additionally, the patient must be able to provide at least one of the following three samples: EPS, VB3, or semen. If he is unable to provide one of the three, he cannot be entered into the study, and is considered a screening failure.

The RC will complete this form upon availability of the CC's laboratory report. The form date should correspond to the date that the urine and EPS samples were obtained.

Q8-10: This information will be obtained from the dipstick, and is collected for the **VB2** sample only (See Chapter 8: *Laboratory Procedures*).

7.3.6 FOUR GLASS TEST SPECIMEN CULTURE (FGTSC)

Purpose: To collect specimen culture information on the four samples taken during the Four Glass Test, including the Voided Bladder (VB)1, VB2, EPS sample, and the VB3. These culture counts will be taken at 48 hours and 5 days after collecting the sample.

Who: Research Coordinator Completed

When: Screening Contact - Visit #1; Follow-up Contact Months: 12, 24, and 36

Instructions:

The four glass test should be performed at the first screening visit. The patient should remain abstinent for 48 hours prior to the four glass test.

The semen sample must not be taken the same day as a four glass test. Additionally, the patient must be able to provide at least one of the following three samples: EPS, VB3, or semen. If he is unable to provide one of the three, he cannot be entered into the study, and is considered a screening failure.

The RC will complete this form upon availability of the CC's laboratory report. The form date should correspond to the date that the urine and EPS samples were obtained.
Specimen cultures are counted 48 hours after the sample is cultured and again 5 days after the sample is cultured. The culture count is measured in CFU/ml.

Specimen Code Table: The first page of the FGTSC form is the table containing all the specimens to be identified from the lab report. If any of the indicated specimens are on the lab report, the code should be recorded in the appropriate place on pages 2 through 5.

Culture Count Tables: For each measurement, if "no growth" was indicated for the sample, for that time frame, the culture count table does not need to be completed. If growth was identified in the sample, the culture count table should be completed as follows:

> *Specimen Code:* The code for the specimen, as identified in the specimen code table, should be listed in this column. There should be a separate entry for each specimen identified on the lab report.
> *<100,000 or ∃100,000:* Check the appropriate box according to the count listed on the lab report.
> *If <100,000, please enter actual count:* If the count is less than 100,000 CFU/ml, then enter the exact count that is listed on the report.

7.3.7 INCLUSION CHECKLIST (INCL)

Purpose: To assess the patient's eligibility for the study according to the inclusion criteria.

Who: Research Coordinator Completed

When: Screening Contact - Visit #1

Instructions:

This is the first case report form that is to be completed.

Q1: The Informed Consent must be signed before the screening process can continue. If the patient is at least 18 years of age, then he is responsible for signing the consent. If the patient is younger than 18, then his parent or legal guardian must sign the consent.

7.3.8 INTERIM HEALTH CARE (IHC)

Purpose: To collect information regarding medical events and treatments a patient may have had since his last contact.

Who: Patient Interview Completed

When: Contact Months: 6, 12, 18, 24, 30, and 36

Instructions:

Q2: If the patient has been in the hospital, then the RC must complete the reason exactly as it is described by the patient.

Q6: These questions are the original exclusion criteria. If the patient reports any of these conditions during the course of the study, the information will be reported here. The patient will not be excluded from future participation in the study.

Q7: These questions are the original deferral criteria. If the patient reports any of these conditions during the course of the study, the information will be reported here. The patient will not be deferred from future participation in the study.

Q9: Refer to the Treatment Reference Table (Appendix E) if the patient has any questions regarding these medications or treatments.

7.3.9 MEDICAL HISTORY (MED)

Purpose: To collect information regarding the patient's prostatitis and general medical history.

Who: Patient Interview Completed

When: Screening Contact - Visit # 1

Instructions:

Q1a: If the patient does not recall the month, but does recall the year, then enter '06' for the month, and enter the correct year. The year must be four digits.

Q2a: If the patient does not recall the month, but does recall the year, then enter '06' for the month, and enter the correct year. The year must be four digits.

Q5-15: Because patients are not necessarily adept with medical terminology, it is helpful to read the list of specific ailments for the patient when asking about the general system. The patient may not recognize that he has a gastrointestinal disease, but he may remember that he has been diagnosed with diverticulitis.

7.3.10 PATIENT COMPLETION (COMP)

Purpose: To officially close out a patient file at the culmination of the CPC Study.

Who: Research Coordinator Completed

When: The patient's final contact, or at the end of the study

Instructions:

The RC should complete this form for every patient who has participated in the CPC Study, including patients who are currently continuing in the study, as well as withdrawn patients. This will be done for each patient at the end of the study, or at the patient's final contact.

The Last Contact Month is the last contact the patient completed, prior to completing the study.

7.3.11 PATIENT REINSTATEMENT (REIN)

Purpose: To officially reinstate a withdrawn patient for future participation in the CPC Study.

Who: Research Coordinator Completed

When: If needed

Instructions:

The RC should complete this form if a previously withdrawn patient expresses a desire to be reinstated in the study, or if the patient has returned after being considered lost to follow-up.

The Next Contact Month is the next contact for which the patient is eligible. The patient will resume the follow-up phase of the study at the point where he would have been if there had been no interruption in his status. Refer to the Follow-up Contact Schedule to determine the correct contact month.

7.3.12 PATIENT WITHDRAWAL (WITH)

Purpose: To officially withdraw a patient from future participation in the CPC Study.

Who: Research Coordinator Completed

When: If needed

Instructions:

The RC should complete this form if the patient expresses a desire to withdraw from participating in the study, or if the patient has been lost to follow-up for at least six months.

The Last Contact Month is the last contact the patient completed, prior to withdrawal from the study.

7.3.13 PHYSICAL EXAM (EXAM)

Purpose: To collect information obtained during the patient's physical examination.

Who: Principal Investigator Completed, or designee (physician) and reviewed by the RC

When: Screening Contact - Visit #1; Follow-up Contact Months: 6, 12, 18, 24, 30, and 36

Instructions:

Q1-2: It is preferable that height and weight be measured without shoes. However, measurement with shoes is acceptable.

7.3.14 PRIOR TREATMENTS (PRIOR)

Purpose: To collect information regarding prior procedures and current/prior treatments specifically for chronic prostatitis.

Who: Patient Interview Completed

When: Screening Contact - Visit #1

Instructions:

The RC should refer to the Treatment Reference Table (Appendix E) to classify the medications the patient is taking, or if the patient has any questions regarding the procedures, medications, or treatments.

For medications or treatments, if the patient is currently taking the treatment, check "Yes, presently". If the patient has taken the treatment *before*, but is *not currently* taking it, check "Yes, in the past".

7.3.15 SCREENING CONFIRMATION (SCR)

Purpose: To ensure that the Research Coordinator and the Principal Investigator have verified all screening phase criteria and that the patient is eligible for the CPC study; to notify the DCC that the screening phase has been completed.

Who: RC and PI Completed

When: Screening Contact - Final Visit

Instructions:

This should be the last form completed during the entire screening phase. The form should not be completed and signed until the patient has completed screening and is eligible.

Q1: The patient can only be registered and entered into the CPC database if the response to this is "Yes".

7.3.16 SEMEN SAMPLE (SEMEN)

Purpose: To collect specimen culture information on the semen sample taken.

Who: Research Coordinator Completed.

When: Screening Contact - Visit #2

Instructions:

This semen sample should be taken at the second screening visit. The patient should remain abstinent for 48 hours prior to providing the semen sample. If a patient is unable to provide a semen sample, or he refuses to for personal reasons, this will be captured on the form.

The semen sample must not be taken the same day as a four glass test. Additionally, the patient must be able to provide at least one of the following three samples: EPS, VB3, or semen. If he is unable to provide one of the three, he cannot be entered into the study, and is considered a screening failure.

The RC will complete this form upon availability of the CC's laboratory report. The form date should correspond to the date that the semen sample was obtained.

Specimen cultures are counted 48 hours after the sample is cultured and again 5 days after the sample is cultured. The culture count is measured in CFU/ml.

Specimen Code Table: The first page of the SEMEN form is the table containing all the specimens to be identified from the lab report. If any of the indicated specimens are on the lab report, the code should be recorded in the appropriate place on the second page.

Culture Count Tables: For each measurement, if "no growth" was identified for the sample, for that time frame, the culture count table does not need to be completed. If growth was identified in the sample, the culture count table should be completed as follows:

> *Specimen Code:* The code for the specimen, as identified in the specimen code table, should be listed in this column. There should be a separate entry for each specimen identified on the lab report.
> *<100,000 or ∃100,000:* Check the appropriate box according to the count listed on the lab report.
> *If <100,000, please enter actual count:* If the count is less than 100,000 CFU/ml, then enter the exact count that is listed on the report.

7.3.17 SERUM SAMPLE (SERUM)

Purpose: To determine if a blood sample was taken and stored for future research.

Who: Research Coordinator Completed

When: Screening Contact - Visit #1

Instructions:

The form date should be the date the serum sample was drawn from the patient.

7.3.18 SYMPTOM INDEX (SXIND)

Purpose: Collect information regarding the patient's assessment of his discomfort and/or pain, the impact of his symptoms, and his quality of life.

Who: Patient Completed.

When: Screening Contact - Visit #1; All Follow-up Contact Months

Instructions:

This form consists of three sections: the NIH Chronic Prostatitis Symptom Index, the Follow-up of Symptoms, and the Quality of Life Index (SF-12) (8). If the patient is in the clinic, he should complete this form himself.

If the contact is a telephone contact, then a copy of the SXIND, along with an addressed and stamped envelope, should be mailed to the patient, to be completed at home and mailed back to the CC. The RC should not complete the date at the top of the form prior to mailing the SXIND. This date must be filled in by the patient on the day he completes the SXIND form. It is helpful for the RC to remind the patient of this fact by highlighting or circling the date field as a reminder.

7.3.19 URETHRAL SWAB (SWAB)

Purpose: To collect specimen culture information on the sample taken during the urethral swab.

Who: Research Coordinator Completed

When: Screening Contact - Visit #2

Instructions:

The RC will complete this form upon availability of the CC's laboratory report. The form date should correspond to the date that the swab sample was obtained.
Specimen cultures are identified 5 days after the sample is cultured. There is no count taken, simply a list of the specimens present after 5 days.

Specimen Code Table: The top of the first page of the SWAB form is the table containing all the specimens to be identified from the lab report. If any of the indicated specimens are on the lab report, the code should be recorded in the appropriate place on the bottom of the page.

Culture Table: If there was no growth identified for the sample, the culture table does not need to be completed. If there was growth identified in the sample, the culture table should be completed as follows:

> *Specimen Code:* The code for the specimen, as identified in the specimen code table, should be listed in this column. There should be a separate entry for each specimen identified on the lab report.

7.3.20 UROFLOW STUDY (URO)

Purpose: To collect information obtained during the patient's uroflow analysis.

Who: Research Coordinator Completed

When: Screening Contact -Visit #2

Instructions:

The RC will complete this form upon availability of the CC's laboratory report. The form date should correspond to the date that the uroflow was performed.

Q4: A bladder ultrasound will be performed to determine the post-void residual volume.

7.3.21 VOIDING LOG (VOID)

Purpose: To collect information on a patient's voiding pattern over a 24-hour period.

Who: Patient Completed

When: Screening Contact - Visit # 2; Follow-up Contact Months: 12, 24, and 36

Instructions:

The patient should complete the voiding log within the window for the contact month. For contact months 12, 24, and 36, the voiding log should be mailed to the patient's home prior to the clinic appointment, and the patient should complete the log and bring it with him to the clinic.

7.4 INSTRUCTIONS FOR COMPLETION OF ADMINISTRATIVE FORMS

7.4.1 GENERAL INSTRUCTIONS FOR ADMINISTRATIVE FORMS

Specific instructions for completing the administrative forms are specified in Section 7.4.2. The following general guidelines should be maintained when completing any of the administrative forms.

All administrative forms should be completed in ***black*** ink.

Responses should be printed legibly. When making changes to answers or correcting mistakes or incorrectly recorded information, put a single line through the middle of the incorrect information. Record the correct information, and initial and date the correct answer. Circle the correct answer if further clarification is necessary.

7.4.2 SPECIFIC INSTRUCTIONS FOR ADMINISTRATIVE FORMS

This section contains specific directions for completing administrative forms correctly. The forms are listed in alphabetical order. If you are unable to find specific information that you

need to complete the form, please contact the CPC Data Manager.

7.4.2.1 Clinic-Initiated Correction Form

The Clinic-Initiated Correction Form is initiated at the CC and sent, via email, to the DCC to notify the DCC of any necessary corrections to data already submitted to the DCC. This form should be used for items which cannot be queried or have not been queried and is not intended to be used to record corrections already recorded on a query form.

Correction forms should be printed out and filed with the patient's file. In addition, the patient's file should be updated to reflect the change indicated on the correction form so that the clinical center records match those maintained at the DCC. Changes in the patient's file should be made by crossing out the error with a single line in black ink, entering the correct information, with the initials and date of change.

7.4.2.2 Contact Checklists

There is a checklist for each contact type identifying all the procedures and forms to be completed during the contact. This checklist should be reviewed before the patient leaves the clinic or gets off the phone, and must be stored along with the contact packet in the patient's file.

If a form has been completed and is enclosed in the packet, check "Yes". If a form has not been completed due to extenuating circumstances, check "No" and indicate the reason.

7.4.2.3 Contact Reminders

There is a separate Contact Reminder for each type of follow-up contact. The appropriate contact reminder should be mailed to the patient two weeks before his scheduled contact, and should be accompanied by any forms that must be completed by the patient and mailed to the CC or brought to the clinic at the time of the patient's contact.

7.4.2.4 Data Processing Cover Sheet

This form is designed to track any completed packets or forms through the data entry and verification process. This form must be attached to the packet before data entry, and must be completed at each stage of the entry/verification process at the CC.

7.4.2.5 How To Complete Your Voiding Log

This handout provides the patient with detailed instructions regarding the completion of the Voiding Log. It is best to distribute this handout with the Voiding Log.

7.4.2.6 Informed Consent

The Informed Consent is the tool whereby patients or parent/legal guardian of patients under the age of 18, consent to participate in the CPC Study. This form must be signed by the patient or parent/legal guardian of patient, prior to collecting any information or performing any procedure for the purpose of the CPC Study. This form is to be kept and filed by the CC and not sent to the DCC.

7.4.2.7 Lab Tracking Log

This form is a tool to enable the RC's to track the specimens they have stored at their clinic's lab. It does not need to be forwarded to the DCC.

7.4.2.8 Missing Contact

If all attempts to reach a patient to complete a contact have failed, the contact must be considered missed, and the Missing Contact form must be completed. The reason for the missed contact should be documented and stored in the patient's file. The form will be entered into the database (see also section 7.6.2.)

7.4.2.9 Patient Contact Information

This form is used to collect patient contact information, and is strictly confidential. It is for Clinical Center use ***only***, and it must be stored in a secure location. This form should ***never*** be forwarded to the DCC. The Patient Contact form should be completed at the first screening visit. If a patient's contact information changes during the course of the study, a new form should be printed, completed, and filed with the old one.

7.4.2.10 Patient Log

This form contains a list of all the patient ID's and identifies the name and initials of the patient assigned to each ID number. This log is for CC use ***only***, and should ***not*** be forwarded to the DCC. The Patient Log must be stored in a secure location.

7.4.2.11 Patient Refusal Log

This log is used to track why patients have refused to participate in the CPC Study, to help improve the study and the recruiting techniques at the Clinical Centers, and help the investigators assess the design of the study. The information in the Patient Refusal Log should be used when reporting to the DCC (Section 11.4.1.5).

7.4.2.12 Patient Transfer

This form is used to notify the DCC and the receiving CC if a patient wishes to transfer from one CC to another. This is an electronic form that should be sent via e-mail to both the DCC (the CPC Data Manager) and the receiving CC (the center to which the patient is transferring).

7.4.2.13 Query Forms

Query forms are initiated at the DCC and sent to the CC via email, requesting clarification of missing, unclear, illogical or problematic responses on a case report form. The queried item should be clarified with the patient, patient's file, and/or the patient's medical records, as appropriate.

The RC should respond to the query by sending the original email, with the requested information back to the CPC Data Manager. Queries should be resolved as quickly as possible.

Resolved queries should be printed out and filed with the patient's file. In addition, the patient's file should be updated to reflect the change indicated on the query form so that the clinical center records match those maintained at the DCC. Changes in the patient's file should be made by crossing out the error with a single line in black ink, entering the correct information, with the initials and date of change.

7.4.2.14 Status Tracking Log

This form may be used by the RC as a guide to determine the patient's current status in the CPC study. It does not need to be forwarded to the DCC.

7.4.2.15 Telephone Log

If the RC thinks a patient may be lost to follow-up, then it is important to maintain a telephone log, indicating the date and reason for the call to document the attempts to retain the person in the study. This log is for CC use ***only***, and should ***not*** be forwarded to the DCC.

7.4.2.16 Uroflow Study - Patient Information

This handout is an information sheet for the patients, detailing what is involved in the uroflow study. It can be distributed to the patient at Screening Contact - Visit #1, since the uroflow study will be completed at Screening Contact - Visit #2.

7.5 REVIEW OF COMPLETED FORMS

It is the RC's responsibility to review ***all*** case report forms and administrative forms for accuracy, completeness and legibility ***before*** they are filed. This should be done while the patient is still available in order to facilitate any clarification of questionable answers or provide missing information. If clarification is required, the RC will review the item in question with the patient.

7.5.1 CORRECTIONS OR CHANGES TO CASE REPORT FORMS

All responses should be in legible print. ***Any*** change to information should be made as follows:

- Cross out recorded information by placing a single line through the recorded information.
- Write in the correct information next to (above or below) the incorrect information.
- Provide initials and date of change next to the information that has been changed or corrected.
- For clarification purposes, if multiple changes have been made to an entry, circle the correct answer.

7.6 UPDATING THE DATABASE

Only completely screened and eligible patients will be registered into the database, and this section only refers to these patients. For these patients, all contact packets and single forms should be entered in the database and verified. Forms for a contact should not be entered or verified in the database until ***all*** forms in that packet are completed. Entry and verification ***must*** be done by two separate individuals. Specific instructions for updating the database can be found in Chapter 9.

7.6.1 REGISTERING THE PATIENT

Once the Screening Confirmation (SCR) form has been signed and dated by both the RC and the PI, the patient is ready to be registered into the database. Registration should be done by the RC, as soon as possible. The RC will only be able to enter a Patient ID that is valid for the CPC Protocol and his/her Clinical Center.

7.6.2 ENTRY

First data entry should be done by designated data entry personnel. It is recommended that the RC complete verification. The forms will appear in sequential order to be entered. Any form that was not completed, for whatever reason, should be noted by clicking the "Missing Form" button.

If the entire contact has been missed, and a Missing Contact (MISS) form was completed, then during entry, the "Missing Contact" button should be clicked. It is important to make the database aware of a missing contact, so the database and the DCC do not expect the contact to be completed. This will also end the entry application, since no further entry will need to be done.

7.6.3 VERIFICATION

It is recommended that the RC complete verification, since any discrepancies that arise would be best resolved by the RC.

Any field that is different during verification from first entry will be appear as an error, and should be resolved immediately. The person doing verification will be presented with the first entry response, the verification response, and the option of choosing the first entry response, the verification response, or enter another response.

7.7 SUBMISSION OF FORMS TO THE DCC

The DCC may request a copy of any forms or contact packets for patients at any time during the course of the study. Copies of forms could be requested for several reasons, including data auditing and forms completion review.

If a request is made, the CC is responsible for making photocopies of all forms requested. The original should remain in the patient's study file and the photocopies should be sent to the DCC.

All multi-page forms should be stapled and an entire packet should be paper-clipped.

It is preferred that copies should be sent to the DCC via Fed Ex. It is very important that requests are sent to the DCC as quickly as possible to ensure data quality.

All forms mailings and all correspondence to the DCC regarding forms should be addressed as follows:

University of Pennsylvania
Clinical Research Computing Unit
CPC Data Manager
423 Guardian Drive
503 Blockley Hall
Philadelphia, PA 19104-6021

8. LABORATORY PROCEDURES

8.1 SPECIMEN COLLECTION PROCEDURES

The following five procedures, with the exception of the Four-Glass Test, will be performed only during the screening phase of the study. The Four-Glass Test will be repeated for microscopy study only at the brief clinic visit, and for culture and microscopy at the extensive clinic visit. ***It is mandatory that the following procedures be performed using sterile technique.***

8.1.1 FOUR GLASS TEST PROCEDURE

The four glass urine test will be performed by the physician or designated health care professional.

Equipment:

Non-sterile gloves, sterile urine cup, microscope, Colombia agar with 5% sheep blood, 10 µl loop.

Procedure:

Important: The patient should be instructed to be abstinent (no ejaculation) for the two (2) days before the four-glass test procedure.

1. Uncircumcised men should retract their foreskin.
2. The head of the penis should be cleansed with an alcohol pad.
3. The patient should void approximately 10ml (VB1) directly into a sterile container.
    A) A portion of this specimen (5ml) should be transferred into a test tube, centrifuged and examined as described below (see microscopy methods).
    B) The remaining portion should be sent to the laboratory for culture (see culture methods).
4. The mid-stream sample (VB2) should be collected. This is done by having the patient place the sterile container into his urine stream while he is voiding and at least 5ml (Range 5-200ml) should be collected.
    A) A portion should be sent to the laboratory for culture (see culture methods).
    B) A portion of this specimen should be tested with a dipstick for pH, glucose, and protein. Record results on the case report form.
    C) A portion of the specimen should be centrifuged (5 mls) and examined as described below (see microscopy methods).
5. EPS (Expressed Prostatic Secretion) – during/after prostatic massage collect the EPS on a sterile surface (example: lid of a sterile urine cup).

A) The volume should be estimated in drops. About 5µL should be examined at 400X power and WBCs, and RBCs recorded per HPF. Note yeast as present or absent.

B) Using a 10µL sterile, disposable loop spread the EPS onto Columbia agar plus 5% sheep blood and incubate at 37°C for 5 days. Record results at 48 hours and 5 days. Isolate colonies and send to laboratory for identification.

Interpretation: 1 colony = 100 CFU/ml

10 colonies = 1000 CFU/ml

100 colonies = 10,000 CFU/ml

C) Any remaining volume of EPS should be restored in cryovials and snap frozen in liquid nitrogen for storage later at -70°C.

6. Collect the first 10ml of post massage urine (VB3) within 30 minutes (Range 5-30ml).

A) A portion of the specimen should be sent to the laboratory for culture (see culture methods).

B) A portion of the specimen should be centrifuged (5 mls) and examined as described below (see Microscopy Method I).

8.1.1a ALTERNATIVE MICROSCOPY AND CULTURE METHODS

Method I. VB1, VB2, and VB3 Microscopy

Procedure:

1. Centrifuge 5 mls. of urine for 5 minutes at maximum table top speed (1500 rpm).
2. Pour off supernatant, break up pellet using a disposable pipette and place a drop onto a clean microscope slide, and cover with a cover slip.
3. Examine using a microscope at 400X power.
4. Count WBC, RBC, and yeast (average of three fields rounded to nearest whole number). Record results on the case report form.

Method II. VB1, VB2, and VB3 Culture

A minimum of 1.0 ml of urine is generally required for hospital laboratories for microbiological culture. Each hospital laboratory should have a Standard Operating Procedure (SOP) and these should be kept on file in each Clinical Center (and at the DCC) for examination. For those Clinical Centers that do their own culture, the following is a standard microbiological procedure for urine culture.

Procedure:

1. Pipette 100 µl of urine into a sterile test tube containing 0.9 ml of sterile phosphate buffered (pH 7.2) saline (PBS) and another 100 µl directly onto a Colombia agar with 5% sheep blood.

2. Spread the plate using a sterile loop (or a sterile plate spreader).

3. Dip a sterile 10 µl loop into the diluted urine and plate onto Colombia agar with 5% sheep blood.

   Interpretation:

   - 100 µl plate: 1 colony = 10 CFU/ml
     10 colonies = 100 CFU/ml
     100 colonies = 1000 CFU/ml
   - 10 µl plate: 1 colony = 1000 CFU/ml
     10 colonies = 10,000 CFU/ml
     100 colonies = 100,000 CFU/ml
     >100 colonies = >100,000 CFU/ml

4. Isolated colonies are sent to a laboratory for identification using standard urine culture identification techniques.

8.2 SEMEN SAMPLE PROCEDURE

The physician or designated health care professional will instruct the patient**.**

Equipment:

Sterile specimen cup, sterile pipette, sterile cryovials**.**

Procedure:

1. The patient should be instructed to be abstinent (no ejaculation) for the two (2) days before the semen sample collection.
2. Patient should wipe the glans penis with an alcohol prep. The patient should be instructed to avoid touching the inside of the container with the penis.
3. The sample is produced by masturbation into a sterile specimen container.
4. After the sample is obtained the lid is replaced on the container.
5. The specimen is kept at ambient temperature for 30 minutes.
6. At the end of the 30 minute interval an aliquot of the whole semen is submitted for culture (see VB1, VB2, VB3 Culture above).
7. After the aliquot is submitted for culture the remaining semen is pipetted with a sterile, disposable pipette into a sterile 15 ml conical centrifuge tube.
8. The semen is centrifuged in a standard table top laboratory centrifuge for 10 min at 1500 RPM. This translates into 450-500g with a typical rotor diameter.
9. The supernatant (seminal plasma) is aspirated with a sterile pipette and placed in 0.5 ml aliquots into sterile cryovials labeled with the patient ID number, date and labeled “Seminal plasma.”

The 1.8 ml Nunc vials are ideal.

10. The samples are placed in a freezer and stored at B70°C. Record the number of vials.
11. Specimens collected at home must be transported on ice to the clinical center immediately.

Peroxidase Staining Procedure:

Prepare Benzidine-Cyanosine stock solution:

1. Dissolve 62 mg Benzidine (Sigma catalog# B3383) in 24 ml Methanol.

2. Add 75mg Cyanosine. (Phloxine B, Sigma catalog # P2759)

3. Add 26 ml boiling deionized or triple distilled H_2O. (Solution will precipitate if room temperature water is used).

4. Store in brown bottle (solution is light sensitive) at room temperature for less than 1 year.

Immediately prior to counting sample, make Benzidine-Cyanosine working solution:

1. Combine 1 ml Benzidine-Cyanosine stock solution and 4 uL 3% H_2O_2.

2. Mix semen and Benzidine-Cyanosine working solution in 1:1 ratio:
   20uL semen with 20uL working solution.

3. Place 20uL of combination on microscope slide and coverslip.

4. Scan slide under microscope at low power to assure even distribution of cells.

5. Count number of WBC per 5 high power fields (400X) after 5-10 minutes. WBC will be stained brown. Round cells which are not WBC (immature spermatids) will not be stained brown. The background will be pink. There may also be bubbles as a result of the H_2O_2.

8.1.3 SERUM SAMPLE PROCEDURE

To be performed by medical technologist or appropriate health care professional.

Equipment:

Tourniquet, Vacutainer apparatus, centrifuge, cryovials.

Procedure:

1. Place patient in a comfortable seated position providing a surface on which to rest patient's arm at approximately the level of the heart.

2. Place a tourniquet around the upper arm and ask patient to open and close fist several times to accentuate venous filling.
3. After identifying a suitable vein for venipuncture cleanse the skin surface several times with an alcohol prep swab.

4. Using the Vacutainer (Beckton-Dickinson) needle apparatus, insert the needle bevel edge up in to the vein at approximately a 45 degree angle. Use caution in inserting the needle so as to avoid going through the back wall of the vessel.

5. Once needle is in the lumen of the vein, engage Vacutainer collection tube into the needle apparatus and once blood starts to flow into the tube remove the tourniquet with your free hand. Use Becton Dickinson SST brand serum separation tubes – "tiger top" - red/gray silicone lubricated rubber stoppers, 9.5 ml draw containing inert barrier material and clot activator on interior walls (Becton Dickinson reorder number 6510).

6. After blood has filled the tube, completely remove the needle from the vein and apply a 2" X 2" gauze pad over the puncture site and ask the patient to apply pressure with the opposite hand. Discard the needle into an appropriately labeled biohazard sharps container. After homeostasis has been achieved, place a Band-Aid over the venipuncture site.

7. After collection gently invert tube 5 times and allow to clot for 30 minutes at room temperature.

8. Centrifuge at 1,000 - 1,300 X G for 10 minutes to separate serum (top layer) from clotted material.

9. Remove rubber stopper and pipette 0.5 ml aliquots of serum into 4-6 cryovials.

10. Label vials and store in ultra cold freezer (-70°C).

8.1.4 URETHRAL SWAB PROCEDURE

This test will be performed by the urologist or designated health care professional.

Equipment:

Alcohol prep, cotton tipped or calcium alginate swab, Colombia agar with 5% Sheep Blood plate.

Procedure:

1. Preparation of the penis:
   - have the patient lying supine and retract the foreskin, if present.
   - wipe glans with an alcohol swab.

2. Collection of specimen:
   - remove sterile swab from culture collection kit, taking care not to touch it to any surface.
   - holding penis at the base of the glans with the left hand, use right hand to insert cotton swab into urethra approximately 1-2 inches and slowly remove with a swirling motion.

- immediately plate swab onto Colombia media with 5% sheep blood.

3. Culture report:
   - report presence and type of bacteria at 5 days.

8.1.5 UROFLOW STUDY PROCEDURE

This test will be performed by the urologist or designated health care professional.

Equipment:
Urodynamic monitor, portable ultrasound machine.

Procedure:

1. On arrival, the patients should be asked to drink water or other fluids: the men should be instructed to drink enough fluids to give the patient a feeling of bladder fullness (up to a point that the men would normally void). The patient's bladder should not be uncomfortably full. At this point, it is important to perform the uroflow study without delay.

2. Any of the standard uroflow machines may be used. The results must include:
   1) total voided volume (in cc's),
   2) maximum void velocity (cc's / sec),
   3) average void velocity (cc's / s)
   4) flow strip.

   The uroflow machine's accuracy and internal variability should be provided by the company and documented for study purposes.

3. The uroflow procedure itself should be performed in the standard fashion. Either sitting or standing (whichever technique the man normally uses) the man should void to completion into the uroflow container. This should mimic the man's normal voiding pattern as closely as possible. If there is less than 150 cc's of voided urine or the patient states that the stream was not typical for his voiding pattern, the study should be repeated.

4. Post-uroflow, an abdominal ultrasound will be performed to measure post-void residual, which will be reported in cc's. Regular ultrasound machines with curvilinear or linear arrays or ultrasound units specifically designed to measure bladder volume may be used. Because of the variety of types of ultrasounds which will be available to the researchers, it is critical that each

center determine and document the accuracy and variability of their particular ultrasound's determination of post-void residual.

8.2 SPECIMEN LABELING AND STORAGE

Specimens will be stored at each clinical center as described in the specific procedures above. Every specimen should be labeled with the following information: CPC Study, date of procedure, patient initials, and patient ID. Specimens are not to be used for any purpose other than CPC Study research purposes. Access to study specimens will be controlled by a sub-group of the PP&AS Committee, entitled the Committee on Access to CPC Study Data and Patient Specimens.

9. DATA BASE APPLICATION USER GUIDE

9.1 CLINICAL CENTER CPC APPLICATION MENU

Purpose: To allow access to CPC clinical center database system applications. These applications allow entry of patient contact data into the database located at the DCC and viewing of registered patient status.

Users: Clinical center personnel:

1 Data Management/Data Entry Personnel
2 Research Coordinator

User Actions:

1 Start the application by selecting the "CPC CC Menu" icon from the Windows NT Workstation desktop or from the Windows NT Menu. The database login dialog box will appear.

1 Log on the database:
- .1 Enter User ID
- .2 Enter User Password
- .3 Enter database name
- .4 Press "Connect" button

1 The CC Menu appears with the following options:

.1 Register Patient
- .1 Starts the Patient Registration Application
- .2 Requires Patient ID and Patient Initials

.1 Entry Status
- .1 Starts the Entry Status Application
- .2 Requires Patient ID to view a specific patient contact form status.
- .3 Presents the registered patient status and contact forms status.

.1 Packet Entry
- .1 Start the Packet Entry Application
- .2 Requires a packet of forms for a specific patient and contact.
- .3 Requires the Patient ID, Patient Initials, Clinical Center Number, Contact Month, and the Contact Forms Packet.

.1 Single Form Entry
- .1 Start the Single Form Entry Application
- .2 Requires a single form for a specific patient and contact.
- .3 Requires the Patient ID, Patient Initials, Clinical Center Number, Contact Month, and the single form.

.1 Packet Verification

.1 Starts the Packet Verification Application.

.2 Requires a packet of forms for a specific patient and contact that has completed entry.

.3 Requires the Patient ID, Patient Initials, Clinical Center Number, Contact Month, and the Contact Forms Packet.

.1 Single Form Verification

.1 Starts the Single Form Verification Application.

.2 Requires a single form for a specific patient and contact that has completed entry.

.3 Requires the Patient ID, Patient Initials, Clinical Center Number, Contact Month, and the Contact Forms Packet.

.1 Reports: Opens the Reports Menu Application

.1 Cancel: Exits the CPC CC Menu

.1 The User chooses the desired application (Register Patient, Entry Status, Enter Forms, Verify Forms, Reports Menu) or chooses Cancel to exit the application.

Purpose: To allow registration of a new patient into the DCC database system. This is required prior to entering patient contact forms.

Users: Clinical center personnel:

1 Data Management/Data Entry Personnel

2 Research Coordinator

User Actions:

1 Enter the Patient ID:

.1 Patient ID must be exactly 5 numeric characters.

.2 The first digit must be a "1" to represent the CPC protocol.

.3 The last three digits will represent the sequence of patient enrollment using the center number for the first digit (1001..1999 for center one, 2001..2999 for center two, ... , 6001..6999 for center six).

.4 An error will occur if fewer than or more than 5 digits are entered or any non-numeric characters are entered.

.5 An error message given for duplicate Patient IDs.

1 Enter the Patient Initials:

.1 Patient Initials must be 2 to 3 uppercase letters.

.2 Error message is given if less than 2 or more than 3 letters are entered or any character that is not a letter is entered.

.3 Warning message given for duplicate initials.

1 Patient ID and Patient Initials are mandatory fields, neither may be left blank.

1 The entered Patient ID and Patient Initials must be confirmed by re-entering both fields:

.1 If either field differs from the first entry, an error message is given and the both fields must be re-entered for confirmation.

.2 Each field has the same constraints as indicated above.

1 After the new Patient ID and Patient Initials are entered and confirmed, repeat the process

9.2 CLINICAL CENTER PATIENT REGISTRATION APPLICATION

to register another patient into the DCC database system or return to the CPC CC Menu by selecting the Cancel button.

9.2 CLINICAL CENTER PATIENT REGISTRATION APPLICATION

Purpose:

1 Logs the patient contact and patient contact forms into the DCC database system.

2 Allows entry of the patient contact form data into the DCC database system.

Users: Clinical center personnel:

-- Data Management/Data Entry Personnel

User Actions:

1 Enter the patient ID

.1 Patient ID has the same requirements as in the Registration Application

.2 The patient ID will be checked against the registration table to verify that the patient does exist.

.3 If the Patient ID is not registered for the Clinical Center in the database, an error message will be generated and the user will not be allowed to proceed unless a Patient ID registered with the Clinical Center is entered.

1 Enter patient initials

.1 The patient initials will be cross checked with the patient initials for the corresponding patient ID in the registration table

.2 If initials do not match, then an error message will be generated and user will not be able to proceed until the correct initials are entered

1 Enter Clinical Center Number

.1 This number must be the number assigned to the Clinical Center for the study.

.2 If the CC number entered is not the same as that assigned to the

center, an error message is given.

1 Enter Contact Month

.1 The contact month must be 1 to 2 numeric characters.

.2 An error will occur if contact month is not a valid contact or if you try to enter any other character that is not a number.

.3 If the contact has already been entered, an error should appear.

.4 If any previous contacts have not yet been entered, an error is given, and will prevent entry of contact forms.

1 All four fields (Patient ID, Patient Initials, Clinical Center Number, and Contact Month) are mandatory.

1 After entering the mandatory fields, choose:

.1 Proceed to enter the packet

.2 Packet Missing to mark the packet as missing

.3 or Cancel to exit the Entry Application.

1 After choosing packet entry:

.1 The system will open the entry screens for each form in the appropriate order.

.2 If a form has been previously entered or marked as missing, a message will be issued indicating the form status. After acknowledging any form status messages, the next form is presented.

.3 The form entry screens will look like the case report forms.

.4 If the form is missing from the packet, mark the form as missing and proceed to the next form in the packet. Forms marked as missing cannot be entered.

.5 For all forms, the heading in the upper right hand corner will display the patient ID, patient initials, clinical center number, and the contact month automatically as a standard heading.

.6 Proceed by entering the visit date in the upper right hand corner.

This date is the date the form was completed, and it must be entered. The range for the date must be between the study start date, and the current date.

.7 Enter the Interviewer ID in the upper right hand corner.

.8 Enter all data on the forms into the appropriate fields.

.9 The data fields fall into the following categories: alphabetic letter, alphanumeric, categorical, date, numeric, time, and free text. Specifications for these fields are described in Appendix A.

.10 For case report forms with multiple pages, the option to either proceed and move forward to next page of the form or move backwards to the preceding page is available.

.11 Upon completing data entry for each case report form a Commit button will allow the entries for that form to be saved and move onto the next.

.12 The data cannot be changed after it has been saved.

.13 After the last form has been entered, the entry process can be repeated for the next patient.

1 You will have the option of exiting the entry process at any time. The data entered on any unsaved forms will be lost.

1 Special Form Requirements for VOID, FGTSC (four-glass test), SWAB, & SEMEN:

.1 The number of specimens or voids on the form must be entered.

.2 If there are a different number of records than initially indicated, an error message is given.

.3 Any number of records can be entered.

.4 Extra (or incorrect) records can be deleted prior to saving the form data.

Purpose:

1 Logs the patient single forms into the DCC database system.

2 Allows entry of the patient single form data into the DCC database system.

Users: Clinical center personnel:

-- Data Management/Data Entry Personnel

User Actions:

1 Enter the patient ID

.1 Patient ID has the same requirements as in the Registration Application

.2 The patient ID will be checked against the registration table to verify that the patient does exist.

.3 If the Patient ID is not registered for the Clinical Center in the database, an error message will be generated and the user will not be allowed to proceed unless a Patient ID registered with the Clinical Center is entered .

1 Enter patient initials

.1 The patient initials will be cross checked with the patient initials for the corresponding patient ID in the registration table

.2 If initials do not match, then an error message will be generated and user will not be able to proceed until the correct initials are entered

1 Enter Clinical Center Number

.1 This number must be the number assigned to the Clinical Center for the study.

.2 If the CC number entered is not the same as that assigned to the

center, an error message is given.

1 Enter Contact Month

.1 The contact month must be 1 to 2 numeric characters.

.2 An error will occur if contact month is not a valid contact or if you try to enter any other character that is not a number.

.3 If the contact has already been entered, an error should appear.

.4 If any previous contacts have not yet been entered, an error is given, and will prevent entry of contact forms.

1 All four fields (Patient ID, Patient Initials, Clinical Center Number, and Contact Month) are mandatory.

1 After entering the mandatory fields, choose the single form to enter.

1 After choosing the form:

.1 select Proceed to enter the form

.2 or select Cancel to exit the Single Form Entry Application.

1 Form Entry:

.1 The system will open the entry screens for the single form selected.

.2 If a form has been entered, a message will be issued indicating the form status.

.3 The form entry screen will look like the case report form.

.4 The single forms can not be marked as missing.

.5 For all forms, the heading in the upper right hand corner will display the patient ID, patient initials, clinical center number, and the contact month automatically as a standard heading.

.6 Proceed by entering the visit date in the upper right hand corner. This date is the date the form was completed, and it must be entered. The range for the date must be between the study start date, and the current date.

.7 Enter the Interviewer ID in the upper right hand corner.

.8 Enter all data on the forms into the appropriate fields.

.9 The data fields fall into the following categories: alphabetic letter, categorical, date, numeric, time, and free text. Specifications for these fields are described in Appendix A.

.10 Upon completing data entry for the form a Commit button will allow the entries for that form to be saved and return the user to single form entry screen.

.11 The data cannot be changed after it has been saved.

.12 This entry process can be repeated for the single form.

1 You will have the option of exiting the entry process at any time. The data entered on any unsaved forms will be lost.

Purpose: Allow second entry verification of all entered forms for a patient contact.

Users: Clinical center personnel: -- Research Coordinator

User Actions:

1 The user action items 1-8 in the Packet Entry Application apply.

1 The data entered for each form field are compared to the data from first entry.
- .1 If it is different a message is given (indicating first entry value, verification entry value, and other value), you must choose which entry is correct. If Other is chosen, you must enter the new value.
- .2 You are not allowed to proceed to the next field without choosing the correct value.

1 Special Form Requirements for VOID, FGTSC (four-glass test), SWAB, & SEMEN:
- .1 You are required to enter the number of specimen or void entries.
- .2 If this is different from the number of records entered in first entry, an error message is given.
- .3 If you enter a different amount of records than initially indicated, an error message is given prompting you to correct the problem.
- .4 Any number of records can be entered.
- .5 Extra (or incorrect) records can be deleted prior to saving the form data.
- .6 All verification entries are compared with first entry as described above.

9.6 CLINICAL CENTER SINGLE FORM VERIFICATION APPLICATION

Purpose: Allow second entry verification of single forms for a patient contact.

Users: Clinical center personnel: -- Research Coordinator

User Actions:

1 The user action items 1-8 in the Single Form Entry Application apply.

1 The data entered for each form field are compared to the data from first entry.
- .1 If it is different a message is given (indicating first entry value, verification entry value, and other value), you must choose which entry is correct. If Other is chosen, you must enter the new value.
- .2 You are not allowed to proceed to the next field without choosing the correct value.

9.7 CLINICAL CENTER ENTRY STATUS APPLICATION

Purpose: Allow viewing the registered patients and the entry status of patient contact forms.

Users: Clinical Center Personnel:

1 Data Management/Data Entry Personnel

2 Research Coordinator

User Actions:

1 Select status type (Patient or Forms) to view and enter Patient ID if Forms Status for a specific Patient is desired, then select Proceed to view the list or select Cancel to exit and return to the CPC CC Menu.

2 Registered Patient List is presented with registration dates and the user code of the registering application user.

3 Contact Forms List is presented with registration dates, entry dates, and the code of the application user.

9.7 CLINICAL CENTER ENTRY STATUS APPLICATION

Purpose: To allow the generation of monitoring reports.

Users: Clinical Center Personnel:

1 Data Management/Data Entry Personnel
2 Research Coordinator

User Actions:

1 The Report Menu appears with the following options:
- .1 Patient
- .2 Registered With No Contacts
- .3 Patient Registered With Outstanding Contacts
- .4 Patient Contact Not Completely Entered
- .5 Patient Contact Entered But Not Completely Verified
- .6 Patient Follow-up Contact Schedule
- .7 Clinical Center Patient Contact Schedule
- .8 Cancel

1 Choose the desired report or choose Cancel to exit the application and return to the CPC CC Menu.

Appendix A -- Data Field Specifications

Alphabetic Letter Fields: The patient initials is the only alphabetic letter field in the case report forms. Patient initials must be 2 to 3 uppercase letters. Errors will occur if you tr to enter fewer than 2 or more than 3 letters, or any characters that is not a letter.

Alpha-numeric Fields: The zip code on the EPI form is the only alpha-numeric field.

Categorical Fields: A categorical field is a set of numeric choices as indicated in the case report forms. The user must enter a number, and it must be contained within the range specified on the annotated case report forms. If user enters an out of range number, then the system should make user aware that an illegal number has been entered and needs correction before proceeding to next question.

Date Fields: There are two types of date fields: mm-dd-yy and mm-yy. For the mm-dd-yy fields, the user may enter 5 or 6 digits. The month may be represented by one digit, but the date and the year must be represented by two. For the mm-yy fields, the user may enter 3 or 4 digits. The month may be represented by one digit, but the year must be represented by two. A slash (/) or dash (-) are not needed to separate the month, day, or year, however, if a slash or dash are entered when date field recorded, the system should accept it. The range for each date field is indicated on the annotated forms.

Numeric Field: Numeric fields must contain numbers only, and an error should prevent the user from entering any value other than a number. The size of the field should correspond to the size indicated on the case report form. The ranges for each field are indicated on the annotated forms.

Time Field: The user may enter 3 or 4 digits for the time field. The hour may be represented by one or two digits, and the minutes must be represented by two digits. The user is not required to enter the semicolon (:) between the hour and

Appendix A -- Data Field Specifications

the minutes, but the system should accept it.

Free text fields: There are several places where a free text answer is requested. These fields are identified on the annotated forms, and none of them will be entered into the database.

10 STUDY SUPPORT PLAN

The DCC will provide technical and managerial support to all aspects of the CPC Study. Computing support specifically related to the computer system and CPC Study application and data base will be provided to the Clinical Center by the Data Coordinating Center help desk. In addition, as a back up to the network system, the DCC has established an external Internet Service Provider (ISP) for clinical centers in the event of a network failure. Requests for DCC support will generally fall into the following three areas:

Computer Systems
Questions and problems related to your computer system should be directed to the DCC CPCRN help desk. Tell the person that you are experiencing a problem with your CPCRN computer system.

Clinical Data Management
Questions related to the administration of case report forms, administrative forms, patient enrollment, and visit scheduling and administration should be directed to the DCC Clinical Data Manager.

Project Management
Questions related to the study protocol, organization, general policies regarding publication and ancillary studies, and internal and external communication should be directed to the DCC Project Manager.

10.1 CPCRN COMPUTER SYSTEM

Each Clinical Center has been provided with a computer. This computer is equipped with several software packages. A brief description of each package is provided here. If any problems are experienced while using these programs, please contact the CPCRN Helpdesk at the DCC.

Microsoft Windows NT Operating System
Before you can use any of the software on the computer, you must log in to Windows NT. Instructions on doing this are provided in appendix G. If you are in need of a user-id and password, please contact the CPCRN Helpdesk at the DCC.

Microsoft Office
Each computer is equipped with the Microsoft Office suite of software. This includes Microsoft Word for word processing and Microsoft Excel for creating spreadsheets, as well as many other useful applications. A complete description of using Microsoft Office is beyond the scope of this manual. There are many sources of information on the use of this package. On-line help is available from within any of the Office applications. Usually, help can be brought up by pressing the F1 key, or selecting an option from the Help menu.

Netscape Communicator
Netscape Communicator provides the ability to browse information on the World Wide Web and communicate using electronic mail. Instructions on the use of Netscape Communicator are provided in appendix G.

Adobe Acrobat for Viewing and Printing Study Forms and Documents
Study forms and documents are accessible on your computer, and can be viewed and printed using the Adobe Acrobat Reader.

To view a single document, double click on the folder icon on your desktop labeled ACPC Study

Documents@. This will bring up a window showing several folders. Double click on the folder holding the form or document you wish to view. This will show all documents held in this folder, and double clicking on any of these will cause the Adobe Acrobat Reader to show this document. Once the Adobe Acrobat Reader program has started, information on using this program can be accessed by choosing the Reader Online Guide from the Help menu.

Laplink

This software enables the help desk to have remote access to the clinical sites. It allows for remote desktop control and file transfer. Laplink is used primarily by the help desk at the DCC.

11 CLINICAL CENTER RESPONSIBILITIES

11.1 STAFFING REQUIREMENTS

Each Clinical Center is responsible for staffing one Research Coordinator to coordinate all activities at the clinical center level required to achieve the goals of the CPC Study. The Research Coordinators play an integral part in keeping the CPC Study on course, and therefore every effort should be made to retain these individuals throughout the course of the study. If a Research Coordinator leaves the study, however, the Clinical Center investigator is responsible for hiring a replacement immediately to ensure overlap among the relevant individuals. The departing Research Coordinator is responsible for training the replacement on issues concerning the CPC Study specific to the Clinical Center. The new coordinator should attend a 1 - 2 day training session at the University of Pennsylvania.

11.2 PATIENT RECRUITMENT REQUIREMENTS

The CPC Study is a multi-center, observational, longitudinal study. It is expected that each clinical center will enroll 35 new chronic prostatitis patients per year for 3 years of recruitment. This will result in an annual accumulation of 210 patients in the CPC Study per year. During the course of the 3-year accrual period, a minimum of 630 patients will be enrolled into the study. Depending upon date of last screening visit, patients will participate in the follow-up phase at varying lengths of time. The attrition rate will be monitored by the DCC as well as by each clinical center. Table 11.1 provides an estimate of clinical research center workload, based on enrollment figures and patient contacts.

11.3 PATIENT RETENTION

The success of the CPC Study depends heavily on the ability of the Clinical Centers to retain enrolled patients throughout their follow-up phase. The onus of keeping patients interested in the study therefore resides in the hands of the Clinical Center staff. Potential ways of accomplishing this are:

- emphasizing advantage of having a dedicated RC available to answer phone calls;
- emphasizing advantage of receiving education about chronic prostatitis during participation in study and of having first access to clinical trials;
- making a dedicated phone line and answering machine available to study patients;
- offering reduced fees to study patients.

11.4 REPORTING TO THE DCC

11.4.1 GENERAL INSTRUCTIONS

The CPC Study represents the first Protocol to be implemented by the CPCRN. Reporting to the DCC will generally be accomplished in two ways: (1) sending ***copies*** of completed sets of contact packets via Federal Express, when requested; (2) reporting via e-mail.

11.4.1.1 First Seven Patients Enrolled

During the course of the study, the first seven patients enrolled at each Clinical Center will be tracked closely by the DCC. As these patients complete each contact, and once the data has been entered and verified in the database, the RC=s are responsible for mailing a copy of all the completed CRF=s to the DCC. The DCC should receive the completed forms for all of the contacts for the first seven patients enrolled into the CPC Study at each Clinical Center. (This should include the two pilot patients at each CC and the first five main study patients.) Instructions for submitting forms to the DCC are provided in Section 7.7.

Note: regardless of the type of contact (screening, telephone, clinic visit), the Clinical Center should send a complete packet of forms for each patient. The complete package includes the appropriate CRF=s, the contact checklist, and the Data Processing Cover Sheet (DPCS).

11.4.1.2 Additional Sets of Forms, Upon Request

The DCC will review completed forms to determine the level of completion of the forms themselves, difficulty with specific forms across all centers or by center, adherence to procedures, and the like. Based on review of all completed forms sent to the DCC at the beginning of the study (pilot study and first five patients enrolled), the DCC will determine the frequency of additional form submission.

Note: copies of completed forms or lab results sent to the DCC should ***never*** contain patient names. Clinical Centers will have to be especially careful to remove patient names from lab results before sending copies to the DCC.

11.4.1.3 Data Audits

Throughout the course of the study, the DCC periodically will request form submission on a random selection of patients and/or forms. These internal data audits will be conducted in an effort to ensure data quality across all clinical centers.

11.4.1.4 Monthly Patient Count

The monthly patient count will provide accountability for all assigned Patient ID numbers. It will also give the DCC an opportunity to track the patient accrual process and to identify reasons why patients choose not to participate in the CPC Study. Since patients who refuse participation in the CPC Study are not assigned a Patient ID, these patients should be tracked on the Patient Refusal Log

(REF) form. An e-mail template will allow each Clinical Center to report all patient activity on a monthly basis. This will consist of a manual count of patients according to the following categories:

- eligible, fully-screened and registered patients in the database for the given month
- deferred patients
- excluded patients
- screening failures, other than exclusions
- patients in screening process who are expected to complete screening in the next month
- patients who refused to participate in the study, as well as a breakdown of why patients have refused.

The Patient Refusal Log (REF) form should be completed according to the instructions provided in Section 7.

12 DATA COORDINATING CENTER RESPONSIBILITIES

12.1 CLINICAL CENTER SITE VISITS

The CPC is a cooperative agreement study in which all investigators and the NIDDK have a shared responsibility for the overall quantity and quality of the data collection. The primary purpose of the CPC Clinical Center (CC) site visit is to ensure to the Chronic Prostatitis Collaborative Research Network (CPCRN) the accuracy and quality of data which have been submitted for the Chronic Prostatitis Cohort (CPC) Database, and adherence of data collection procedures to established protocol policies. While it is the responsibility of the Data Coordinating Center to monitor the quantity and quality of data being collected, the DCC will not conduct a formal audit. By the time the site visit occurs, the DCC will have conducted extensive queries of the database and many concerns already will have been addressed. The site visit will help the DCC identify concerns that had not been identified through database queries and will assist the Clinical Centers in improving their overall performance on the CPC Study. To accomplish this goal, the Steering Committee has developed a CPCRN Quality Assurance Committee.

It is suggested that the following issues should be assessed at each site visit:

- CC organizational and administrative structure
- Adequacy of support systems and environment
- Quality control systems established within the CC
- Data collection process
- Adherence to the protocol
- Data processing procedures

The site visit team will consist of representatives of the DCC and the Clinical Centers. The team is likely to include the Principal Investigator of the DCC, or his designee, the Project Manager, or her designee, members of the Clinical Data Management group at the DCC, and designated individuals from the Clinical Centers, based upon availability. The CC will have at least four weeks written advance notice. The major determinant of scheduling will be the availability of the CC=s Principal Investigator and Research Coordinator. The absence of other clinical personnel will not necessarily preclude a site visit. A letter describing the requirements and expectations of the site visit team will be sent to the CC's Principal Investigator, with a copy to the Research Coordinator, at least four weeks before the scheduled visit. A Clinical Center Site Visit Checklist, following a general, standardized outline, will be submitted to the NIDDK Project Officer, the Director of Quality Assurance and Compliance and Project Manager, the Principal Investigator and the Research Coordinator at the Clinical Center, with copies to the site visit team within two weeks of completing the site visit.

12.1.1 INITIATION AND NOTIFICATION OF SITE VISITS

Clinical Centers will be visited for quality assurance purposes at least once a year, pending NIDDK funding, or as determined by the NIDDK Project Officer. The Project Manager will work with the NIDDK Project Officer and the Director of Quality Assurance and Compliance to coordinate the visit dates and order. The DCC will be responsible for notifying the Principal Investigator and Research Coordinator at the selected CC, as well as members of the site visit team, of the scheduled site visit dates with at least four weeks written notice.

12.1.2 SITE VISIT ACTIVITIES

Each CC has received a copy of and is responsible for upholding quality assurance guidelines, as set forth in the **CPCRN Quality Assurance Clinical Center Site Visit Guidelines** document. Each site visit will last one or two days. The site visit team will come prepared to evaluate the CC=s day-to-day activities with respect to patient contact (including the CC=s patient environment), patient scheduling, data collection, and organization and completeness of the patient=s study file. Prior to evaluation of the patient study file, the site visit team will meet with the CC's Principal Investigator to provide an overview of the visit and discuss patient confidentiality and privacy issues. The site visit will then proceed to include review of some pre-selected and some randomly selected patient records, comparing key items with the source documents (i.e., patient=s medical records), patient scheduling procedures, and organization and environment of the CC. Patient confidentiality will be maintained at all stages of the review process. In the event that conflicts exist between the source documents and the study documents, the reviewer will make a notation to this effect on the study document and initial and date the notation. A second reviewer will be designated by the site visit team to independently review the source and study documents to verify that the conflict does exist and also initial and date the notation on the study document. **Confidential patient records will <u>not</u> be copied.** The site visit team may also meet with the CC=s Research Coordinator to discuss solutions/improvements of any data collection and/or patient record organizational problems.

The site visit team will meet with the CC=s Principal Investigator at the end of the site visit to provide verbal feedback. All major issues will be discussed at that time. **Note:** The Clinical Center Site Visit Checklist should not include issues, which have not been verbally discussed with the CC Principal Investigator prior to termination of visit. This allows the CC's Principal Investigator an opportunity to clarify any issues. This form should be signed by the Principal Investigator or his designee and either the CC=s Principal Investigator or the Research Coordinator. A copy of this checklist should be made for the CC and the original returned to the DCC for filing.

12.1.3 SITE VISIT REPORT

The Site Monitor or designee will be responsible for writing and submitting an official Clinical Center Site Visit Checklist to the NIDDK Project Officer, the Director of Quality Assurance and Compliance, and the CC=s Principal Investigator and Research Coordinator within two weeks of the completed site visit. These reports will be marked CONFIDENTIAL and released only to those listed in12.1.1.

The Clinical Center Site Visit Checklist should include the following sections:

- A general overview of the purpose of the site visit
- Assessments of protocol adherence
- Data collection process
- Clinic organization and environment
- Recommendations, including a time frame for their implementation

12.1.4 GRIEVANCE PROCESS

If the CC Principal Investigator does not agree with the recommendations outlined in the Clinical Center Site Visit Checklist, a formal letter of grievance should be sent to the NIDDK Project Officer, with copies to the Director of Quality Assurance and Compliance and the CC's Principal Investigator, within four weeks of the submission of the Clinical Center Site Visit Checklist. The grievance will be reviewed by the NIDDK Project Officer and the Director of Quality Assurance and Compliance. The NIDDK Project Officer should provide a formal response to the grievance within two weeks, with copies to the Director of Quality Assurance and Compliance and the DCC Principal Investigator.

12.1.5 FOLLOW-UP VISIT

A follow-up site field may be performed in an appropriate time frame that allows for implementation of the Clinical Center Site Visit Checklist recommendations. The scope of the visit will include the activities listed in 12.1.2 as well as verification of implementation of the recommendations resulting from the initial site visit. The follow-up site visit should be completed within three months of the submission of the initial report. Requests for an exemption from the three-month time limit should be made to the NIDDK Project Officer by the CC's Principal Investigator.

12.2 DATA COORDINATING CENTER SITE VISITS

(As determined by the NIDDK Project Officer and the Director of Quality Assurance and Compliance.)

12.2.1 EXTERNAL SITE VISIT OF DCC

The primary purpose of the CPC Data Coordinating Center (DCC) site visit is to ensure to the Steering Committee the accuracy and quality of data once they have been submitted to and processed by the DCC.

The following issues will be assessed at each site visit:

- Infrastructure and organization
- Project management
- Data management, including quality assurance (QA) monitoring
- Database management systems
- Statistical analysis plans
- Administration and budget issues

The NIDDK Project Officer will be responsible for assembling the site visit team. The DCC will have at least four weeks written advance notice. The major determinant of scheduling will be the availability of the DCC=s Principal Investigator, the Project Manager and Clinical Data Management. The absence of other DCC personnel will not necessarily preclude a site visit. A letter describing the requirements and expectations of the site visit team will be sent to the CC's Principal Investigator, with a copy to the Project Manager, at least four weeks before the scheduled visit. A Clinical Center Site Visit Checklist will be submitted to the Director of Quality Assurance and Compliance, and the DCC's Principal Investigator, with copies to the site visit team and the Project Manager, within two weeks of completing the site visit.

12.2.2 INITIATION AND NOTIFICATION OF SITE VISITS

The Data Coordinating Center will be visited for quality assurance purposes at least once a year, pending NIDDK funding, or as determined by the NIDDK Project Officer. The NIDDK Project Officer will work with the DCC=s Project Manager to coordinate the visit dates. The NIDDK Project Officer will be responsible for notifying the CC's Principal Investigator and the Project Manager, as well as members of the site visit team, of the scheduled site visit dates with at least four weeks written notice.

12.2.3 SITE VISIT ACTIVITIES

The focus of the site visit will be an evaluation of the issues previously described in Section 12.2.1.

The site visit team will meet with the CC's Principal Investigator at the end of the visit to provide verbal feedback. All major issues will be discussed at that time. Note: The Clinical Center Site Visit Checklist should not include issues, which have not been verbally discussed with the CC's Principal Investigator prior to termination of visit. This allows the CC's Principal Investigator an opportunity to clarify any issues. This form should be signed by the NIDDK Project Officer or his designee and either the DCC=s Principal Investigator or Project Manager. A copy of this form should be made for the DCC and the original sent to the NIDDK Project Officer for filing.

12.2.4 CLINICAL CENTER SITE VISIT CHECKLIST

The Site Monitor or designee will be responsible for writing and submitting an official Clinical Center Site Visit Checklist to the NIDDK Project Officer, the CC's Principal Investigator, the DCC's Director of Quality Assurance and Compliance and the and Project Manager within two weeks of the completed site visit. These reports will marked CONFIDENTIAL and released only to those listed in 12.2.2.

The Clinical Center Site Visit Checklist should include the following sections:

- A general overview of the purpose of the site visit
- Assessment of infrastructure, organization, and project management
- Evaluation of data management and Quality Assurance procedures
- Evaluation of computing systems and network support, and backup and security procedures
- Determination of adequacy of staff and budget
- Recommendations, including a time frame for their implementation

12.2.5 GRIEVANCE PROCESS

If the CC's Principal Investigator does not agree with the recommendations outlined in the Clinical Center Site Visit Checklist, a letter of grievance should be sent to the NIDDK Project Officer, with copies to the Director of Quality Assurance and Compliance, within four weeks of the submission of the Clinical Center Site Visit Checklist. The grievance will be reviewed by the NIDDK Project Officer and the Director of Quality Assurance and Compliance. The NIDDK Project Officer should provide a response to the grievance within two weeks, with copies to the Director of Quality Assurance and Compliance.

12.2.6 FOLLOW-UP VISIT

A follow-up site visit may be performed in an appropriate time frame that allows for implementation of the Clinical Center Site Visit Checklist recommendations. The scope of the visit will include the activities listed in 12.2.3 as well as verification of implementation of the recommendations resulting from the initial site visit. The follow-up site visit should be completed within three months of the submission of the initial report. Requests for an exemption from the three-month time limit should be made to the NIDDK Project Officer by the CC's Principal Investigator.

12.3 MAINTENANCE AND DISPOSITION OF STUDY DOCUMENTS, DATA, AND MATERIALS

This Section describes the procedures, which will be employed for maintenance and disposition of study documents, data forms, tapes, results of analysis and materials during and at the conclusion of the CPC Study.

12.3.1 INTERNAL DISTRIBUTION OF STUDY DOCUMENTS

The DCC is responsible for maintaining a record of all documents, reports and meeting minutes pertaining to the CPC Study. During the conduct of the CPC Study, the DCC will be responsible for the distribution of the Protocol, Manual of Procedures, and study reports to CPC participants. At the end of the study, these documents will be archived by the DCC and forwarded to the National Technical Information Service (NTIS).

Minutes of all appropriate committee meetings will be maintained in the files of the DCC. At the conclusion of the study, these minutes will be archived and forwarded to the NIDDK.

12.3.2 EXTERNAL DISTRIBUTION OF STUDY DOCUMENTS

The NIDDK will be responsible for the distribution of study documents and manuscripts requested by individuals not associated with the CPC Study. See Section 4.2.8: *Acknowledgment of Support and Reprint Addresses.*

12.3.3 CASE REPORT FORMS (DATA FORMS)

While it is not required that all case report forms be sent to the DCC during the course of the study, the DCC will ask the Clinical Centers, at various times in the study, to send complete sets of case report forms or lab reports on selected patients or on a randomized sample of patients. At the close of the study, these forms, without personal identifiers, will be archived and stored at the DCC. Clinical centers will maintain a file on each patient which will become a part of the individual=s medical record at the conclusion of the CPC Study.

12.3.4 DATA TAPES AND ANALYSIS OF RESULTS

The DCC will prepare a computer tape of the study data, results, and analyses at the conclusion of the study. This tape will be accompanied by appropriate documentation. One copy will be forwarded to NIDDK and one to the NTIS, U.S. Department of Commerce, Springfield, Virginia so that the information may be generally available, at a small charge, to the scientific community.
The DCC will prepare a data tape of analysis pertaining to each major study paper. At the end of the Data and Analysis Phase (Phase 3), all of these tapes with appropriate accompanying documentation will also be submitted to NIDDK and NTIS.

The DCC will provide documentation of all formulas and statistical analyses used in the study or referred to in the study documents. This information will also be made available to NIDDK and NTIS.

12.3.5 LABORATORY SPECIMENS AND MATERIALS

Specimens collected by the clinical centers will be kept for long-term storage until the end of the CPC Study. At that time, the Steering Committee will decide as to the disposition of these specimens. All specimens and materials not claimed or undesignated by the Steering Committee will be destroyed.