

Standard Operating Procedure 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, Statistical 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 generally 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.

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 focus groups, as well as the Statistical Core. Additionally, CPs that include requests for samples are reviewed by the 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 is made by the RCC at the time of initial triage of the proposal for assignment to a focus group and prioritization.

2.3.1 Routine track: A formal, quarterly 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 Statistical 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 maintains a calendar of the beginning and end of each quarterly review cycle, keeps track of submission and receipt dates of proposals, and allocates each CP to a given review cycle. In general, a CP received within 2 weeks of the beginning of the next quarterly review cycle must be allocated to the subsequent cycle, although the RCC and the EC can consider exceptions on a case-by-case basis.

3.2 Periodic solicitations for new concept proposals

The Administrative Core circulates the yearly calendar (generally in October of each year), with deadlines for each quarterly review cycle, among all CNICS investigators. The schedule is also posted for permanent consultation on the CNICS website. All CPs submitted by the quarterly deadline are reviewed in context together. The proposals to be reviewed under this process may be either unsolicited investigator-initiated proposals that focus on specific high-priority research areas of CNICS or proposals submitted in response to a solicitation from 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 Statistics 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 RCC chair will have the flexibility to refer individual ad hoc proposals at "pre-review" to individual focus area sub-committees for either the formal review process or for a fast-track review. Once these decisions are complete, the RCC Chair and/or Vice-Chair (usually within one week of receipt of the CP), submit

the CP to the designated focus group leader, who designates the primary reviewer for the proposal (usually him/herself). 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 focus group assigned by the RCC to each CP. The leadership of the Focus Area Sub-Committee (FAS) may seek outside expertise (e.g., representatives from the other FASs) to include in their committees' formal reviews of focused topics, as a strategy to avoid the creation of additional consultative review groups. The FASs 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. Whenever a proposal cannot be assigned to an established FAS, or a reviewer with sufficient expertise in the area of the proposal is not available, the RCC leadership, or its designate, will take primary responsibility of review of that proposal.

3.4.1 Scientific scoring of new proposals. The FASs 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 include a priority score using the following scale:

<p><i>1.0-1.9= High Priority</i></p> <p><i>2.0-2.5= Moderate Priority</i></p> <p><i>2.6-5.0= Low Priority</i></p> <p><i>Please provide your priority vote for CNICS CP XX as currently written.</i></p> <p><i>Priority vote: _____ (please use the scale provided above)</i></p>
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The priority score is assigned by the vote of the corresponding FAS, on the basis of the primary reviewer's input. A score in the high priority range triggers the subsequent step in the review process (described below). Low priority scores generally prompt a communication to the investigator without further processing of the proposal, until the concerns raised by the FAS are addressed. Moderate priority proposals may proceed to the next step of review at the discretion of the RCC leadership.

3.4.2 Statistical review of new proposals. Unless the FAS determines that a given proposal does not fulfill a minimum standard of quality (discussed below), all CPs will be reviewed for statistical validity and feasibility by the Statistical Core concurrently with the FAS group review. Once the FAS determines that the proposal is acceptable from the scientific standpoint (even if it recommends substantial revisions), the proposal is forwarded by the FAS leader to the Statistical Core for completion of the statistical review.

Comments from the Statistical Core will be incorporated in the final RCC review letter.

- 3.4.3 Approval for proposals requesting repository specimens. Submission to the Repository Core for review occurs at the same time as submission to the Statistical 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, the proposal will be forwarded to the RCC for review and approval, rather than initiating a lengthy correspondence between the FAS and the proposing investigators. The recommended modifications would be made during the study development process and overseen by the FAS and RCC, if the concept proposal is approved by the RCC. However, some proposals may need major, fundamental changes; or the FAS may decide that two or more proposals should be combined into a single document. In such cases, the RCC should specify to the proposing investigators whether or not the RCC needs to review the revised version
- 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 FAS leader will notify the RCC immediately upon reaching a decision that a proposal has received a designation of “not approvable”. If the FAS recommends disapproval of the concept proposal, this will be further discussed on the RCC calls. The RCC will use the draft letter from the FAS to write the final letter 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 FAS 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 EC 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 will receive a list of all concept proposals reviewed by each FAS, will be copied on FAS letters, and could discuss with the FAS leadership the reasons for the priority score and merits or deficiencies in the proposal on the regularly scheduled conference calls. All review letters for those proposals forwarded to the RCC for consideration will be sent after the RCC review and will incorporate the comments from both the FAS and the RCC reviews.

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

- 4.1 **Criteria for fast-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 quarterly 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 fast-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 FAS, to determine whether to refer the proposal for routine review or expedited review, depending on the justification provided.

4.3 Limitation in eligibility for fast-track processing.

It should be made clear that not all CP will be reviewed according to this fast-track 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 Executive Committee 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.

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 final approval. The EC will make final decisions about all CP after careful consideration of the FAS 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. At the time of EC review, each CNICS site will declare their intention to provide data and/ or specimens for each CP. Note that every site does not need to participate in every CP.