NIH RECOVER Clinical Trials Research Opportunity Announcement (ROA) Frequently Asked Questions

This document contains triaged questions that have been populated by the NIH or submitted between **May 3, 2022 and May 6, 2022**.

This FAQ review covers the following topics regarding the Clinical Trials Research Opportunity Announcement OTA-21-015H:

1. Application Preparation and Submission

1.1 Q	**The ROA states, "For best consideration, applications should be emailed by May 19, 2022…". We are developing our proposal, but the limited timeframe is making obtaining the necessary documents for subcontracts extremely difficult, any guidance to how to go about this? We are just not sure we can have all subcontracts in time for submission on the 19th. Will applications be accepted after May 19?**
A	Applicants are highly encouraged to submit their applications by May 19, but applications received after May 19 may be considered. A future ROA for clinical trials in children is anticipated.
1.2 Q	**Do I need to submit a full protocol?**
A	The applicant should provide enough information about what would be in the protocol to inform the reviewers, analogous to what would be provided in a 12-pp grant application. The requested information is listed in the ROA.
1.3 Q	**Who will make the final selection of outcomes and interventions?**
A	NIH will make the final decisions informed by consultations with patients, practitioners, researchers and other external experts, and the RECOVER Executive Committee.
1.4 Q	**If multiple intervention clinical trials are being proposed at once, should they be submitted as one multi-component trial, or as multiple separate proposals for each trial?**
A	You may submit one proposal for a multi-component trial, if appropriate to answer the scientific question for each of the components, but may submit multiple applications, if scientifically more appropriate.
1.5 Q	**How much detail should we provide for usual human subjects' sections? Do we need a complete human subjects section and typical NIH clinical trial sections?**
A	The application should contain risks to the participants and what would be appropriate monitoring and risk mitigation procedures.

1.6 Q	**May sites submit more than one application, e.g., a different clinical trial proposal with a different PI?**
A	Yes, institutions may submit more than one application.
1.7 Q	**Are companies able to apply?**
A	For profit companies may apply. Applications must include the information requested in the ROA.
1.8 Q	**Can submitters focus on providing a treatment modality/capability without a clinical trial design (i.e., to be integrated into ongoing RECOVER trials) or does it need to be provided in the context of a clinical trial proposal?**
A	Applications solely proposing an intervention without the clinical trial design would not be considered responsive.
1.9 Q	**Are applications designed to develop improved diagnostics to segregate populations for treatments responsive?**
A	The purpose of this funding announcement is to identify effective treatment strategies for PASC. If the diagnostic is integral to answering the scientific question it may be included.
1.10 Q	**I am reaching out with a question about biosketches. The ROA states biosketches are limited to 4 pages instead of NIH's standard 5 pages. Is a 4-page biosketch indeed a requirement?**
A	Please feel free to use the standard 5-page NIH biosketch.
1.11 Q	**Will there be further opportunities to apply for Long Covid therapy proposals?**
A	Given the breadth of the need and the evolving science, the search for strategies to treat and prevent PASC will be an ongoing endeavor. Applications received after May 19 may be considered, if feasible.
1.12 Q	**How do I apply for OTA-21-015H, RECOVER Clinical Trials?**
A	For best consideration, applications should be emailed by May 19, 2022, to NHLBI_OTA@mail.nih.gov by an authorized business official of your institution. Proposals must be submitted as one single .PDF file and should address the ROA requirements.
1.13 Q	**What is the format of the grant application – more like a study protocol such as that we submit to FDA/ IRB for a clinical trial or more like an RO1 grant with specific aims/research strategies etc.?**
A	No specific format is required, focus on responding to the ROA.
1.14 oQ	**Are budget justification, facilities and environment, and key personnel included in the 50-page limit?**
A	Yes, budget justification is included in the 50-page limit, but the key personnel and facilities and environment are not included.

2. ROA Requirements: Clinical Trials

2.1 Q	**Will there be a firm definition of PASC used to qualify patients for intervention studies?**
A	The definition of PASC is evolving. Each trial may propose specific inclusion/exclusion criteria as appropriate for the research question being proposed.
2.2 Q	**Can an investigational drug that requires monitoring by a manufacturer be integrated?**
A	Yes, NIH encourages collaboration with industry and has mechanisms for doing so.
2.3 Q	**Are trials that have already been initiated eligible for consideration? If a trial is starting imminently, can it still be submitted with retroactive funding?**
A	As noted in the ROA, the CT-DCC is responsible for developing the final trial protocol in collaboration with awardees. The trial may or may not be implemented as it was submitted. Awardees may be asked to work with other awardees in the development of a protocol with multiple interventions. Therefore, a trial protocol must have the flexibility to be modified to be appropriate for this ROA. Funding would be for the work going forward that has not already received funding.
2.4 Q	**If a protocol involves two steps 1) a first step of optimizing an existing device for PASC, and then 2) conducting the trial - would this be responsive to this mechanism?**
A	If the intervention has not been fully developed and ready for testing in a Phase IIb trial or Phase III trial, it is not appropriate for consideration at this time. There are other funding announcements available at NIH that would be appropriate.
2.5 Q	**Since trials are anticipated to start in the 3rd/4th quarter, will trials that test an active drug that takes 6-8 months to formulate be considered? (Which means enrollment would start in 2023)**
A	As our understanding of PASC improves or new interventions become available, NIH will review them and prioritize them for testing. If you have enough information, including a timeline, to design at least a Phase IIb trial, NIH will consider the application responsive to the ROA.
2.6 Q	**What end points will be acceptable? Are patient reported subjective end points acceptable?**
A	Any type of endpoint appropriate to answer the scientific question can be proposed and will need to be justified. This includes patient-reported outcomes.

3. Proposal Budget

3.1 Q	**What is the maximum # of years for the grant award duration under the OTA award? What is the budget limit per year?**

A	Awards issued under OTA-21-015H are not grants and there is no set number of years or budget limit per year. Funding and award period will be driven by the requirements of the protocol parameters and the time it takes to reach completion. We are emphasizing rapid results.
3.2 Q	**The ROA states, "It is anticipated that awards pursuant to this ROA will be issued as sub-agreements under the CT-DCC". Does this have any implications for application and budget preparation?**
A	No, you should follow the instructions outlined in the ROA. In particular, please be sure to consolidate all materials into a single .PDF document. Proposals must be emailed by your institution's authorized business official.
3.3 Q	**For drug repurposing trials, should we budget to buy the drug or try to get the pharma company to donate the drug (IIT)?**
A	The budget for the drug and any placebo should be included. Having funding from the manufacturer is not required but encouraged.
3.4 Q	**Should we include costs of providing compensation to participants in the clinical trial protocol, or will those costs be covered by the CT-DCC?**
A	Yes, you should include proposed patient compensation as a line item in your budget.
3.5 Q	**Are we submitting a budget for this proposal as if our institution was conducting the protocol (i.e., patient care, radiology or drug costs, clinical staff efforts) or directing it (ex. leadership and oversight)?**
A	The CT-DCC will conduct the protocol but the budget in your proposal should include fully justifiable costs for conducting the protocol.

4. Clinical Trials Data Coordinating Center (CT-DCC)

4.1 Q	**The ROA states, "The RECOVER CT-DCC will provide overall project coordination, administration, comprehensive data management, final protocol development, site selection, operational support for the trials including regulatory submissions, study materials and training, safety monitoring, biostatistical support, and rapid results dissemination…". Could you please, clarify how each proposal should plan to perform these functions? Do I need to plan for IRB submissions?**
A	The RECOVER CT-DCC will perform the functions listed in the ROA, including IRB submissions, so these do not need to be included in your budget. However, if there are particular functions or expertise, such as a biostatistical collaboration, that you think are necessary for your proposal, you may put them forward for consideration.
4.2 Q	**The ROA mentions that the RECOVER CT-DCC will provide overall project coordination, including site selection. Does this mean that we don't need to identify potential trial sites, clinicians, and other related personnel, before we apply? I am part of the multi-site study.**

A	The CT-DCC is responsible for selecting recruitment sites and implementing enrollment of study participants. If you are part of a multi-site study and want to propose your collaborators, you may propose them to the CT-DCC for consideration and include them in your application as well as other relevant personnel.
4.3 Q	**If the trial(s) will be finalized and implemented by the CT-DCC, what will be the role of the applicant PI?**
A	The applicant PI brings needed scientific expertise and will have a key role in the final design, execution of the protocol or portion of the protocol with the proposed intervention, and dissemination of the results, including publications. For multi-arm protocols, there will likely be multiple PIs.
4.4 Q	**Can you speak to the requirement for an SAP for the application considering CT-DCC will be providing statistical support?**
A	The reviewers will want to be able to evaluate the feasibility of answering the scientific question, so will need to understand sample size, proposed outcomes, effect size, and general statistical methods. It is not expected for you to provide a detailed SAP.
4.5 Q	**Will the CT-DCC or the investigator handle 1572 for the proposed treatment? Should we budget preparation of 1572?**
A	CT-DCC will handle the 1572 and other site-level regulatory documents.
4.6 Q	**Can we subcontract a CRO for a multi-site study?**
A	The CT-DCC will perform many of the functions of a CRO, so a CRO may not be needed to implement the study. However, if you think your application would be enhanced by proposing a specific role for a CRO, you may do so for consideration.

5. Sites

5.1 Q	**Can investigators from non-RECOVER study sites apply and if chosen will they be able to enroll their patients at their site?**
A	Yes, the announcement is open to all. The CT-DCC is responsible for selecting recruitment sites and enrolling study participants. Applicants may propose sites to the CT-DCC.
5.2 Q	**Can we use an IRO to recruit because we have already established a collaboration with an IRO who has a large database from their COVID-19 testing service for another COVID-19 trial?**
A	If you think your application would be enhanced by proposing an IRO, you may propose it for consideration. The final selection of sites will be made by the CT-DCC.
5.3 Q	**If we want to propose multi-sites and multi-PIs, are we required to include subawards in our May 19 submission? Is it acceptable if we suggest these sites and collaborators and use generic placeholders for subawards that will be finalized during negotiations?**

A	It is acceptable to suggest sites and collaborators but because these sub-awards will be negotiated by the CT-DCC, you will not need a formal letter of support for sites or collaborators.
5.4 Q	**Will the ability to enroll participants/patients at the applicant's own (clinic) site be a review factor?**
A	The reviewers will want to know that the patient population proposed in the trial will be available and willing to participate in the numbers needed to answer the question, whether at your site or others. The CT-DCC will be responsible for selecting the recruitment sites.
5.5 Q	**Can a proposed protocol be implemented at other RECOVER-funded sites?**
A	The CT-DCC is responsible for selecting the recruitment sites and will consider both RECOVER and non-RECOVER sites.
5.6 Q	**What if we have a registry of PASC to recruit from? Are we also able to serve as enrollment sites?**
A	The CT-DCC is responsible for selecting the recruitment sites. Applicants may propose sites to the CT-DCC and can serve as enrollment sites.
5.7 Q	**Does the sample size for which the proposed trial is powered have to only include patients enrolled at the proposing site(s) or can the sample size assume that multiple sites will be involved?**
A	The reviewers will want to know the sample size required to answer the scientific question(s). It is expected that most scientific questions will require more than one site to have an adequate sample size.

6. Miscellaneous

6.1 Q	**Can you explain further what you expect from patient involvement?**
A	Patients may be included in study design and implementation. As described in the ROA, an important component of RECOVER is the active engagement and contribution of people suffering with PASC and their caregivers in the development of the research program. Applicants should provide documentation and a description of processes and ways in which the proposed protocol incorporates patient and other stakeholders input. Additionally, applicants should provide a plan for the ongoing inclusion of patients and caregivers in the development and conduct of the protocol and selection of interventions and outcomes. The final plan for engagement of patients and stakeholders will be developed by the CT-DCC in collaboration with the study PI.
6.2 Q	**What data are collected by the RECOVER m-Health platform?**
A	If you plan to collect data via a m-Health platform, you should indicate in your application what data you would recommend be captured by mHealth and how.
6.3 Q	**Can this mechanism fund add-on studies (PGx etc.) added to ongoing trials?**

A	No, not at this time.
6.4 Q	**Would there be any concerns/considerations about an investigator serving as a co-investigator on one application and a co-primary investigator on a separate/distinct application?**
A	No, there would not be any concerns or considerations for this specific situation.
6.5 Q	**Where can we find the list of the common data elements?**
A	There are many common data elements lists that would be acceptable. Ones used in the RECOVER Observational Cohort are listed in the https://recovercovid.org/ website. Two others can be found here: https://cde.nlm.nih.gov/home or https://tools.niehs.nih.gov/dr2/index.cfm/resource/24250.