Pilot Clinical Trials in CKD Manual of Operations Revision of 10/31/2017		
Chapter #	**General Chapters**	**Revision Date**
3	Publications and Presentations Policies	07/02/2015
4	Ancillary Studies	03/11/2014
6	Event Review System	05/25/2016
7	Clinical Site Set-Up and Management	
	Investigator Study Team Face-to-Face Meeting Log	03/05/2015
	Appendix 1: Early steps in setting up a Pilot Clinical Trials in CKD Clinical Center	06/24/2014
8	Forms Completion, Data Entry and Data Discrepancy Resolution	04/19/2017
9	Data and Lab Quality Control	
	Appendix 1: CKD Study eGFR Equation	05/12/2016
	Appendix 2: BSA formula	05/12/2016
11	General Recruitment Issues and Strategies	03/30/2015
	Appendix 1: Study Participant Information	11/13/2014
Chapter #	**BASE Study Chapters**	**Revision Date**
30	BASE Study Overview and General Information	
	Appendix 1: Items to have on hand when BASE Study starts	05/12/2016
	Appendix 2: Reasons Candidates Approached for BASE but Di Not Consent	10/08/2015
31	Managing BASE Study Participants	02/16/2017
	Appendix 1: Listing of Common PPIs and H2 Blockers	12/30/2015
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32	BASE Study Participant Educational Materials	01/07/2016
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33	BASE Laboratories Overview	04/12/2016
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34	BASE Study Litholink Central Lab	11/10/2016
	Appendix 1: Material Safety Data Sheet – Preservative	05/30/2006
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	Appendix 3: Litholink Supply Order Form	09/21/2015
35	NIDDK Biorepository for BASE Study Samples	10/02/2015
	Appendix 2: NIDDK Biorepository Kit Re-Order Form	02/16/2016
36	BASE Study Anthropometry Ankle Measurement	01/30/2017
	BASE Study Anthropometry Ankle Measurement PowerPoint	03/15/2015
	Handouts - BASE	
	24-Hour Urine Collection Instructions (female) – BASE template	12/22/2014
	24-Hour Urine Collection Instructions (male) – BASE template	12/22/2104

Chapter #	**COMBINE Study Chapters**	**Revision Date**
50	COMBINE Study Overview and General Information	05/12/2016
	Appendix 1: Items to have on hand when the COMBINE study starts	01/16/2015
	Appendix 2: Reasons Candidates Approached for COMBINE but Did Not Consent	05/21/2015
	Appendix 3: Reasons Some Candidates Were Not Approached	12/22/2014
51	Managing COMBINE Study Participants	08/03/2016
	Appendix 1: Participant Re-enroll Flowchart	04/01/2015
52	COMBINE Participant Dietary Educational Materials	
	Dietary Phosphorus Quick Start	V1.0
	Fast Food Choices: Better vs. Poor Choices	V1.0
	Fast Food Restaurants: Phosphorus Found in Foods	V1.0
	Fast Food Restaurants: Better Choices	V1.0
	Food Smart: Understanding Food Labels	V1.0
	Overview for Physicians Letter	V1.0
	Overview for Participants Brochure	V1.0
	Your Plate: Fruits, Vegetables, Protein and Grain Portions	V1.0
	Pre-Enrollment Recruitment Telephone Script	V1.0
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53	COMBINE Laboratories Overview	
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54	COMBINE Study Spectra Central Laboratory	09/07/2016
	Appendix 1-Adding Acid to Urine Containers	10/20/2015
	Appendix 2-Spectra Critical Lab Values for Randomized Participants	10/31/2017
	Spectra Supply Reorder Form	06/13/2017
	Spectra 24-Hr Urine Collection Participant Instructions	V1.0
	Hydrochloric Acid Information Sheet	05/25/2016
55	UW FGF23 Core Laboratory Manual	06/22/2015
56	Cardiac and Renal MRI Core Laboratory	02/26/2015
	Appendix 1: CTI Safety Questionnaire	06/10/2014
	Appendix 2: MRI Appointment Reminder and Instructions	10/01/2014
57	NIDDK Biorepository for the COMBINE Study	03/03/2015
	Appendix 1: NIDDK Biorepository Supply Reorder Form	06/17/2015
58	Drug Distribution Center	
	Material Safety Data Sheet – Endur-amide	09/03/2014
	Material Safety Data Sheet – Lanthanum Carbonate	01/2007
	Ingredient Listing for Placebo for Endur-amide	08/22/2014

Chapter #	TarGut Microbiome Study Chapters	Revision Date
	Interviewer instructions for starting a new FFQ session	12/18/2014

CHAPTER 3: PUBLICATIONS AND PRESENTATIONS POLICY

3.1 Group Definitions

CKD Study Investigators

For the purposes of this policy, *CKD Study Investigators* are all individuals affiliated with the CKD Study to whom this policy will apply. The *CKD Study Investigators* are categorized into three groups:

1) CKD Study PIs
    a) CKD Study Principal Investigators at the Clinical Centers and Data Coordinating Center
    b) NIDDK Project Scientist
    c) Steering Committee Chair
2) CKD Study Investigators
    a) Typically, investigators who are at the Clinical Centers, Data Coordinating Center and Central Cores, other than *CKD Study Principal Investigators.*
    b) Research staff and study coordinators
3) Ancillary Study Investigators
    a) Individuals who propose, receive approval from the PAS Committee, and obtain funding for a CKD ancillary study.

Publications and Ancillary Studies (PAS) Committee

The CKD PAS Committee will be chaired by the Steering Committee Chair. Other members are the CKD Study voting Steering Committee members, or alternative designee from each site.

3.2 Publication Policy Principles

1) Publication of scientific research papers is a central and critical aspect of each CKD Study because:
    a) Scientific publications will be the principal mechanism by which each CKD Study will communicate its scientific findings.
    b) Scientific publications represent one of the most important mechanisms for CKD Study Investigators to achieve scientific and academic recognition for their participation in CKD Study.
2) Research questions and hypotheses to be addressed using CKD Study data should be formulated *a priori* and clearly stated in a manuscript.
3) Publication policies should promote scientific inquiry within and productivity from the CKD Study.
4) To avoid premature publication of results that might compromise the performance of the study (such as by publication of trends of 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).
5) Publication of scientific findings from each CKD Study should proceed in a timely fashion once relevant analyses are complete.
6) Abstracts, presentations, and publications based on CKD Study material must be accurate and objective and must not compromise the scientific integrity of Study.
7) The publications arising from each CKD Study should avoid overlap (except for review articles) and conflicting representation of Study findings.

8) Recognition through authorship will be distributed among the *CKD Study Investigators* so that:
    a) *CKD Study PIs* have equitable opportunity to lead and co-author CKD Study publications.
    b) *CKD Study Investigators* have opportunity to lead and be co-authors on publications resulting from analyses made possible through their collaboration, and participate in publications reporting scientific findings to which they have contributed.
    c) *Ancillary Study Investigators* have the opportunity to lead and be co-authors on publications resulting from analyses made possible through their collaboration.
9) The CKD Study promotes the career development of junior faculty by providing them opportunity to lead and to be recognized as co-authors of CKD Study publications, as appropriate.
10) Authorship on CKD Study publications will adhere to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals of the International Committee of Medical Journal Editors.

To adhere to these principles, it is the policy of the Study that preparation of all publications or presentations, other than materials prepared for local publicity purposes (see Section 23.3), must be assigned by the Chair of the Publications and Ancillary Studies (PAS) Committee to specifically appointed writing committees. Materials must be reviewed and approved by the PAS Committee and/or the Steering Committee before publication or presentation.

3.3 Scope of Policy, and Exception for Local Informational Materials

All material to be presented orally, as poster, or submitted for publication for dissemination by individuals associated with the Study and dealing with any aspect of the Study must receive prior review and approval by the PAS Committee with the following exception:

Material prepared for informational purposes within the recruitment region of a CKD Clinical Center, or presented orally or as handouts or posters to local professional audiences solely for the purposes of informing the profession of the Study and its objectives, need not be reviewed by the PAS Committee. Such material must be limited to a background discussion of chronic kidney disease treatment and a description of the 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 include discussion of any study data not previously presented or published. Informational material for national dissemination, including lay summaries, does need to be reviewed and approved by the PAS Committee.

3.4 Source of Suggestions for Publications of the Study

Suggestions for topics appropriate for preparation of abstracts or peer-reviewed papers are made by the PAS Committee. In addition, all investigators and staff in the Study are invited to suggest topics appropriate for preparation as abstracts and peer-reviewed papers from the Study. Such suggestions should be made to the DCC and the Chair of the PAS Committee, who shall review the request to be certain that there is no overlap with materials previously assigned, or planning to be assigned, to other writing committees. Where such overlap exists, the Chair of the PAS Committee may make recommendations that the suggestion be referred to an existing writing committee, that additional study investigators be added to existing writing committees, or make other suggestions to resolve the overlap. However, final decision in this matter will be made by the Chair of the PAS Committee.

It is the intent of this policy to encourage non-physician professionals to prepare scientific presentations to 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 well overlap with material being prepared by writing committees for medical journals, it is the policy of the 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 23.7.

It is also the intention of this policy to promote the conversion of as many abstracts as possible into full manuscripts and to discourage the production and presentation of abstracts that do not represent an intermediate step towards the preparation of a full scientific manuscript.

In addition, the PAS Committee will formulate and maintain a list of suggested topics that should be prepared for publication, to assure that all completed aspects of the work of the Study are reported to the scientific community in a timely fashion.

3.5 Assignment of Writing Committees

Topics suggested for presentation or for publication that do not overlap with an existing committee will be circulated to CKD Study PIs and CKD Study investigators. Writing committees should be formed with the intent of writing a paper for publication. This committee can also prepare abstracts for submission to professional meetings. Volunteers for the writing committee solicited are from all investigators. Persons are requested to suggest and justify names for lead authors (Chair of writing committees) and co-authors. This information will be collated and reviewed by the Chair of the PAS Committee and the DCC PI. The Chair of the PAS Committee will decide on the final composition of the writing committee.

If a topic is suggested by an investigator of the Study, and approved by the PAS, the writing committee will be formed as just described and the person making the suggestion will be considered as the potential lead author. The Principal Investigator of an ancillary study should be considered for lead author of material derived from that ancillary study. If only a subset of clinical centers participate in an ancillary study, only investigators from these centers should be considered to be on writing committees relating to this study.

Appointments of writing committee chairs will be made fairly to all professionals -- physicians, study coordinators, nurses, statisticians, and others -- in a manner that recognizes the unique contributions of each member of the Study to its performance. Any dispute about the selection of the lead author or co-author will be settled by the Chair of the PAS Committee. In all cases, writing committees requiring analysis of data by the Data Coordinating Center will have at least one 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 PAS Committee is authorized to make such changes with the consensus of the members of the writing committee, or on his own authority where there is clear cause.

3.6 Classes of Reports of the Study

There are four types of reports of each CKD Study:

A. Reports of the major outcomes of each CKD Study.

B. Reports addressing in detail one aspect of the 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 Study (e.g., substudies or ancillary studies), or originally conceived analyses of data from the entire Study (original analyses).

D. Reports of investigations initiated outside the Study, but using data or samples collected by the Study. The investigators may be CKD or other investigators, but the source of the ideas and the funding for the study will have been derived outside the Study itself. Writing committees for this type are formed and presentations and publications made in accordance with the general policy rules for CKD publications. However, the Principal Investigator of an ancillary study should be assigned the prerogative and should take primary responsibility in publishing the results of the study.

3.7 Authorship Policy

The authorship policy of the 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 CKD professional staff. Thus, reports of Types A and B must give recognition to all the investigators of the Study, and other Types must give primary recognition to those participating in the specific investigation. On the other hand, it is recognized that the preparation of a manuscript places special demands on the assigned writing committee, and especially on the Chair of the 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 Study. The CKD authorship policy attempts to recognize each of these goals. The authors of CKD Study publications will be listed as detailed below for each type of publication.

Type A publications:

Abstracts: [*specific study name*, e.g., The CKD Optimal Management with BIinders and NicotinamidE (COMBINE)] Study Group[1], presented by XXXX.

Papers: [*specific study name*, e.g., The CKD Optimal Management with BIinders and NicotinamidE (COMBINE)] Study Group[1], prepared by XXXX.

[1]The CKD participant box, detailed below, must be included in these papers. If a society's or journal's policy does not allow authorship by a group, the authors will be listed first as in Type B publications.

Type B publications:

Abstracts and papers: Authors' names, and [*specific study name*, e.g., The CKD Optimal Management with BIinders and NicotinamidE (COMBINE)] Study Group[1]

[1]The *specific study* participant box will be included in all papers if this can be arranged with the publisher. Otherwise it will be referenced to one of the Type A papers. It will not be practical to publish the entire list of participants in abstracts.

Type C and Type D publications:

Abstracts and papers: authors' names for [*specific study name*, e.g., The CKD Optimal Management with BIinders and NicotinamidE (COMBINE)] Study

[1]The participant box will be included in all Type C papers if this can be arranged with the publisher. Otherwise it will be referenced to one of the Type A papers. In Type D papers, the list of research personnel will be referenced in all cases. It will not be practical to publish the entire list of participants in abstracts.

3.8 Listing of Professional Participants in the Participant Box

The CKD Study participant box will list all professionals who have participated in the 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 or investigators listed alphabetically. Each participant will be listed only by his/her professional and academic degrees, not by the specific position that he/she held in the study. The centers will be listed in the following order:

Steering Committee Chair
Clinical Centers (in alphabetical order by center name)
DCC
Cores/Repositories
NIDDK

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

3.9 Acknowledgement of Support

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

The Study is supported by the Division of Kidney, Urologic and Hematologic Diseases of the National Institute of Diabetes and Digestive, and Kidney Diseases, NIH. Additional support is provided by the (list of any industrial or other support).

3.10 Schedule for Completion of Writing Assignments and Resolution of Overlaps among Writing Committees

At the time that a writing committee is constituted, the PAS 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 should provide the Chair of the PAS Committee a general outline of the proposed publication within a month of receiving its assignment, to permit the PAS Committee to identify any overlap with the assignments of other writing committees, and to permit establishment of an appropriate timetable. Where overlaps of materials to be covered by different writing committees are detected, the Chair of the PAS 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 PAS Committee. The Chair of the PAS Committee will report at each meeting of the Steering Committee on the progress of the various writing committees.

3.11 Review of Abstracts and Presentations by the PAS 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:

1) The writing committee shall contact the Chair of the PAS Committee and the DCC P.I. should be contacted. The Chair (or designee) will name a subcommittee of two members of the PAS Committee to review the submitted material and will inform the submitter and this subcommittee of their appointment. The submitted material should be sent by the submitter directly to these two reviewers so as to reach them no fewer than seven (7) days prior to the deadline for submission.

2) The members of the subcommittee shall review the material and notify the Chair (or designee) of their approval or disapproval. If there is unanimous approval, the PAS Committee Chair (or designee) shall inform (through the DCC) the submitter that he/she has approval for the submission.

3) All materials submitted for approval in this fashion will be distributed, together with notice of the disposition, to all members of the PAS Committee.

Approval for submission of an abstract or oral presentation does not automatically grant approval of the material ultimately to be presented. This material must also be submitted for review and approval in accordance with the above rules at least seven (7) days prior to the scheduled oral or poster presentation. Normally this review will be done by the same subcommittee of the PAS Committee that reviewed the initial abstract.

1) In the case of an oral presentation, an outline of the talk and a copy of any slides to be used must be submitted for review.

2) In case of a poster presentation, the content of the poster material must be submitted for review.

Also, if there is a meeting proceedings paper, the lead author must notify the PAS Chair at the time the abstract is proposed and receive approval for both abstract and the affiliated proceeding paper.

3.12 Review of Papers by the PAS Committee

All materials for which there is no explicit deadline, and all full papers that may result in a citable scientific reference (including book chapters and reviews), whether or not there is a deadline for submission, must be submitted to the DCC for distribution to and formal review by the entire PAS 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 Chair, PAS Committee, at least 14 days prior to the deadline, to permit such review. This review will be conducted as follows:

1) The Chair of the PAS Committee, shall appoint at least two primary reviewers, one of which must be a PAS Committee member, and one of whom may be any professional member of the Study Group with appropriate expertise. The Chair (through the DCC) shall distribute the material to all members of the PAS Committee. The two primary reviewers shall each prepare and send to the Chair a written critique of the submitted material for distribution to the entire PAS Committee. The PAS Committee will be given a deadline by which any comments or critiques must be received by the Chair of the PAS Committee.

2) The Chair of the PAS Committee may schedule a conference call of the PAS Committee, to review papers and other non-time critical materials as agenda items. The reviews of the panel members and any comments received from the center PIs will be distributed to the committee with the agenda. Alternatively, the Chair can decide if the review can be done by email input, rather than by conference call.

3) While discussion of the submitted paper(s) and other materials will be led by the two appointed reviewers, all members of the PAS Committee will be invited to participate and all shall vote on final disposition.

4) 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.

5) The Chair of the PAS Committee shall be responsible (through the DCC) for communicating the decision of the Committee to the authors, together with a summary of suggestions for revision, if any.

6) In the event that editors of a scientific journal to which an approved CKD scientific manuscript is submitted suggest or require major revisions of the manuscript, the revised manuscript must be reviewed again by the PAS Committee prior to resubmission in the same manner as described above. Generally, the Chair will appoint the same reviewers who first read the paper to review the revision, and every effort will be made to expedite such repeat reviews.

3.13 Criteria for Review of Materials by the PAS Committee

All materials submitted to the PAS Committee will be reviewed for acceptability on two grounds:

1) Materials shall be evaluated for scientific accuracy, quality, importance, and style. The intent is to assure that all approved CKD materials reflect well on the Study.

2) Materials shall be reviewed to assure appropriateness of the content. The material shall be reviewed to assure that it conforms to the assignment to the writing committee, addressing satisfactorily the assigned topics and not encroaching on material assigned to other writing groups. In addition, the material shall be reviewed to assure that it does not divulge prematurely the outcomes or findings of the Study or compromise the eventual publication of CKD findings in high quality peer-reviewed journals. In this later 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.

3.14 Maintenance of Records of Publications and Presentations

The DCC will maintain a record of all publications and presentations of the CKD Study, separated into the following categories:

1) Peer-reviewed accepted or published papers in professional journals
2) Abstracts published in citable journals
3) Presentations at regional, national or international meetings

This listing will be updated at least every six months and will be distributed to the all investigators in the Study, together with copies of any scientific papers or abstracts published since the last update. This is intended to inform investigators of all study findings and to facilitate the updating of curricula vitae.

3.15 Acknowledgement and Acceptance of CKD Study Policies on Publications and Presentations by the Study Investigators

To assure that all investigators (the three groups defined in Section 23.1) involved with the Study are aware of the policies of the Study, and to minimize the possibilities of misunderstandings after initiation of the Study, each investigator (except vascular function personnel, sonographers) will be given a copy of this Chapter and will be asked to sign a Statement of Understanding Form (see next pages) listing the major provisions of the Chapter and attesting to his/her acceptance of these policies. The original of the signed Statement of Understanding Form should be returned to the DCC. A copy of the Chapter and their signed Statement of Understanding Form should be kept by each CKD investigator.

CHRONIC KIDNEY DISEASE STUDIES

Statement of Understanding of Policy Concerning Publications and Presentations

To assure that all professionals involved with the CKD Study know and understand the policies of the CKD Study regarding publications and presentations, and to preclude the possibilities of misunderstandings after initiation of the Study, each professional member will be given a copy of the Manual of Operations Section 23 detailing these policies and will be asked to sign this form attesting to his/her acceptance of these policies, which are summarized below.

I. Material Covered by These Policies

All material to be presented at meetings or submitted for publication or dissemination by individuals associated with each CKD Study and dealing with any aspect of the Study must receive prior review and approval by the Publications and Ancillary Studies (PAS) Committee with the following exception:

Material prepared for publicity purposes within the recruitment region of a CKD Clinical Center, or presented orally or as handouts or posters to professional audiences solely for the purposes of informing the profession of each CKD Study and its objectives, need not be reviewed by the PAS Committee. Material for national dissemination does need to be reviewed and approved by the PAS Committee. Such material must be limited to a background discussion of the issue involved and a description of the specific CKD 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 include discussion of any previously not presented or published CKD Study outcomes or results, and must not itself result in publication of an abstract or other citable professional reference.

II. Assignment of Writing Committees for Publications

The PAS Committee will solicit volunteers for each writing committee for abstracts and publications and make a recommendation on the writing committee and topic to the CKD Steering Committee Chair. The CKD PAS Chair will decide on the final composition and topic of the committee. All interested individuals will be given a chance to request appointment to the various writing committees, but the final appointments will be determined by the Chair of the PAS Committee.

III. Authorship

The CKD policies specify the authorship for each of the four different classes of publication or abstract (See Section 3.6 of the Manual of Operations). These policies are binding and must be followed in all publications derived from the CKD Study.

IV. Review of Abstracts

All abstracts must be reviewed and approved by the PAS Committee before being submitted (See Section 3.11 of the Manual of Operations). These abstracts must be delivered to the reviewers at least seven (7) days before the submission deadline to permit time for this review. Abstracts not approved in this fashion will be withdrawn by the CKD Study.

V. Review of Materials for Presentations

Approval for submission of an abstract does not automatically grant approval of the material ultimately to be presented. This material must also be submitted for review and approval by members of the PAS Committee at least seven (7) days prior to the scheduled oral or poster presentation.

VI. Review of Papers

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 PAS Committee for formal review by the entire Committee (see Section 3.12 in the Manual of Operations). 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 Chair of the PAS Committee at least 30 days prior to the deadline, to permit such review.

VII. Certification by CKD Study Participant

This is to certify that I have read the above statement of policies of the CKD Study with regard to publications and presentations, understand it, and agree to abide by it in matters of all publications and presentations derived from the CKD Study.

_____ _____

(Signature) (Date)

_____

(Print or Type Name and Institution)

CHAPTER 4: ANCILLARY STUDIES

4.1 Purpose

To enhance the value of the CKD Study, the Steering Committee welcomes proposals from individual investigators to carry out ancillary studies in collaboration with the CKD Study investigators.

4.2 Definition of Ancillary Study

An ancillary study is one based on information, images or biospecimens from the CKD Study participants in an investigation that is relevant to, yet not described in the CKD Study protocol, and derives support from non-CKD Study funds. It is anticipated that a typical ancillary study will propose the collection of additional data not collected or analyzed as part of the CKD Study parent data set.

4. 3 Ancillary Study Principles

1) Participation in, and approval of, an ancillary study is subject to review by the CKD Study Publications and Ancillary Studies (PAS) Committee. See Section 23.1 for composition of the PAS Committee. Also, the CKD Study Data, Safety and Monitoring Board is notified of all ancillary studies.

2) Approval by the PAS Committee will be defined as a majority of votes in favor of the proposal. In the case of an ancillary study which includes subject participation at all clinical centers, two-thirds approval of the PAS Committee membership will be required. Furthermore, the centers participating must each approve.

3) An ancillary study must receive PAS Committee approval before a grant to support it is submitted to a funding agency or to local institutional authorities (e.g., IRB), and before the study is permitted to begin.

4) All CKD ancillary study proposals initiated by a non-CKD investigator as PI must include as a Co-investigator at least one CKD Study PI or Co-investigator.

5) Ancillary studies require external (non-CKD Study) funding. Any ancillary study must have sufficient funding to cover the costs incurred by the CKD Study Clinical Centers and Cores (e.g., to process or ship samples), and the Data Coordinating Center (DCC) (for tasks such as sample selection, data management, preparing and documenting analysis files, participating in statistical analysis, and integrating the new ancillary data into the combined CKD Study database). Also, studies using Repository biospecimens must have adequate support for handling and using the specimens. Special consideration will be given to requests for ancillary studies to be funded through training grants or career development awards through the NIH or other peer-reviewed funding sources.

6) Considerations for approval of ancillary studies
   The proposed study:

a) must meet requirements of the highest scientific merit.
b) must not, or minimally, interfere with the completion of the main objectives of each CKD Study.
c) must not, or minimally, adversely affect participant cooperation or compliance with each CKD Study.
d) must not create a serious diversion of CKD Consortium Study resources.
e) must put minimal demand on scarce CKD Study Consortium resources, such as blood samples.
f) must require the unique characteristics of the CKD Study patient data to accomplish its goals.
g) must have adequate resources to effectively complete the project.
h) must agree to provide the ancillary data to the CKD Study Consortium (also see 10 and 11).
i) must not jeopardize the public image of the CKD Study Consortium.
j) consider using the entire cohort for testing, rather than individual centers or isolated subgroups when appropriate.

7) Once an ancillary study is approved, if a change occurs in the structure or concept of the study (for example as a result of the NIH review process), including any change in data elements to be collected or analyzed, or any change to study aims, such changes must be disclosed to the PAS Committee and the CKD Study Steering Committee, for review and approval before the proposal is (re-)submitted to a funding agency.

8) A written progress report on ancillary studies must be made periodically (e.g., at time of Steering Committee meetings) to the Steering Committee.

9) All data collected under the auspices of an ancillary study is expected to adhere to the same high standards of quality applied to data collected in the CKD Study Consortium. A plan for quality control must be submitted to the DCC for funded studies. In addition, once the ancillary study is initiated, periodic quality control reports must be sent to the DCC.

10) Data from ancillary studies will be made available to the DCC either on a real time basis using direct data entry into the DCC's computer server or through periodic (e.g., quarterly) transfers of ancillary data to the DCC.

11) An archival copy of the collected data and/or laboratory results not already held at the DCC will be sent to the CKD Study Data Coordinating Center at the conclusion of the data analysis and publication of the main ancillary study results. This transfer is the responsibility of the ancillary study CKD Study collaborator(s). Once transferred back to the CKD Study Consortium, these ancillary data will become part of the aggregate CKD Study data.

12) Images, tracings and biosamples may usually be kept by the ancillary study investigators. During the CKD Study operation, further use of the samples beyond the objectives that have been approved by the PAS is prohibited without additional

consent from the PAS Committee. The restrictions on specimens imposed by the Veterans Affairs for specimens collected at the VA sites must be observed. Also, the NIDDK has the option to require that the images, tracings (or copies of) and remaining biosamples be transferred to the NIDDK Repository at the end of the CKD Studies.

13) Unless specifically arranged, all analyses will take place at the DCC and be conducted under the supervision of its biostatistician-investigators in collaboration with the ancillary study investigators. Under specifically approved circumstances, datasets will be released to external investigators for local analysis.

14) Proposals for abstracts and manuscripts resulting from all ancillary studies shall be submitted to the PAS for review and approval before establishment of a writing committee or a submission for publication or presentation. It is anticipated that principal investigators of approved ancillary studies will lead at least one scientific paper emerging from the ancillary study analyses.

15) Information about proposed ancillary studies, and progress and results from approved ancillary studies are considered to be confidential and are not to be shared with others outside of the CKD Study Consortium except as provided for by the CKD Study Publications and Ancillary Studies Policy. Ancillary study investigators can share information among their co-investigators and with CKD Study investigators.

4.4 Funding of Ancillary Studies

Ancillary studies will not be funded by the CKD Study, but will require an independent source of funding.

4.5 Approval Procedures

1) Proposals may be generated by a participating clinical center or by other interested investigators providing at least one CKD Study PI or Co-investigator is included as a co-investigator. These applications are submitted to the Data Coordinating Center for review by the CKD PAS Committee.

2) There will be a two-step review by the PAS Committee. The first step is to have the proposal reviewed for its concept and general acceptability. This will be done in 2-4 weeks after submission. A short description of the study including the following information should be submitted.
   a) Hypotheses to be tested.
      Specific outcome variables that will be assessed.
      Need for data and specimens from the DCC or Repositories.
   b) Significance of the proposed ancillary study.
   c) How will performance of this ancillary study affect each CKD Study?
      Specifically:
      i. Will there be any data/specimen/image collection beyond that specified in each CKD Study protocol? If so, what additional information/samples will be obtained? What, if any, impact will this additional information/sample

have on the main study, including study coordinator burden?
   ii. How much additional participant burden and time will be required to complete this ancillary study?
   iii. Will additional funds be requested for the study and what will their source be?

3) If this proposal is acceptable in concept to the PAS Committee, a more detailed proposal should be written and submitted for review. This proposal should include detailed information on:
   a) Hypotheses to be tested.
   b) Background and significance of the study.
   c) Conduct and performance of the study including specifying the study population and the data to be collected.
   d) CKD Study staff and DCC burden. Costs for this work need to be included in the project's support.
   e) Sample size justification.
   f) Quality control of the data.
   g) Data analysis methods.

4) The PAS Committee will review the proposal within 2-4 weeks. The decision can be for approval, modifications with further review, or disapproval.

4.6 Publication of Ancillary Study Results

The policies regarding publications and presentations of the result of ancillary studies are the same as those governing the publications and presentations of results of the main study (see Chapter 23). These policies are designed to:

1) Assure timely publication of the results to the appropriate professional audiences.
2) Avoid premature publications of results that might compromise the performance of the main study or that might compromise the ability to publish the results in high quality peer reviewed journals.
3) Maintain high standards of the published material.
4) To guard against duplicate publication of results, unless in review articles after the results have been published in a peer-reviewed article.
5) Assure equitable attribution of credit to all of the professionals participating in the ancillary study and the CKD Studies.

CHAPTER 6. EVENT REVIEW SYSTEM

6.1 Event Review Committee Review

The Event Review Committee (ERC) reviews serious adverse events. The Event Review Committee adjudicates whether an SAE was possibly, probably, or definitely caused by CKD procedures or by CKD random treatment group assignment. The ERC also recommends or confirms study treatment end points by which a participant continues to be followed in CKD but physicians discontinue treatments aimed toward reaching the participant's randomized treatment group assignment.

6.2 COMBINE Review of SAEs

The COMBINE Study ERC will review the first 10 SAEs occurring at each site in the COMBINE Study. After that, the ERC will review all deaths, all SAEs that the site investigators categorized as possibly related, probably related, or related and a 10% QC subset of the SAEs that the site investigator categorized as unrelated.

The following SAEs will be reported in detail to the DCC, Data Safety Monitoring Board (DSMB) and the ERC:

1. Death
2. Life-threatening event
3. Hospitalization
4. Prolongation of hospitalization
5. Congenital anomaly
6. Persistent or significant disability/incapacity
7. Important medical event requiring medical or surgical intervention to prevent serious outcome
8. Spontaneous abortion

Participants will stop treatment with nicotinamide and/or lanthanum carbonate, but data collection will continue as usual, if the site investigator and the ERC agree that an SAE was possibly, probably, or definitely related to treatment and that it is unsafe for the patient to continue on the specified treatment (nicotinamide and/or lanthanum carbonate).

The ERC will review SAEs and any events that the clinical centers categorize as requiring treatment discontinuation for safety reasons.

6.3 BASE Review of SAEs

The BASE Study ERC will review the data for any participant who is told to stop blinded medications for safety reasons. The ERC will confirm whether or not the participant met the protocol definition to stop blinded medications for safety reasons.

Emergency unblinding is not expected to be necessary as knowledge of the treatment group would not affect clinical care. The *potential* side effects of sodium bicarbonate, such as edema, hypertension, and hypokalemia are common in CKD and those taking diuretics and can be managed without unblinding the treatment assignment of the participant. In the rare circumstance that the investigator feels that unblinding would be helpful or influence participant

management, the investigator will formally request unblinding. Unblinding will be reviewed and confirmed by the ERC.

The following SAEs will be reported in detail to the DCC, Data Safety Monitoring Board (DSMB) and the ERC:

1. Death
2. Life-threatening event
3. Hospitalization
4. Persistent or significant disability/incapacity
5. Emergency room visit for:
   a) Edema, heart failure, or pulmonary edema
   b) Hypertension
   c) Low serum potassium level
   d) High serum potassium level
   e) High serum bicarbonate level
   f) Low serum bicarbonate level.

6.4 Event Review Committee Membership and Calls

Event Review Committee membership consists of John Middleton, M.D., from Duke University, Thomas Hostetter, M.D., from University Hospitals and Linda Fried, M.D., from the VA Pittsburgh Healthcare System. Event Review Committee conference calls will also include representatives from the DCC.

6.5 Processing documents for review

Site SAE/Death data packets are generally 5 to 10 pages long. Given that all data from the CKD database is also included in the reports sent to the Event Review Committee (ERC), it is anticipated that most SAEs would include 20 or fewer pages of additional information from the site. If a clinical center is considering sending documentation more than 30 pages in length, the site PI should carefully consider whether the physicians on the ERC need to see each page in order to understand the SAE. We are trying to keep the maximum pages for each case to 20 pages, but certainly can send more if relevant information supporting the case exceeds 20 pages.

<u>Primary material that should be included, if available</u>

- For hospitalizations: Discharge summary
- For ER visits: an ER summary note
- For deaths: an expiration summary, autopsy report, or death certificate

If these are not available, the CKD physician who is most familiar with the SAE should write a narrative explaining what is known about the SAE.

<u>Supporting material that should be included, if available</u>

- Results of laboratory tests that clarify what happened, support a primary or secondary diagnosis, or support causation. For example, if the primary diagnosis was MI and cardiac enzyme tests are available, these should be included.
- Results of procedures that clarify what happened, support a primary or secondary diagnosis, or support causation. For example, if relevant EKG tracings or biopsy reports are available, these should be included.

Be sure to list any other supporting material on Form 540 in the "Other information sent" field. If other information is sent, describe other material provided in the text box on the form. Please do not send the participant discharge instructions, as this document does not yield adequate information for the reviewing physicians.

Material that need not be included

- Do not include CKD data forms. The DCC will create a report with demographic information, labs, medications, and the contents of Form 532 (for deaths) or Forms 512 and 522 (for other SAEs and hospitalizations) that have already been entered into the CKD database.
- Discuss other documentation with the site PI or the CKD physician who is most familiar with the SAE.

6.6 How is the documentation de-identified?

DCC staff will coordinate the receipt and distribution of documents. All supporting patient documentation to be sent to the ERC should be de-identified by the clinical center staff before it is sent to the DCC. This can be done by copying the original documents and placing white out or white correction tape over patient identifiers and then using a black Sharpie marker to black areas that were covered with the white out or correction tape. This "double cover" will ensure that patient identifiers cannot be seen.

Reports that are generated are for internal CKD use and are only seen by the DCC and the ERC. Therefore, any patient information (discharge summaries, autopsies, lab tests, etc.) that is sent to the DCC will need to be de-identified. Sites should remove all types of direct identifiers that we do not store in the CKD Database. These include:

1. Names, initials (name of the participant, doctor, PI, and name of hospital)
2. Addresses
3. Phone numbers
4. Social Security numbers
5. Local medical record numbers or other local codes that directly link to an individual patient's identification
6. Health insurance numbers or other account numbers
7. Device identifiers or serial numbers
8. Date of birth

6.7 How is the documentation sent?

Before sending material to DCC, the local clinical center personnel should write the participant study ID number and alphacode on each page of the packet being sent.

Complete Form 540 Event Information Sent to the DCC on paper prior to emailing hospitalization, ER visit or death information packets to DCC. Documentation should be scanned and sent via email to: brittak@ccf.org and sherers@ccf.org. *Please do not send to ckd_dcc@bio.ri.ccf.org*. Enter the Form 540 once the packet has been emailed successfully.

6.8 Adjudication Process

The DCC will coordinate Event Review Committee conference calls to discuss the cases. Before forwarding the information to committee members, the DCC will check that the clinical center staff appropriately de-identified the material. If necessary, they will complete the de-identification process.

The Event Review Committee will receive and review the supporting documentation surrounding the event and material from the completed SAE form and elsewhere in the CKD database to make their assessment.

A "Primary Reviewer" will be assigned to each SAE. All reviewers are sent all documentation and should review every case that will be discussed on the call. The appropriate Event Review Committee forms (Forms 612, 622 and/or 632) will be completed based on the discussions for each event reviewed.

6.9 Email Alerts

If the Event Review Committee feels that a SAE is "possibly", "probably", or "definitely" related to the blood pressure regimen, device, procedure or intervention that was specifically done as part of the CKD Trial Protocol, then the clinical center will receive an email alert.

All email alerts should be discussed at the next clinical staff meeting. If the center PI would like to discuss the case, the center PI should contact members of the Event Review Committee.

Revision of 03/05/2015

MOP Chapter 7, Appendix 2
Pilot Clinical Trials in CKD SITE PERSONNEL
INVESTIGATOR STUDY TEAM
Face to Face Meeting Log

Site PI: _____ Study: BASE, COMBINE or BOTH

Study Site: _____ (Circle whichever applies)

Use this log to document routine or specially scheduled meetings of study team members.

Date/time	Attendees	1) Major topics discussed and 2) ID numbers of participants discussed*

*The "Ready for Baseline Placebo" report should be reviewed for each participant who has not yet started Baseline Placebo. The Ready to Randomize report should be reviewed for each participant from this site who is not yet randomized. Each randomized participant should be discussed at least once each month. For example, if a site has 32 participants in follow up, discuss 8 participants at each of four weekly meetings.

June 24, 2014

Manual of Operations Chapter 6
Setting up the Clinical Sites
Appendix 1. Early steps in setting up a Pilot Clinical Trials in CKD Clinical Center

The following local Clinical Center questions can be investigated at any time before participant enrollment begins:

- Where is the -80 freezer that the COMBINE Staff will use for FGF23 samples?
- Where will meds be shipped and to whose attention? Where will meds be stored? Who will keep track of what is received (likely by kit)? (What is dispensed will be recorded by bottle number in the study database.)
- Will a physician need to write a prescription for the study meds?
- Where will the pills be counted (out of the patient's site)?
- Is there a shelf for the patient 3-ring binders?
- Where is there a Windows desktop or laptop for data entry, or does one need to be ordered?
- How will we order the screening lab tests in such a way that they will be billed to the study and not to a participant?
- The Core Lab Spectra will supply blood draw kits and 24-hour urine jugs. Where will these be stored?
- Where will the local screening blood be drawn? Who will draw them? Is this the same person who will draw the follow up bloods?
- Where will the follow up bloods to be sent to the repository be spun? Will the same person who draws the blood be the one who spins it in a centrifuge?
- Where is the dry ice kept at this hospital? What do I need to do to get dry ice?
- Will one of our study coordinators need to be certified to do hazardous shipments or is someone else at our hospital designated to do this?
- Who do we contact to schedule the MRIs?
- How will we order the MRIs in such a way that they will be billed to the study and not to a participant?
- Who will prescribe the IV furosemide for the BOLD Renal MRIs? How will we cover lunch after morning fasting MRI, before afternoon blood draw?
- Order the cryovials you will use to ship samples from your site to the University of Washington Core Lab. You'll be shipping 2 serum and 1 plasma at B1 and F12. You'll be shipping 1 plasma at B2, F1, F2, F3, F6, F9.

CHAPTER 8: FORMS COMPLETION, DATA ENTRY AND COMPUTING

8.1 Forms Completion

The Study Coordinator will review all data forms for completeness and accuracy and to ensure timely submission to the Data Coordinating Center. Data forms will be filed in an area convenient for study personnel's access. To ensure that the study has quality data, team members must know the purpose of the study, the protocol design, and the sections of the Manual of Operations that are pertinent to their role in the study. If protocol expectations and study goals are clear and common to all team members, then protocol adherence by staff will help ensure quality data collection and a pleasant working environment.

All study forms should be completed legibly using a blue or black pen. If an error occurs when completing an entry on a form, put an "x" through the incorrect entry and write the correct entry next to it. In the margin, next to the fixed entry, write your initials and the date the change was made. Never, try to place the correct entry over the incorrect entry. Do not transcribe a form from the original completed version onto another form. However, in the rare case that a form gets something like coffee spilled on it and you are worried that you will no longer be able to read some of the values, complete another form, let the coffee spill dry out and staple the coffee stained form to the transcribed form.

Each form has a "**Clinical Center Use Only**" box which is located at the end of every form. This box should only be completed once the form is successfully data entered into the database. If you receive an error message and are unable to commit the form, do not complete any of the information in this box. Once the form is successfully saved, write the username of the person entering the data and the date the form was entered into this box. This information will also be displayed on the database screen.

All data entered into the study database should always match the paper form. Data should be entered within 3 business days from the date the visit was held.

8.1.1 Screening Forms and dropout

If the Screening Form shows that the participant is not eligible for the study, a dropout form is not needed.

8.1.2 De-Identifying the Participant Consent and Forwarding to the DCC

In order for a participant to be randomized, the DCC will need to receive a de-identified copy of the signature page only of the consent form for the participant to be randomized. We do not need the entire consent; only the signature page. Please make sure that all participant information cannot be seen by DCC staff. This can be best done by using a black marker. The DCC should be able to see the date the participant signed the consent though.

Write the Participant ID and Alphacode in the middle of the page. This way, if it is faxed to the DCC, we will be able to see it and this information will not be cut off.

It is best if this document is scanned and emailed to ckd_dcc. However, if you do need to fax it, please send an email to ckd_dcc stating that you are doing this.

8.2 CKD Study Computing

The CKD Study Data Coordinating Center's recommended specifications for your PC are as follows:

Internet Explorer 6.0 or higher, Adobe Acrobat Reader, and the Sun JRE download for the Oracle 11g application. These can be downloaded from the DCC's website as specified in Appendix A.

8.3 Accessing the DCC Website to Enter Data

See Appendix A for instructions on how to set up your PC to access the DCC's website.

After you have successfully entered the website, you will see a menu titled 'CKD Study'. At this point, resize the window to the largest that will fit on the screen for optimal viewing. You can then choose a form or report from the menu, or you can go to the 'Inquiry' menu to answer or view your data inquiries.

8.4 Usernames and Passwords

You will have an Oracle database username and password. The usernames are assigned by the DCC's Database Administrators and are usually set up in the following format: first six letters of your last name followed by the first letter of your first name. There are up to seven letters in a username. Please do not share passwords. Passwords are not case sensitive.

Passwords will need to be changed every 75 days. You will be notified via email when your oracle password needs to be changed. If you do not change your password in the allotted time, you will need to send an email message to CKD_DCC@bio.ri.ccf.org asking to have your password reset. A new temporary password will be sent to you in a secure e-mail and you will need to retrieve it from the secure site. This temporary password is only valid for one day..

8.4.1 Selecting a Good Password

Here are some good references for picking a good password:

- http://www.net.berkeley.edu/dcns/faq/good_pw.html
- http://www.msc.tamu.edu/services/cops/security/goodpasswd.html and
- http://www.cs.umd.edu/faq/Passwords.shtml

Please read them all as they all have good advice.

8.4.2 Changing Your Password

There is a menu option available to change your password.

1. Go into the CKD Study website https://qhsapps.ccf.org/ckdp/ and click on 'Logon to the CKD System'

2. Enter your username and current password then hit 'enter' or click on 'connect'.
3. At the top of the screen, click on 'Change your password' and follow the prompts. Be sure to select 'RDP10' as the database. Passwords for the CKD Study will require 8 or more alphanumeric characters (alphanumeric characters include letters and numbers only). An alpha character must always appear in the first position of the password.

8.5 Instructions: How to Enter Study Data into the Database

Press enter, tab or click your mouse to move from field to field within a form. Note that you will see bubble help when you move your mouse over the toolbar buttons. The upper left button should be the 'Save' button. When you are finished entering data for a form, click on the save button, or choose 'Save' from the 'Action' menu, or press the Ctrl+K to identify which key is the 'Save' or 'Commit' function key. The Ctrl+S key corresponds to the Oracle function 'Save' or 'Commit'.

Maximize window to see messages at the bottom of the screen. You will see a message indicating how many new records were added to the database. You can get out of a form by pressing the 'Exit' button or choosing 'Exit' from the 'Action' menu. 'F4' is the speed key to exit.

If you want to enter another form you should navigate to the top of the form, and press the 'Insert Record' button. 'Insert' can be selected from the 'Record' menu. Unfortunately, you are not permitted to remove records once you have saved/committed them. You will need to send the DCC a data change request via the Inquiry system to do that. You are also not permitted to change certain key fields or fields that determine eligibility. Again, you will need to send a query to the DCC.

When entering data, if you receive an error message stating the value is out-of-range, then back out of the form without saving the information and review the data with other staff members and possibly the PI. If the value on the paper form is correct, notify the DCC with the information and we can investigate further. It may be that the range needs to be adjusted for that particular field. **Never** enter a value as a placeholder thinking that you will come back and fix the data at a later date.

If a form requires that all fields have a response but your paper version of the form has fields that are blank, **never** enter a value as a placeholder thinking that you will come back and fix the data at a later date. Instead, back out of the form without saving it. Discuss the form with other study personnel and the PI to obtain values for those fields that were missing.

8.5.1 Obtaining the ID and Alphacode for a Participant

When data entering the Screening Form for each study, question 1 "Identification Number" will have a list of values key (^), click on the "^". Select the first identification number that is listed. Once you have selected that number, that number will not be displayed the next time a Screening Form is entered. The Alphacode will be populated once you have successfully committed and saved the Screening Form. Make sure to write the Identification Number and the Alphacode on the Screening Form. This ID and alphacode will follow the participant throughout the study.

8.5.2 Keymappings

Ctrl+K means hold down the <Ctrl> key and then simultaneously press the 'K' key. Now release 'K' and then <Ctrl>. Another way to get to the key mappings is to choose 'Keys' from the 'Help' menu.

8.5.3 List of Values (LOV)

Note that you may see messages on the bottom of your screen. If you see 'List of Values', that means you can choose 'Display List' from the 'Edit' menu, or press Ctrl+L to retrieve a list of values to your screen which you can scroll through and make a selection. You can also click on the 'v' button next to the field to select the response you need.

8.5.4 Editing

If the box for the field is smaller than the text you are typing into it, you can choose 'Edit' from the 'Edit' menu, or press Ctrl+E when your cursor is in that field. This will open up a pop-up box containing a larger view of that field.

8.5.5 Navigation

Other useful Oracle functions that you can use are 'Next Record' and 'Previous Record'. You can find buttons and speed keys for these and they are also on the 'Record' menu. Use these to navigate between forms or detail records (for example, in the medication form).

8.5.6 Error Messages

If you skip over a required field, you will see the error message:

> Field must be entered.

If you enter a value that is not possible for that field, you will see the error message:

> Invalid value for field name.

If you enter a non-numeric character in a numeric field, you will see the error message:

> Legal characters are 0-9 - + E or Item must be formatted as, for example, 90.0 (or some specific format)

If you try to update previously entered data without using the [Change Value] button, you will see:

Field is protected against update.

If you try to enter a Form that has already been entered, you will see the error message:

Error while inserting: ORA-00001: unique constraint (P200723.BID_CC_PK) violated.

You will also see other various error messages as well. If you can't figure out why you are getting that particular error message, please write down the complete message, and also choose Help->Display Error while the message is on the screen to see if a further explanation pops up before contacting the DCC. If you get stuck, it may help to use Cancel Query or Query->Cancel (if you see 'Enter-Query' on the bottom of your screen), Action->Clear All or Record->Clear

8.6 Instructions: How to Change Study Data in the Database

8.6.1 Retrieving Data

Once the data has been entered, you can retrieve it to your screen for viewing:

- Access the form # you want to view.
- Press the F11 [Enter Query] key, query icon or use the pull down menu option under 'Query'.

Note the hint line will say 'Enter-Query'.

- Enter the Patient ID, Visit Type and Visit Number (visit number may not be applicable).
- Press the Ctrl+F11 [Execute Query] key, execute query icon or use click on the pull down menu option under 'Query' to execute query.

8.6.2 Data Change Within 7 Days

- Retrieve the form you want to view.
- Put the cursor on the field that needs to be updated.
- Press the [Change Value] button.
- Change the value by entering the appropriate value.
- Press 'enter' or [Save] button.
- A pop-up box will appear with a Data Change Number.
- Write the Data Change Number on your form next to the question that was changed.

- Press the [OK] button to return to the form.
- No further action is required.
- The database should always match the paper copy of the form you entered.

8.6.3 Clinical Center Change to Data After 7 Days (send 'Data Change Request' to DCC)

- Retrieve the verified data and the form you want to view.
- Position the cursor on the field to be changed.
- Press the [Change Value] button.
- A new screen will appear that will allow you to enter a 'New Value' and an explanation.
- Enter the new value in the 'New Value' field and text describing the desired change in the 'CC Text' field. Please give as much detailed information as possible as to why the value should be updated. (The DCC will use this response to investigate the request.)
- Press the [Save and Exit] button.
- You will receive an inquiry number or 'data change request' number after you save the request. Write this number on your form. You can use this number to check to see if the DCC signed off on your inquiry.
- The DCC will take the appropriate action, and then use the DCC Sign-Off screen to indicate the final status of the request.
- A 'DCC Sign-Off to CC Initiated Data Inquiry' will be sent to the DCC and CC.
- No further action is required.
- The database should always match the paper copy of the form you entered.

8.6.4 Data Change for Forms 9 and 10

- Data on Forms 9 and 10 can be changed at any time.
- Retrieve the data and the form you wish to view.
- Put the cursor on the field that needs to be updated.
- Change the value by entering the appropriate value
- Press the [Save] button.
- No further action is required.

8.7 Instructions: How to Initiate and Respond to Data Change Requests/Queries

8.7.1 Clinical Center Initiation of Queries

Queries, or Data Change Requests, can be initiated by the Clinical Center as described in the above section on changing data.

8.7.2 Clinical Center Response to a DCC Initiated Inquiry

- You will receive a DCC initiated inquiry report through e-mail, or you can go to the 'Inquiries' menu and choose 'Center Response to DCC Inquiry' to find unanswered queries.

- To respond to an inquiry, you **must** use the database Inquiry System. The DCC is unable to accept e-mail responses.

- When the screen appears you can press [Execute Query] to retrieve all unanswered queries, or press [Enter Query] and enter the specific query # and then press [Execute Query].

- If you do not enter an inquiry number, all unanswered queries will be retrieved. You need to press [Next Record] or use the 'up' or 'down' arrow' key to navigate to the other queries. Keep pressing [Previous Record] to get back to a previous query.

- Position your cursor on the 'DCC text' field'.

- Choose Edit->Edit if you want to read the entire explanation from the DCC as to why you are being queried.

- Navigate to 'New Value'.

- Type a new value for the field being inquired. If a different field requires changing, leave it blank or enter N/A for not applicable.

- Navigate to 'CC text', and enter an explanation for your value. This field must be answered in order for the DCC to take action. Please make sure that your explanation is specific and complete.

- The explanation can be up to 2000 characters. Click on the [Save and Exit] button on the bottom of the screen to save the text. Click on [Exit and Don't Save] if you do NOT want to save the text.

- The DCC will then make the appropriate updates to the database.

- It is very important that the CC respond within 3 business days.

8.8 Retrieving Data from Forms

8.8.1 Introduction

Data can be retrieved in several ways from the form application. In order to 'query' data available in the database for the information on a given form application, the [Enter Query] and [Execute Query] keys can be used. The screen will be populated with the first set of patient data for the form application being accessed. By pressing the [next record] or [previous record] keys, you will have the ability to view the next or previous set of data.

There are different ways to retrieve data. You can execute simple queries that meet specific criteria, as well as complex queries that satisfy several conditions. The following topics are discussed.

- Matching exact values
- Entering variable conditions
- Matching values that meet a specified pattern

8.8.2 Matching Exact Values

Suppose you want to check on all instances of visits of the 'B' or 'F' type for a given patient ID (110001 for example). The data entry screens can retrieve the record(s) that contains specifically these values. The following are general steps for retrieving records that match exact values:

1. Access the appropriate form via the menu system.
2. Press [Enter Query]
3. Type the values you want to match into the appropriate fields.
4. For this example, cursor to the Patient ID field and type 110001.
5. Press [Execute Query]
6. Press [Next Record] or [Previous Record] to view the retrieved data.

NOTE: If there is not any data that meets the specified criteria, the following message will be displayed on the status line of your screen:

'FRM-40301: Query caused no records to be retrieved. Re-enter.'

8.8.3 Entering Variable Conditions

Sometimes it is not practical to enter the exact values that you want retrieved data to match. For example, you might want to retrieve the following:

- A specific form with visit type = 'F'

To select data that have a visit type = 'F', press [Enter Query] and enter the patient ID number, visit type of 'F' and press [Execute Query]. This will bring up all of the forms with a visit type of 'F' for that participant.

8.8.4 Populating WHOdrug and MedDRA Data Fields

A. The WHO Drug database is used for recording medications on Form 214-Concomitant Medications, Part A and Form 215-Concomitant Medications, Part B. You will need to select the name of the medication from a [List of Values] to populate these forms; you cannot type freehand the name of the medication as there is a chance of misspelling.

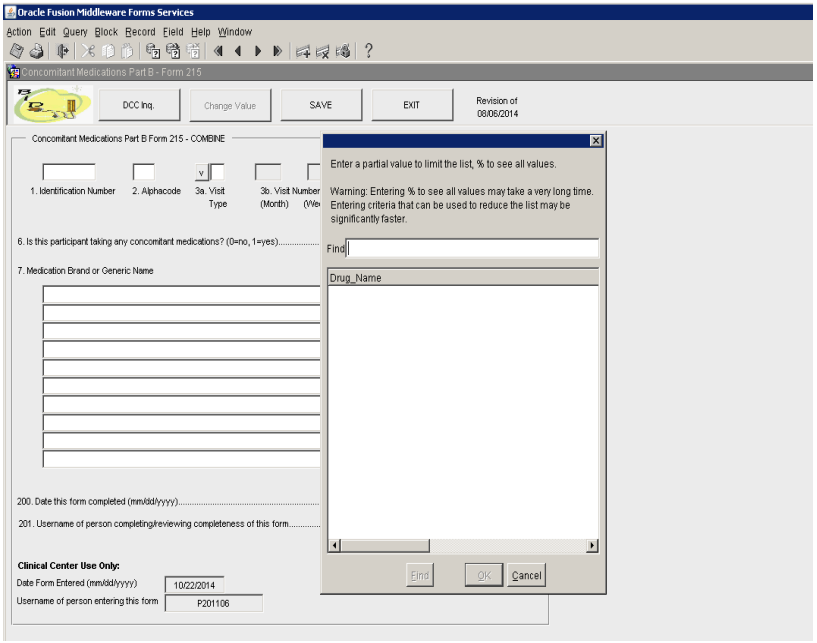
For example, a patient is taking a non-antihypertensive medication, Rolaids, on Form 215:

1. Access the Form 215 data entry screen and enter the patient information in Q1 - 6.

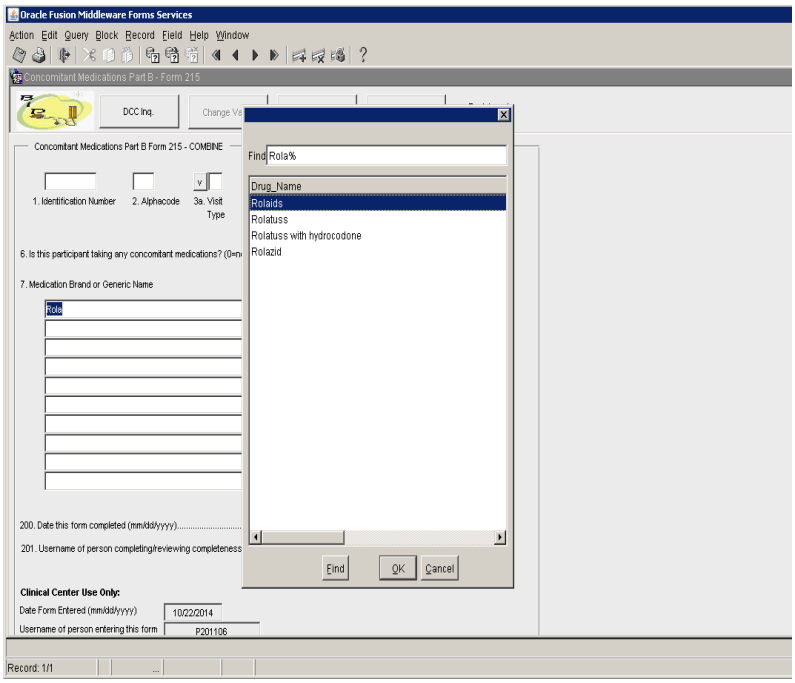
2. Database will automatically pop you into a blank medication field.

3. Obtain the medication name by clicking on the [List of Values] box on the left side of the field and you should get an empty pop-up box.

(*pop-up box shown on next page*)



4. In the 'Find' box, type the first few letters of the medication name 'Rolai' (not case sensitive) and the window will automatically add the % sign. Either hit the 'Enter' key or click on the 'Find' button at the bottom of the window. The window will populate with all medications starting with those 5 letters.



5. Scroll through the list of medications to identify the name of the medication the patient is taking. (*Disregard the country and drug code number*.)

6. You can further refine this same list of 413 medications by going to the 'Find' line and typing in the additional letters and the window will provide a smaller subset of medications.

7. Using your mouse, highlight the medication name and click the 'OK' button. The blank medication field will now be populated with the medication name. Another option is to highlight the medication and double-click. The field will be populated.

8. **Note:** if you determine that the name of the medication is different than what you originally typed, you must click on the 'Cancel' button or the 'X' box and start over.

9. If there are no other medications to be entered, you can either press the "enter" key twice to go to the next question or use your mouse to go to the next question. However, if you press "enter" and type something in the blank row and delete it, you will not be able to exit that row since the computer is expecting you to enter another medication. If there are no other medications to be entered, and the cursor will not go to the next field, select "Record" from the task bar, then select "Remove". You will then be able to use your mouse to get to the next question on the form.

B. The Medical Dictionary for Regulatory Activities (MedDRA) is a clinically validated international medical terminology. The CKD Study uses this software for miscellaneous signs and symptoms that patients may report that are not already listed in previous questions.

For example, a patient tells you he had 'hip pain':

1. Access the Form 285 data entry screen and enter the patient information up until you reach Q36.

2. Database will automatically pop you into a blank 'Symptom' field in Q37.

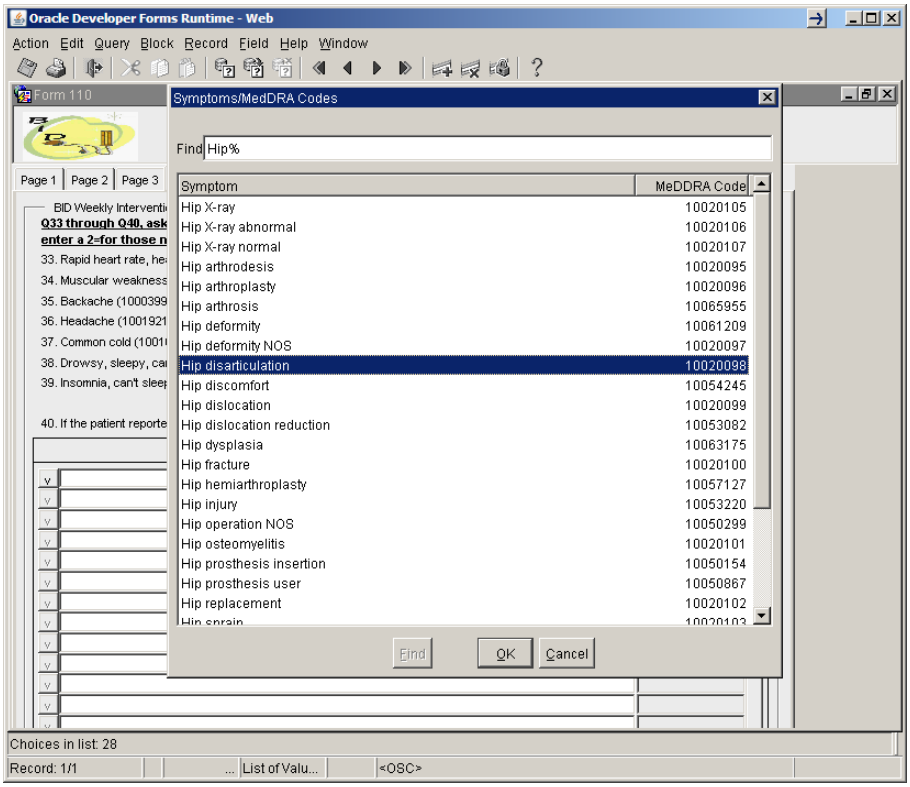
   To pop out of blank Symptom field, simply hit 'Tab' or 'Enter' button. Database will automatically place your cursor in Q37.

3. Obtain the symptom name by clicking on the [List of Values] box on the left side of the field and you should get an empty pop-up box. (*The pop-up box is the same as the picture shown in the medication section 8.7.4. above.*)

4. MedDRA advises that in searching for symptoms, use what the patient reports. Do not attempt to interpret what the patient reports.

5. In the 'Find' box, type the first few letters of the symptom 'hip' (not case sensitive) and the window will automatically add the % sign. Either hit the 'Enter' key or click on the 'Find' button at the bottom of the window. The window will populate with all symptoms starting with those 3 letters.

(*pop-up box shown on next page*)

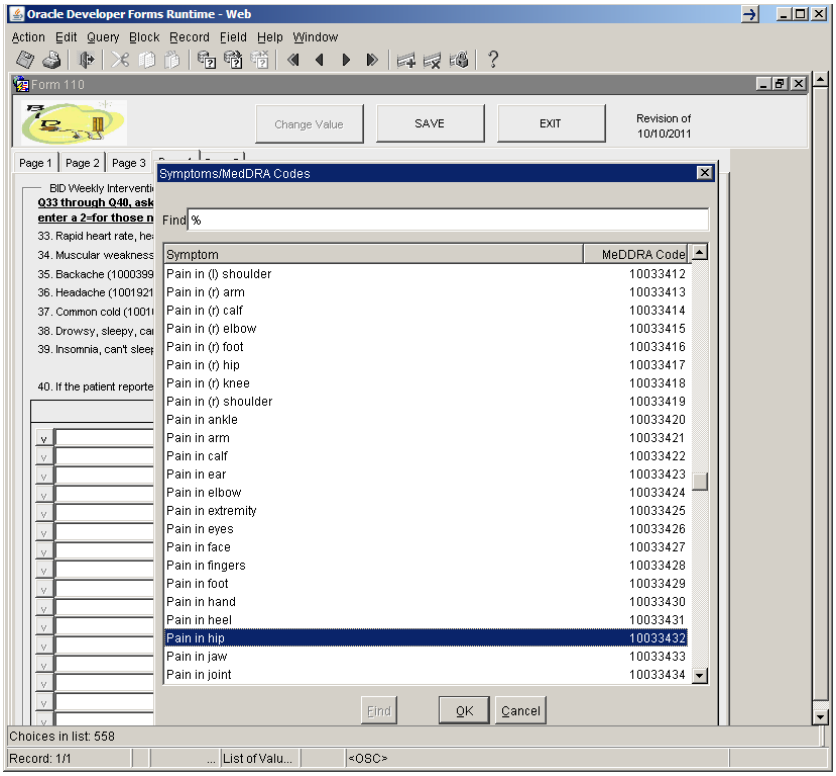


6. Scroll through the list of hip-related symptoms to identify what the patient reported. (Disregard the country and drug_code number.)

7. You can further refine this <u>same</u> list of 28 hip-related symptoms by going to the 'Find' line and typing in additional letters; the window will provide a smaller subset of symptoms.

   In this example, there is no 'hip pain' listed. Cancel out and start over by typing a slight variation of 'Pain in hip' typed as 'pain' %. This brings up 558 symptoms with 'pain' as part of the description. As you can see in the pop-up box shown on the next page, two symptoms 'Pain in (l) hip', 'Pain in (r) hip' or 'Pain in hip' are identified.

   (*pop-up box shown on next page*)



   Select the symptom that best represents 'hip pain' reported by the patient.

8. Using your mouse, highlight the symptom name and click the 'OK' button. The blank symptom field will now be populated with the symptom description. Another option is to highlight the symptom and double-click; the field will be populated.

9. **Note:** if you determine that the symptom is different than what you originally typed, you must click on the 'Cancel' button or 'X' box and start over.

10. If there are no other symptoms to be entered, you can either press the "enter" key twice to go to the next question or use your mouse to go to the next question. However, if you press "enter" and type something in the blank row and delete it, you will not be able to exit that row since the computer is expecting you to enter another symptom. If there are no other

symptoms to be entered, and the cursor will not go to the next field, select "Record" from the task bar, then select "Remove". You will then be able to use your mouse to get to the next question on the form.

8.9 Patient Confidentiality and Data Security

Patient confidentiality of medical records and identity will be maintained at the highest level. All patient data submitted to the DCC will be transmitted as secured encrypted files and reported anonymously with no names, Social Security numbers, etc. It will be emphasized to all staff of the CCs, and any centeral cores, the need for strict confidentiality of all study data, with a specific plan for later data sharing as required by NIH. HIPAA privacy regulations will be followed carefully. All forms, CDs and tapes will be kept in locked cabinets. All computerized files will be protected by means of a password system. All reports prepared by the Data Coordinating Center will be such that no individual patient can be identified. Any publication of trial data will be reported as a group, thus avoiding identification of an individual subject.

8.9.1 System Physical Security

The Server Room is located on the Cleveland Clinic main campus in the JJNorth Building. Building and department access is limited to authorized Cleveland Clinic and contracted maintenance employees via ID Badge swipe access device at building entrances. The Server room access is restricted to authorized personnel only via ID Badge swipe access device at the server room entrance.

Devices and systems for fire detection are installed and available. Server room undergoes periodic fire marshal inspection by the Department of Safety.

Temperature and humidity are automatically controlled by the heating and air conditioning equipment. Server and battery room temperatures are monitored automatically. Facility Engineering is notified of high temperature alerts for remediation automatically. The System Group is notified at the same time.

A UPS (uninterruptible power supply) is installed, maintained and tested periodically to allow for proper computer equipment shutdown in the case of extended power outages. The UPS automatically sends a page if it goes on.

8.9.2 Storage and Back-up

The database is backed up weekly in its entirety using Oracle Recovery Manager hot back-ups. Then incremental 'hot' back-ups are done on a daily basis. These are all written to disk where they are in turn copied to tape backup. In addition, transactions between backups are stored in archive logs that are also on hard disk. The tapes are kept in a fireproof safe on site for one month and then moved to Iron Mountain for long-term storage.

8.9.3 Auditing

CKD Study data are contained within an Oracle database. Access is through password protected user accounts. Passwords are forced to be changed at least every 75 days.

All inserted data records are stamped with the date, time and username of the person entering the information.

All changes to data records have a copy of the existing record saved in an audit table and the date, time and username of the person making the change is saved.

All data record deletions have the existing record copied into an audit table along with the date, time and username of the person deleting the record.

8.10 E-mail Alias Lists

There are several useful e-mail aliases, including:

ckd_steering@bio.ri.ccf.org -	Steering Committee
ckd_dcc@bio.ri.ccf.org -	DCC personnel
ckd_exec@bio.ri.ccf.org -	Executive Committee
ckd_forms@bio.ri.ccf.org -	Forms Committee

Other alias listings can be found in the CKD Study Address Directory.

Appendix A

CKD Study Website

WEB SITE DOWNLOADABLE UTILITIES

The upgrade/install to our Oracle Forms application for the CKD Study is to allow sites to use Java 8. Please follow the steps below to update your Java. Please note that if you don't have permission, you may need to contact your local IT support.

A. Go to:

http://www.java.com/en/

1. Click on the link "Do I have Java?" to obtain your current version.
2. Click on "Verify Java version"
3. Click on "Download Java Now" to get Version 8 Update 111 32 bit
4. Click "Agree and Start Free Download"
5. If you get a pop-up box at the bottom of your screen that says "Do you want to run or save JavaSetup8…..exe (721 KB) from sdlc-esd.oracle.com?, then click "Run"
6. On the "Welcome to Java" page click "install"
7. Uncheck the box "RECOMMENDED……" by checking 'Do Not Update Browser Settings' and click "Next"
8. Java will install
9. If 'Out-of-Date Java Version Detected' – press 'Uninstall' (older version)
10. If you see: "Restore Java security prompts" Uncheck and click "Next"
11. Once finished, close all browsers and restart

You have successfully installed Java and may or may not need to do the following steps below in 'B':

B. Please leave the check mark in "Restart my browser now to complete the installation" and click "Close"
   1. Java will close and re-open in another window. Click "Enable" where it says "The Java™ Plug-In SSV Helper add-on from 'Oracle American, Inc.' is ready for use"

C. Go to the computer Start button, left click and select the Control Panel.
   1. Select Java and click on the "Security" tab.
   2. Click on "Edit Site List"
   3. Click "Add" and type the following into the box labeled 'location': https://qhsapps.ccf.org and press "OK".
   4. Close your browser and restart to access the CKD Database.

Appendix B

Key Mapping

FUNCTION	KEY
Block Menu	Ctrl+B
Clear Block	F7
Clear Field	F5
Clear Form	F8
Clear Record	F6
Commit	Ctrl+S
Count Query	F12
Delete Record	Ctrl+↑
Display Error	Shift+Ctrl+E
Down	↓
Duplicate Item	Shift+F5
Duplicate Field	Shift+F6
Edit	Ctrl+E
Enter Query	F11
Execute Query	Ctrl+F11
Exit	Action menu, select Exit
Help	Ctrl+H
Insert Record	Ctrl+↓
List of Values	Ctrl+L
List Tab Pages	F2
Next Block	Shift+PageDown
Next Field	Tab
Next Primary Key	Shift+F7
Next Set of Records	Shift+F8
Previous Block	Shift+PageUp
Previous Field	Shift+Tab
Print	Ctrl+P
Return	Return
Show Keys	Ctrl+K
Up	Up
Update Record	Ctrl+U

Appendix C

Instructions on Running the "Bottle Number Assignment Report"

Login to the CKD database

Under "Forms", click on "Assign Bottles-COMBINE"

Enter ID and Alphacode for the participant

After entering the participant ID and Alphacode, your site will receive a message that the query produced no records. (That is fine because this is the participant's first bottle assignment.)

Place a "B" in the "Visit Type" field and a "0" in the "Visit #" field for the Baseline Visit. For follow-up visits, place a "F" in the "Visit #" field.

Press the ***Assign Bottle(s)*** button and the bottle assignment should populate under "Bottles Assigned But Not Dispensed".

Your site will receive an email with this same information which you may use to pull the bottles for participant.

Note: This report can be run the day before the participant receives the baseline study medications. This allows time for your research pharmacy to gather the medications and will not hold up the participant visit.

Appendix D

Instructions for Clearing your IE Cache

If you are unable to see an updated report, try cleaning out your ‘cache’ in your web browser and then try running the report again.

You can follow these steps:
a. Open Internet Explorer and then click on Tools.
b. Then click on Internet options.
c. Click the General tab, and then, under Browsing history, click Delete.
d. Here you can select history, cookies, temporary internet files and then click delete.

This will clear your Internet Explorer cache.

Chapter 9, Appendix 1: CKD Study eGFR Equation

CKD-EPI equation expressed as a single equation:

$$GFR = 141 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018 \text{ [if female]} \times 1.159 \text{ [if black]}$$

where:

S_{cr} *is serum creatinine in mg/dL,*

κ *is 0.7 for females and 0.9 for males,*

α *is -0.329 for females and -0.411 for males,*

min indicates the minimum of S_{cr}/κ *or 1, and*

max indicates the maximum of S_{cr}/κ *or 1.*

Chapter 9, Appendix 2: BSA Formula

The DuBois formula is used to calculate BSA.

$$BSA = 0.007184 \times W^{0.425} \times H^{0.725}$$

CHAPTER 11. GENERAL PRINCIPLES OF RECRUITMENT FOR THE U01 CKD STUDIES

11.1 General Issues of Recruitment

Recruitment is essential for the success of this study. Consider the following points when recruiting participants:

1. Emphasize the importance of the study.
2. Emphasize the nutritional information that will be provided during the study.
3. Emphasize close follow-up of laboratory results during the study.
4. Explain that a stipend for participation will be provided.
5. Approach potential participants more than once, if necessary.
6. Be courteous, attentive and professional.
7. Show interest and enthusiasm in the study.
8. Make sure that potential participants fully understand the potential risks and benefits of the study. Explain all aspects of the study detailed in the informed consent. Make sure that participants understand the information you present. Allow the participant enough time to consider and sign the informed consent document.
9. Emphasize that participation in the study will advance medical knowledge. Potential participants may be told, "We don't know the answers, but here is a chance to help medical science."
10. Some potential participants will be motivated by stressing that the results may benefit future generations of patients with chronic kidney disease and that they may have a chance to help society.

11.2 General Issues Regarding Contact with Providers and Participants

Several tools are available for establishing contact with providers and participants.

11.2.1 Provider Cooperation

Providers are busy, and it is not their responsibility to recruit participants for this study. But you can ask for their support.

1. Take the initiative. Do not wait for providers to contact you regarding potential participants.
2. Mail a study brochure with a personal letter to providers requesting their cooperation.
3. Ask providers for permission to contact their patients and ask them to encourage their patients to enroll.
4. Reassure providers that their patients will be followed by individual CKD study (COMBINE, BASE, Microbiome) investigators for study purposes only.
5. Let the providers know that you will inform them of the participant's course in the study.

11.2.2 Contact with Providers

Direct involvement of investigators is essential for successful recruitment. Possible strategies include:

- **Formal and informal presentations** (Grand rounds, research conferences, house staff rounds, clinic in-services)
- **Distribution of brochures** in clinics
- **Direct conversations** with physicians and other providers (physician assistants, nurse practitioners, nurses)
- **Consistent and frequent screening** in CKD and other clinics
- **Data base searches and mass mailings**

To promote collaboration, investigators should reassure the providers that their patients will be followed by their individual CKD study (COMBINE, BASE, Microbiome) investigators for study purposes only and that providers will be informed of the patients' status throughout the study.

11.2.3 The Participant Brochure

The recruitment brochure describes in easy-to-understand language the purpose of an individual CKD study (COMBINE, BASE, Microbiome) and what is expected of the participants. It can be used as a tool to briefly review the study requirements with potential participants upon initial introduction, prior to the screening visit and the actual informed consent process. Sample participant brochure will be provided in Appendix and on the study website. This brochure requires approval by your local Institutional Review Board before it should be distributed to potential participants or providers.

11.2.4 Letters to Patients and Providers

Sample letters will be provided in Appendix and on the study website. These letters require approval by your local Institutional Review Board before it should be distributed to potential participants or providers.

11.3 Approach to Recruitment

11.3.1 Recruitment Plan

Each site will develop a recruitment plan that may use some or all of the following recruitment strategies: clinic-based recruitment; referrals from providers; community-based recruitment campaigns.

Clinic-based recruitment:

- After HIPAA waivers and waivers of Informed Consent are obtained, if required by local Institutional Review Boards, electronic medical records will be reviewed to identify potential patients who are eligible for participation.
- Study staff will approach patients during their clinic sessions and invite them to learn more about the study. Recruitment letters may also be used instead of verbal contact during the course of providing medical care. Following introduction, study staff will communicate with interested individuals and set up a screening visit.

Referral from providers:

Providers will be introduced to the study and will be provided with list of inclusion and exclusion criteria. The primary providers will be encouraged to discuss the study with potentially eligible participants, and to either provide the participant with contact information for the study, or alternative ask if study personnel may contact the participant to discuss the study in more detail. Study staff will initiate contact with interested and potentially eligible patients and

describe the study to them. Recruitment letters may also be used instead of phone contact. Following introduction, study staff will set up screening visits with interested individuals.

Community-based recruitment:

The site investigators will initiate contact with community leaders and introduce them to the study. Community leaders will suggest possible ways to disseminate information regarding the study to potential participants in the community. Study staff will respond to contact initiated by interested individuals and briefly describe the study to them. Following introduction, study staff will communicate with interested individuals and set up a screening visit. Additional strategies, including targeted mailings, advertisements within healthcare settings and external promotions will also be considered.

Additional strategies may include:

- provider referrals
- participants referrals
- targeted mailings
- advertisements within local health care settings
- external promotion

11.3.2 Monitoring Recruitment Progress

Investigators and study staff will meet weekly to discuss progress of weekly goals. Appropriate actions may include:

- Increase number of chart reviews
- Increase time in targeted clinics
- Determine what is working and what is not
- Review barriers and problems
- Revise the plan as necessary
- Consider other means of recruitment, including outside promotion

CKD Study Participant Information

These informational items are for local center adaptation only. Note: information on this sheet should be reviewed with the patient beginning at baseline and, if randomized, at F3, F6, F9 and F12.

CKD Identification Number
CKD Alphacode
Participant's Name (Last, First, Middle/Maiden)
Participant title preference (Mr., Mrs., Ms, no preference)
Social Security Number
Age, Birth date
Preferred Method of Contact/Best Time(s)
Check if Medical Records Release Form is signed
MRN (local dialysis unit, other medical establishment)

<u>Contact Information</u>
Pt complete addresses (home and alternate)
- Pt telephone numbers (home, work, cell, alternate, fax #s)
  - (pt communicate by telephone? TTY phone may be an option)
- Pt email addresses: (home, work, alternate)

Spouse or Significant Other: (Last, First, Middle/Maiden), title preference
- Telephone numbers: (home, work, cell, alternate, fax #s)
- Additional Notes

Alternate Contact(s) not living with participant (Last, First, Middle/Maiden, title preference, relationship to pt)
- Telephone numbers (home, work, cell, alternate, fax #s)

Emergency Contact (Last, First, Middle/Maiden, title preference, relationship to pt)
- Telephone numbers (home, alternate numbers)

<u>Health Care Information:</u>
Primary Care/Referring Physician Name
- Address (Street, Bldg/Floor/Suite, Box/Dept, City, State, Zip)
- Telephone numbers (office, fax #s)
- Notes

Nephrologist or Other Physician Name
- Address (Street, Bldg/Floor/Suite, Box/Dept, City, State, Zip)
- Telephone numbers (office, fax #s)
- Notes

Type of Insurance

Notes

Interviewer instructions for starting a new FFQ session

Note: For online use, the user account must already have been set up.

1. For an online session, use a web browser to go to the URL:
   https://www.nutritionquest.com/login/

2. At the "Welcome to the Block Food Questionnaire" screen, enter:

   User Name: _____ (enter User Login Name assigned for user)

   Password: _____ (enter Password assigned for user)

   Group Id: _____ (enter 3-digit number provided by NutritionQuest)

   Click the button: **Submit**

3. On the webpage **BDDS Food Frequency Questionnaire**

   A. First time, click the button: **Start a new Questionnaire**

   B. If you log in for the second (third, etc) time to resume and complete the questionnaire session, click the link: **RESUME**

4. Enter responses to all of the questions on each screen. To move to the next screen, Click the **NEXT** button.

5. If you need to stop temporarily,
   Click the **Stop Survey** button (upper right corner of the screen).

   When you are ready to start up again, follow steps 1, 2, and 3B. The system will automatically take you to the screen where you left off.

6. You can change answers any time before the ending the questionnaire session.
   Click the **BACK** button. *[Caution: Do **not** use the browser Back button.]*

7. On the last FFQ screen – "You have completed the final section of the survey. Thank you!" –
   Click the **NEXT** button so that all responses are recorded to the online system.

9. In the final screen click the button that reads
   CLICK HERE TO END THE SESSION