Frequently Asked Questions (FAQs) for RFA-HD-21-016: Collaborative Pediatric Critical Care Research Network (CPCCRN) (PL1, Clinical Trial Required)

The following FAQs and answers are related to RFA-HD-21-016.

What is the purpose of this Funding Opportunity Announcement (FOA)?

The purpose of this FOA is to invite applications to form a research network to conduct multisite clinical studies in pediatric critical care medicine. The network is designed to investigate the efficacy of treatment and management strategies to care for critically ill and injured children, as well as to better understand the pathophysiological bases of critical illness and injury in children.

How many sites will be in the network?

The network will include 7 to 12 clinical sites and a Data Coordinating Center (DCC). Each clinical site is encouraged to identify at least one ancillary site (pre-application) to participate in enrolling subjects in the proposed clinical trial (and additional studies, as applicable).

What is the PL1 mechanism and how is it different from the UG1 mechanism and U01 mechanisms used in the previous CPCCRN funding cycle?

A PL1 is a Research Program Project or Center – Linked Center Core Grant. The previous CPCCRN awards used the UG1 mechanism for sites, and the U01 cooperative agreement award mechanism for the DCC, meaning that there was substantial involvement of an NIH project scientist in the research the network conducted. NICHD recently re-evaluated the use of cooperative agreements and decided that the network was well-established in the Pediatric Critical Care community and no longer needed the level of involvement from NIH staff beyond normal program oversight. There is no direct “non-cooperative agreement” mechanism equivalent to the UG1.

The PL1 mechanism is a “group” application in which at least 7 clinical sites, along with a site serving as the DCC, will work together in the pre-application period to develop, at a minimum, a single, shared protocol for the conduct of a large-scale, multisite clinical trial of high priority to pediatric critical care (i.e., the sites will predetermine who will participate in the network based on the submitted application). This process differs significantly from the previous CPCCRN cycles in which investigators submitted individual site applications, and the NIH formed the network from the individual applications that were most well-received.

At the time of the award, the PL1 components will be disaggregated so that each clinical site will be awarded an individual, but linked research project (RL1) grant. The DCC will retain the PL1 grant. Therefore, the DCC Principal Investigator (PI) must be the PI for the overall PL1 application responding to the FOA.

The other significant difference from the previous cooperative agreement mechanisms and the PL1 is that all studies to be conducted as part of the grant must undergo NIH peer review and be included in the initial grant application. Delayed Onset studies are not allowed; however, Delayed Start studies are allowed, as long as they can be completed within the funding cycle and are included in the initial application. Should the network members wish to conduct a study within the CPCCRN, they may seek additional funding from another institute (and possibly NICHD) to conduct that study as long as all costs of the study are included in the awarded funds.

Should current CPCCRN sites submit a renewal application or a new application? Are resubmission applications allowed?

Because the mechanism has significantly changed from the cooperative agreement (UG1/U01) to an investigator-led non-cooperative agreement grant (PL1), all applicants should submit as new applicants. Resubmission applications are not allowed. This is a one-time-only submission.

Can the Multiple PI (MPI) option be used for this application?

Yes, the MPI option may be used for both the DCC and each clinical site.

Can a clinical site be made up of more than one institution?

Yes, more than one institution may come together to form a consortium and submit their application as a single site. The institution submitting the application will be considered the lead institution and that PI will serve as the contact PI. If funded, the NIH will issue a single RL1 award to the applicant institution which will administer the award using the traditional subcontract approach to the other collaborating sites. No additional base funds will be provided beyond the base budget maximum request of $175,000 direct costs per clinical site.

Is a Letter of Intent required? When is it due?

No, a Letter of Intent is not required, is not binding, and does not enter into the review of a subsequent application; however, the information contained in the Letter of Intent allows NICHD staff to estimate the potential review workload and plan the review. The Letter of Intent is due by **July 1, 2020, to Tammara Jenkins** (tjenkins@mail.nih.gov).

The FOA says that NICHD "intends to commit up to $4.3 million in Fiscal Year 2021 to fund one (1) award." Is that the amount for the entire funding cycle or per year? Does the amount span the entire 5 years of the award? Does the amount include indirect (F&A) costs? How does the funding get divided among the clinical sites and DCC?

The dollar amount indicated is the committed funds for FY 2021 to cover all awards (PL1 and RL1s), including direct plus indirect costs. Because future budget years have yet to be approved by Congress, the amounts only represent funds for the initial award year. However, as with other NIH FOAs, the expectation is that comparable funding will be available for the non-competing years of each award.

An applicant for a clinical site may request a budget for direct costs up to $175,000/year, but the total costs for clinical sites in the PL1 application may not exceed $125 million. The grant may fund 7 to 12 clinical sites as long as the total cost for the sites does not exceed $125 million in direct costs. Clinical sites need not request the same amount of funding.

For the PL1 DCC award, there are two financial components: (1) the base award for the DCC, and (2) the patient and protocol funds for distribution to the CPCCRN clinical sites, and for support for required monitoring, a Data and Safety Monitoring Board (DSMB), and the Family Network Collaborative. The DCC base award includes direct plus indirect costs. An applicant for the DCC may request a budget for total costs up to $900,000/year. The required clinical trial must request protocol costs of at least $700,000. Indirect costs are not awarded on protocol costs. Applicants may manipulate the budget as long as the base award is no more than $900,000 and the protocol costs are no less than $700,000 (i.e., the more allocated to protocol costs, the less the DCC base award.) Protocol funds must be commensurate with the proposed work.

The total costs for all components (direct costs and indirect/F&A costs) may not exceed $4.3 million.

I am an appointed study section member with continuous submission privileges. Does that apply to this Request for Application (RFA)?

No. Continuous submission only applies to R01s, R21s, and R34s submitted to FOAs using standard due dates. This RFA does not use any of these mechanisms and does not use standard due dates; therefore, applications are not eligible for continuous submission.

I recently submitted an R01 on the same topic as our CPCCRN application. Can I include any part of that project in the PL1 application?

No. NIH policy states that you cannot have duplicate or highly overlapping applications under review at the same time. (An application is considered “under review” until the summary statement is issued.)

Will the applications be reviewed in a standing NIH study section?

No. This RFA will be reviewed in a Special Emphasis Panel (SEP) convened by the review staff of the NICHD Scientific Review Branch.

The overall component is supposed to address the network function and organization, as well as convey the clinical trial, but is only allowed 12 pages. How can I fit all that information in 12 pages?

The network function and organization, etc., should only be discussed in a broad overall description in the Overall Section (e.g. one paragraph), with the remaining part of the overall component dedicated to the clinical trial.

The majority of the description of the network function, organization, communication, etc., should be included as an attachment in the “Research & Related Other Project Information (Overall)” section. There are two required attachments in that section: (1) CPCCRN Network Organizational Structure, and (2) Population Available for Clinical Research. Each clinical site applicant must describe its pediatric critical care population as directed in the FOA (may include ancillary sites) and disclose any ongoing or pending clinical studies/trials that will limit availability of patients for CPCCRN trials.

Do we have to submit an Additional Research Project? If we do include one, does it have to be a clinical trial? Can we get additional funds for the Additional Research Project?

Additional Research Projects are optional and not required. If the applicants wish, they may submit up to 2 additional research projects. These additional projects may or may not be clinical trials and/or clinical research. The research plan for such projects should be prepared according to the SF424 Guide instructions for the appropriate NIH/NICHD parent FOA, such as an R01, R21 or R03 application.

There are no additional funds available for Additional Research Projects. All costs for such projects must fit within the total PL1 budget of $4.3 million (total costs).

Is the DCC PI required to be a clinician (i.e., physician)? If so, is there any mechanism by which the DCC PI can combine with a clinician so the DCC has co-PIs?

The Eligibility section of the FOA states that the DCC PI applicant ***should*** have clinical experience in pediatrics, critical care medicine, or preferably both. The FOA does not

state the applicant ***must*** have such experience, so such experience is not required. The intent of the preference towards an applicant with clinical experience is to have a network-specific DCC with a PI with extensive experience in conducting clinical trials with critically ill or injured children. Preferably, the PI would have an appreciation of the unique needs of conducting clinical research with this highly vulnerable population and would be knowledgeable about the science of pediatric critical care. Individuals who are not clinicians, but who have demonstrable experience in conducting trials with this population are eligible and will be considered.

MPIs are allowed within this application. Additionally, the FOA requires the DCC PI designate a Senior/Key Person to "direct the DCC in the absence of the PI." These two factors provide a mechanism by which a non-clinician expert may partner with a clinician to apply as MPIs for the DCC on the application. (NOTE: NIH defines "co-PI" as a collaborator, not someone carrying out the role of the PI. The proper term for more than one PI applying together is "Multiple-PI" and requires following the instructions for multi-PI in the SF424 and RFA).

Can an investigator design a trial after the network is underway? For example, submit for an R01 that gets awarded in years 2 or 3, then get the second (or third) trial underway late in year 3?

Yes. The FOA states: *If the Network chooses to do so, it may develop additional studies, solicit external funding and conduct such research throughout the 5-year funding cycle, as long as the external funding provides full funding for the project(s), including infrastructure costs. Ideas for these subsequent studies may come from investigators within the Network, or from the pediatric critical care field at large. All proposed studies must go through the standard peer review process and be selected for funding of all aspects of the study.* The Steering Committee of the network will need to vote to agree to participate in such a study. Additionally, if an additional outside study gets awarded in years 2 or 3, the members of the network will need to agree to continue with the fully funded study for the duration of the study, even if they are not successful for recompetition at year 5 of the network funding cycle. The outside study must not negatively impact the ability to complete the study(ies) originally put forward in the PL1 application.

Will the pre-application technical assistance webinar be recorded and available online?

Yes. Both the slides and the complete recording will be posted on the NICHD Pediatric Trauma and Critical Illness Branch website shortly after the webinar, under the "Highlights" section.

The FOA references the "assurance of cooperation with the policy for capitation of research costs […] from the departmental and institutional offices of sponsored programs." (1) Is it expected that

this assurance is separate from Institutional Letter of Support (CEO/COO)? (2) If so, will both a Departmental and Institutional Assurance letter be required? (3) If so, can the Departmental Assurance be included in the department chair letter? (4) For the ancillary site, is it implied that applicants will need the same assurances as the clinical site or will the Institutional Letter of Support (CEO/COO) be sufficient?

It is expected that the letters of support will come from the Signing Official (SO)/Authorized Organizational Representative (AOR) and have their concurrence. The way it is worded in the RFA is as follows: "Assurance of cooperation with the policy for capitation of research costs should also be provided from the departmental and institutional offices of sponsored research programs." The questioner is interpreting this statement as an addition to Letters of Support. If the assurance is included and clearly stated in the chair letter and has the Sponsored Research Program's Office concurrence, then that should be acceptable. If the SO/AOR wishes to be most transparent, they can submit two separate letters (Departmental and Institutional Assurance, respectively) as long as AOR concurrence is there. The Letters of Support are no different than what is stated in the current RFA. The most important point is that the documents must come from the Sponsored Research Program's Office. Ancillary sites should follow the same instructions, and instructions in the RFA.

Can you confirm that the Facilities and Administrative (F&A) restriction on capitated costs is not just for Patient Care Costs?

The RFA states, "In general, capitation costs are not subject to facilities and administration costs." The intent of this statement is that NIH will not pay F&A costs on the funds that are designated as capitation/patient care costs in the application in order to maximize the available funds for conducting the clinical trial(s)/research project(s). All capitation costs are included in the DCC on the subcontract line and are disbursed to the clinical sites at the DCC's discretion, based on the clinical sites' protocol needs. However, F&A costs will be paid by the NIH on all clinical site base awards and the DCC base award.

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