RECOVER
Researching COVID to Enhance Recovery

An Initiative Funded by the National Institutes of Health

RECOVER Ancillary Studies Oversight Committee (ASOC)

Proposal Questions

Submission Form for RECOVER Ancillary Studies Proposals (Paper Version)

Note: **This paper version of the Submission Form is for REFERENCE ONLY. Investigators who are interested in submitting a RECOVER ancillary study proposal and/or requesting a letter of support from the ASOC must complete the online submission form.**

Introduction

RECOVER biospecimens are available by request to interested investigators, with associated phenotype data accessible through BioData Catalyst (BDC). In addition, multi-omic data generated by the RECOVER Systems Biology project will be made available to the scientific community beginning in 2025.

Applicants will be asked to justify any potential overlap with existing publications, funded Pathobiology Research Opportunity Announcements (ROAs), and the Systems Biology project. Please refer to Section T of this submission form for more information and to indicate your acknowledgment of any potential study overlap.

A. Lead Principal Investigator (PI) and Associated mPIs

Lead PI *(one individual only, responsible for the proposal)*:

1. First Name:
2. Last Name:
3. Middle Initial:
4. Lead PI NIH Biosketch *(please attach the biosketch as a separate Word Document or PDF*).
5. Will this proposal use a Multiple Principal Investigator (mPI) system?

   ☐ Yes
   ☐ No

6. If this proposal uses an mPI system, then please list the full names of each mPI and provide Biosketch for each:

mPI 1	
mPI 2	
mPI 3	

7. Please indicate if the proposed ancillary study includes a collaboration with a current NIH RECOVER Investigator serving as a co-investigator or mPI in the ancillary study.

   ☐ Yes
   ☐ No

8. If the proposed ancillary study includes a collaboration with a current NIH RECOVER Investigator serving as a co-investigator or mPI in the ancillary study, then please provide the name of the NIH RECOVER Investigator, the investigator's affiliation (name of Hub or core) and e-mail address, and their role in the ancillary study. If there are multiple collaborations with existing NIH RECOVER Investigators, please complete for all such collaborations.

Name	Affiliation	Email	Role

B. Lead PI Contact Information

Note: E-mail address will be listed publicly with other research proposals that are approved

1.	E-mail Address:	
2.	Affiliated Institution:	
3.	Telephone Number:	
4.	Address Line 1 (if applicable):	
5.	Address Line 2:	
6.	Address Line 3:	

C. Areas of Research Expertise Needed for Review of Proposal

Please select the areas of research expertise that are needed for the review of your proposal *(select all that apply)*:

☐ Cardiopulmonary
☐ Immunology and Hematology
☐ Mechanistic Pathways
☐ Metabolic Disorders
☐ Microbiology
☐ Neuropsychiatric
☐ Omics
☐ Other (please describe): _____

D. Plans for Funding

1. Funding mechanism:
2. Do you have existing funding?

   ☐ Yes
   ☐ No

3. If yes, please provide award number:
4. If not, please list the funding mechanism and solicitation you are targeting:
5. Deadline for submission date (if applicable):

E. Title

1. Provide the title of the proposal:
2. *(Optional)* Please attach the mother grant specific aims and research strategy. *Note: not including this could lead to a delay in the final determination.*

F. Hypothesis and/or Specific Aims of the Study

Provide a brief statement ***(maximum 1–2 sentences)*** describing the proposal's main hypothesis. If the proposal has multiple aims, please provide a brief statement for each aim:

G. Background, Significance, and Feasibility

Provide a brief statement summarizing the background, significance, and feasibility ***(maximum 250 words for each)*** of the proposed research.

1. **Background:**
2. **Significance:**
3. **Feasibility:**

H. Study Design, Including Primary Outcomes and Covariates

If this is a clinical study, please use a **CONSORT** (Consolidated Standards of Reporting Trials) flow diagram to delineate study design (including groups for comparison), list the primary and secondary

outcomes of interest for this proposal and requests for modeling these outcomes, any covariates of interest, and any of the main variables that may need to be considered (e.g., for adjustment) in the analysis. *You may attach this as a separate Word Document or PDF file, or include it as plain text in this document.*

I. Need for RECOVER Resources and Justification of Use

Please select the type of RECOVER resources the proposal is requesting to use (*select all that apply*):

1. ☐ Retrospective collection of samples and data
    - ☐ Stored samples and data
        - ☐ Adult
        - ☐ Pediatric
        - ☐ Autopsy
    - ☐ Stored data only
        - ☐ Adult
        - ☐ Pediatric
        - ☐ Autopsy
2. ☐ Prospective recruiting/interaction/collection *(Please specify the types of groups being requested)* **Note:** Prospective studies are allowed only for RECOVER Consortium investigators. _____

J. Phenotype Requirements

(Complete this section only if your request is for stored samples and/or data)

1. Please specify the phenotypes for which you would like samples and/or data by completing the chart below. You can build up to 8 distinct cohorts. For each cohort, specify the infection status [either "Infected: Acute" (infected within last 30 days) OR "Infected: post-acute" (infected >30 days ago) OR "Uninfected"], the PASC status, the number of subjects, list of symptoms, and the time points (you can request any or all of the following): Adult Cohort: baseline, 3-months, 6-mo, 12-mo, 24-mo, 36-mo, 48-mo; Pediatric Cohort: baseline, 8-week (acute cohort only), 6-mo, 12-mo, 24-mo, 36-mo, 48-mo). Adult Cohort time points are calculated starting from the first known infection date or negative test; Pediatric time points are follow-up timepoint based on enrollment date. Please refer to the participant surveys for the specific symptoms that RECOVER captures.

Group	Cohort	Infection Status	PASC Status	# Subjects	Timepoints	Symptom List
Example	Adult/Pediatric/ Autopsy	Infected: Acute	PASC+	20	3-mo 12-mo 36-mo	(list the symptoms)
1						
2						
3						
4						

Group	Cohort	Infection Status	PASC Status	# Subjects	Timepoints	Symptom List
5						
6						
7						
8						

2. Please describe your phenotype of interest:

3. Provide brief justification of the proposed cohort size (number of subjects) inclusive of statistical analysis plan and power calculations:

4. If you are requesting more than one sample type, do you only want to include participants who have all of the sample types requested?

5. If you are requesting samples from multiple timepoints, do you only want to include participants who have samples available at each timepoint?

K. Biospecimen Requirements – Adult

(Complete this section only if applicable)

1. Please specify the biospecimen type *(select all that apply)*:
   NOTE: Specify the minimum sample amount required for proposed assays. In order to distribute samples as widely as possible, we are only distributing the minimum required for proposed assays. Requests for larger volumes per collection event may impact sample availability and could extend processing time.

☐ Plasma
- Specify minimum aliquot volume in microliters (µL): _____
- Specify the treatment type for the Plasma samples by selecting one of the following:
  - ☐ EDTA
  - ☐ Sodium Citrate
  - ☐ Sodium Citrate-CPT
  - ☐ Doesn't matter

☐ Serum
- Specify minimum aliquot volume in microliters (µL): _____

☐ PBMC
- Note: Vials contain 5 million cells on average and cannot be divided. Requests that require multiple vials may require further review.
- Please specify the **minimum** number of cells required _____

☐ PAXGene RNA Whole Blood • Note: Some PAXgene RNA whole blood samples will have already undergone RNA extraction. • Please specify total mass of RNA you are requesting in micrograms (ug): _____
☐ Oragene OGR-600 Saliva • Note: Some saliva samples will have already undergone DNA extraction. • Please specify the total mass of DNA you are requesting: _____
☐ Urine • Specify the minimum required volume in microliters (µL): _____
☐ Stool • Specify the minimum required volume in milliliters (mL):_____
☐ White Blood Cells • Note: Some White Blood Cell samples are having DNA extracted. • Please specify the mass of DNA you are requesting in micrograms (µg): _____
☐ Nasal Cells
☐ Nasopharyngeal Cells

2. Provide minimum required volume/mass and a brief justification of the proposed quantity of biospecimen needed:

3. Please describe the type of assay(s) you plan to perform on each sample type requested. Failure to provide assay description will lead to the proposal being ineligible for review:

L. Biospecimen Requirements – Autopsy

(Complete this section only if applicable)

1. Please specify the biospecimen type *(select all that apply)*:
   NOTE: Specify the minimum sample amount required for proposed assays. In order to distribute samples as widely as possible, we are only distributing the minimum required for proposed assays. Requests for larger volumes per collection event may impact sample availability and could extend processing time.

   NOTE: The RECOVER Autopsy Cohort will generate various histopathological special and immunohistochemical (IHC) stains on select autopsies as a priority outcome for the cohort. A subset of autopsies and tissue blocks have been selected for this project. Sample selection and processing is ongoing and will continue through the remainder of 2025. Ancillary study requests for autopsy samples may be considered, but biospecimen distributions will be delayed through this time period. When feasible, concurrent sample processing can be considered for funded proposals.

☐ Serum • Specify minimum aliquot volume in microliters (µL): _____
☐ Blood Spot
☐ Stool • Specify the minimum required volume in milliliters (mL): _____

☐ CSF Fluid • Specify minimum aliquot volume in microliters (µL): _____
☐ Bronchial Cells
☐ Fresh Frozen Tissue
☐ Formalin Fixed, Paraffin-Embedded (FFPE) Sections • Note: Full, uncut FFPE blocks will not be released. • Please specify minimum quantity needed: _____

2. Provide minimum required quantity (volume, section thickness, etc.) and a brief justification of the proposed quantity of biospecimen needed:

3. Please describe the type of assay(s) you plan to perform on each sample type requested. Failure to provide assay description will lead to the proposal being ineligible for review:

M. Biospecimen Requirements – Pediatric

(Complete this section only if applicable)

1. Please specify the biospecimen type *(select all that apply)*:
   NOTE: Specify the minimum sample amount required for proposed assays. In order to distribute samples as widely as possible, we are only distributing the minimum required for proposed assays. Requests for larger volumes per collection event may impact sample availability and could extend processing time.

☐ EDTA Plasma • Specify minimum aliquot volume in microliters (µL): _____
☐ Serum • Specify minimum aliquot volume in microliters (µL): _____
☐ Blood Spot (Tasso) • Specify minimum number of sponges: _____
☐ PBMC • Note: Vials contain 2 million cells on average and cannot be divided. Requests that require multiple vials may require further review. • Please specify the **minimum** number of cells required _____
☐ Oragene OGR-600 Saliva • Note: Some saliva samples are having DNA extracted. • Please specify the mass of DNA you are requesting in micrograms (µg) _____
☐ White Blood Cells • Note: Some White Blood Cell samples will have undergone DNA extraction. • Please specify the mass of DNA you are requesting in micrograms (µg) _____
☐ Red Blood Cells
☐ PAXGene RNA Whole Blood • Note: Some PAXgene RNA whole blood samples will have already undergone RNA extraction. • Please specify total mass of RNA you are requesting in micrograms (µg): _____

2. Provide minimum required volume/mass and a brief justification of the proposed quantity of biospecimen needed:

3. Please describe the type of assay(s) you plan to perform on each sample type requested. Failure to provide assay description will lead to the proposal being ineligible for review:

N. Data Requirements

(Complete this section only if applicable)
Data availability can be determined using the BioData Catalyst PIC-SURE.

1. Please describe the data that you need for your study:

2. Provide brief justification of the request for data:

O. Participant Recruitment/Interaction Requirements (Allowed only for RECOVER Investigators)

(Complete this section only if applicable)

1. Will you be recruiting existing RECOVER participants or participants not currently enrolled in RECOVER? *(Select all that apply)*
   - ☐ RECOVER participants
   - ☐ Participants not currently enrolled in RECOVER

2. What will you ask the existing RECOVER participants to do? *(Select all that apply)*
   - ☐ Collect additional samples (Please describe):
   - ☐ Collect additional data *(Please **describe**):*
   - ☐ Other *(Please **describe**):*

3. Please state the proposed cohort size (number of subjects) for RECOVER participants:

4. Please provide brief justification of the proposed cohort size (number of subjects) for RECOVER participants:

5. Please state the proposed cohort size (number of subjects) for participants not currently enrolled in RECOVER:

6. Please provide brief justification of the proposed cohort size (number of subjects) for participants not currently enrolled in RECOVER:

P. Inclusion and Exclusion Criteria

(Complete this section only if applicable)

1. Briefly describe the proposal's cohort inclusion and exclusion criteria. Refer to the protocol as needed to describe these criteria.

2. List the RECOVER enrolling site(s) from which participants will be recruited (Note: RECOVER participant recruitment is allowed only for RECOVER investigators).

   ☐ I want to recruit from a single RECOVER site *(please **provide the name of the site** you want to recruit from):*

   ☐ I want to recruit from multiple RECOVER sites *(please **provide the names of all the sites** you want to recruit from):*

Q. Protection of Human Subjects Plan

(Complete this section only if applicable)

Provide a brief description of the risks, benefits, consent process, and protection against risk, making particular note of approaches for vulnerable subjects. If applicable, please describe the safeguards that will be put in place to reduce or prevent participant burden.

R. Patient or Community Engagement

1. Please indicate whether you conferred with patient communities, such as a community advisory board or a group of patients, on your proposal. If you would like more information about engagement with Community Representatives, please contact RECOVER_ACC@rti.org.

   ☐ Yes

   ☐ No

2. If you did confer with patient communities on your proposal, then please provide more details regarding (1) at what point during the study development period did you choose to consult with patient communities, (2) the composition of the patient community you conferred with, and (3) examples of how you assessed and implemented patient feedback into your proposal:

3. If you did **not** confer with patient communities on your proposal, then please provide more details, such as justification for why patient/community consultation was not obtained, or a brief description of plans to include patient/community consultation in the future:

S. Additional Study Impact

Please indicate whether this study will require new/additional testing or new/additional data collection. If so, then what are the measures being proposed to minimize site/staff burden?

T. Study Overlap

1. RECOVER maintains a list of consortium publications, and research summaries on a subset of these publications. Additional perspectives from expert presenters are available via recordings of presentations from the RECOVER Research Review Seminar Series. Are you aware of any significant overlap between your proposed study and the current RECOVER studies?

   ☐ Yes *(**Please provide details** to justify this overlap, such as how your proposal is complementary to the studies or promotes necessary replication):*

   ☐ No

2. Please refer to the list of funded RECOVER pathobiology awards available at recoverCOVID.org. Are you aware of any significant overlap between your proposal and any of the funded RECOVER pathobiology awards?

   ☐ Yes *(**Please identify** the funded RECOVER pathobiology awards that your proposal overlaps with, and please provide details to justify this overlap):*

   ☐ No

3. The RECOVER Systems Biology project will generate omic data via the Trans-Omics for Precision Medicine (TOPMed) program. A subset of adult participants at timepoints with sufficient biosamples (i.e. plasma, buffy coat, and RNA Paxgene tube) for processing and available symptom data have been selected for omics. A subset of Pediatric participants who have agreed to Tier 2 promotion, have sufficient samples (i.e. plasma, buffy coat) for processing and available symptom data have been selected for omics. **Note:** RNA Paxgene collection for the Pediatric cohort started in July 2024, and transcriptomic data may not be available until 2026. Generated omic data will be made available to the scientific community starting in 2025. Additional information about requesting data access will be provided at a later date.

Omic data to be available through the BDC

Omic	Sample Source	Platform	Number of Timepoints	
			Adult	Pediatrics
Metabolomics	Plasma	Metabolon	18,000	6,000
Proteomics	Plasma	5000 PLEX	18,000	6,000
Epigenetics	Buffy Coat (DNA)	Epic V2-935K	9,000	3,000
Genomics	Buffy Coat (DNA)	Illumina 30x	9,000	3,000
Transcriptomics	Paxgene (RNA)	Illumina 75M Reads	18,000	6,000

Are you aware of any significant overlap between your proposal and RECOVER Systems Biology Study? **NOTE: Proposals which duplicate data generated in the RECOVER Systems Biology Study without sufficient justification will not be considered.**

☐ Yes *(**Please provide details** to justify this overlap, such as how your proposal is complementary to the study or promotes necessary replication):*

☐ No

U. References

List relevant literature citations; maximum of 10

1 _____

2 _____

3 _____

4 _____

5 _____

6 _____

7 _____

8 _____

9 _____

10 _____