Advancing Toward Recovery from Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)

NIH RECOVER Initiative

Technical Assistance Workshop
for Applicants to the RECOVER Clinical Trials Research Opportunity Announcement

May 6, 2022
Zoom Orientation

The graphic below highlights the Zoom Bar features that you have as a registrant.

- **Your microphone is automatically muted.** If you have a question, please submit it via the “Q&A” icon.
- **Chat functionality is unavailable during the webinar.** To ask a question, use the “Q&A” icon.
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- **Click here if you would like to leave the meeting.**
Technical Assistance Webinar (TAW) Overview

Purpose

To enhance potential applicant understanding of the RECOVER initiative, the Clinical Trials Research Opportunity Announcements (ROAs), and to facilitate preparation of responsive applications.

Objectives

- Gain an understanding of the vision and specific objectives of the RECOVER initiative.
- Outline the key scientific & research elements of the ROAs—including the specific research components.
- Review the OTA framework, application process, and requirements.
- Address prospective applicant questions.
## Agenda

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NIH Researching COVID to Enhance Recovery (RECOVER) Initiative on Post-Acute Sequelae of SARS-CoV-2 Infection (PASC)
Overview
NIH RECOVER Initiative

Goal
Rapidly improve our understanding of and ability to predict, treat, and prevent PASC.

Key Scientific Aims
1. Understand clinical spectrum/biology underlying recovery over time.
2. Define risk factors, incidence/prevalence, and distinct PASC sub-phenotypes.
3. Study pathogenesis over time and possible relation to other organ dysfunction/disorders.
4. Identify interventions to treat and prevent PASC.

Guiding Principles
Patient-centered, participants as partners
National scale with inclusive, diverse participation & community engagement
Platform protocols, standardized methodologies, and common data elements
Adaptive approaches based on emerging science

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RECOVER Study Components

**RECOVER Cores**

- Clinical Trial Data Coord. Center
- Clinical Science Core
- Data Resource Core
- Biorepository Core

**Elements**

- **RECOVER Clinical Trials**
  - Clinical Platform with Multi-therapeutic domains
  - ~40,000 participants

- **RECOVER Enrolling Cohorts**
  - ~4 million+ COVID cases

- **EHR/ Health Systems Studies**
  - 60 million+ records;
  - ~4 million+ COVID cases

- **Pathobiology Studies**
  - Mechanistic studies of pathogenesis

- **Tissue Pathology Studies**
  - 50+ tissue types

**Data Resources**

- **Clinical**
- **Imaging**
- **Mobile and Digital Health**
- **EHR / Other Real-World Data**
- **Pathology**

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RECOVER Clinical Trial Development and Design: Critical Inputs

• **Patients** • **Clinicians** • **FDA**
• **Clinical Researchers** • **CMS** • **PCORI**

Phase IIb-III clinical trials that leverage fit-for-purpose design strategies to maximize rigor, efficiency, and flexibility.

- Adaptive platform design and classic RCT as appropriate.
- Frequentist/Bayesian approaches as needed.

Clinical trials developed through a consultative process with engagement of patient, practitioner, and research communities.

Clinical trial proposals solicited from broad research community, OTA-21-015H.

Input from Partners

- Patients
- Clinicians
- FDA
- Clinical Researchers
- CMS
- PCORI

Goal: Clinical trials launched Q3/Q4 2022
RECOVER Clinical Trials Data Coordinating Center (CT-DCC) Overview and Mission
RECOVER Clinical Trials Data Coordinating Center (CT-DCC)

Roles
Support simultaneous multi-intervention platform trials targeting adult and/or pediatric populations, focused on cognitive/behavioral, rehabilitation, complementary alternative medicine, drug, or device interventions.

Operationalized through provision of:

- Program-wide Infrastructure
- RECOVER Clinical Trials Patient Registry
- Clinical Trials Support
RECOVER CT-DCC Responsibilities

**Program Infrastructure**
- Scientific & operational leadership.
- Enterprise-wide project oversight & management.
- QA/QC compliance & auditing.
- Subcontractor & vendor selection and oversight.

**Registry**
- Support participant recruitment, screening, diverse enrollment, consent & assent.
- Coordinate efforts across existing RECOVER and ACTIV platforms for centralized CT access.
- OEC education materials
- Integrate with RECOVER mobile health platform for device data collection.

**Clinical Trials**
- Protocol & study design for approved interventions leveraging an adaptive protocol template.
- Operations: regulatory, study materials & training, site selection & management, pharmacovigilance support.
- Data management leveraging RECOVER CDEs & statistics
- Study reporting.
CT-DCC Relationships with RECOVER

Play a critical role in fostering and coordinating the collaboration across numerous institutions participating in the RECOVER Program, as well as leveraging and integrating associated resources in support of RECOVER Clinical Trials.

Research Resources
- RECOVER Mobile Health Platform
- RECOVER Community Engagement

RECOVER Observational Cohorts

Other Patient Cohorts
- ACTIV Platform Trials
- CONNECTS Trials
- Re-CONNECTS

CT-DCC

Registry
Centralized access to research resources & patient cohorts

CT-ROA

Clinical Trials

RECOVER
- Adaptive Platform Protocol initial design & template
- Common Data Elements integration
- PASC Intervention Prioritization Panel (PIPP)
RECOVER Clinical Trials ROA
RECOVER Clinical Trials Solicitation: Overview

• **Goal:** Well-designed clinical trials to identify safe and effective treatments and preventive strategies for PASC.
  • Protocols to be finalized and executed rapidly in collaboration with the RECOVER CT-DCC.
  • Interventions across multiple domains (registration/non-registration pharmacologic/non-pharmacologic/devices/behavioral health and lifestyle/intervention strategies with an evidence base for addressing other relevant conditions).
  • Diverse trial types are acceptable.
• Awards are anticipated to be issued as sub-agreements under the RECOVER CT-DCC.
• A future ROA is anticipated for trials in children.
• NIH puts high priority on obtaining rapid results and expedited data sharing.
Other Important Provisions

• The final protocol(s) will be developed in collaboration with the RECOVER CT-DCC to align with the guiding principles below.
  • The proposed trial may not be conducted as submitted.
  • Multiple awardees may be asked to work to develop a new protocol that incorporates multiple intervention strategies.
  • Additional interventions may be prioritized and selected by NIH for testing in awarded clinical trials.
• The RECOVER Clinical Trial Data Coordinating Center will provide administrative, data management, monitoring and pharmacovigilance and statistical support across all RECOVER clinical trials, including selection of appropriate sites.
• Evidence of active engagement and contribution of people suffering with PASC, as well as their caregivers, in the development of the research program.

Patient-centered, participants as partners
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National scale with Inclusive, diverse participation & community engagement

Platform protocols, standardized methodologies, and common data elements

Adaptive approaches based on emerging science
Additional

- Strong strategies proposed to address potential implications of participant co-enrollment in the RECOVER observational cohort study and other clinical trials.
- Results of the study will have potential applicability to clinical practice.
Other Transactions Authority (OTA) Discussion
Other Transaction Authority (OTA) Framework

An Other Transaction Authority provides the NIH greater flexibility to identify and engage nontraditional research partners, to engage traditional partners in new ways, and negotiate terms and conditions that will concentrate their efforts, spur innovation, and facilitate collaborative problem solving.

Defined in the negative:
• Not a grant.
• Not a contract.
• Not a cooperative agreement.

Defined in the positive:
• Is an agreement between the government and a legal entity.
• Is used primarily for R&D.
• Is funded from the NIH (usually).
OTA Framework Considerations

Proposal Formatting:

- Proposals must be submitted as one single .PDF file and should address the ROA requirements.

- Unless otherwise specified, you have flexibility to make formatting decisions if the content requirements are addressed.

- Additional content in the proposal such as bio-sketches, appendixes, or letters of support will not count towards page limits.
OTA Framework Considerations

预算和谈判:

• OTA是通过谈判审查和授予的。

• 如果审查结果需要，我们将与您联系讨论。

• 奖金水平基于要求。没有为奖项预设的预算。

• 参考ROA获取具体预算说明，R&R形式推荐但非必需。

• 预计将作为CT-DCC的子奖项颁发。
OTA Framework Considerations

What do we mean by negotiation?

- Unlike with a grant, you can expect that we will work with you to revise elements of what we fund.
- You should aim to propose what you believe you can readily offer at the time of submission.
- The CT-DCC is able to provide multiple services (e.g., sites, statistical services, IRB, DSMB support, etc).
- The application submitted is not your final opportunity to propose elements to be funded.
Submission Information

• For best consideration applications are due by **May 19th, 2022**.

• Submit to [NHLBI OTA@mail.nih.gov](mailto:NHLBI OTA@mail.nih.gov) by an authorized business official of your institution.

• Address financial, administrative, and technical programmatic questions to [NHLBI OTA@mail.nih.gov](mailto:NHLBI OTA@mail.nih.gov).

• Reference **OTA-21-015H** in the title of all inquiries.

Applications will be accepted after May 19th and may be given future review consideration but, at this time, that is not guaranteed.
Q&A

Please Post Questions in the Q&A Box
For any questions related to the Clinical Trials ROA, you can reach out to NHLBI_OTA@mail.nih.gov.

As a reminder, questions that we did not cover today will be shared in an FAQ document.
Closing Remarks & Next Steps
Staying connected with the RECOVER Initiative

Visit the RECOVER Initiative website
https://recovercovid.org/.

View the RECOVER Clinical Trials ROA
https://recovercovid.org/docs/RECOVER_CT_ROA.pdf