

Pilot Clinical Trials in CKD Manual of Operations Revision of 10/31/2017		
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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 BInders and Nicotinamide (COMBINE)] Study Group¹, presented by XXXX.

Papers: [*specific study name*, e.g., The CKD Optimal Management with BInders and Nicotinamide (COMBINE)] Study Group¹, prepared by XXXX.

¹The 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 BInders and Nicotinamide (COMBINE)] Study Group¹

¹The *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 BInders and Nicotinamide (COMBINE)] Study

¹The 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.

Primary material that should be included, if available

- 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.

Supporting material that should be included, if available

- 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.

**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.

**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

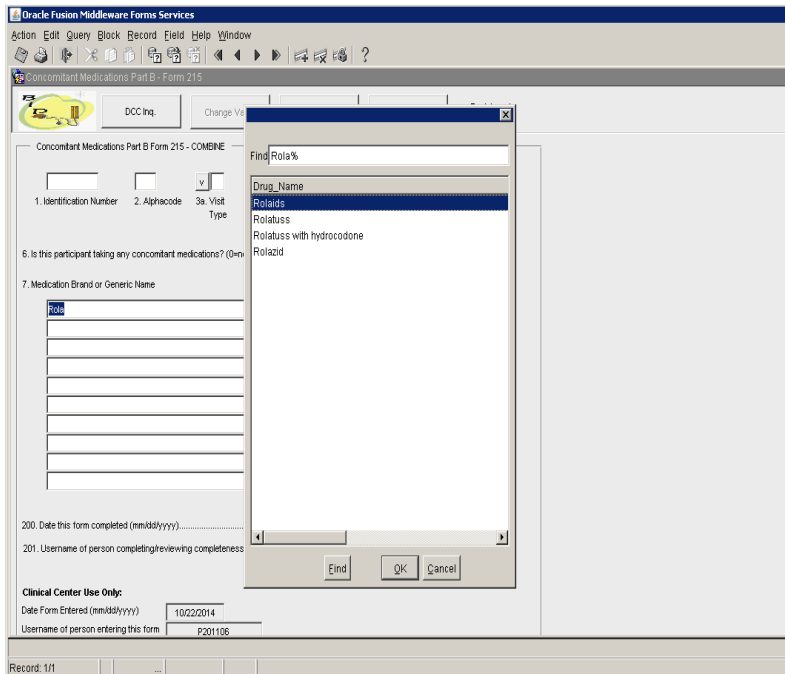
A. The WHO Drug database is used for recording medications on Form 214-Concomitant Medications, Part A and Form 215-Concomitant Medications, Part B. You will need to select the name of the medication from a [List of Values] to populate these forms; you cannot type freehand the name of the medication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

For example, a patient is taking a non-antihypertensive medication, Rolaid's, 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.

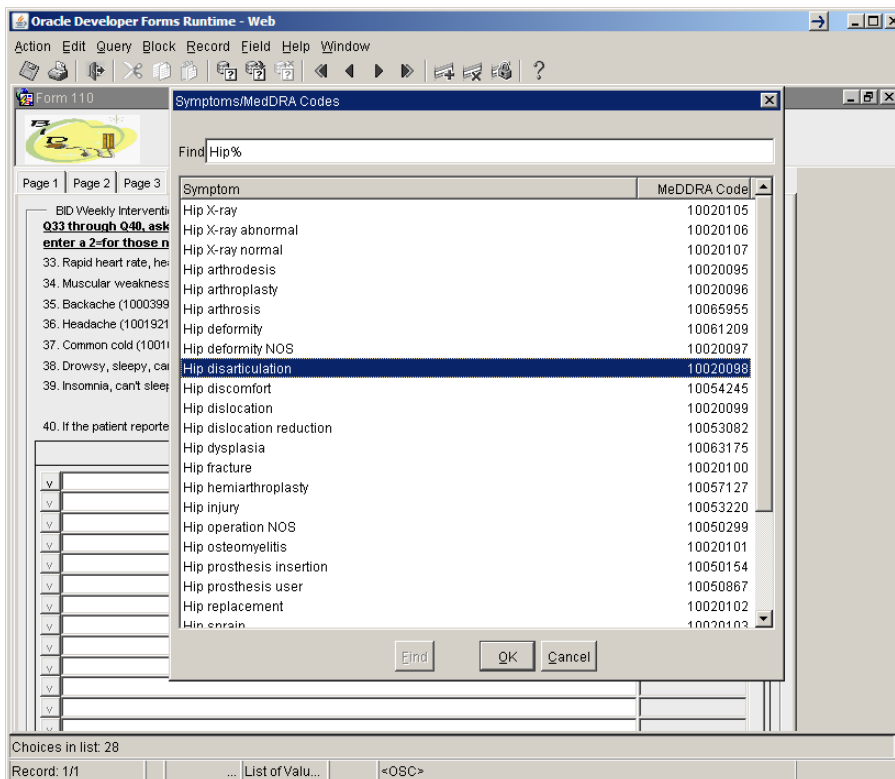
For example, a patient tells you he had 'hip pain':

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)

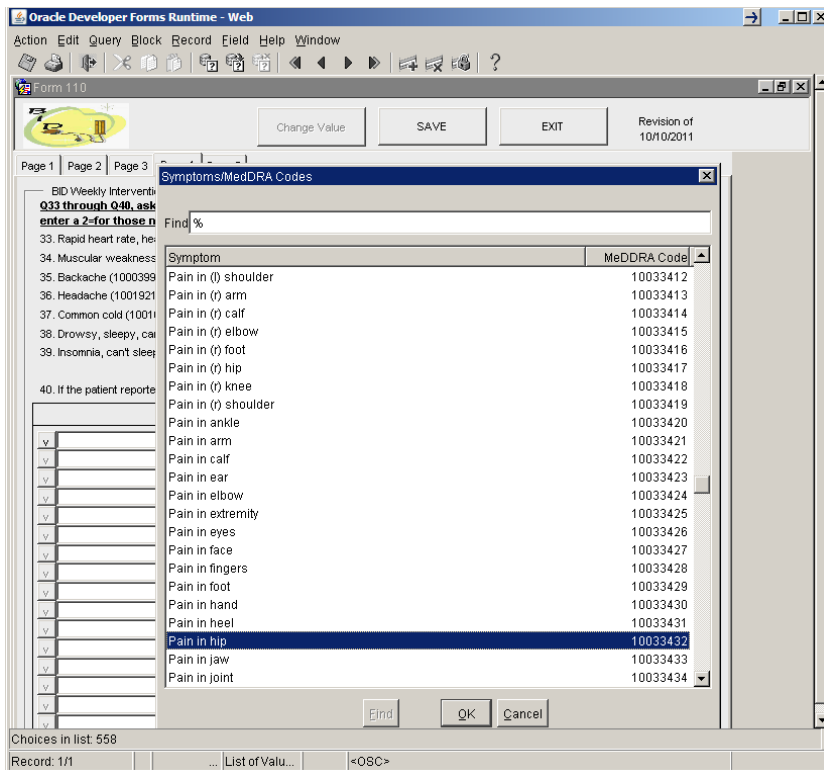


6. Scroll through the list of hip-related symptoms to identify what the patient reported. (Disregard the country and drug_code number.)

- You can further refine this same 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.

- 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.
- 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.
- 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 central 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:

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

where:

Scr 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 Scr / κ or 1, and

max indicates the maximum of Scr / 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)

Contact Information

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)

Health Care Information:

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

Pilot Clinical Trials in CKD**Bicarbonate Administration to Stabilize eGFR: The (BASE) Trial****Items to have on hand for when the BASE Study starts**

- Tape Measures (to measure ankle circumference) - Order at least 3 **Gulick II** tapes measures (Fisher Scientific at www.fishersci.com, Catalog No.: NC9678141). *Please note: there is a regular Gulick and Gulick II Plus available, but be sure to purchase the **Gulick II**. Retail cost is around \$54 but your institution may already have an established account and get a volume discounted price.*
- Weight scale
- Weight scale to measure urine weight
 - Two BASE standard table top weight scales (one to use to measure urine weight; one on hand, stored, as a back-up). The standard scale chosen for BASE is the KD8000 Scale by My Weight - Baker's Math Kitchen Scale. (Available on Amazon.com for \$32.32)
- 500 g calibration weight
 - Need not be standardized. However, if you need to order one, you might consider the one offered by American Weigh Scales 500WGT 500 Gram Calibration Weight for \$7.65 on Amazon.com
- 200 g calibration weight
 - Need not be standardized. However, if you need to order one, you might consider the one offered by American Weigh Scales 200WGT Carbon Steel 200gm Calibration Weight Scale for \$7.21 on Amazon.com
- Sphygmomanometer (to measure blood pressure, pulse)
- Stadiometer (to measure height)
- Urine collection aids (female 'urine collection hats', male (urinals, as needed) (to make it easier for patients to do their 24-hour urine collection)
- Pill counting tray that can handle ¾" pills and a pill-counting spatula
- Centrifuge – capable of spinning at 3000 rpm for 15 minutes
- Freezer (-20° C or colder) to freeze backup containers of urine for Litholink
- Blood drawing and lab processing supplies:

Local lab requisition form or method to order local labs	Pipettes
Blood tubes for local labs	Sharps containers
Tourniquets	Gauze
Butterflies/needles (21G and 23G)	Coban/tape
Vacutainer (needle holders)	Alcohol wipes
Specimen racks/boxes for temporary storage of samples	

- Extra Biohazard bags/absorbent material/container for transport (extra shipment box provided by Litholink)
- Extra 15 ml tubes to freeze back-up 24-hour urine for Litholink (*need two 15 ml tubes containing 10 ml of urine per participant*)
- Permanent fine-tip marker (Sharpie)
- Labels for Biorepository tubes and urine cup (provided by DCC)

Other start up items to consider:

- A Windows desktop or laptop available for data entry
- Convenient printer
- Three-ring binders for completed data collection forms and other source documents
- Folders for giving hand-outs to study participants
- Shipping supplies, e.g., packaging tape and a box cutter
- Storage for:
 - Lab supplies
 - Study meds if you are storing the blinded meds with the PI, not the pharmacy
 - Participant study binders (follow guidelines for storing in locked cabinet, room, etc.)

Pilot Clinical Trials in CKD

Bicarbonate Administration to Stabilize eGFR: The (**BASE**) Trial

- IATA certification – Necessary for any study staff member that is packaging samples for shipment
- CLIA Certificate of Waiver – If study personnel will be performing the urine pregnancy test, the site needs to check if they are covered by an institutional CLIA. If not, a CLIA Certificate of Waiver is necessary.

**Primary Reasons Why Candidates Who Were Approached
For BASE Did Not Consent**

	Reasons Approached Candidates for BASE Did Not Consent	Number of Patients
A.	Do not want to be in a research study / “feels like a human guinea pig” / Feels he does not need research done on his kidneys	
B.	Particularly does not want to take sodium bicarbonate capsules	
C.	Particularly does not want to be randomized to treatment	
D.	Not willing to take a placebo	
E.	Says BASE Pills are too big to swallow	
F.	Doesn’t want to take so many pills or so many additional pills	
G.	Too busy / Busy schedule / Doesn’t want to attend so many visits	
H.	Doesn’t want to collect the 24-hour urines	
I.	Says study is too long / doesn’t want to stay 32 weeks	
J.	Not willing to do some other BASE requirement [please keep a list] <i>(Remember that you do not need to consent to the biosample repository in order to join BASE)</i>	
K.	Says that overall, the study requirements are just too much for him/her	
L.	Significant others do not support patient participating	
M.	Primary care doc, other nephrologist does not support patient participating	
N.	Not ready at this time / Thinking about it / Will approach later	
O.	Patient said no (or refused to respond despite prompting) without giving a reason	
P.	In another interventional study	
Q.	Participant lives too far away	
R.	Participant does not live here all year around	
S.	Participant does not speak English	
T.	Institutionalized (nursing home or rehab center)	
U.	Participant reports being a vegetarian	
V.	Participant reports two or more UTIs in the past year	
W.	Participant reports becoming out of breath when walking on flat surfaces or at rest	
X.	Patient does not want to participate for some other specific reason [keep a list]:	
	TOTAL NUMBER OF CANDIDATES THAT DID NOT CONSENT	

CHAPTER 31: MANAGING BASE STUDY PARTICIPANTS

31.1 Review of medications during the Screening Visit

All medications that the participant is currently taking should be reviewed at the screening visit for eligibility purposes.

Eligibility criteria states “Chronic immunosuppressive therapy for any indication. This does not include oral steroids ≤ 10 mg per day, inhaled steroids, or topical steroids.”

The participant is exempted if they are on a stable oral steroid < 10 mg of prednisone/day or inhaled steroids or an equivalent. The following corticosteroids can be taken by the participant and would not be an exclusion:

Prednisone 10 mg is equivalent to:

Cortisone 50 mg

Hydrocortisone 40 mg

Prednisolone 10 mg

Methylprednisolone 8 mg

Dexamethasone 1.5 mg

As long as the dose is less than noted above, the participant meets this criterion.

31.2 Re-Enrollment of a Previously Enrolled Participant

The procedure for re-enrolling is similar for BASE as it is in COMBINE.

All screening forms should be entered. If a participant is eligible based on Form 106 (BASE Screening Form) but becomes ineligible on Form 121 (Local Lab Serum Pregnancy) or Form 202 (Visit Form) or Form 213 (Concomitant Medications) or Form 351 (Local Lab Serum Results) or Form 356 (Local Lab Spot Urine Results), a Form 162 (BASE Baseline Drop Out Form) will need to be entered. *Note, if the participant was not eligible based on the information alone on Form 106 (Screening Form), a Form 162 (Drop Out Form) is not needed.*

A BASE participant can be re-screened after at least one month has passed from the date the Baseline Dropout Form 162 is entered into the database as noted in the instructions on Form 402 (Re-Enrollment of a Previously Enrolled Participant). When the participant returns for the Screening Visit, the screening forms are completed and Form 402 (Re-Enrollment of a Previously Enrolled Participant) is completed on paper (this form is not data entered) and scanned and emailed to the DCC. The DCC would then prepare the database so the new data for the visit could be entered.

31.3 Randomization

Prior to randomizing the participant, the site should run the “Ready to Randomize Report.” The report must show that the participant is eligible. Sites may want to print this report showing eligibility for the participant’s file. It is very important that you randomize the participant the day of or the day before the participant is scheduled to come in.

31.4 Time between W28 and the W32 visit

Participants are taken off of BASE study medications at W28. There should be 4 weeks between the W28 visit and the W32 visit. Results from blood chemistries done at W28 and W32 will be compared to see what changes occurred after study medications were discontinued.

31.5 Washout for those who complete BASE and want to start COMBINE

A participant can begin COMBINE after 1 week has passed from the “Date the PI determined no more data will be coming for this patient” (Q4) on BASE Form 476 Study Closeout Form. Please notify the DCC via email one week prior to the screening visit. Participants will continue to keep the same ID and alphacode when starting COMBINE.

**Listing of Common H₂ Blockers and PPIs – BASE
Appendix 1**

H₂ Blockers (Acid Reducers) for Gastroesophageal Reflux Disease (GERD)


Examples

Generic Name	Brand Name
cimetidine	Tagamet
famotidine	Pepcid
nizatidine	Axid
ranitidine	Zantac

Proton pump inhibitors

Drug
Aciphex [®] (rabeprazole)
Dexilant [®] (dexlansoprazole) (formerly Kapidex)
Nexium [®] (esomeprazole)
lansoprazole* (Prevacid [®])
Prevacid 24-HR** (lansoprazole)
omeprazole* (Prilosec [®])
omeprazole ** (Prilosec OTC [®])
pantoprazole* (Protonix [®])

Listing of Common H₂ Blockers and PPIs – BASE Appendix 1


omeprazole/ sod
bicarbonate*

(Zegerid®)

Zegerid OTC®

(omeprazole/ sod
bicarbonate)

**Common Antihypertensive Medications: ACEI and ARB – BASE
Appendix 2**

	WHODrug Generic/Brand Name	WHODrug Code (DRUG REC)	ACE	ARB
1.	Accupril	008106	Y	
2.	Accuretic	011336	Y	
3.	Aceon	007907	Y	
4.	Altace	008856	Y	
5.	Amlodipine and Benazepril, Amlodipine Besylate and Benazepril HCL	016216	Y	
6.	Atacand	013495		Y
7.	Atacand HCT	014216		Y
8.	Avalide	013508		Y
9.	Avapro	013396		Y
10.	Azilsartan. Azilsartan medoxomil, Azilsartan kamedoxomil	067648		Y
11.	Azilsartan medoxomil w/Chlortalidone	073882		Y
12.	Benazepril, Benazepril HCL, Benazepril Hydrochloride	009091	Y	
13.	Benazepril and Hydrochlorothiazide, Benazepril Hydrochloride/Hctz	011663	Y	
14.	Benicar	016354		Y
15.	Benicar HCT	016429		Y
16.	Capoten	004984	Y	
17.	Captopril	004984	Y	
18.	Captopril/Hydrochlorothiazide	007296	Y	
19.	Cozaar	011216		Y
20.	Diovan	013196		Y
21.	Edarbi	067648		Y
22.	Edarbyclor	073882		Y
23.	Enalapril Maleate	005749	Y	
24.	Enalapril Maleate/Hctz	008968	Y	
25.	Exforge	026260		Y
26.	Exforge Hct	062959		Y
27.	Fosinopril	008940	Y	
28.	Fosinopril Sodium	009153	Y	
29.	Fosinopril Sodium / Hctz Fosinopril sodium and hydrochlorothiazide	013241	Y	
30.	Hyzaar	012848		Y
31.	Lexxel	013462	Y	
32.	Lisinopril	008940	Y	
33.	Lisinopril and Hydrochlorothiazide, Lisinopril/Hctz	064007	Y	
34.	Losartan Potassium/Hctz, Losartan potassium and hydrochlorothiazide	012848		Y
35.	Losartan, Losartan Potassium	011216		Y
36.	Lotensin	009091	Y	
37.	Lotensin HCT	011663	Y	
38.	Lotrel	016216	Y	
39.	Mavik	011483	Y	
40.	Micardis	014218		Y
41.	Micardis HCT, Micardis hct	064150		Y
42.	Moexipril Hcl / Hctz, Moexipril Hcl and Hydrochlorothiazide	013835	Y	
43.	Moexipril Hcl, Moexipril Hydrochloride	012939	Y	

**Common Antihypertensive Medications: ACEI and ARB – BASE
Appendix 2**

	WHODrug Generic/Brand Name	WHODrug Code (DRUG REC)	ACE	ARB
44.	Monopril	009153	Y	
45.	Monopril-hct, Monopril HCT	013241	Y	
46.	Perindopril, Perindopril Erbumine,	007907	Y	
47.	Prinivil	008940	Y	
48.	Prinzide	016139	Y	
49.	Quinapril Hcl / Hctz, Quinapril Hcl and Hydrochlorothiazide	011336	Y	
50.	Quinapril, Quinapril Hcl, Quinapril Hydrochloride	008106	Y	
51.	Ramipril	008856	Y	
52.	Tarka	013234	Y	
53.	Teveten	013473		Y
54.	Teveten Hct	094180		Y
55.	Trandolapril	011483	Y	
56.	Trandolapril/Verapamil Hcl, Trandolapril and verapamil hydrochloride	013234	Y	
57.	Uniretic	013835	Y	
58.	Univasc	012939	Y	
59.	Valsartan	013196		Y
60.	Vaseretic	008968	Y	
61.	Vasotec	005749	Y	
62.	Zestoretic	064007	Y	
63.	Zestoric	016139	Y	
64.	Zestril	008940	Y	

CHAPTER 32: BASE PARTICIPANT EDUCATIONAL MATERIALS

32.1 Dietary Education Handout

The “Sodium dietary education” handout should be given and reviewed with the participant at the B0 visit. This handout is an appendix to this chapter.

Sodium and Your CKD Diet: How to Spice Up Your Cooking

What is sodium?

Sodium is a mineral found naturally in foods and is the major part of table salt.

What are the effects of eating too much sodium?

When your kidneys are not healthy, extra sodium and fluid build up in your body. This can cause swollen ankles, puffiness, a rise in blood pressure, shortness of breath, and/or fluid around your heart and lungs. See the following table for suggestions on how to reduce sodium in your diet.

LIMIT THE AMOUNT OF...	FOOD TO LIMIT BECAUSE OF THEIR HIGH SODIUM CONTENT	ACCEPTABLE SUBSTITUTES
SALT & SALT SEASONINGS	<ul style="list-style-type: none"> Table salt Seasoning salt Garlic salt Onion salt Celery salt Lemon pepper Lite salt Meat tenderizer Bouillon cubes Flavor enhancers 	<ul style="list-style-type: none"> Fresh garlic, fresh onion, garlic powder, onion powder, black pepper, lemon juice, low-sodium/salt-free seasoning blends, vinegar
SALTY FOODS	<p>High Sodium Sauces such as:</p> <ul style="list-style-type: none"> Barbecue sauce Steak Sauce Soy sauce Teryaki sauce Oyster sauce 	<ul style="list-style-type: none"> Homemade or low-sodium sauces and salad dressings; vinegar; dry mustard; unsalted popcorn, pretzels, tortilla or corn chips
	<p>Salted Snacks such as:</p> <ul style="list-style-type: none"> Crackers Potato chips Corn chips Pretzels Tortilla chips Nuts Popcorn Sunflower seeds 	

CURED FOODS	Ham Salt pork Bacon Sauerkraut Pickles, pickle relish Lox & Herring Olives	Fresh beef, veal, pork, poultry, fish, eggs
LUNCHEON MEATS	Hot Dogs Cold cuts, deli meats Pastrami Sausage Corned beef Spam	Low-salt deli meats
PROCESSED FOODS	Buttermilk Cheese Canned: Soups Tomato products Vegetable juices Canned vegetables Convenience Foods such as: TV Dinners Canned raviolis Chili Macaroni & Cheese Spaghetti Commercial mixes Frozen prepared foods Fast foods	Natural cheese (1-2 oz per week) Homemade or low-sodium soups, canned food without added salt Homemade casseroles without added salt, made with fresh or raw vegetables, fresh meat, rice, pasta, or unsalted canned vegetables

Why do I need to limit my sodium intake?

Some salt or sodium is needed for body water balance. But when your kidneys lose the ability to control sodium and water balance, you may experience the following:

- thirst
- fluid gain
- high blood pressure
- discomfort during dialysis

By using less sodium in your diet, you can control these problems.

Hints to keep your sodium intake down

- Cook with herbs and spices instead of salt. (Refer to “Spice Up Your Cooking” section for further suggestions.)
- Read food labels and choose those foods low in sodium.
- Avoid salt substitutes and specialty low-sodium foods made with salt substitutes because they are high in potassium.
- When eating out, ask for meat or fish without salt. Ask for gravy or sauce on the side; these may contain large amounts of salt and should be used in small amounts.
- Limit use of canned, processed and frozen foods.

Some information about reading labels

- Understanding the terms:

- Sodium Free - Only a trivial amount of sodium per serving.
- Very Low Sodium - 35 mg or less per serving.
- Low Sodium - 140 mg or less per serving.
- Reduced Sodium - Foods in which the level of sodium is reduced by 25%.
- Light or Lite in Sodium - Foods in which the sodium is reduced by at least 50%.

- Simple rule of thumb: If salt is listed in the first five ingredients, the item is probably too high in sodium to use.

All food labels now have milligrams (mg) of sodium listed. Follow these steps when reading the sodium information on the label:

1. **Know how much sodium you are allowed each day.** Remember that there are 1000 milligrams (mg) in 1 gram. For example, if your diet prescription is 2 grams of sodium, your limit is 2000 milligrams per day. Consider the sodium value or other food to be eaten during the day.
2. **Look at the package label.** Check the serving size. Nutrition values are expressed per serving. How does this compare to your total daily allowance? If the sodium level is 500 mg or more per serving, the item is not a good choice.
3. **Compare labels of similar products.** Select the lowest sodium level for the same serving size.

How to Spice Up Your Cooking

Giving up salt does not mean giving up flavor. Learn to season your food with herbs and spices. Be creative and experiment for a new and exciting flavor.

What kinds of spices and herbs should I use instead of salt to add flavor?

Try the following spices with the foods listed.

Allspice:

Use with beef, fish, beets, cabbage, carrots, peas, fruit.

Basil:

Use with beef, pork, most vegetables.

Bay Leaf:

Use with beef, pork, most vegetables.

Caraway:

Use with beef, pork, green beans, cauliflower, cabbage, beets, asparagus, and in dips and marinades.

Cardamom:

Use with fruit and in baked goods.

Curry:

Use with beef, chicken, pork, fish, green beans, carrots and in marinades.

Dill:

Use with beef, chicken, green beans, cabbage, carrots, peas and in dips.

Ginger:

Use with beef, chicken, pork, green beans, cauliflower and eggplant.

Marjoram:

Use with beef, chicken, pork, green beans, cauliflower and eggplant.

Rosemary:

Use with chicken, pork, cauliflower, peas and in marinades.

Thyme:

Use with beef, chicken, pork, fish, green beans, beets and carrots.

Sage:

Use with chicken, pork, eggplant and in dressing.

Tarragon:

Use with fish, chicken, asparagus, beets, cabbage, cauliflower and in marinades.

Tips for cooking with herbs and spices

- Purchase spices and herbs in small amounts. When they sit on the shelf for years they lose their flavor.
- Use no more than $\frac{1}{4}$ teaspoon of dried spice ($\frac{3}{4}$ of fresh) per pound of meat.
- Add ground spices to food about 15 minutes before the end of the cooking period.
- Add whole spices to food at least one hour before the end of the cooking period.
- Combine herbs with oil or butter, set for 30 minutes to bring out their flavor, then brush on foods while they cook, or brush meat with oil and sprinkle herbs one hour before cooking.
- Crush dried herbs before adding to foods.

Can I use salt substitutes?

Caution! If you are told to limit potassium in your diet, be very cautious about using salt substitutes because most of them contain some form of potassium. Check with your doctor or dietitian before using and salt substitute.

CHAPTER 33: BASE LABORATORIES OVERVIEW

33.1 Mean of serum bicarb in Baseline

When looking at baseline eligibility criteria for serum bicarbonate, the “Ready to Randomize Report” will look at the mean of the two most recent baseline serum bicarbonate values that are entered on Form 351 Local Lab Serum Results Form. If the mean of the two most recent values is 19.5, this value will be rounded to 20 and the participant will meet the serum bicarbonate criteria on the “Ready to Randomize Report.”

BASE STUDY - SPECIMENS COLLECTION and SHIPPING GUIDE *as of 05/11/2015*

	Serum (sent to Local Lab)	Serum (sent to NIDDK Repository)	Plasma (sent to NIDDK Repository)	Spot Urine (sent to Local Lab)	24-Hour Urine (sent to Litholink)	24-Hour Urine (saved as backup for Litholink)	Spot Urine (sent to NIDDK Repository)
Collect:	<i>Collect and process according to Site's Local Lab guidelines</i>	<i>4ml SST gold top tube</i>	<i>4.5 ml PST light green top tube</i>	<i>Collect and process according to Site's Local Lab guidelines</i>	<i>Jug, then transfer to 50 ml to green top urine tube (minimum 40 ml urine needed)</i>	<i>Transfer additional urine to 15 ml tubes (minimum 10 ml/tube)</i>	<i>Collect in 90 ml urine cup</i>
Form #	<i>351</i>	<i>F302</i>	<i>F302</i>	<i>F356</i>	<i>F335</i>	<i>F327, F328</i>	<i>F303</i>
Local Storage	<i>See local lab</i>	<i>See local lab</i>	<i>See local lab</i>	<i>See local lab</i>	<i>Room temperature</i>	<i>-20° C freezer locally</i>	<i>Fridge</i>
Ship on	<i>-</i>	<i>Cold pack</i>	<i>Cold pack</i>	<i>-</i>	<i>Room temp</i>	<i>If needed- room temp</i>	<i>Cold pack</i>
Screening	<i>See local lab guidelines</i>	<i>-</i>	<i>-</i>	<i>See local lab guidelines</i>	<i>-</i>	<i>-</i>	<i>-</i>
B0	<i>See local lab guidelines*</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
B1	<i>See local lab guidelines</i>	<i>1 – 4ml SST gold top</i>	<i>1 – 4.5 ml PST lt. green top</i>	<i>-</i>	<i>50 ml urine cup (minimum 40 ml urine needed)</i>	<i>2-15 ml tubes with 10 ml urine/tube minimum)</i>	<i>1 - 90 ml cup</i>
B2	<i>See local lab guidelines</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
W0[†]	<i>See local lab guidelines</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
W4	<i>See local lab guidelines</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
W8	<i>See local lab guidelines</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
W12	<i>See local lab guidelines*</i>	<i>1- 4ml SST gold top</i>	<i>1 – 4.5 ml PST lt. green top</i>	<i>-</i>	<i>50 ml urine cup (minimum 40 ml urine needed)</i>	<i>2-15 ml tubes with 10 ml urine/tube minimum)</i>	<i>1 - 90 ml cup</i>
W20	<i>See local lab guidelines</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
W28	<i>See local lab guidelines*</i>	<i>1 – 4ml SST gold top</i>	<i>1 – 4.5 ml PST lt. green top tube</i>	<i>See local lab guidelines</i>	<i>50 ml urine cup (minimum 40 ml urine needed)</i>	<i>2-15 ml tubes with 10 ml urine/tube minimum)</i>	<i>1 - 90 ml cup</i>
Action item check-as needed	<i>See local lab guidelines</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
W32	<i>See local lab guidelines</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>

** phos collected at this visit*

† If the participant had serum collected at B2 baseline visit and is randomized at the same visit, a separate W0 serum collection is not required

CHAPTER 34. BASE 24-HOUR URINE COLLECTION – LITHOLINK CORE LAB

34.1 Background

Participants who are enrolled in the CKD BASE Study will collect urine over a 24-hour period at B0, W12 and W28. A 50 ml tube of urine will be shipped overnight to Litholink Corporation in Chicago, Illinois. Two additional tubes containing 10 ml of urine will be saved as back up and frozen at each local site.

For general collection and processing questions, call 1-800-338-4333. For additional supplies needed and shipment notification, contact Susan Donohue at donahus@labcorp.com and Ignacio Granja at granjai@labcorp.com. Contact information can be found in the CKD BASE Address Directory.

34.2 Schedule, Type and Volume of Urine Required

BASE 24-Hour Urine Samples Collected for Litholink

Tube Size	Collection Periods, Quantity Required, Storage and Shipping		
	B	W12	W28
50 ml – provided by Litholink	1 x 50 ml urine Storage: room temperature	1 x 50 ml urine Storage: room temperature	1 x 50 ml urine Storage: room temperature
15 ml – provided by local sites	2 – 10 ml urine Storage: In -20° or colder freezer locally	2 – 10 ml urine Storage: In -20° or colder freezer locally	2 – 10 ml urine Storage: In -20° or colder freezer locally

34.3 Training Requirements for Personnel Sending Samples

Each person shipping diagnostic specimens should be trained according to DOT and IATA regulations. Someone at each BASE site will be responsible for training the appropriate personnel.

34.4 Logistics for Litholink

Overview: The Litholink Corporation will provide 24-hour urine collection kits – see section 34.5 for specific contents. Participants will collect their urine over the course of 24-hours and bring in the urine collection container(s) for processing by the study coordinator or other designated person. The labels to be used locally for the backup tubes will be supplied to the sites by the DCC with detailed completion instructions provided. The tube labels include space to write in the BASE participant's 6 digit-identification number. The labels will also include two spaces in which the study staff should mark the participant's alphanumeric code, which will be used as an alternative ID. Tubes should be labeled immediately prior to when urine from the participant is poured into the tubes.

34.5 Kits and Shipping Materials

Litholink Kit Contents include:

- 1–Orange urine collection container
- 1–Sealed tube of liquid urine preservative (contains Gentamicin 20 mg, Germall II 1.25 g, Potassium Fluoride 306 mg)
- 1–Green-topped 50 ml tube
- 1–Safeguard Specimen (biohazard) Bag with absorbent material
- 1–Pre-addressed shipping box (printed with appropriate DOT labels)
- 1–Preprinted Fedex Priority Overnight label (See address directory for name of individual at Litholink who will receive the specimen box)
- 1–Customer service card with toll-free phone number

Note: Litholink will send female collection aids (‘hats’) in one bulk shipment.

Local Site provides:

- Extra 15 ml tubes (for storing and freezing two additional tubes containing 10 ml/tube of backup urine)
- Tube labels (provided to each site by DCC)
- Freezer rack/storage box to hold frozen urine tubes ‘backup’
- 20° or colder freezer

34.6 Instructing the Participant on Collecting Urine

Provide the participant with items needed for urine collection including: orange urine collection container, sealed tube of liquid urine preservative, ‘how to’ instructions, and if female, urine collection aid ‘hat’. (It is suggested that the urine jug be marked with some identifying information to separate multiple samples in the event that more than one participant comes in for a study visit on the same day.). For the initial collection, it is recommended that the participant be given two jugs since each 4 liter jug should not be filled more than 4,000 mls of urine. In the event that the participant’s output exceeds the 4,000 mls, the second jug could then be used to complete the collection. Note, any collections of over 4,500 mls in a jug will need to be repeated. If the participant does not use the second jug for the collection, the participant should return the unused jug to the site and the site could use it for another participant. However, if the participant does use the second jug or the urine volume is close to 4,000 mls, a second jug should be given at subsequent visits where a 24-hour collection is needed.

Thoroughly review the instructions with the participant (and caregiver, if he or she is accompanying the study participant). Urine collection should start the date prior to the in-person study visit* and should be written on participant’s instruction sheet. Be sure to provide the participant with study personnel contact information and an emergency contact, if needed. Remind the participant that all urine is collected even if there is nighttime urination. Collections should be as close to 24-hours as possible prior to the in-person study visit. Urine jug can be stored at room temperature. Collection time should be between 20 and 28 hours. If during Baseline, the collection is <20 or >28 hours, an additional collection is required for randomization.

*For in-person visits requiring 24-hour urine collection (B1, W12 and W28), it is helpful to schedule in-person visits on a Monday so urine can be collected over the weekend and brought in to the visit.

Participant Instructions sheets on collecting their urines are provided in this chapter's appendices. Appendix A includes two IRB-reviewed participant instructions for females and for males prepared by University of Utah. Appendix B provides a generic template that can be modified accordingly. Any participant urine collection instructions must be submitted to your local IRB.

For female participants, instruct the participant to try to avoid collecting the sample during their menstrual cycle. If they happen to do the collection during this time, the sample should still be sent to Litholink with a note stating that the sample was collected during the participant's menstrual cycle.

If the participant comes in for the W28 visit, does not bring in a 24-hour urine collection, and study medications are stopped, the 24-hour urine collection for W28 will be missing and should not be recollected. If the 24-hour urine was collected after the participant stopped study medications at W28, the urine results would not provide the pharmacodynamics data that is needed since the pharmacodynamic effect is expected to dissipate within a day or so of stopping BASE study medications.

34.7 Litholink Urine Sample Processing Information

Participant will return urine collection jug and instruction sheet where actual dates and times of start/stop urine collection are written in by the participant. Record this information on Form 326 (start and end date of urine collection and start and end time of urine collection).

Process any urine regardless of under or over collection. If during baseline, if the collection is < 20 hours or > 28 hours, the collection will need to be repeated in order for the participant to be randomized. Also, filling a 4-liter jug with more than 4,000 mls of urine may compromise results from Litholink. Any collection that exceeds 4,500 mls in one jug will need to be repeated.

24-Hour Urine Collection processing – (for 1 or 2 jugs)

1. Before measuring urine volume, it is important to tighten the lid.
2. Place the collection container on a flat surface turning the jug upright so the handle is vertical.
3. Use the measuring tool along the side of the container (jug lines) to read how much fluid is inside the container. Estimate to the nearest 100 mls and record on Form 326 item 14a (Estimated volume of this 24-hour urine collection to the nearest 100 mls). If a second jug was used, estimate the second jug to the nearest 100 mls and record on Form 326 item 14b (Estimated volume of additional urine (second jug) collected to the nearest 100 mls).
4. Weigh the urine collection (includes the urine, jug with lid and the preservative). Enter value on Form 326 item 15a (Weight of the 24-hr urine collection jug). If a second jug was used, weigh the second jug urine collection (includes the urine, jug with lid and the

preservative). Enter the value on Form 326 item 15b (Weight of the second 24-hr urine collection jug).

5. Thoroughly mix or shake the urine collection container(s).
6. Fill the green-topped tube marked Collection 1 about $\frac{3}{4}$ full with the urine sample. If a second jug was used, fill a second green-topped tube marked Collection 2 about $\frac{3}{4}$ full with the urine sample.
7. Twist green top(s) tightly to seal. Make sure that the top(s) is on secure and evenly so this does not leak when shipping to Litholink. Be sure the 50 ml tube(s) used for shipping is labeled with the BASE study participant identification number and alphacode, start date/time of urine collection, and visit type. Do not spin the tube(s). Tube(s) can sit at room temperature until ready to ship.
8. Proceed to processing the backup tubes in Section 34.8.

Complete a paper copy of Litholink 24-Hr Urine Mailing form (Form 326) and make sure a copy is made of the completed document so it can be included in the shipment to Litholink. The information on the form must also be entered in the database.

All efforts should be made to ship the 50 ml tube of urine to Litholink the day the collection ends. The urine collection will no longer be good if the urine collection is received at Litholink > 96 hours after the time the urine collection ended as documented on Form 326 (Litholink 24-hr Urine Mailing Form). Specimens older than four days (96 hours) yield suboptimal results that could impact the quality of study data thus the participant should be instructed to re-collect the sample.

In Baseline, the following criteria must be met in order for the 24-urine to meet randomization eligibility criteria:

- Form 326 shows preservative observed in urine container (Q9=1)..... Yes
 - Form 326 shows preservative added (Q10=1 or 2)..... Yes
 - Form 326 shows that collection was complete (Q11=1) Yes
 - Form 326 shows tube sent to Litholink (Q16=1 or 2) Yes
 - Collection was between 20 and 28 hours? Yes
- At least one Litholink urine results Form 355 with ammonium results YES

34.8 Processing Backup Tubes for Freezing

1. Complete and attach the participant ID labels provided by the DCC to the urine tubes prior to filling. Place the label lengthwise on the tubes – do not overlap. DO NOT write the participant’s name or any other personal identification information (e.g., SS#, DOB) on the tubes.

Sample label:

BASE Study-Litholink
ID: _____ - _____
Visit: Baseline W12 W28
Start Date: ____/____/_____

The tube labels include 8 spaces on which the study team member will write in the CKD BASE Participants' 6 digit ID and alpha code with a fine-tipped permanent marker (like a Sharpie). Circle the visit: Baseline, W12 or W28. Write the start date of the urine collect.

2. Pour 10 ml of urine into each tube and make sure seal is closed tightly. Place tubes in storage container (rack/box) in the designated -20° or colder freezer. Every effort should be made to freeze the back-up samples within 48 hours from the time the urine collection ended as documented on Form 326 (Litholink 24-hr Urine Mailing Form). Note, if two urine collection jugs were used by the participant, than two back up samples are needed from each jug for a total of four back-up samples.
3. Dispose of any remaining urine and urine jug according to your site's local disposal policy.
4. Do not ship tubes to Litholink unless told to do so. Await word from either Litholink or the DCC indicating the status of the original 50 ml urine tube.
5. After receiving successful receipt and status information on the 50 ml urine tube from either Litholink or the DCC, complete Form 15 - Back-up Litholink Sample Discard Form. This form documents the disposition of the two frozen tubes for the urine collection.
 - a. If the 50 ml sample was analyzed and results reported, dispose of the frozen tubes according to your site's local policy and by completing Form 15.
 - b. If the original sample could not be analyzed sufficiently, Litholink will contact your site to ship the tubes that were frozen previously. Complete Form 327-Litholink Back-up Mailing Form indicating that frozen tubes are being shipped.
6. If shipment to Litholink is required, remove frozen tubes from freezer. Verify ID and alphacode and other information that appears on the tubes' labels. Do not thaw out the urine. Place frozen tubes into the biohazard bag with the absorbent material included. Ship at room temperature. (Do not ship on a cold pack.)
7. Complete Form 327 Litholink Back-up Mailing Form and make a copy for your files. Place the completed F327 inside the shipping box and send by FedEx to Litholink.

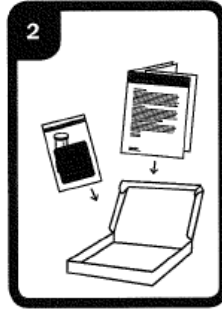
Note: If frozen urine is requested on a Friday, keep the tubes in the freezer and ship on Monday.

34.9 Shipping Instructions

Shipping Instructions

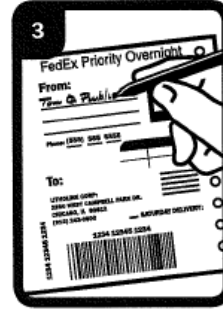


Place the green-topped tube(s) in the biohazard bag with the absorbent paper and seal the bag.

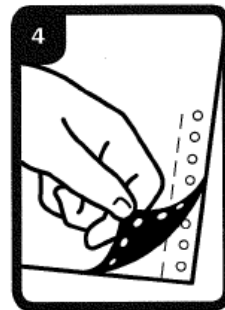


Enclose the following into your Litholink Patient Sample Shipping Box:

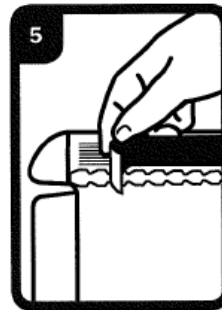
- 1) Sealed biohazard bag
- 2) Completed Collection Data



Complete the return address portion on the right-hand side of the FedEx form.



Peel the backing off the back of the FedEx form and stick the form to the top of the box.



Remove the adhesive strip under the front flap of the Litholink Patient Sample Shipping Box and seal.



Call 1-800-Go FedEx (1-800-463-3339) to schedule a pickup or to find a FedEx drop box near you.

Appendix A: Consent Form – Univ. of Utah

**BASE Study
Instructions for Collecting the Urine Sample - Female**

Collecting a 24-hour sample of urine is a very important part of this study. This sample will be used to do tests that will help us determine if sodium bicarbonate might be helpful for patients like you.

If you have any questions about how to collect the sample, please contact one of the following people:



Katt Mackin at (801) 587-8547
Megan Varner at (801) 585-2511
Jennifer Zitterkoph at (801) 585-1897
Dr. Kalani Raphael at (801) 582-1565 ext. 1794

Before starting:

Check to be sure you have:

- 1 large orange collection jug
- 1 collection aid (aka “hat”)
- 1 tube of liquid urine preservative
- Pen or pencil



Instructions:

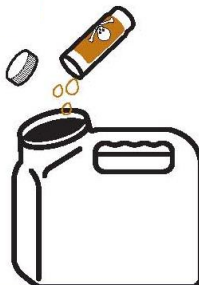
- The urine collection will start the day before your study visit.

My urine collection will begin on _____

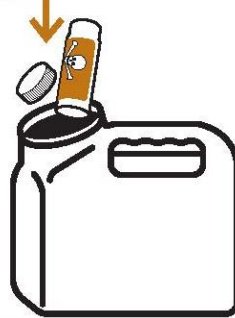
- When you wake up in the morning, flush your first urine in the toilet. **DO NOT** collect this urine.

Please write down the exact time: _____

- Open the tube of urine preservative and empty it into the collection container.



- Drop the urine preservative tube and lid into the collection container. This ensures that every drop of the preservative gets into the container. **Important: When you bring your urine collection to the study visit, the study coordinator will check to make sure the preservative tube and lid are inside the collection container. If they are not, you will be asked to repeat the urine collection.**



- Collect all of your urine into the container over the next 24 hours, including the very first urine the following morning and any urine produced during the night. To perform the collection, place the collection aid (“hat”) over the toilet and then carefully pour the urine into the orange collection container. The first urine collected the following morning is your stop time.

Please write down this exact time: _____

- Bring the orange jug with the lid firmly attached to your study visit.

Appointment Information:



Date: _____

Time: _____

Location: Center for Clinical and Translational Science (CCTS) on the 5th floor of the hospital.

BASE Study Instructions for Collecting the Urine Sample - Male

Collecting a 24-hour sample of urine is a very important part of this study. This sample will be used to do tests that will help us determine if sodium bicarbonate might be helpful for patients like you.

If you have any questions about how to collect the sample, please contact one of the following people:



Katt Mackin at (801) 587-8547
Megan Varner at (801) 585-2511
Jennifer Zitterkoph at (801) 585-1897
Dr. Kalani Raphael at (801) 582-1565 ext. 1794

Before starting:

Check to be sure you have:

- 1 large orange collection jug
- 1 tube of liquid urine preservative
- Pen or pencil



Instructions:

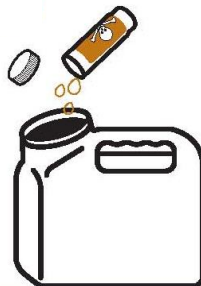
- The urine collection will start the day before your study visit.

My urine collection will begin on _____

- When you wake up in the morning, flush your first urine in the toilet. **DO NOT** collect this urine.

Please write down the exact time: _____

- Open the tube of urine preservative and empty it into the collection container.



- Drop the urine preservative tube and lid into the collection container. This ensures that every drop of the preservative gets into the container. **Important: When you bring your urine collection to the study visit, the study coordinator will check to make sure the preservative tube and lid are inside the collection container. If they are not, you will be asked to repeat the urine collection.**



- Collect all of your urine into the container over the next 24 hours, including the very first urine the following morning and any urine produced during the night. The first urine collected the following morning is your stop time.

Please write down this exact time: _____

- Bring the orange jug with the lid firmly attached to your study visit.

Appointment Information:



Date: _____

Time: _____

Location: Center for Clinical and Translational Science (CCTS) on the 5th floor of the hospital.

Appendix B: Template Consent Form

BASE Study - Instructions for Collecting the Urine Sample

Collecting a 24-hour sample of urine is a very important part of this study. This sample will be used to do tests that will help us determine if sodium bicarbonate might be helpful for persons with kidney conditions like you.

If you have any questions about how to collect the sample, please call one of the following people:



BASE Study Team Contacts:

Coordinator: _____ XXX-XXX-XXXX
Coordinator: _____ XXX-XXX-XXXX
Study Nurse: _____ XXX-XXX-XXXX
Study PI: _____ XXX-XXX-XXXX

Before starting:

Check to be sure you have:

- 1 large orange collection jug
- 1 tube of liquid urine preservative
- 1 collection aid, if needed (*“hat” for females, urinal for males, if requested*)
- Pen or pencil
- This instruction sheet



Instructions:

- The urine collection will start the day before your study visit.

My study coordinator says to start on this day (*write in day, date*): _____

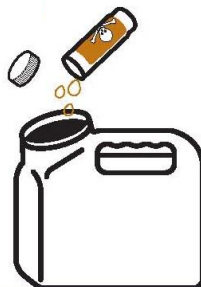
My actual urine collection began on (*write in day, date*): _____

- When you wake up in the morning, flush your first urine in the toilet. DO NOT save this urine.

This is the time I first went to the bathroom after waking up:

_____ Circle one: **am** **pm**

- Open the tube of urine preservative and empty it into the collection container.




- Drop the urine preservative tube and lid into the orange jug. This ensures that every drop of the preservative gets into the container. **Important: When you bring your urine collection to the study visit, the study coordinator will check to make sure the preservative tube and lid are inside the collection container. If these two items are not in the jug, you will be asked to repeat the urine collection.**



- Collect all of your urine into the container over the next 24 hours. Keep the jug at room temperature (no need to refrigerate it). To perform the collection, place the collection aid (“hat”) over the toilet and then carefully pour the urine into the orange collection container.
- Collect all urine produced during the night. The last time you collect your urine in the jug is the very first urine the following morning. The first urine collected the following morning is your stop time.

This is the time I first went to the bathroom after waking up the next day:

- _____ Circle one: **am** **pm**
- Bring the orange jug with the lid firmly attached to your study visit instruction sheet.

	<p>Appointment Information:</p>
	<p>Date: _____</p>
	<p>Time: _____</p>
	<p>Location: _____</p>

MATERIAL SAFETY DATA SHEET

AMRESKO INC.
6681 Cochran Road
Solon, Ohio 44139

EMERGENCY TELEPHONE NUMBER:
CHEMTREC (800) 424-9300

TELEPHONE NUMBER FOR INFORMATION:
(800) 448-4442 OR (440) 349-1199

DATE PREPARED: 3-16-06

DATE REVISED: 5-30-06

SECTION 1. ----- CHEMICAL IDENTIFICATION -----

CODE#: N299
NAME: URINE PRESERVATIVE
CAS#: N/A

SECTION 2. ----- COMPOSITION/INFORMATION ON INGREDIENTS -----

CHEMICAL NAME:	CAS#:	RTECS #:
GERMALL II	78491-02-8	YS2717000
GENTAMYCIN SULFATE	1405-41-0	LY2625000
POTASSIUM FLUORIDE	7789-23-3	TT0700000

SEE ACTUAL ENTRY IN RTECS FOR COMPLETE INFORMATION

SECTION 3. ----- HAZARDS IDENTIFICATION -----

LABEL PRECAUTIONARY STATEMENTS

IRRITANT
IRRITATING TO EYES, RESPIRATORY SYSTEM AND SKIN.
CORROSIVE
CAUSES BURNS
HIGHLY TOXIC
HARMFUL BY INHALATION, IN CONTACT WITH SKIN AND IF SWALLOWED.
SENSITIZER
MAY CAUSE SENSITIZATION BY INHALATION AND SKIN CONTACT.
SUSPECTED TERATOGEN
POSSIBLE RISK OF IMPAIRED FERTILITY
TARGET ORGAN(S):
KIDNEYS
EYES
TEETH
CNS
HEART
BONES
EARS
IN CASE OF ACCIDENT OR IF YOU FEEL UNWELL, SEEK MEDICAL ADVICE
IMMEDIATELY (SHOW THE LABEL WHERE POSSIBLE).
WEAR SUITABLE PROTECTIVE CLOTHING, GLOVES AND EYE/FACE
PROTECTION.
DO NOT BREATHE VAPOR.

SECTION 4. ----- FIRST-AID MEASURES -----

IN CASE OF CONTACT, IMMEDIATELY FLUSH EYES OR SKIN WITH COPIOUS
AMOUNTS OF WATER FOR AT LEAST 15 MINUTES WHILE REMOVING CONTAMINATED
CLOTHING AND SHOES.

IF INHALED, REMOVE TO FRESH AIR. IF NOT BREATHING GIVE ARTIFICIAL RESPIRATION. IF BREATHING IS DIFFICULT, GIVE OXYGEN.
IF SWALLOWED, WASH OUT MOUTH WITH WATER PROVIDED PERSON IS CONSCIOUS.
CALL A PHYSICIAN.

SECTION 5. ----- FIRE FIGHTING MEASURES -----

EXTINGUISHING MEDIA
NONCOMBUSTIBLE.
USE EXTINGUISHING MEDIA APPROPRIATE TO SURROUNDING FIRE CONDITIONS.
SPECIAL FIREFIGHTING PROCEDURES
WEAR SELF-CONTAINED BREATHING APPARATUS AND PROTECTIVE CLOTHING TO PREVENT CONTACT WITH SKIN AND EYES.

SECTION 6. ----- ACCIDENTAL RELEASE MEASURES -----

EVACUATE AREA.
WEAR RESPIRATOR, CHEMICAL SAFETY GOGGLES, BOOTS AND HEAVY GLOVES.
ABSORB ON SAND OR VERMICULITE AND PLACE IN CLOSED CONTAINERS FOR DISPOSAL.
VENTILATE AREA AND WASH SPILL SITE AFTER MATERIAL PICKUP IS COMPLETE.

SECTION 7. ----- HANDLING AND STORAGE -----

REFER TO SECTION 8.

SECTION 8. ----- EXPOSURE CONTROLS/PERSONAL PROTECTION -----

WEAR APPROPRIATE NIOSH/MSHA-APPROVED RESPIRATOR, CHEMICAL-RESISTANT GLOVES, SAFETY GOGGLES, OTHER PROTECTIVE CLOTHING.
USE ONLY IN A CHEMICAL FUME HOOD.
SAFETY SHOWER AND EYE BATH.
DO NOT BREATHE VAPOR.
DO NOT GET IN EYES, ON SKIN, ON CLOTHING.
AVOID PROLONGED OR REPEATED EXPOSURE.
WASH THOROUGHLY AFTER HANDLING.
HYGROSCOPIC
KEEP TIGHTLY CLOSED.
STORE IN A COOL DRY PLACE.

SECTION 9. ----- PHYSICAL AND CHEMICAL PROPERTIES -----

APPEARANCE
LIQUID

SECTION 10. ----- STABILITY AND REACTIVITY -----

STABILITY
STABLE.
INCOMPATIBILITIES:
MOISTURE
HAZARDOUS COMBUSTION OR DECOMPOSITION PRODUCTS
CARBON MONOXIDE, CARBON DIOXIDE
NITROGEN OXIDES
HAZARDOUS POLYMERIZATION
WILL NOT OCCUR.

SECTION 11. ----- TOXICOLOGICAL INFORMATION -----

ACUTE EFFECTS

HARMFUL BY INHALATION, INGESTION, OR SKIN ABSORPTION.

CAUSES EYE AND SKIN IRRITATION.

MATERIAL IS EXTREMELY DESTRUCTIVE TO TISSUE OF THE MUCOUS MEMBRANES

AND

UPPER RESPIRATORY TRACT, EYES AND SKIN.

PROLONGED OR REPEATED EXPOSURE MAY CAUSE ALLERGIC REACTIONS IN CERTAIN SENSITIVE INDIVIDUALS.

CHRONIC EFFECTS

TARGET ORGAN(S):

KIDNEYS

EYES

TEETH

CNS

HEART

BONES

GASTROINTESTINAL TRACT

EARS

MAY CAUSE CONGENITAL MALFORMATION IN THE FETUS.

TO THE BEST OF OUR KNOWLEDGE, THE CHEMICAL, PHYSICAL, AND

TOXICOLOGICAL PROPERTIES HAVE NOT BEEN THOROUGHLY INVESTIGATED.

SECTION 12. ----- ECOLOGICAL INFORMATION -----

DATA NOT YET AVAILABLE.

SECTION 13. ----- DISPOSAL CONSIDERATIONS -----

OBSERVE ALL FEDERAL, STATE AND LOCAL ENVIRONMENTAL REGULATIONS.

SECTION 14. ----- TRANSPORT INFORMATION -----

NOT REGULATED

SECTION 15. ----- REGULATORY INFORMATION -----

EUROPEAN INFORMATION

IRRITATING TO EYES AND SKIN.

R: 36/37/38

IRRITATING TO EYES, RESPIRATORY SYSTEM AND SKIN.

R 34

CAUSES BURNS.

R 42/43

MAY CAUSE SENSITIZATION BY INHALATION. MAY CAUSE SENSITIZATION BY SKIN CONTACT.

R 60/61

MAY IMPAIR FERTILITY. MAY CAUSE HARM TO THE UNBORN CHILD.

R 26/27/28

VERY TOXIC BY INHALATION, IN CONTACT WITH SKIN AND IF SWALLOWED.

S 36/37/39

WEAR SUITABLE PROTECTIVE CLOTHING, GLOVES AND EYE/FACE PROTECTION.

SECTION 16. ----- OTHER INFORMATION -----

THE ABOVE INFORMATION IS BELIEVED TO BE CORRECT BUT DOES NOT PURPORT TO BE ALL INCLUSIVE AND SHALL BE USED ONLY AS A GUIDE. AMRESKO INC. SHALL NOT BE HELD LIABLE FOR ANY DAMAGE RESULTING FROM HANDLING OR FROM CONTACT WITH THE ABOVE PRODUCT. SEE REVERSE SIDE OF INVOICE OR PACKING SLIP FOR

ADDITIONAL TERMS AND CONDITIONS OF SALE.

BASE – 24-hour Urine Collection Kit Procedures

Items that will be in the LitholinkStone Shipping box as provided by Litholink:

- Sealed tube of liquid urine preservative
- Green-topped 50 mL tube
- Safeguard specimen biohazard bag with absorbent material
- Pre-addressed shipping box
- Preprinted Fedex Priority Overnight label
- Customer service card with toll-free number
- Research test forms
- Litholink collection instructions
- MSDS for the urine preservative
- Litholink's notice of privacy practices

Items to throw away:

- Customer service card
- Research test forms
- Litholink collection instructions
- MSDS*
- Litholink notice of privacy practices*

Place the following items in a bag or other container to give to the participant:

- Orange urine collection container
- Sealed tube of liquid urine preservative
- Collection aid, if needed
- IRB-approved BASE urine collection instructions and contact information

Items that should remain in the box at the study site for processing/shipping:

- Green-topped 50 mL tube
- Safeguard specimen biohazard bag with absorbent material
- Pre-printed Fedex Priority Overnight label

*Keep one copy on file

BASE – Appendix 3: Litholink Supply Order Form

For additional supplies needed, contact Litholink Team:

Susan Donohue at donahus@labcorp.com

Ignacio Granja at granjai@labcorp.com

Contact ckd_dcc@bio.ri.ccf.org for tube labels.

Qty Requested	Item Requested
	Orange urine collection container, 4L
	<p>LitholinkStone Shipping Kit* includes:</p> <ul style="list-style-type: none"> • Sealed tube of liquid urine preservative • Green-topped 50 mL tube • Safeguard specimen biohazard bag with absorbent material • Pre-addressed shipping box (pre-printed with appropriate DOT labels) • Preprinted Fedex Priority Overnight label • Customer service card with toll-free number • Research test forms • Litholink collection instructions • MSDS for the urine preservative • Litholink’s notice of privacy practices <p><i>Items to throw away before giving kit to participant :</i></p> <ul style="list-style-type: none"> <input type="checkbox"/> <i>Customer service card</i> <input type="checkbox"/> <i>Research test forms</i> <input type="checkbox"/> <i>Litholink collection instructions</i> <input type="checkbox"/> <i>MSDS*</i> <input type="checkbox"/> <i>Litholink notice of privacy practices*</i>

*See Manual of Operations Chapter 34.

35. Specimens for NIDDK Repository

35.1 Background

Participants who are enrolled in the CKD BASE Study will be invited to volunteer to provide biological samples to be stored for use in possible future studies. A separate repository informed consent will be required, although it may be part of the main consent form (Note: NIH approval is required for Repository Consents before specimens can be taken out of the Repository). Template repository consent verbiage is provided in Appendix 1. Among those participants who consent for storage of biological specimens, serum, plasma and random (spot) urine samples will be collected at various time points as identified in the table below. Samples from BASE sites will be shipped to the NIDDK Biosample Repository at Fisher BioServices, Germantown, Maryland.

Contact information can be found in the CKD Address Directory. For general questions and biosample shipment notification, use bio-niddkrepository@thermofisher.com.

35.2 Schedule, Type and Volume of Samples

Samples Collected for NIDDK Repository

Specimen Type	Collection Periods		
	B	W	W
Serum	1 x 4.0 ml	1 x 4.0 ml	1 x 4.0 ml
Plasma	1 x 4.5 ml	1 x 4.5 ml	1 x 4.5 ml
Spot Urine	>20 ml	>20 ml	>20 ml

A biorepository kit contains the following items:

Qty	Biorepository Kit Item
1	90 ml sterile urine container with lid (for spot urine sample)
1	4.0 ml SST vacutainer (gold top) tube (serum)
1	4.5 ml light green PST tube (lithium heparin additive) (plasma)
1	Bubble wrap sleeve (for tubes)
1	Bubble wrap (big cells)
2	Biohazard bags with absorbent material (urine and blood)
1	Label: 'Exempt Human Specimen'
1	Label: Fisher Bioservices return address
1	Label: Pre-printed Fedex Airbill
1	Freezer cold pack
1	Set of instructions for processing PST, SST tubes, and packing/shipping
1	Cardboard Box with styrofoam shipper

35.3 Training Requirements for Personnel Sending Samples

Each person shipping diagnostic specimens should be trained according to DOT and IATA regulations. Someone at each BASE site will be responsible for training the appropriate personnel. No sample test kit submission is required for the BASE Study.

35.4 Logistics for Biosample Repository

Overview: The BioRepository will provide sample collection kits including the necessary blood collection tubes, packing and shipping materials and Federal Express labels for collection and shipping of the samples. The sample collection kits will be shipped to the sites by Fisher. The tube labels to be used with all repository specimens will be supplied to the sites by the DCC with detailed completion instructions provided.

The tube labels include pre-printed 3-digit identification numbers, in which the first 3 digits designate the NIDDK BioRepository Site Identification code; the study team member will write in the CKD Participants' ID in the final 6 spaces on the label. The labels will also include two spaces in which the study staff should mark the participant's CKD alpha code, which will be used as an alternative ID by Fisher BioServices. Circle the appropriate type of specimen (plasma/serum/urine). Tubes and urine cup should be labeled immediately prior to when blood is drawn from the patient or participant collects a spot urine sample.

Follow the procedure identified in Section 35.5 for specific sample processing information.

For consenting participants, study staff will fill one serum shipping tube (SST tube) and one plasma shipping tube (PST tube) and then store them in a refrigerator at +4 degrees Centigrade that is roughly equivalent to 39 degrees Fahrenheit. They should be shipped refrigerated to Fisher BioServices using the shipping kits and packing materials provided by Fisher.

A completed paper copy of the BASE Biorepository Serum and Plasma Mailing Form (Form # 302) as well as BASE Biorepository Spot Urine Mailing Form (Form # 303) and should also be included in the kit shipped to Fisher. The information on the form must also be entered in the database. Be sure to write in the intended visit number.

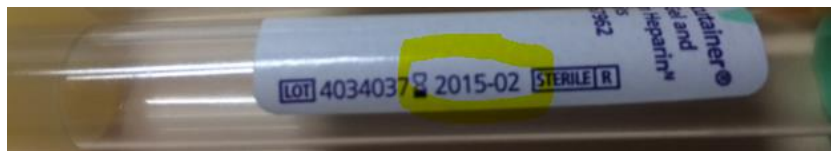
On arrival at the BioRepository, a Fisher BioServices staff member will divide the samples into aliquots according to the table below. Barcodes will be placed on each cryovials and entered in the repository database. Cryovials will then be placed in -70° C freezer for future ancillary studies.

Sample Type	0.2 ml Aliquots	0.5 ml Aliquots	1.0 ml Aliquots	5.0 ml Aliquots
Serum – 4.0 ml tube	qty. 10	(remainder of tube)	--	--
Plasma tube – 4.5 ml tube	qty. 10	(remainder of tube)	--	--
Spot urine >20 ml urine cup	--	--	qty. 10	qty. 2 (remainder is discarded)

35.5 Fisher BioServices Repository Procedure Instructions

Blood - Serum and Plasma

1. Be sure that the vacutainer tubes have not expired. Check that the date shown to the right of the hourglass on the BD label is equal to or later than the current month.



2. In preparation for collecting the serum/plasma: complete and attach the participant I.D. labels provided by the DCC to the blood samples immediately prior to collection. Use the labels provided and place them lengthwise on the tubes. DO NOT write the participant's name or any other personal identification information (e.g., SS#, DOB) on the tubes.
3. Complete and attach the participant I.D.

Sample label:

BASE Study – NIDDK Repository	
B X X -	_____ - _____
Serum	Plasma Spot Urine
Collect Date:	___/___/___

Note: The tube labels include pre-printed 3-digit identification numbers, in which the first 3 digits designate the NIDDK BioRepository Site Identification code; the study team member will write in the CKD BASE Participants' ID in the final 6 spaces on the label. The labels include two spaces in which the study staff should mark the participant's BASE alpha code, which will be used as an alternative ID by the BioServices Repository.

Sites	NIDDK BioSpecimens Site Number
Ctr 11-George Washington Univ.	B10
Ctr 21-Northwestern Univ.	B11
Ctr 31-UCSD	B12
Ctr 32-Denver Nephrology	B13
Ctr 41-Univ. of Utah	B14
Ctr 42-Baylor Scott & White	B15
Ctr 43-Utah VA	B16

4. Collect the specimen in the appropriate container; either SST/PST vacutainer tube.
5. After filling:
After filling: (please see guides on Preparing a Quality Sample for serum and plasma on next pages as provided by the biorepository.)

Continued on next page.

SERUM:

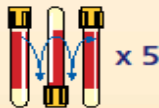


Helping all people
live healthy lives

How to Prepare a Quality Sample

Using BD Vacutainer® SST™ Tubes

Invert
5
Times



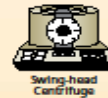
- Gently invert 5 times to mix clot activator with blood.

Clot
30
Minutes



- Allow blood to clot for a minimum of 30 minutes in a vertical position.
- Observe a dense clot.

Spin
10
Minutes



- Centrifuge at **FULL SPEED** (between 1100 and 1300g) for 10 minutes for swing-head units or 15 minutes for fixed angle units (balance tube in centrifuge).
- Barrier will form, separating serum specimen from clot.
- Transport spun tube to laboratory.

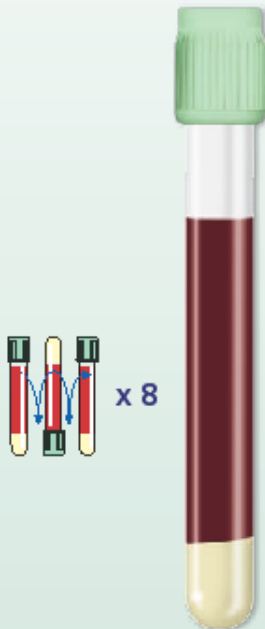
PLASMA:



Helping all people
live healthy lives

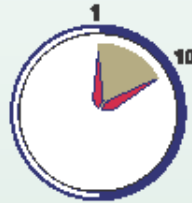
How to Prepare a Quality Sample Using BD Vacutainer® PST™ Tubes

Invert
8-10
Times



- Gently invert 8-10 times immediately after collection to mix lithium heparin anticoagulant with blood.
- Insufficient mixing may lead to microclot and fibrin strand formation.

Spin
10
Minutes



Centrifuge at
1100 - 1300g



- Centrifuge at full speed
1100 – 1300g for 13 mm Plus Plastic tubes
1000 – 1300g for 16 mm Plus Plastic tubes
for 10 minutes in a swing-bucket unit or
15 minutes for a fixed-angle unit
(balance tubes in centrifuge).
- Gel barrier will form to separate plasma from red blood cells.

Ready
for
Analysis



- Use in laboratory for plasma determinations in chemistry.

Then move the tubes to the refrigerator until the shipment is ready to be sent. Be sure that the refrigerator is securely closed.

6. Double check the subject ID, and verify that ID information on the vacutainer tubes matches that on the Form 302-Biorepository Serum and Plasma Mailing Form (Form # 302). Be sure to write in the intended visit number in the space provided on this Form.
7. Date and identify the person completing the Form 302-Biorepository Serum and Plasma Mailing Form (Form # 302). Make a copy of each form; keep the copy and send the original with the shipment.
8. If more than one BASE participant's serum and plasma has been collected, then it is acceptable to ship both in the same shipper. Make sure each BASE participant's samples are well-marked and placed in separate bags.

**All BASE samples must be sent in a shipping box separate from any other CKD study's samples.
This will minimize risk of samples being mixed up.**

Urine - Random (Spot)

1. Be sure that the seal on the urine cup has not been broken prior to giving to the participant and requesting a urine collection
2. Complete and attach the participant I.D. label provided by the DCC to the urine container immediately prior to collection. DO NOT write the participant's name or any other personal identification information (e.g., SS#, DOB) on the container.

Sample label:

BASE Study – NIDDK Repository
B x x - _____ - _____
Serum Plasma Spot Urine
Collect Date: ____/____/____

The urine container label includes a pre-printed 3-digit identification number, in which the first 3 digits designate the NIDDK BioRepository Site Identification code*; using a fine-tipped permanent marker (like a Sharpie), the study team member will write in the CKD BASE Participants' ID in the final 6 spaces on the label. The label also includes two spaces in which the study staff should mark the participant's CKD BASE alpha code, which will be used as an alternative ID by the BioServices Repository. Write the date spot urine collected in the space provided.

*Refer to Section 35.5 for NIDDK Site repository numbers

3. Then move the urine container to the refrigerator until the shipment is ready to be sent. Be sure that the refrigerator is securely closed.
4. When preparing to ship, double check the subject ID, and verify that ID information on the urine container matches that on the Form 303-Biorepository Random (Spot) Urine Mailing.
5. Date and identify the person completing the Form 303-Biorepository Random (Spot) Urine Mailing. Make a copy of each form; keep the copy and send the original with the shipment.

See next page for preparing sample shipments to Fisher.

Instructions For Shipping COMBINE Urine and Blood to the NIDDK BioSample Repository

1. Freeze the gel pack included in the shipping kit prior to sample collection.
2. Collect the urine in the specimen cup and screw the lid on the cup. Verify that the lid is secured tightly, and wipe any urine off the outside of the container.
3. Place the urine cup into the biohazard zip-lock bag with the absorbent sheet. Seal the bag. (Pic.1)
4. Insert the Vacutainers into the bubble wrap pouch (Pic.2). Place the pouch into the zip-lock bag with the absorbent sheet. Seal the bag. (Pic.3)
5. Place the frozen ice pack in the bottom of the foam cooler. (Pic.4)
6. Place the zip-lock bags containing the urine and Vacutainers on top of the gel pack. Make sure the urine container is in an upright position. Place additional bubble wrap or packing material inside the foam cooler to prevent the contents from shifting during shipment. (Pic.5 & 6)
7. Place the foam lid on the foam cooler. Place the Biorepository Mailing Forms on top of the foam lid. (Pic.7)
8. Close and seal the box with packing tape. Affix the "Exempt Human Specimen" label to the top of the box in the upper right corner. Affix the repository address label to the top of the box in the upper left corner. (Pic.8)
9. Use the pre-printed FedEx air bill to ship specimens to the NIDDK Repository:
 - a. Section 1, From: Fill in your name, return address, phone number and the date. Leave "Sender's FedEx Account Number" blank.
 - b. Section 2, Your Internal Billing Reference: Enter the study name "COMBINE".
 - c. Section 6, Special Handling: Place a check mark next to "No" under "Does this shipment contain dangerous goods?"
 - d. Section 7, Payment: Enter "1" under "Total Packages" and the total weight of the package under "Total Weight".
 - e. Follow the peel-and-stick instructions on the back of the preprinted air bill. As shown, affix the air bill to the side of the box.
10. If your organization does not have a regularly scheduled FedEx pickup, call Federal Express, 1-800-GO-FEDEX (1-800-463-3339). Tell them the account number (in Section 7, Payment) on the preprinted FedEx air bill and your pickup address. FedEx will dispatch a courier to pick up the package. Please schedule shipments Monday through Thursday. **The repository is closed on weekends so do not ship specimens on Fridays.** Specimens may be refrigerated and shipped on the following Monday.
11. Send a shipment notification to bio-niddkrepository@thermofisher.com on the day the package is picked up by FedEx. Include the 12-digit FedEx tracking number, study name and your contact information in the notification.
12. Contact the NIDDK Biosample Repository via email or call Heather Higgins (240-686-4703) or Sandra Ke (240-686-4702) regarding questions about packaging and shipping.



Pic.1



Pic.2



Pic.3



Pic.4



Pic.5



Pic.6



Pic.7



Pic.8

Revision date: 11 Nov 2014

fedex.com 1800.GoFedEx 1800.463.3339



FedEx Tracking Number 8062 8133 3753

Form 0215

Sender's Copy

1 From Please print and press hard

Date _____ Sender's FedEx Account Number **RECIPIENT'S FEDEX ACCOUNT NUMBER 0476**

Sender's Name _____ Phone (____) _____

Company _____

Address _____ Dept./Floor/Room _____

City _____ State _____ ZIP _____

2 Your Internal Billing Reference (OPTIONAL)

Print 25 characters will appear on invoice

3 To

Recipient's Name **HEATHER HIGGINS** Phone (____) **240.686-4706**

Company **FISHER BIOSERVICES, INC GOVT**

Address **2001 CENTURY BLVD** HOLD Weekday
We cannot deliver to PO boxes or P.O. ZIP codes. Dept./Floor/Room HOLD Saturday
 HOLD (HOLD) with exception
Address **BLDG. 6, Suite 400** HOLD Saturday
 HOLD (HOLD) with exception
Use this line for the HOLD location address or in continuation of your shipping address. HOLD Saturday
 HOLD (HOLD) with exception
City **GERMANTOWN** State **MD** ZIP **20874-9172**

0115214309

Ship it. Track it. Pay for it. All online. Go to fedex.com

4 Express Package Service * To local locations. Packages up to 150 lbs. For packages over 150 lbs., use the new FedEx Express Freight 25 A-M.

Next Business Day

FedEx First Overnight: Delivered next business morning. Delivery is subject to location. FedEx Signature will be obtained on Monday unless SATURDAY Delivery is selected.

FedEx Priority Overnight: Next business morning. * FedEx shipments will be delivered on Monday unless SATURDAY Delivery is selected.

FedEx Standard Overnight: Next business afternoon. * Saturday Delivery NOT available.

2 or 3 Business Days

FedEx 2Day A.M.: Second business morning. * Saturday Delivery NOT available.

FedEx 2Day: Second business afternoon. * Thursday shipments will be delivered on Monday unless SATURDAY Delivery is selected.

FedEx Express Saver: Three business days. * Saturday Delivery NOT available.

5 Packaging * Declared value limit \$500

FedEx Envelope* FedEx Pak* FedEx Box FedEx Tube Other

6 Special Handling and Delivery Signature Options

SATURDAY Delivery: Will be delivered on SATURDAY. * FedEx Standard Overnight, FedEx 2Day A.M., or FedEx Express Saver.

No Signature Required: Package may be left without signature at recipient's address. * Signature required for delivery. See options.

Direct Signature: Someone at recipient's address must sign for delivery. See options.

Indirect Signature: If no one is available at recipient's address, someone at a neighboring address may sign for delivery. See options.

Does this shipment contain dangerous goods?

No Yes (See options) Yes (See options) Dry Ice (Dry Ice 2, UN 1845) _____ to _____

Dangerous goods (including dry ice) cannot be shipped in FedEx packaging. Cargo Aircraft Only

7 Payment Bill to: Enter FedEx Acct. No. or Credit Card No. below:

Sender FedEx No. Sender Recipient Third Party Credit Card Cash/Check

FedEx Acct. No. **2820-0902-1** Co. Code _____

Total Packages _____ Total Weight _____ Total Declared Value* _____

*Your liability is limited to \$5000 unless you declare a higher value. See options for details. By completing this bill you agree to the service conditions of the back of this bill or in the current FedEx Service Guide, including terms stated on our facility.

Form 0215 • Part #0215 • ©1996-2015 FedEx • PRINTED IN U.S.A. 2/15

PULL AND RETAIN THIS COPY BEFORE AFFIXING TO THE PACKAGE. NO POUCH NEEDED.

Appendix 1: Template Repository Verbiage

OPTIONAL STUDY ELEMENT:

Tissue Bank

As part of this study, we would like to send some of your blood and urine specimens to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Repository, a research resource supported by the National Institutes of Health. The Repository collects, stores, and distributes biological samples and associated data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples available for use in research for the study of chronic kidney disease after the current study is completed. Sending samples to the Repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent diseases. These specimens will also be labeled by a unique code and without your personal health identifiers. Therefore, the Repository will not be able to give out your name, or other information that identifies you to the scientists who receive the samples. Also, because your sample cannot be linked back to you, we will not share the results from future studies with you or your doctors.

This study does not plan to collect your DNA or to do any studies with DNA. Your samples will be used only for research and will not be sold.

Tissue or blood samples obtained from you in this research may help in the development of a commercial product by the NIH or its research partners. There are no plans to provide financial compensation to you should this occur.

Requests for samples: An appropriate external panel will review all requests to use Repository samples. That panel will include a bioethicist and other individuals with expertise in one or more areas including: clinical research, epidemiology, physiology, and statistical analysis.

If you agree to have your sample(s) stored in the Repository, you can change your mind up until the end of the study – at that time, the list that links names and study ID numbers will be destroyed. When study researchers receive written instructions from you, they will destroy your sample(s). After the study ends, you will not be able to withdraw your sample(s) because the Repository will not know which one is yours. The sample(s) will stay in the Repository indefinitely.

You do not have to participate in the tissue bank to be in the main part of this study. No matter what you decide to do, your decision will not affect your medical care. You can tell us your choice by initialing one of the choices below:

_____ I consent to banking of my blood and urine specimens for future research.

_____ I do not consent to banking of my blood and urine specimens for future research.

NIDDK Biorepository Kit Re-Order Form CKD BASE Study

Request Date: _____ Date needed by: _____

Study Coordinator: _____ Phone Contact #: _____

NIDDK Repository #: B ____ ____

Shipping Address:

ITEM	UNITS	QUANTITY REQUESTED
Biorepository Kit	EACH	

Scan and email to: Bio-NIDDKRepository@thermofisher.com

or Fax supply re-order sheet to: 301-515-4049

--PLEASE ALLOW 7-10 BUSINESS DAYS FOR DELIVERY--

Each kit will contain the following items:

Qty	Biorepository Kit Item
1	90 ml sterile urine container with lid (for 24-hr urine sample)
1	4.0 ml SST vacutainer (gold top) tube (serum)
1	4.5 ml light green PST tube (lithium heparin additive) (plasma)
1	Bubble wrap sleeve (for tubes)
1	Bubble wrap (big cells)
2	Biohazard bags with absorbent material (urine and blood)
1	Label: 'Exempt Human Specimen'
1	Label: Fisher Bioservices return address
1	Label: Pre-printed Fedex Airbill
1	Freezer cold pack
1	Set of instructions for processing PST, SST tubes, and packing/shipping
1	Cardboard Box with styrofoam shipper

CHAPTER 36: ANTHROPOMETRY

36.1 Anthropometry Training

Centers were trained in measuring ankle circumference at the BASE Central Training Session held at the O'Hare Hilton in Chicago on Tuesday, March 17, 2015.

Jennifer Zitterkoph ([ZITTERJ](#)) and Katherine Mackin ([MACKINK](#)) trained the following staff:

Ctr. 11-GWU: Maria Wing ([WINGM](#)), Christina Franco ([FRANCO](#))

Ctr. 21-Northwestern: Gina Schwartz ([SCHWARG2](#)), Michelle Bradley ([BRADLEM](#))

Ctr. 31-Univ. of California, San Diego: Erick Castro ([CASTROE](#))

Ctr. 32-Denver Nephrology: Beth Shamblyn ([SHAMBLE](#)), Martha Persky ([PERSKYM](#))

Ctr. 41-Univ. of Utah/Utah VA: Jennifer Zitterkoph, Katherine Mackin - TRAINERS

Ctr. 42-Baylor/Scott & White: JoAnn Nichols ([NICHOLJ](#))

The following were trained in measuring ankle circumference at the BASE Anthropometry Training during the Study Coordinators' Meeting/Steering Committee Meeting at the Marriott Suites, Bethesda, Maryland on Wednesday, November 18, 2015.

Jennifer Zitterkoph ([ZITTERJ](#)) trained the following:

Ctr. 11-GWU: Michelle Dumadag ([DUMADAM](#))

Ctr. 42-Baylor/Scott & White: Theresa Strakos ([STRAKOT](#))

The following were trained in measuring ankle circumference prior to the Study Coordinators Meeting in Bethesda, Maryland on Wednesday, January 25, 2017.

Jennifer Zitterkoph and Megan Varner trained the following:

Ctr. 21-Northwestern: Patrick Fox ([FOXP](#))

Ctr. 22-Northshore: Sangeetha Rao ([RAOS](#))

Ctr. 31-UCSD: Brenda Thomas ([THOMASB](#))

Ctr. 51-Duke Univ: Ashley Broome

Only the individuals noted above who have been trained centrally can train and certify other staff at their clinical site. If those staff members who were trained centrally leave the study, then the center must appoint another staff representative to be trained by Jennifer Zitterkoph or Katherine Mackin.

36.2 Measuring ankle circumference in BASE

The Gulick II tape measure will be used to measure ankle circumference. The link below can be used for ordering.

<https://www.fitnessmart.com/products/gulick-ii-tape-measure?variant=27555940167>

36.3 Severe edema

Severe edema is defined as $\geq 10\%$ increase in total ankle circumference from baseline. The most recent baseline measure will be used. If ankle circumference was measured at both B1 and B0, then the B1 measure will be used to determine severe edema. If there was no measure done at B1, then the measure done at B0 will be used to determine severe edema.

Measuring ankle circumference

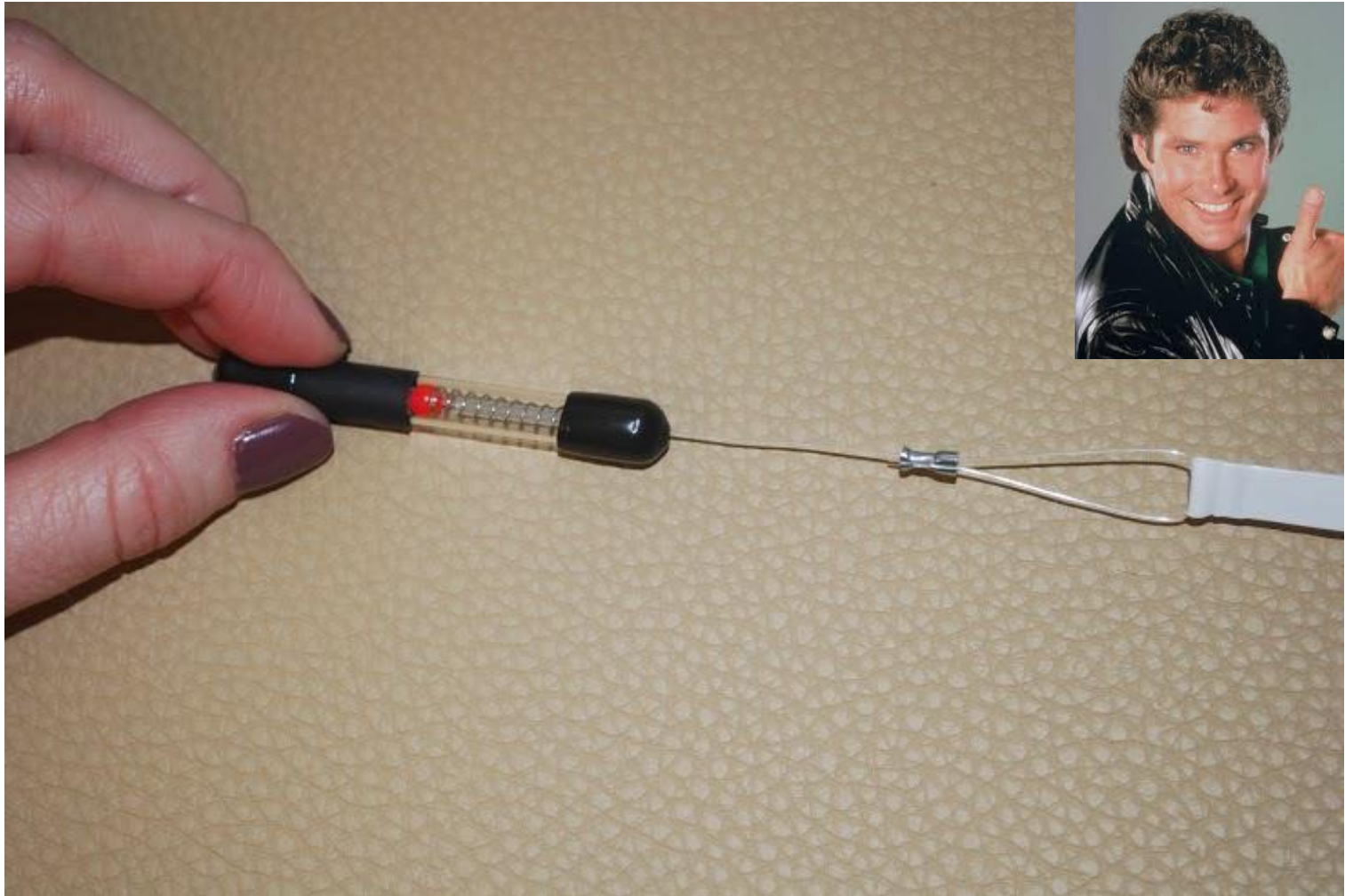
Gulick II Tape Measure- two sides



Red =
centimeters

~~Black = inches~~

Gulick II Tape Measure - tension control



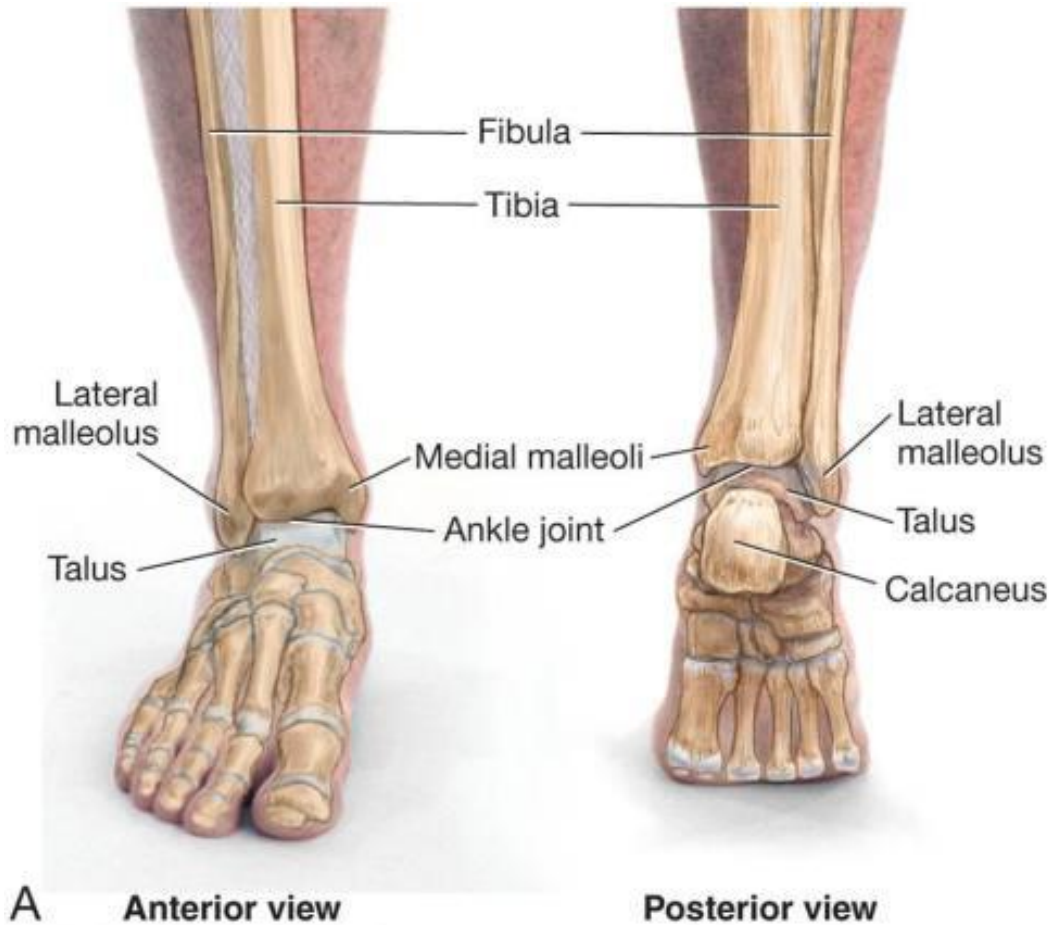
Two red balls = too much tension



Expose lower leg

- Remind participants to dress comfortably
- Take off shoes and socks if necessary
- Roll up pant leg, etc
- Do not remove compression stockings

1. Identify medial malleolus



A Anterior view

Posterior view

Medial =
Middle

~~Lateral = Little
toe~~

1. Identify **Medial malleolus** – **Middle**



1. Identify medial malleolus



2. Place 0 cm mark at center of medial malleolus



3. Measure 7 cm above medial malleolus



Keep in line
with the leg

4. Mark at 7cm





5. Wrap measuring tape around ankle at 7 cm mark
(centimeter side should be showing)



Perpendicular
with the leg

5. Wrap measuring tape around ankle at 7 cm mark



TIP: switch hands here



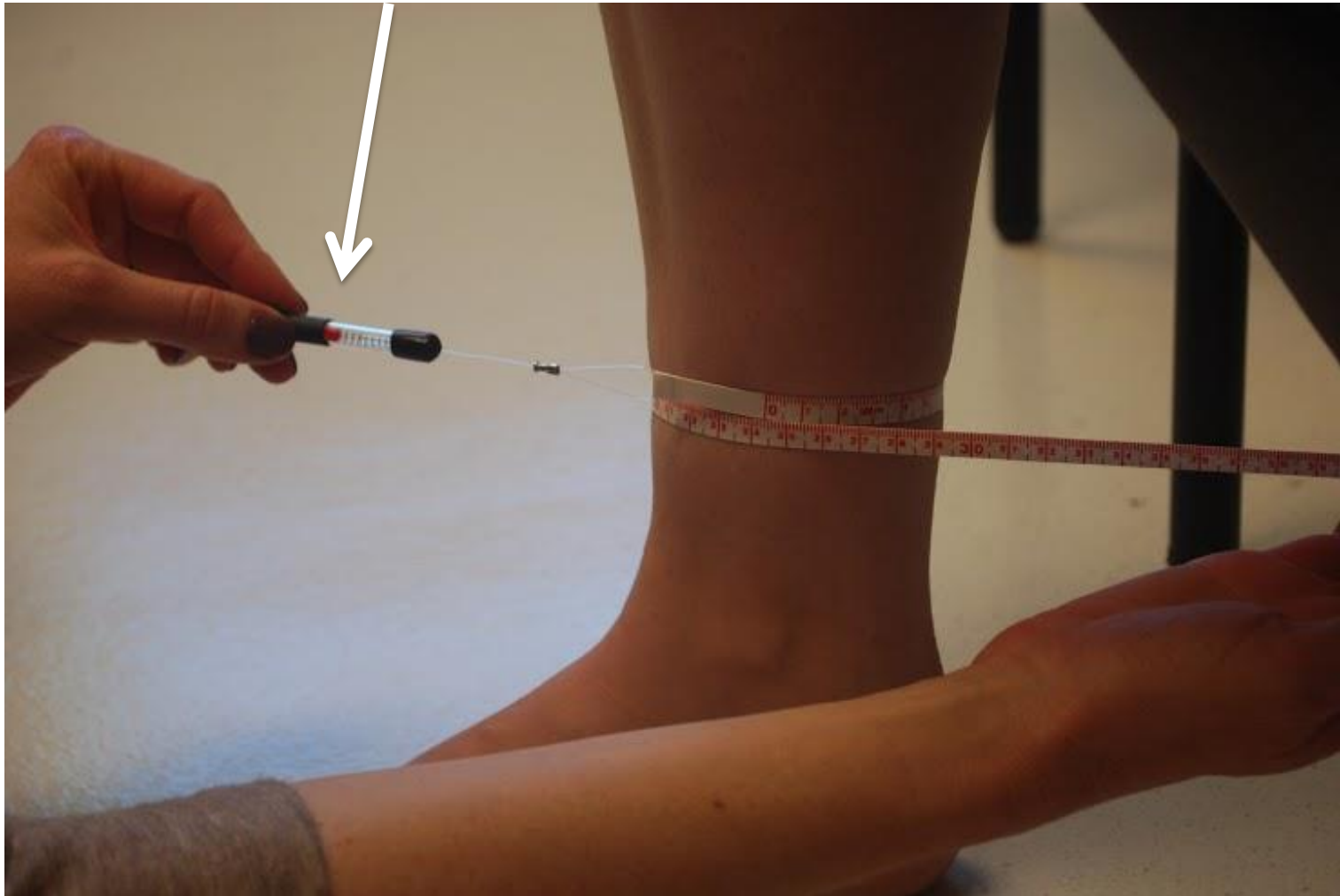
6. Maneuver the tape into position

Line you drew should be in between the upper and lower portions of the tape measure

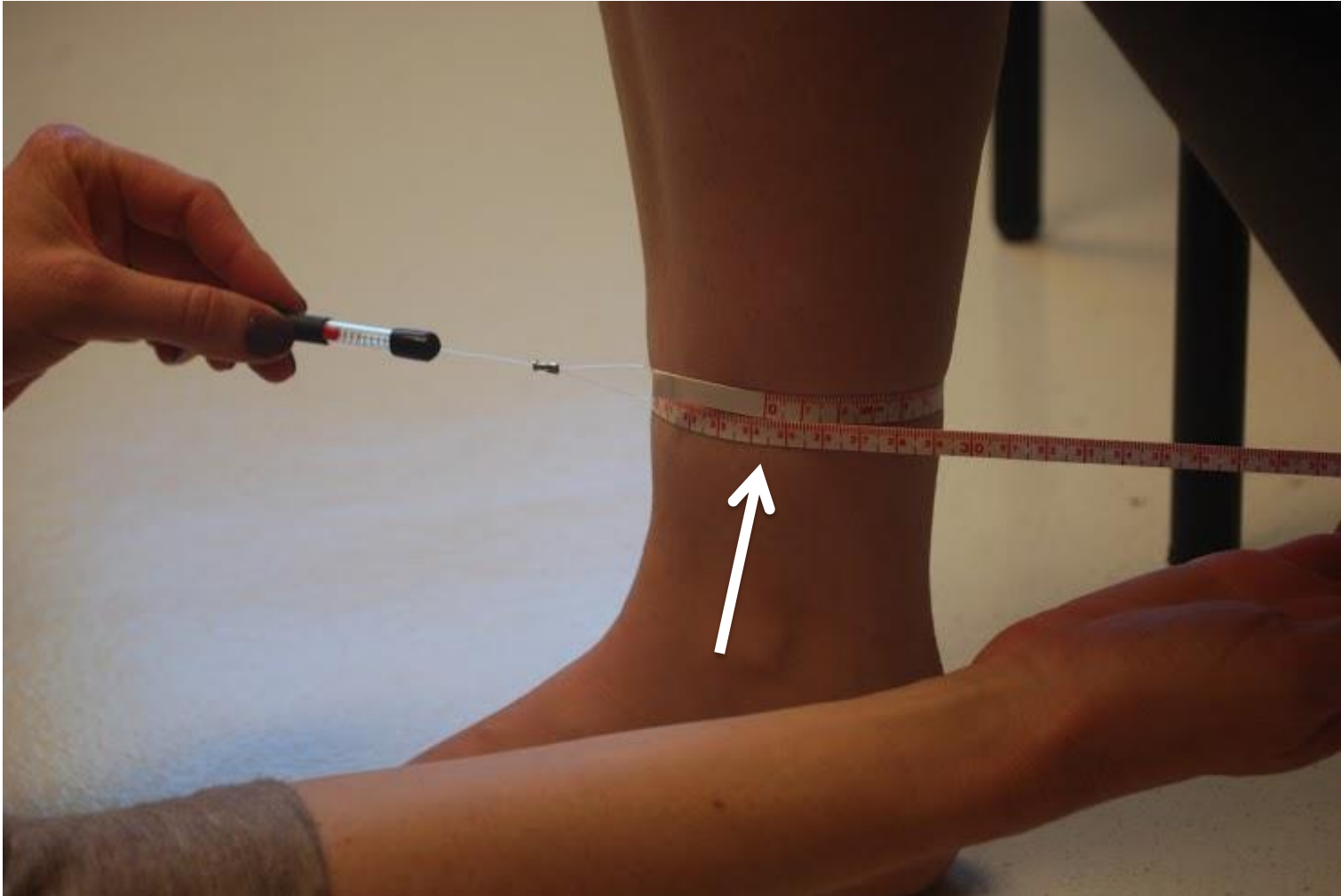


Upper portion of TM
Lower portion of TM

7. Apply appropriate tension- 1 red ball visible



8. Measure in centimeters, record



Tips

- Easiest way: stand on one leg and put other leg on chair
- Knee at 90 degrees as much as possible



Tips

- If can't stand on one leg, have patient sit and extend one leg onto a chair
- If compression stockings, use athletic tape near the 7cm spot, mark with pen

BASE Study

Instructions for Collecting the Urine Sample - Female

Collecting a 24-hour sample of urine is a very important part of this study. This sample will be used to do tests that will help us determine if sodium bicarbonate might be helpful for patients like you.

If you have any questions about how to collect the sample, please contact one of the following people:



Katt Mackin at (801) 587-8547
Megan Varner at (801) 585-2511
Jennifer Zitterkoph at (801) 585-1897
Dr. Kalani Raphael at (801) 582-1565 ext. 1794

Before starting:

Check to be sure you have:

- 1 large orange collection jug
- 1 collection aid (aka “hat”)
- 1 tube of liquid urine preservative
- Pen or pencil



Instructions:

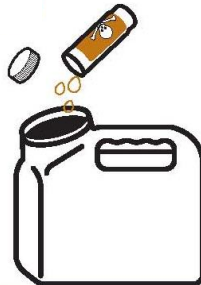
- The urine collection will start the day before your study visit.

My urine collection will begin on _____

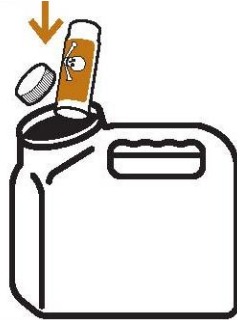
- When you wake up in the morning, flush your first urine in the toilet. **DO NOT** collect this urine.

Please write down the exact time: _____

- Open the tube of urine preservative and empty it into the collection container.



- Drop the urine preservative tube and lid into the collection container. This ensures that every drop of the preservative gets into the container. **Important: When you bring your urine collection to the study visit, the study coordinator will check to make sure the preservative tube and lid are inside the collection container. If they are not, you will be asked to repeat the urine collection.**



- Collect all of your urine into the container over the next 24 hours, including the very first urine the following morning and any urine produced during the night. To perform the collection, place the collection aid (“hat”) over the toilet and then carefully pour the urine into the orange collection container. The first urine collected the following morning is your stop time.

Please write down this exact time: _____

- Bring the orange jug with the lid firmly attached to your study visit.

Appointment Information:



Date: _____

Time: _____

Location: Center for Clinical and Translational Science (CCTS) on the 5th floor of the hospital.

BASE Study

Instructions for Collecting the Urine Sample - Male

Collecting a 24-hour sample of urine is a very important part of this study. This sample will be used to do tests that will help us determine if sodium bicarbonate might be helpful for patients like you.

If you have any questions about how to collect the sample, please contact one of the following people:



Katt Mackin at (801) 587-8547
Megan Varner at (801) 585-2511
Jennifer Zitterkoph at (801) 585-1897
Dr. Kalani Raphael at (801) 582-1565 ext. 1794

Before starting:

Check to be sure you have:

- 1 large orange collection jug
- 1 tube of liquid urine preservative
- Pen or pencil



Instructions:

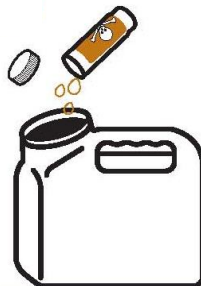
- The urine collection will start the day before your study visit.

My urine collection will begin on _____

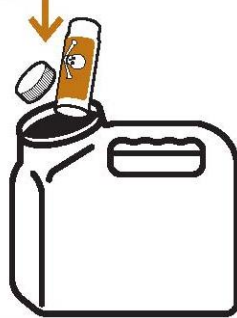
- When you wake up in the morning, flush your first urine in the toilet. DO NOT collect this urine.

Please write down the exact time: _____

- Open the tube of urine preservative and empty it into the collection container.



- Drop the urine preservative tube and lid into the collection container. This ensures that every drop of the preservative gets into the container. **Important: When you bring your urine collection to the study visit, the study coordinator will check to make sure the preservative tube and lid are inside the collection container. If they are not, you will be asked to repeat the urine collection.**



- Collect all of your urine into the container over the next 24 hours, including the very first urine the following morning and any urine produced during the night. The first urine collected the following morning is your stop time.

Please write down this exact time: _____

- Bring the orange jug with the lid firmly attached to your study visit.



Appointment Information:

Date: _____

Time: _____

Location: Center for Clinical and Translational Science (CCTS) on the 5th floor of the hospital.