Section 1: ANCILLARY STUDIES POLICY

Revised July 2015

I. General Policy and Process Overview

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

To protect the integrity of the CRIC Study, such ancillary studies must be reviewed and approved by the Primary and Ancillary Measures Committee (PAM) and the Steering Committee before their inception or submission of a proposal for external funding consideration.

Ancillary submissions are reviewed by the PAM Committee and comments are collated and returned to the Investigator. At that time the Investigator may address any issues and resubmit the proposal for reconsideration.

The ancillary study proposal template is at the end of this document. See section XII for instructions on the submission process. Section XIV details the procedural steps involved in the review.

II. Definition of Ancillary Study

An ancillary study is one based on information from CRIC Study participants, which includes hypotheses, specific aims, anticipated publications and sufficient non-CRIC Study funding to support an investigation or analysis which is relevant to, yet not described in, the CRIC Study protocol. It is anticipated that a typical ancillary study will propose the collection of additional data not collected or analyzed as part of the routine CRIC Study data set. Ancillary studies may be submitted by investigators within the CRIC Study or by investigators without a prior relationship to the CRIC Study. Investigators who are not part of the core CRIC Study must collaborate with a CRIC investigator. Ancillary studies require external funding; there are no funds available for these purposes within the CRIC Study. Examples include studies funded by investigator-initiated NIH research awards (e.g. RO1), grants from academic institutions or private sources (e.g. private foundations, pharmaceutical companies). Ancillary studies must have sufficient funding to cover the costs that may be incurred by the CRIC Study Clinical Centers, laboratories (e.g., to process or ship samples), Reading Centers and the Scientific and Data Coordinating Center (for tasks such as sample selection, preparing and documenting analysis files, participating in statistical analysis, and integrating the new ancillary data into the combined CRIC Study database).

III. Requirements and Procedures for Approval of an Ancillary Study

IIIa. Overview

Participation in, and approval of an ancillary study is subject to review by the CRIC PAM Committee, and formal approval by the CRIC Steering Committee. The role of the PAM Committee is to provide feedback to a potential ancillary study investigator regarding the suitability of the incorporation of their protocol into the CRIC Study, feasibility, potential issues of overlap with existing CRIC Study activities and any concerns regarding the proposed science or methods Feedback about the proposal from the assigned PAM Committee reviewers will be returned to the Investigator for responses prior to circulating for formal Steering Committee vote.

The investigator's response to PAM reviewer feedback will then be circulated back to the reviewers and a final recommendation to approve or reject the proposal will be noted. A formal decision regarding approval of all ancillary studies is provided by the Steering Committee. Approval by the Steering Committee will be defined by seven of nine votes in favor of the proposal. Votes from the Steering Committee will be based on review of the submitted proposal and de-identified versions of the reviews completed by assigned PAM reviewers. Dissenting voters must provide the explicit reason for their dissent. Any issues of concern to dissenting voters will be shared with the applicant and opportunities for clarification provided. In the case of an ancillary study which requires subject participation at **all** sites, a unanimous Steering Committee vote will be required for approval. All sites (Clinical Centers, Scientific and Data Coordinating Center, NIH) agree to cooperate with approved ancillary studies regardless of their individual vote in studies where that center/site that disapproved is not required to enroll subjects.

An ancillary study must receive approval before a grant to support it is submitted. Investigators are encouraged to discuss potential proposals with the Chair or Co-chair of the PAM Committee, or the CRIC Steering Committee Chair prior to submitting a concept proposal. As an increasing number of ancillary studies are reviewed and implemented, the need to manage overlap is occurring more frequently. An important step in the review process is identification of conflicting or overlapping aims with other proposed or approved ancillary studies. When overlap is identified between a newly submitted proposal and an already approved proposal, the degree of overlap will be assessed and classified as minimal, moderate, or insurmountable. To the extent possible, the proposing investigator will be provided with advice as to how their aims could be modified in order to avoid overlap with already approved aims. CRIC will not broker discussions between investigators with overlapping aims. The ancillary studies policy and processes are contingent upon the work of the membership and chairs of both PAM and the Steering Committees. In the event of conflict of interest, the Chair or membership of either committee is expected to recuse him/herself from the approval process. A co-Chair or SDCC delegate can act as a proxy throughout the PAM feedback and Steering Committee vote processes.

All within-CRIC ancillary study proposals must include at least one CRIC investigator as a co-investigator (see section XV for Investigators submitting from outside the 7 Clinical Centers). Willingness to include additional CRIC investigators as co-investigators of the ancillary study is mandatory. If another site wishes to participate in the ancillary study, they should contact the SDCC to facilitate communication with the proposing investigator, with the assistance of the Chair or Co-chair of the PAM Committee, if needed.

III b. Requests for Ancillary Studies as Part of Training or Career Awards

See additional information in section XIV specifically dedicated to this issue. The CRIC Study investigators and the NIH anticipate that the CRIC Study will be an important resource for career development and training among members of the academic community. Special consideration, therefore, will need to be given to requests for ancillary studies to be funded through training grants or career development awards through the NIH or other funding sources. Since these funding mechanisms typically do not provide funding for additional data collection,

such proposals will generally consist of research questions and analyses that could possibly be considered part of the core CRIC Study. In these cases, consideration of what analyses will be authorized could present a conflict with the interests of the CRIC investigators. Evaluation should consider the scientific gain to the CRIC study from the addition of the proposed ancillary analyses as well as the training and career development opportunities afforded to the applicant by the proposed ancillary study. (See section 2 for more information on training submissions).

Evaluation in the case of proposals to be funded through training grants will be limited to trainees of **CRIC study investigators**, to promote quality analyses that will be greatly dependent on the mentor identified in the training grant. All training proposals must identify a CRIC investigator who will have a formal mentoring role on the project. In the case of faculty career awards, evaluation of ancillary study applications will need to consider the anticipated scientific contribution of the applicant, including their ability to perform data analyses that may not be able to be performed at the SDCC without additional funding. Further, willingness to adhere to the requirements of the Publications and Presentations Committee with respect to authorship will be particularly important.

The review process will have two steps. The first step is review of the proposal concept and acceptability by the PAM Committee. The proposal concept should be summarized in 2-4 pages; a template is provided below in Appendix A.

III c. Considerations for Approval of Ancillary Studies

A. Must meet requirement of the highest scientific merit
B. Must not create undue burden - The proposed study must:
    a. be acceptable to the participants (e.g. time, discomfort, privacy).
    b. not interfere with any part of the CRIC Study protocol.
    c. not hamper continued participation the CRIC Study.
    d. put minimal demand on CRIC Study resources such as biological specimens, personnel, and equipment.
C. Must require the unique characteristics of the CRIC Study cohort to accomplish its goals.
D. The investigators must have adequate resources to effectively complete the project, including:
    a. Sufficient financial resources and personnel
    b. Staff who have the requisite expertise to meet the objectives of the project.
E. The ancillary study investigators must agree to provide to the CRIC SDCC any data collected as part of the ancillary study
F. Must not jeopardize the public image of the CRIC Study.
G. Must document involvement of the CRIC investigators as part of the research team.
H. Investigators are encouraged to consider the entire cohort for testing, rather than isolated subgroups, whenever possible to minimize sample handling issues and to provide assay data for the entire cohort.

III d. Instructions for Preparation of Requests for Approval of an Ancillary Study

All proposed ancillary studies must be submitted to the CRIC PAM Committee in time for circulation and subsequent review by the Steering Committee before submission to a funding

agency. It is encouraged for proposals to be submitted four months in advance of the anticipated grant submission deadline. Studies submitted for review less than 8 weeks before a funding application deadline may not receive approval. The following are the elements to be included in an ancillary study proposal.

III e. Proposal Format

Prior to submitting the proposal for the first review within PAM, each Investigator must consider the possible participation of other CRIC centers, if the study involves clinical center participation. There will be times when the study cannot accommodate all interested sites because of budgetary constraints. It is important that adequate communication exists before sites are included/excluded. The Steering Committee will ultimately arbitrate any process in which a dispute arises regarding an ancillary study and site exclusion based on budget (or any other) constraints.

A written request for approval of an ancillary study should be submitted as a two to three page summary to the PAM Committee containing the following information (use the template in Appendix A):

1) Identifiers:
   a) Initiating investigators, collaborators, CRIC Study co-investigator
   b) Planned starting date and project timeline
   c) Funding plans and estimated cost
   d) Anticipated grant submission deadline (if applicable)
2) Design and Methods
   a) Brief background and rationale
   b) Study questions or hypotheses
   c) Specific data collection methodology, including questionnaires and coding forms, if available.
3) Specific answers to the following questions
   a) What is the expected burden to participants? What are the time burdens, discomfort and expected participation rates?
   b) What CRIC Study core data and/or analyses are needed for the ancillary study?
   c) Is blood or other biologic samples (either fresh or from the CRIC Study's repository of stored samples) required?
      i) What quantity of specimens will be needed? Specify time points and number of specimens at each time point.
      ii) What is the desired location for the testing of biologic samples (CRIC Central Lab or other)?
         (1) If the desired location for testing is not the CRIC Central Lab please explain the rationale for choosing this lab and provide a description of the methods of analysis, including the volume of samples required). Additional documentation of laboratory procedures may be requested.
   d) What collaboration with CRIC Study investigators is planned? With whom? Have the collaborating investigators approved the proposal?
   e) What, if any, follow-up is needed? Specify length of time and events to be ascertained.
   f) How many participants are required?
   g) When will data be collected? Could the ancillary study be deferred to a later exam cycle?

h) How will the ancillary study be funded?
   i) Would any additional un-reimbursed work or personnel time be expected of the CRIC Study?
   ii) How will the ancillary study budget cover demands on CRIC Study personnel time and Study resources.
i) Where will the data analyses be conducted?
   i) If data analyses will be conducted outside of the CRIC SDCC an analytical plan must be submitted along with the ancillary study proposal
   ii) If data analyses will be conducted outside of the CRIC SDCC the investigator who will lead the analyses must be identified in the proposal.
j) How will the confidentiality and other aspects of protection of human subjects be maintained?
k) When and in what form will a complete data set be returned to the CRIC Study?

4) Data or Specimen Requirements:
   a) Data needed from CRIC Study analysis files
   b) Specimens needed from CRIC Study repositories or specimens that will need to be obtained prospectively from participants, specifying type and amount
5) Handling of CRIC Study Data and Specimens:
   a) Disposition of stored samples from main study and those processed by ancillary study
   b) Disposition of ancillary study data at the conclusion of the ancillary study
6) A Quality Control plan must be provided for any new data elements that will be generated.

The request should begin ***at least 4 months before the due date*** of the agency to which it is anticipated that the proposal will be submitted. All potential Investigators are strongly encouraged to contact the PAM Committee Co-chairs and the Ancillary Management Team (see Appendix B for contact information) as early as possible in the process (**see Section XII**). The SDCC participates in budget development, and is also helpful in planning study design and analyses.

IV. Changes to A Proposed Study

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 PAM Committee, the SDCC and the CRIC Steering Committee, for review and approval before the proposal is (re-)submitted to a funding agency. Send an email to the Ancillary Measures co-chairs and the SDCC (see appendix B for addresses) with a brief summary of the proposed changes and the revised ancillary study proposal with changes tracked. If the changes are considered to be minor by the co-chairs and SDCC the proposal will be circulated directly to the Steering Committee for a re-vote. If the changes are substantial the protocol will need to be routed anew through the Ancillary Measures Committee.

If any changes to approved aims are made prior to the initial submission, the PAM Committee and the SDCC need to be notified of the changes in advance of grant submission. It if is deemed that there is a change in scope re-approval will be necessary before the grant can be submitted. Approved ancillary study proposals are approved only for the aims described in the

proposals. Expansions of scope in the body of the grant, beyond what is described in the approved ancillary study proposal are not approved.

V. Proposal Budget

The investigator applying for an ancillary study must supply all additional funds needed to successfully complete the study. The PAM Committee will be concerned with both the obvious and the hidden costs to the CRIC Study entailed by an ancillary study. Provision of funds for these expenses is essential – an ancillary study cannot begin without such fiscal support to the core study. The need for such support must be stressed in research grant applications since this support is a mandatory ingredient. Such costs include, but are not limited to:

1) SDCC Costs
    a) Data management effort for coordinating the additional data management and analyses
    b) Statistical staff and investigator effort to conduct additional analyses or verify analyses conducted by the ancillary investigator before publication of results
    c) Investigator and project management effort to implement the ancillary study
    d) Expenses involved in altering key identifying data so that subjects' confidentiality will be protected.
    e) Costs for notification of alert values, if relevant.
    f) CRIC Central Laboratory costs
        i) appropriate lab, storage, freezer and office space
        ii) appropriate lab supplies
        iii) if assays conducted at SDCC, cost of assays
        iv) pulling and aliquotting specimens, if necessary
        v) lab tech effort to receive, track, process, and either order tests or ship specimens for testing
        vi) Oversight of quality of laboratory analyses conducted at labs other than the CRIC Central Lab
2) Costs to participating Clinical Centers
    a) If subject recruitment outside of main exams is anticipated, study coordinator to arrange subject appointments.
    b) Personnel (investigator and staff effort), equipment and supplies necessary to complete the project
    c) Expenses involved in altering key identifying data so that subjects' confidentiality will be protected
    d) If work is to occur on site, rental of appropriate clinic, lab and office space
    e) Transportation costs for subjects, if relevant
    f) Costs for notification of alert values, if relevant

Once a study concept is approved, applicants for ancillary studies must work in conjunction with the SDCC to develop a budget that adequately provides for these types of expenses at both the SDCC and Clinical Centers.

VI. Human Subjects/Data Confidentiality

Confidentiality of CRIC participants must be guaranteed. Individually identifiable data may not be released. A signed consent must be obtained from every participant in the ancillary study, if the data collection/request is not covered in the original informed consent process for the main CRIC Study.

a) Any investigator or personnel having access to CRIC data must abide by the terms indicated in the data use agreement. Key personnel of the ancillary study must be certified in the NIH OHSR or equivalent training course.
b) A copy of the local IRB approval letter for the ancillary study is to be sent to the Scientific and Data Coordinating Center. If a separate consent form is required for the ancillary study, a copy of the signed ancillary study consent form for each study participant must be included in the CRIC Study record.

If requested, a written progress report on ancillary studies must be made periodically to the Steering Committee and the Monitoring Board.

VII. Data Management, Analysis, and Publication of Results of Ancillary Studies

Management of Ancillary Study Data

1. 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 core CRIC study. All data from ancillary studies will be scrutinized for quality and consistency using the same mechanisms that are in place for the core CRIC study (e.g. oversight by the Quality Assurance Committee and the evaluation of data collection techniques by site visit teams).
2. All data from ancillary studies will be made available to the SDCC either on a real time basis using direct data entry into the DMS as established by the SDCC or through frequent transfers of ancillary data to the SDCC. The frequency of these transfers will be established prior to the initiation of any ancillary study and ordinarily would be expected to occur no less frequently than on a quarterly basis. This policy regarding data transfer will not only help to assure the highest quality of data from ancillary studies but will enable the SDCC to track recruitment and follow-up of CRIC subjects participation in ancillary studies. In addition, the format of data transfer to the SDCC must conform to standards compatible with the DMS as defined by the SDCC data management group.
3. All cost associated with the collection, transfer, analysis and oversight of data collected by an ancillary study will be borne by the ancillary study. Budgets in support of ancillary studies must be sufficient to address all of these requirements regarding ancillary study data. Proposals that do not have sufficient budgets to assure these data management activities will in general not be approved.

Unless specifically arranged, all analyses will take place at the SDCC and be conducted under the supervision of its biostatistician-investigators. Under specifically approved circumstances, datasets will be released for analysis by external investigators. When data analyses are to be conducted outside of the SDCC an analytical plan and the biostatistician/ epidemiologist who will lead the analyses must be identified. Ancillary studies funded as career or training awards as well as studies taking place in a subset of clinical centers may be situations in which release of data for analysis deserves special consideration. Under these circumstances, the investigator of the ancillary study will provide interim reports on analyses to the SDCC

during data analysis to ensure that all study data used in analysis of ancillary study results are consistent with data in the main study database and to ensure the quality of analytical approaches. Proposals for manuscripts resulting from all ancillary studies shall be submitted to the CRIC Presentations and Publications Committee and require approval by the Steering Committee 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 as specified in the Publications and Presentations Policy. Each manuscript and abstract would be expected to include a CRIC investigator. The phrase "CRIC Study" should be included in the title in all scientific presentations and manuscripts and listed as a key word whenever possible. Manuscripts will also contain an appendix listing CRIC investigators deemed appropriate.

VIII. Feedback of Results of Ancillary Studies to Participants

Results of ancillary studies shall be reported to participants and/or their physicians if medically useful. Such reporting should follow standard CRIC protocol for notification of participants.

IX. Handling of CRIC Data and Specimens

It is the preference of the Steering Committee for all biologic specimen analysis to be performed at the CRIC Central Lab in order to assure quality measurements and to minimize sample use and distribution. If after discussions with the SDCC, it is not feasible for testing to be performed at the CRIC Central Lab, specific arrangements should be made, including budgeting of adequate funds, with the SDCC to insure adequate oversight of testing done elsewhere. When laboratory testing will be performed outside of the CRIC Central Lab, the laboratory performing the testing must provide information upon request regarding procedures for sample handling, data management and management of specimen identity. A quality control plan for the laboratory testing must also be submitted for review by the CRIC QC Committee.

At the time of distribution of CRIC specimens and/or information, the CRIC Collaborating Investigator, with help from the SDCC, will make explicit arrangements with the ancillary study PI for the security of these study materials, and for their final disposition at the conclusion of the ancillary study. The safety and confidentiality of the CRIC data at the collaborating institution is the responsibility of the ancillary study PI, as is the appropriate disposition of these materials after the study has been completed. Leftover DNA and laboratory specimens are destroyed or returned, and files of CRIC data are returned or deleted, as established at the outset of the collaboration. An archival copy of the newly collected data and/or laboratory results not already held at the SDCC will be sent to the CRIC SDCC at the conclusion of the data analysis and publication of the main (ancillary) study hypothesis. Data should be released to the SDCC sooner if these data are needed for CRIC scientific activities with aims separate from the ancillary studies' specific aims. This transfer is the responsibility of the ancillary study CRIC collaborator(s). Once transferred back to the CRIC Study, these ancillary data will become part of the aggregate CRIC data. Subsequent access to these data will be governed by the CRIC Study Policy on Use of Archived Study Data.

If the submitting ancillary Investigator proposes to have a laboratory assay performed on CRIC serum, plasma, urine or DNA in a lab other than the CRIC Central Lab, it is recommended that the Investigator discuss this in advance with the CRIC SDCC (see Appendix B for contact information). For an assay to be done outside the Central Lab the submitting Investigator will need to submit both adequate documentation of Quality Control methods at the proposed assay site, and sufficient details on how sample processing will be handled (amounts, type, shipping, frequency, etc.) in an appendix to the application.

The CRIC Study Central Lab, PAM and the Steering Committee reserve the right to request preliminary data validating an investigators laboratory method against an external standard. In addition, they may also request outside review by independent experts in the area to certify the QA data presented.

X. Steering Committee Vote

Once the ancillary proposal has been reviewed by the assigned PAM committee reviewers, it will then be circulated among the Steering Committee (PIs from the CRIC Centers, the Steering Committee Chair and the NIH project officer) to place their vote to approve or reject the proposal. If a PI does not vote in the given time frame of two weeks (or in expedited circumstances, 1 week), their vote will automatically be counted as approved. However, in instances that a reviewer recommends rejection of a proposal, all investigators must vote unless there have already been 3 votes to reject. In that case, three votes to reject a proposal meet the standard for disapproving.

XI. Timelines, Investigator Departures and Future Considerations

Upon initial approval of an ancillary study proposal, the investigator must submit the grant no more than six months later than the submission date indicated in the proposal and no more than one year from the date of approval. If the grant is not submitted within this time frame, the aims will no longer be protected for that investigator. If he/she decides to submit the grant for a subsequent funding cycle, the proposal would need to be resubmitted for review and approval by the Ancillary Studies and Steering Committees.

The PAM Committee recognizes that a majority of applications will not be funded in their original form. One particular circumstance is when a career development applicant is no longer active in academics or eligible to receive K funding. In many cases, the previously CRIC-approved K award may be adopted by the mentor and reconfigured into an R application. The PAM Committee reserves the right to reconsider such an application since the criteria for approval of a K award are frequently more flexible than those for an R award

If grant is not funded upon initial submission and the investigator plans to resubmit, they must resubmit the grant within one year of receiving the review and funding decision of the initial grant submission. After two submissions or failure to submit a grant within the specified time frame, the aims will no longer be protected for the investigator. Proposals from investigators who have indicated interest in submitting a grant with overlapping aims will be considered at that time.

Once the approval for a proposal expires, the content area will then be considered to be open to future submissions with no consideration of overlap issues related to the proposal with the expired approval.

XII. Ancillary Submission Processes and Inquiries

1. Ancillary studies should be submitted by email to the SDCC (see Appendix) and the PAM Committee co-chairs. See Appendix B for contact information.

2. Upon request the SDCC can provide information about laboratory testing that has been completed or is planned as well as testing that is supported by the CRIC Central Lab. The ancillary investigator should request information about specific laboratory testing from the SDCC.

3. Investigators may contact PAM Committee Chairs (see Appendix B for contact information) to discuss an ancillary study idea, or submit directly to Ancillary Management team (see Appendix B for contact information) at SDCC with a cc to PAM Committee Chair(s).

4. The proposal is reviewed at the SDCC for completeness and clarity and additional data are requested from the investigator, if needed.

5. The proposal is reviewed by the PAM committee (at least two reviewers evaluate the proposal).

6. Reviews will typically take place within two weeks of being distributed to the reviewers. Feedback will be provided to the investigators without identifying the reviewers. The Ancillary Management Team will send PAM committee reviewer feedback to the investigator (with additional comments if warranted) with a cc to PAM Committee Chairs

7. Investigator will clarify any queries or concerns

8. Investigator will resubmit the proposal to PAM Committee Chair(s) with cc to Ancillary Management Team. PAM Committee reviewers assess responsiveness to PAM queries and annotate this assessment for the Steering Committee.

9. The Ancillary Management Team forwards the reviewer summaries along with the ancillary study proposal to the Steering Committee for approval votes.

10. Ancillary Management Team tallies the votes and communicates the decision to approve or disapprove to the ancillary study investigator.

11. For ancillary studies that are approved, the investigator will be notified by email and an approval letter signed by the Chair of the CRIC Steering Committee (or designee) will be provided. For ancillary studies that are not approved, an email to this effect will be sent to the investigator.

XIV. TRAINING GRANT ANCILLARY SUBMISSIONS:

We recognize the need to both protect the integrity of the core hypotheses and yet provide for research training in junior members of our various institutions. The ancillary submission form is now amended to include a box to check for "Training Proposal" which will alter the philosophy of the review process within the PAM Committee as well as the Steering Committee.

When a Training proposal is submitted, the proposal must identify a CRIC investigator who will have a formal mentoring role on the project. A copy of the CV of the mentor(s) is welcomed, but not necessary.

Since "hypothesis overlap" is likely, if not probable, the proposal should include a paragraph in the proposal dealing with whether, and exactly how, the overlap will be handled. Since this is a process, the 'requirements' for this paragraph are vague, and guidelines for this are necessarily general. The paragraph should acknowledge where overlap exists. When substantial overlap exists, the proposal should explain how this proposal will add to CRIC as well as to the development of the research aim(s). Investigators proposing such proposals are encouraged to contact and discuss these proposals within the PAM committee as well as with the SDCC. We encourage ancillary proposals, and we all want to foster training in nephrology. However, there will be circumstances in which the overlap with primary hypotheses is too large to be considered approvable by the Steering Committee. It is best to discuss the proposals candidly with members of the Steering Committee when this is anticipated. Mentors advising mentees for possible ancillary submissions are encouraged to find creative ways of adding additional value to CRIC without needing to capitalize heavily on existing measurements already designated as core hypothesis areas in CRIC.

When the proposal circulates through the PAM committee, the Training Proposal box tick will generate the following checklist in addition to the usual considerations for any ancillary proposal:

__ Does the hypothesis overlap with core hypotheses in CRIC, and has rationale supporting why the overlap is reasonable been presented?

__ Is the mentor(s) clearly identified and do they appear to possess the expertise and commitment to train the candidate?

__ Will the proposal require resources clearly beyond those typically available in a training award, and does the mentor have such resources available?

XV. ANCILLARY SUBMISSIONS FROM NON-CRIC INVESTIGATORS:

The External Scientific Advisory Committee has recommended to the CRIC Steering Committee that Ancillary Study submissions be encouraged from Investigators outside the 7 Clinical Centers. The same general processes for application apply, but the following points will need clarification in a separate page from any External Ancillary Investigator/Investigative Team(See Template, Appendix A):

Will the proposed ancillary study be conducted:

___ 1) independently of the existing CRIC consortium,
___ 2) with an existing clinical center or centers, or
___ 3) only with the SDCC?

Does the proposed ancillary study involve direct contact with research subjects by Investigators outside the 7 clinical centers?

___ Yes
___ No

Does the local IRB forbid or restrict Investigator access to an existing study without de novo submission to the IRB of a full protocol detailing the project? Are such restrictions limited to direct contact, or do they also apply to stored demographic data and biologic samples? Please explain.

Will the proposal bring resources or expertise outside of those already available? Elaborate on this in the actual proposal.

Template for Ancillary Study Submission.
Appendix A

A. Identifiers: (add or delete lines in tables as needed to answer fully)
(Sections A&B should be no more than 3 pages all together)

PI name & E-mail Address				
Affiliation				
CRIC Investigator				
Collaborators				
Start date				
End date				
Proposed funding source and mechanism				
Target grant submission date:				
Is this a resubmission? If so, how many times has it been submitted previously?				
FOA #				
Estimated costs	$			
Is this a training proposal? (Check one.)	Yes		No	

B. Design and Methods: (add lines in tables as needed to answer fully)
(Sections A&B should be no more than 3 pages all together)

Title of Study:	
Keywords:	
Background/Rationale:	
Research Questions or hypotheses/specific aims:	
Data collection methodology:	

Within your proposed aims, please list exposures and outcomes in the table below: (add lines in tables as needed to answer fully)

Aim	Exposure(s)	Outcome(s)

C. Specifics: (add lines in tables as needed to answer fully)

1. Burden to participants (fill in tables; use N/A if segment not applicable)

If your ancillary uses questionnaires, please provide a copy of each proposed questionnaire with application, or explain reason for not doing so:

Name of questionnaire	Time require to complete questionnaire? (in minutes)	Who completes questionnaire? (Participant, Study Coordinator, Other (specify)	How often is questionnaire given, and at what years of follow-up?	What centers will be doing it?

If your ancillary uses already stored blood or urine:

What test will be done?	What will be collected? Plasma? Serum? Urine? Other (specify)?	Specify the volume of specimen needed?	In what years of follow-up will test be conducted?

If your ancillary needs additional blood or urine please describe:

Name(s) of test(s) to be done on the specimens	Type(s) of specimen(s) to be collected (Plasma? Serum? Urine? Other (specify)?)	Volume of each specimen needed.	Years of follow-up when test will be conducted.	When each specimen will be collected. (At regularly scheduled CRIC visit, or additional?)	Special processing specifications, if applicable	Participating Clinical Centers

Please indicate whether you plan to utilize the following assays, and if so, for which years of the CRIC Study? Please list any additional assays under "Other."

Assay	Year	√	Assay	Year	√	Assay	Year	√
25D			Advanced Glycation Endproducts (AGE)			Apolipoproteins		
B12			B6			BNP		
CBC			C-peptide			Creatinine		
Cystatin C			Electrolytes			Fetuin		
FGF			Fibrinogen			Folate		
HbA1C			Homocysteine			hsCRP		
IL-10			IL-1beta			IL-6		
Inflammatory marker s ICAM			Insulin			Ionized calcium		
Lipid panel (LDL Cholesterol, HDL Cholesterol)			Lipoprotein (a)			Magnesium		
Metabolic panel (Albumin, Bicarbonate, Total Bilirubin, Calcium, Carbon Dioxide, Chloride, Creatinine, Glucose, Alkaline Phosphatase, Potassium, Total Protein, Sodium)			pH			Phosphorus		
Potassium			PTH			Sodium		
TGF-beta			TNF-alpha			Transferrin		
Troponin I			Troponin T			Uric Acid		
Urinary Isoprostanes			Vit C			Vit E		
Vit D			Vit A			Zinc		
Other (Specify):			Other (Specify):			Other (Specify):		
Other (Specify):			Other (Specify):			Other (Specify):		

If your ancillary adds an additional procedure or an additional visit:

Name of procedure/ Reason for added visit	Length of time needed to conduct procedure (in minutes)	Does it need additional visit(s)?	Years of follow-up when procedure/visit will be conducted	Participating Clinical Centers	How many subjects per participating Clinical Center

2. What CRIC Study core data and/or analyses are needed for the ancillary study? (Please check all that apply.)

√	Items:
	Plasma
	Serum
	Urine
	DNA
	Existing data in SDCC
	Newly added data to SDCC (examples: questionnaires, X-Rays) – specify item if not shown/detailed in above tables

3. Describe how blood or other biologic sample (either fresh or from the CRIC Study's repository of stored samples) testing will be done? If testing will be done outside of the Core Lab note this fact and provide the following:
a. Description of plan for receiving samples, sample tracking and identity management
b. Description of plan for thawing and aliquotting (if necessary) samples
c. Description of your QA plan for assays
d. Description of your QA plan for data management related to the assay data

4. **In an effort to ensure that ancillary study measurements and analyses adhere to the highest level of quality expected of a federally-funded study such as CRIC, we ask that ancillary investigators prepare a QA and QC plan for their project. The QA/QC plan should address measures specific to the ancillary rather than core measures from CRIC. This plan must include internally and externally valid metrics of quality assurance, appropriate frequency of measurement, and anticipated corrective actions to address any problems or deficiencies. Commitment should be made to regular reports to the CRIC QA/QC committee for review of the quality data from the ancillary. The details of this plan should be described below:**

Quality metric	**Specific aim/measurement**	**Frequency of assessment**	**Means of assessment**	**Plan for corrective action (in case of deficiency)**

5. Collaboration:

√	Site:	√	P.I.	√	Other Investigator?
	Open to all sites		-----		
	Case Western		Rahman		
	Oakland		Go		
	Maryland		Appel		
	Penn		Townsend		
	Ann Arbor		Ojo		
	Chicago		Lash		
	Tulane		He		
	SDCC		Feldman		
	NIDDK		Kusek		
	Other: (add name)				

6. What, if any, follow-up is needed? Specify length of time and events to be ascertained.

7. How many participants are required?

√	Numbers required:
	All CRIC subjects
	All CRIC subjects at sites as above in #4
	# of CRIC subjects (enter a number)

8. When will data be collected? Could the ancillary study be deferred to a later exam cycle?

9. How will the ancillary study be funded?

i. Would any additional un-reimbursed work or personnel time be expected of the CRIC Study?

ii. How will the ancillary study budget cover demands on CRIC Study personnel time and Study resources?

10. Where will the data analyses be conducted? If data analysis is to be conducted outside of the SDCC, a detailed analysis plan must be submitted and approved. Please also indicate the number of manuscripts that you expect to produce from this project.

11. Will you be collecting genetic data? Approximately how much storage will you need?

12. Will you manage data via your own data management system, with clean data to be transferred to the SDCC for inclusion in the CRIC data warehouse?

13. Under the CRIC policy, you will be required to transfer your data at least quarterly. Will you transfer more frequently?

14. How will the confidentiality and other aspects of protection of human subjects be maintained?

15. If data collection is to be performed separately from the CRIC DMS, how will data be transferred to the SDCC. How often will transfers be made? Investigators should contact the SDCC (via the Ancillary Management Team) to develop a transfer plan.

16. If submitted by a Non-CRIC Investigator

i. Will the proposed ancillary study be conducted: (Check one)
   1. ____ independently of the existing CRIC consortium?
   2. ____ with an existing clinical center or centers?
   3. ____ only with the SDCC?

ii. Does the proposed ancillary study involve direct contact with research subjects by investigators outside the 7 clinical centers? (Check one)
   1. ____ Yes
   2. ____ No

iii. Does the local IRB forbid or restrict Investigator access to an existing study without de novo submission to the IRB of a full protocol detailing the project? (Check one)
   1. ____ Yes
   2. ____ No

iv. Are such restrictions limited to direct contact, or do they also apply to stored demographic data and biologic samples? Please explain.

v. Will the proposal bring resources or expertise outside of those already available? Elaborate on this in the actual proposal.
   1. ____ Yes
   2. ____ No

Appendix B

Ancillary Co-Chairs

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Ancillary Management Team - SDCC

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