STANDARD OPERATING PROCEDURE: CFAR Network of Integrated Clinical Systems (CNICS) Concept Proposal Submission, Review and Publication Policy

1) Introduction

a) **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.

b) **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 submit a request for a CNICS collaborator and the CNICS Mentoring Core will identify a CNICS investigator to a given project. 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.

c) **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. Investigators receiving any CNICS data agree to request only the minimum data necessary for their approved analyses, to use those data only in conjunction with approved analyses, and to ensure that any data received are completely deleted or destroyed once there is no longer a legitimate need for those data pertaining to the approved analyses. In the event that an investigator is no longer leading an approved analysis, that investigator agrees that either 1) they no longer have a legitimate need for CNICS data and will completely delete or destroy any data they ever received, or 2) that they will obtain written confirmation from CNICS that the responsibility for these data are being transferred to another investigator, and that the newly responsible investigator has signed a CNICS study initiation agreement.

2) Overview of the review process

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

b) **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 Administrative Core, the Research Coordinating Committee (RCC) and/or focus groups, as well as the Epidemiology and Biostatistical Core and the Data Management Core. Additionally, CPs that include requests for samples are reviewed by the Specimen Repository Core.

c) **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 will be made by the RCC at the time of initial triage of the proposal for assignment for written reviews and prioritization.

(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) 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) Monthly Review Process

a) **Maintenance of the monthly 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 by the study PI followed by general discussion. A CP received within 3 weeks of the next review call may be allocated to the subsequent monthly call, although the RCC can consider exceptions on a case-by-case basis.

b) **Pre-review and submission of concept proposals**

(1) Preliminary input from CNICS investigators. Similar to the process used for NIH grant submissions, proposing investigators are encouraged to seek input from their CNICS collaborator 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 CPs that have received final approval for implementation are posted on the CNICS website as ongoing studies and that they should review these postings prior to developing new proposals in order to limit overlap and redundancy.

(2) Preliminary input from the Epidemiology and Biostatistical Core. Proposing investigator(s) may contact the CNICS Epidemiology and Biostatistics Core for preliminary statistical input, which will be subsequently incorporated into the concept proposal document.

(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 begins the actual review process, described below.

c) **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 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.

(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.

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

(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.

(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.

(5) Rejection of new proposals. Although rare, CPs that are either less meritorious than the others addressing similar topics or which are not high priority for CNICS will be so designated. The RCC will submit a final written summary to the investigator, which will state the reasons for rejection.

(i) 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 Leadership if an investigator requests further analysis of the proposal after detailed review by the RCC.

(6) Coordination and oversight by the RCC leadership. The RCC chair and co-chairs will have oversight of the review of all proposals reviewed, will receive any comments, and could discuss with the reviewers the reasons for final ratings and merits or deficiencies in the proposal on the regularly scheduled RCC conference calls.

(7) **Approved proposals.** Approved projects require further documentation before samples/data are transferred to investigators.

(i) For data requests, a Data Request Form is required from the study team. There are no costs associated with the transfer of the data.

(ii) 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. Specimens are not housed in a central repository but at each individual CNICS site so multiple shipments may be required to fulfill a request.

(iii) Local IRB review and approval must be obtained and sent to the CNICS Administrative Core. Available data/specimens will be transferred to investigators upon receipt of approvals.

(iv) Each site will be queried by the AC by a Site Poll 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 designated in the site poll 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. Please see the below ‘Publcation Policy’ for details regarding authorship.

4) Publication Policy Final abstracts, manuscripts, and presentations must be reviewed and approved by the concept study’s writing team before any presentation to a formal scientific meeting or prior to submission for publication. The dissemination of study outcomes must meet CNICS and NIH guidelines.

a) **Writing Team** The writing team is selected by the polling of the site PIs (Site Poll) for the assignment of a site contact. Only sites who are participating in an approved study will be polled. The Administrative Core will conduct the polling and communicate the contact information for writing team members to the

concept study PI. It is the responsibility of the study PI to contact the writing team members to begin the process for collaboration. The writing team will consist of the study PI, the CNICS collaborator/mentor and the site contacts.

b) **Authorship**

(1) Primary investigations will provide the opportunity for at least one named author from each of the participating sites, as assigned by the site PI. The underlying criteria for authorship should be judged as substantive intellectual contribution to the conception of the work as represented by the manuscript, design of the work, analysis and interpretation of the data or other evidence presented in the manuscript; drafting of the manuscript or revising it for critically important content; and approving the final version of the manuscript for publication. Each such author is expected to participate on the writing team and to make substantive contributions to the conception of the work, design of the analysis, interpretation, and content.

(2) Other co-investigators who make substantive contributions to the publication according to the same criteria and who are recommended by the writing team should also be included as co-authors. Primary authorship shall be fairly distributed among each of the collaborating sites; this distribution shall be monitored and promoted by the RCC and the AC. Each site will be offered the opportunity to participate in the committee and sign off on their level of contribution.

(3) Disagreements or problems with individual author participation should initially be addressed with the site. If this fails, formal grievances regarding credit or authorship shall be directed to the RCC and Administrative Core.

c) **Manuscripts**

(1) Co-author(s) constituting the writing team must participate in the writing and/or review process in a timely manner. It is the responsibility of the study PI, in collaboration with the CNICS collaborator/mentor and the members of the writing team to review the manuscript and use co-authors' comments to decide the outcome of the manuscript. Members of the writing team are required to actively participate in the process and provide their approval/disapproval of the manuscript directly to the study PI. If a co-author does not participate, he or she may be removed from the writing team at the discretion of the RCC or the CNICS Leadership.

(2) If a co-author disagrees with a manuscript, or finds the data or analysis misleading, he/she must resolve these issues with the writing group/co-authors. If a co-author still finds fault with the final version, he or she should address these concerns with the lead investigator. The co-author may also indicate his or her concerns with the CNICS collaborator/mentor. If one or more of the co-authors still disagree with the lead author regarding analyses in the paper, he or she may wish to be removed as a co-author.

(3) The use of CNICS data for a purpose for which it was not approved by the RCC or by the entirety of the designated writing team will be consider a misrepresentation of the CNICS data to the scientific research community. Consequences of such actions include a request from CNICS to the study PI to retract a published manuscript and subsequent communication from the Administrative Core to the journal alerting them that the data was used for an unapproved purpose.

d) **Abstracts and Presentations**

(1) Final abstracts and presentations should be developed, reviewed, and approved by the study PI, the members of the writing team and the CNICS collaborator/mentor, in the same manner as described for manuscripts.

e) **Acknowledgements for Primary Investigations**

(1) All manuscripts will acknowledge that the data were collected through CNICS and credit all collaborating cohorts and institutions, including the NIH, by acknowledging the grant support for the network.

(2) Failure to meet targeted deadlines for submission of manuscripts or resubmission of manuscripts to journals is the responsibility of the study PI and is subject to intervention by the RCC. In instances of delinquent responsiveness, inattention, or failure to carry out analyses within the timeframe agreed upon at the time of study approval may result in reassignment of the PI-ship to another investigator. In most every instance, this will only occur after written warning has been issued to the delinquent PI.