Standard Operating Procedures: CFAR Network of Integrated Clinical Systems (CNICS)
Concept Proposal Submission and Review Process

1.0 Introduction

1.1 Definitions

CNICS concept proposals (CP) are summarized research plans that entail access to CNICS resources. CNICS resources that can be requested include data, Epidemiology and Biostatistical Core support, and CNICS specimens.

1.2 Investigators eligible to submit proposals

Any investigator who can be reasonably expected to be able to conduct the proposed work is eligible to submit a concept proposal to CNICS. This includes, but is not limited to, researchers at CNICS sites, CFAR academic centers, non-CFAR academic centers, funding entities, and biotech and pharmaceutical companies. A CNICS investigator is any researcher affiliated with one of the CNICS member institutions who is either a member of the CNICS key personnel group, or a collaborator of such a member. Investigators who do not fulfill this definition can submit proposals to CNICS, but are required to do so in collaboration with a CNICS investigator. Investigators may request advice on possible CNICS collaborators, and the CNICS Research Coordinating Committee (RCC) may identify a CNICS investigator to a given project, if a CNICS investigator was not originally listed. This step is taken to facilitate interactions with external non-CNICS investigators and to provide mentoring with regard to compliance with CNICS policies, procedures, and administrative and logistic requirements. Occasionally, a proposal may be outside of the spectrum of interests of all CNICS investigators, or the nature of the project may be such that direct involvement of a CNICS investigator is unfeasible or unadvisable. In those circumstances, the proposal can proceed through the approval process, but the investigators are required to abide by all CNICS guidelines and policies.

1.3 Data analyses for studies initiated by biotech and pharmaceutical companies

In addition to undergoing the standard concept review process, these analyses, if approved, will be conducted by the CNICS Epidemiology and Biostatistical Core. CNICS data will not be shared with for-profit or third party entities.

2.0 Overview of the review process

2.1 Goals of the review process

The review process seeks to ensure that approved proposals are
a) scientifically sound; b) methodologically viable; c) feasible within the limits of the CNICS resources; and d) not duplicative of ongoing efforts.

2.2 Committee assignment of proposals Major steps in review of a proposal depend on the CNICS resources required by the project. All CPs are reviewed by the RCC and/or focus groups, as well as the Epidemiology and Biostatistical Core. Additionally, CPs that include requests for samples are reviewed by the Specimen Repository Core.

2.3 Review tracks Depending on priority, resources requested, and specific requirements of each project, CPs can be assigned to either of the tracks described below. Determination of the track a proposal is sent to will be made by the RCC at the time of initial triage of the proposal for assignment for written reviews and prioritization.

2.3.1 Routine track: A formal, monthly review process for concept proposals that are submitted in response to topic-specific solicitations, in addition to general

proposals not specific to a solicitation. These may include larger proposals that use multiple sites data, will require significant resources to prepare the data sets and may require time from the Epidemiology and Biostatistical Core 2.3.2.

Expedited track: A fast-track review process for more time-sensitive proposals that do not require a large amount of group resources, including those considered very high-priority and time-sensitive, and some high-priority ad hoc or industry-initiated submissions.

3.0 Quarterly Review Process

3.1 Maintenance of the quarterly schedule

The Administrative Core keeps track of submission and receipt dates of proposals, and allocates each CP to a regularly scheduled monthly RCC review conference call for discussion of the written reviews with the study PI and any co-investigators. The call lasts approximately 30 minutes and includes a 5-minute overview of the study PI followed by general discussion. A CP received within 2 weeks of the next review call may be allocated to the subsequent monthly call, although the RCC and the EC can consider exceptions on a case-by-case basis.

3.2 Periodic solicitations for new concept proposals

Periodic solicitations may be released by the RCC for ideas that address a specific high-priority research area for which the RCC identifies a scientific need or opportunity. The deadlines will generally be set for times that follow major HIV/AIDS-related conferences to take advantage of ideas generated by new findings in the field. It is anticipated that initially four review deadlines per year will be set, although that number may be revised based on volume, scheduling, or scientific need.

3.3 Pre-review and submission of concept proposals

3.3.1 Preliminary input from CNICS investigators. Similar to the process used for NIH grant submissions, proposing investigators are encouraged to seek informal RCC input regarding their research ideas to assess interest, potential overlap with existing proposals and feasibility at an early stage, prior to developing complete concept proposals for formal submission and review. CNICS investigators are reminded that CP that have received final approval for implementation are posted on the CNICS web site and that they should review these postings prior to developing new proposals in order to limit overlap and redundancy.

3.3.2 Preliminary input from the Epidemiology and Biostatistical Core. Based on RCC assignment, the proposing investigator(s) may contact the CNICS Biostatistics Core for preliminary statistical input, which will be subsequently incorporated into the concept proposal document by means of a standardized statistical submission form. The form will include the title of the concept proposal, preliminary design consultation (comparisons of interest, endpoints, data elements considered), estimated sample size, and a brief statistical rationale.

3.3.3 Triaging and prioritization by the RCC. The Administrative Core will submit the CP to the RCC by way of email for designation of the primary and secondary reviewers. This step is the beginning of the actual review process, described below.

3.4 Scientific review of new proposals. Assessment of the scientific merit of a new proposal is the first step in the review process, and it is the responsibility of the RCC. The RCC may seek expertise from established focus groups to provide expertise on focused topics. The RCC will also have the option at the time of the aggregate reviews to encourage investigators or teams that may have submitted

similar proposals or proposals addressing different dimensions of the same research area to work together in the further development of concept proposals that are approved to move forward. Scientific Review of proposals will include a conference call with the study PI and any co-investigators to discuss the written reviews.

Any approved study carries the imprimatur of the CNICS Network, and therefore, implies a certain level of quality. As such, only those proposals possessing the highest scientific merit will be approved as a CNICS study.

3.4.1 Scientific scoring of new proposals. The RCC will make recommendations about the scientific merit, design and relative priority of the proposals. They will also do an initial assessment of overlap of the new proposal with existing approved CNICS projects. The review will conclude with rating the study using the following criteria: yes, without revisions, yes, with revisions, or no, not applicable to CNICS.

3.4.2 Statistical review of new proposals. All CPs will be reviewed for statistical validity and feasibility by the Epidemiology and Biostatistical Core concurrently with the assigned RCC written reviews. Comments from the Statistical Core will be incorporated in the final RCC review letter and discussed during the review conference call.

3.4.3 Approval for proposals requesting repository specimens. Submission to the Specimen Repository Core for review occurs at the same time as submission to the Epidemiology and Biostatistical Core for projects that require it, as outlined above.

3.4.4 Recommendation to revise a proposal. If an idea has merit but some details need revision, such written recommendations will be forwarded to the study PI and co-investigators. The recommended modifications would be made during the study development process and overseen by the RCC. Some proposals may need major, fundamental changes; or two or more proposals should be combined into a single document. The RCC should specify to the proposing investigators whether or not the full RCC needs to review the revised version or whether the leadership can approve the revisions by way of email.

3.4.5 Rejection of new proposals. Concept Proposals that are either less meritorious than the others addressing similar topics or which are not high priority for the Group will be so designated. The RCC will submit a final written summary to the investigator, which will state the reasons for rejection.

3.4.5.1 Appeal of a “not approvable” decision. In the case of appeal, the RCC chair will review the decision to determine whether the appeal has merit and whether the entire RCC should re-review the proposal. The goal is to establish a clearly delineated "stopping point" in order to avoid encouraging automatic resubmission of rejected proposals. Depending on the specific circumstances, the RCC leadership may refer the proposal to the Executive Committee if an investigator requests further analysis of the proposal after detailed review by the RCC.

3.4.6 Coordination and oversight by the RCC leadership. The RCC chair and co-chair will have oversight of the review of all proposals reviewed by each focus group, will receive any comments, and could discuss with the focus group the reasons for final ratings and merits or deficiencies in the proposal

on the regularly scheduled RCC conference calls. All review summaries for those proposals forwarded to the RCC for consideration will be sent after the RCC review and will incorporate the comments from the reviewers and the full RCC review.

3.4.7 Approved proposals. Approved projects require further documentation before samples/data are transferred to investigators.

- For data requests, a Data Request Form is required from the study team. There are no costs associated with the transfer of the data.
- For specimen requests, a completed Specimen Request Form is required**.** **Please note that investigators are required to pay for costs associated with processing and shipment of specimens.
- Local IRB review and approval must be obtained and sent to the CNICS Administrative Director. Available data/specimens will be transferred to investigators upon receipt of approvals.
- Each site will be queried to determine site participation and a site representative for approved studies based on availability of requested data or specimens and ability of a site to participate in a particular study.
- CNICS leaders will participate in the writing group for the approved study and must approve all written manuscripts and abstracts prior to submission for publication or consideration for presentation. The study PI will receive a listing of site leaders for a particular study, which constitute the study's writing group. Problems with writing groups should be addressed to the Administrative Core (UAB) or the RCC.

4.0 Submission and Review of Proposals for Small Studies or Fast Track CP

4.1 Criteria for expedited-track processing. Proposals for small studies, those that may require few data elements or specimens and would need little central CNICS resources will be reviewed on the regular monthly schedule, unless the time-sensitivity and complexity of the proposed work warrant more expedited review, as determined by the RCC chair.

4.2 Processing of expedited-track proposals. The process for fast-track review will allow for solicited or unsolicited concept proposals, which are proposing time-sensitive or very high-priority research that might be scientifically or logistically compromised by waiting for the general submission and review deadlines, to be submitted in intervening time periods with a request for expedited review. Proposing investigators requesting fast-track consideration must provide justification to the RCC chair for such special handling along with their proposals. It will be at the discretion of the RCC chair, together with the chair of the responsible focus group, to determine whether to refer the proposal for routine review or expedited review, depending on the justification provided.

4.3 Limitation in eligibility for accelerated processing. It should be made clear that not all CPs will be reviewed according to this process. The difficulty in coordinating and prioritizing the group's work includes the large number of CP that address similar questions or areas of research; and without the ability to review similar proposals together in an organized fashion, it will be more difficult to prioritize those efforts to avoid multiple analyses aimed at similar ideas.

5.0 Input from the CNICS Executive Committee (EC)

5.1 Incidental review of specific proposals. As appropriate, the RCC may decide that specific concept proposals should be reviewed by the EC to ascertain the feasibility and prioritization of proposed studies at their sites. This action may be taken

particularly with regard to reviews of proposals involving research topics that would require significant CNICS resources or large numbers of specimens.

All proposals from non-NIH funded investigators including investigators from biotech and pharmaceutical companies will also be examined during the review process by the EC to ascertain feasibility, establish prioritization and provide specific advice on the use of NIH resources so they are directed to the highest priority scientific questions.

5.2 **Overall review of approved proposals.** All proposals that have completed the review process, whatever the final decision, will be sent to the EC for review.

- At the time of final reviews, each CNICS site will declare their intention to provide data and/ or specimens for each CP.
- Requests for participation in CNICS writing groups will be sent to applicable site leaders for approved studies.

The EC has final authority over all CPs after careful consideration of the focus group and RCC scientific and priority reviews. In general, the EC will abide by RCC decisions, but can also act as final arbitrator if there are appeals of disapproved CP.