DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

September 14, 2021

The Honorable Anna G. Eshoo
Chair
Subcommittee on Health
Committee on Energy and Commerce
U.S. House of Representatives
Washington, DC 20515

Dear Chair Eshoo:

Thank you for your letter expressing your ongoing commitment to addressing post-COVID conditions, also known as post-acute sequelae of SARS-CoV-2 infection (PASC). NIH is grateful for the Congressional appropriation for PASC research and has designed a comprehensive research initiative to substantively improve the understanding of and ability to treat and prevent PASC. I share your sense of urgency for addressing this public health challenge and appreciate this opportunity to inform you about NIH's considerable progress with the initiative, now known as RECOVER (REsearching COVID to Enhance Recovery).

Before addressing the specific questions in your letter, I am pleased to inform you that tomorrow, I—along with colleagues working diligently on the RECOVER Initiative—will announce the next set of RECOVER awards. The awards provide the RECOVER Clinical Science Core at New York University (NYU) Langone Health additional funds of nearly $470 million to establish a national study population of diverse research volunteers and support large-scale studies on the long-term effects of COVID-19. With these funds, NYU will be making multiple sub-awards to more than 100 researchers at more than 30 institutions across the country.

In your letter, you asked a series of questions about the RECOVER Initiative. The responses are below. Please note that questions 1 and 2 are addressed together as the strategy and timeline are relevant to both questions.

1) **On April 28th you testified that NIH received 273 responses to your call for research proposals and intended to make awards in the next three weeks. It has now been more than two months since the awards were expected. When does NIH anticipate announcing the remaining awards for ROA OTA-21-015A and ROA OTA-21-015B? How many awards are expected?**

2) **In your testimony, you stated that "intensive laboratory and imaging studies should be underway by summer," but as of July 30th these awards have yet to be made. What is the timeline for these studies to be initiated?**

At the end of May, NIH made awards to New York University to serve as the RECOVER Clinical Science Core (CSC) and to Massachusetts General Hospital to serve as the Data Resource Core (DRC). These awards provide the critical infrastructure for RECOVER. In June, the DRC made

a subaward to establish the PASC Biorepository Core (PBC) and enable PBC Principal Investigators to participate in the development of the RECOVER master protocols.

Funds for PBC operations will be awarded in the next few weeks, and this will complete the selection of Cores solicited by OTA-21-015A.

You also asked about the status of OTA-21-015B, which solicited applications for the SARS-CoV-2 Recovery Meta-cohort (a "cohort of cohorts" that comprise the collectively diverse research participants in the Initiative); the associated Investigator Consortium (cohort leaders and other experts who develop and implement master protocols to screen and evaluate research participants and contribute to multidisciplinary analysis of data); and Electronic Health Record (EHR)/Real World Data (RWD)-based studies.

These are central elements of the RECOVER Initiative and are important means for addressing fundamental scientific questions about PASC, including its incidence/prevalence, epidemiology, clinical spectrum, risk factors, and outcomes.

To achieve the goals of OTA-21-015B, there must be development of master protocols that will guide the clinical assessments conducted across the Recovery Cohort. In June 2021, short-term subawards were made to more than 30 cohort-proposing institutions and three institutions proposing EHR/RWD-based studies—selected through a rigorous merit review process—to support their participation in a multidisciplinary collaboration to develop common master clinical protocols for the study of adult, pregnancy, pediatric, and autopsy populations. The completed protocols will now undergo review by the RECOVER Observational Studies Monitoring Board, as well as Institutional Review Board evaluation. With the master protocols completed, the Recovery Meta-cohort is in the process of being assembled. Over the next few weeks, subawards will be made to the more than 30 institutions that participated in the above-cited protocol development to implement the master protocols.

This strategic, phased approach to cohort development and funding has enabled assembling a cohort of cohorts with the diversity, geographic reach, and age range necessary to inform the understanding of the various manifestations of PASC and its clinical course. It also enabled formation of a multidisciplinary consortium of awardees that are fully aligned to generate and collectively analyze a statistically meaningful and robust evidence base for understanding, treating, and preventing PASC. By using this approach, coupled with milestone-based funding, NIH is enhancing the ability to obtain meaningful answers for patients while reducing costs and risk to the government.

3) **On June 10, 2021, NIH stated "we anticipate subsequent calls for other kinds of research, in particular opportunities focused on clinical trials to test strategies for treating long-term symptoms and promoting recovery from infection." What details can you provide on NIH's strategy for this additional research as part of the RECOVER initiative? When do you anticipate funding these activities?**

The comprehensive and inclusive composition of the Recovery Cohort and the expertise represented in the Investigator Consortium lay the foundation for studies of pathobiology that in

turn can rapidly inform the design of the treatment, prevention, and longitudinal follow-up strategies that are central to the purpose of RECOVER. The Investigator Consortium and other experts will be designing flexible master clinical protocols for the trials, which will likely need to utilize an array of approaches, including pharmacologic and non-pharmacologic interventions, assessed individually or in combination. We anticipate beginning research studies to better understand long COVID this fall. These studies will pave the way for evolving hypotheses to test through RECOVER clinical trials within the next 12-18 months.

4) **Given the urgency of the Long COVID crisis, why has there been such a significant delay in awarding the funds that Congress appropriated to NIH for this critical research? Has NIH's strategy for this initiative changed? What roadblocks has NIH encountered and how can Congress help ensure that this does not continue?**

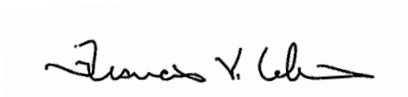
I hope that after reading about the ongoing activities and steady progress in the very complex and ambitious RECOVER Initiative, it is clear that NIH is moving forward with a carefully considered and rigorously planned approach as expeditiously as possible, while concurrently implementing the most rigorous science and appropriate stewardship measures. Again, on September 15, 2021 we will announce additional and substantial awards that position a platform upon which these measures can be executed.

Also, I want to emphasize that one of the key features of RECOVER is the development and use of harmonized master protocols by the Investigator Consortium. This harmonization encompasses scientific aims, clinical tests and procedures, and data structure across cohorts using common terminology and data management and data analysis plans. Development of the protocols was accomplished in record time by the Investigator Consortium. Rather than launching multiple small studies using different methods and terms, our goal has been to launch a harmonized study of national scale that is adaptable and in which all RECOVER investigators speak the same "language" in conducting cross-disciplinary, systematic clinical assessments. This approach will enable rapid generation of statistically significant and broadly generalizable findings and the creation of a national harmonized data and specimen resource that can be utilized by researchers worldwide to better understand, treat, and prevent PASC.

Given how much we have yet to learn about PASC, it is important to note that as the science evolves, it may require us to adjust research directions, increase the number of participants in the Recovery Cohort, and launch additional exploratory trials.

Once again, I appreciate your interest in this vitally important initiative and look forward to providing additional progress reports. NIH would be happy to set up a briefing if you have additional questions.

Sincerely yours,



Francis S. Collins, M.D., Ph.D.
Director