Compiled Public Comments on NIH Virtual Meeting and Listening Session on USG Oversight Framework for Research Involving Enhanced Potential Pandemic Pathogens

April 26, 2022 – April 27, 2022

Public Comments:

1 Nariyoshi Shinomiya, National Defense Medical College (Japan)

2 Edwin Kite, University of Chicago

3 Marc Lipsitch, Harvard University

Submission Date: 4/26/22

Name: Nariyoshi Shinomiya

Name of Organization: National Defense Medical College (Japan)

Comment:

I believe that this conference on Potential Pandemic Pathogens (ePPPs) will provide very important insights into the future of infectious disease-related research. As for me, I would like to raise the following comments:

Regarding the fourth Key Question of the session 2, “How can the research community promote open and honest communication about research involving ePPP?” :

In light of the context of open communication, dialogue and discussion on research involving ePPPs should proceed in an open and transparent manner by keeping pace with international discussions, which include those on the Biological Weapons Convention. This includes in view of the prevention of not only accidental leak (lab safety, influence on public health) but also focusing the true value of the research and its possibility of misapplication.

In this sense, it is necessary for researchers to be honest about the content of their research and to demonstrate not only its significance but also how it has contributed to society as a result, and above all, it is necessary to disclose the process of the research itself in a transparent manner. It is also necessary to be able to verify the research process in retrospect by others.

This comment is submitted by Nariyoshi Shinomiya, President of the National Defense Medical College, Japan on behalf of his research group

Thank you very much for your help in advance. I hope the meeting will be a very fruitful one.

Submission Date: 4/27/22

Name: Edwin Kite

Name of Organization: University of Chicago

Comment:

I hope you are well. This email is public input on the review of limits on ePPP research. I'm an associate professor of planetary science at the University of Chicago.

NASA quantifies low-probability, very-bad-outcome-for-the-public events in at least two contexts: (1) launching many kilograms of plutonium on top of rockets that infrequently explode (NASA-mission nuclear launch approval procedure); (2) returning samples to Earth that might contain life that is harmful to our biosphere, with a special focus on the upcoming Mars Sample Return (Category V Planetary Protection procedure, a.k.a. "back-contamination" of Earth). In both cases, judgement calls are required to quantify the risk, and both the plutonium containers, and Mars sample return canisters, are designed with redundancy to prevent unintended release. Nevertheless, the quantitative flow-through helps to identify the extent to which further limits / risk reduction is necessary. Even an order-of-magnitude quantitative estimate can help to navigate to the line between excessive conservatism and unwarranted risk-taking.

With NASA's examples in mind, perhaps NIH might quantify the risks associated with a future unintended laboratory biosecurity incident leading to a pandemic (e.g., arguably, the 1977 Russian flu), in the context of ePPPs.

The NASA-mission nuclear launch approval process (including quantification) is described in https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.ida.org%2F-%2Fmedia%2Ffeature%2Fpublications%2Fl%2Fla%2Flaunch-approval-processes-for-the-space-nuclear-power-and-propulsion-enterprise%2Fd-10910.ashx&data=05%7C01%7Cirene.cheng%40nih.gov%7C8a3d47518b5343c4705408da29325172%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C637867593329073473%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=LbP1H5sD2sUU3WjdJcvqIkuTkuC2O2SMCGrVSyDpCIU%3D&reserved=0

NASA's planetary protection officer is Nick Bernadini James.N.Benardini@jpl.nasa.gov https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fsma.nasa.gov%2Fsma-disciplines%2Fplanetary-protection&data=05%7C01%7Cirene.cheng%40nih.gov%7C8a3d47518b5343c4705408da29325172%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C637867593329073473%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=QX9MTXLdSZfiktSoF2aoCDV%2FmJXkg%2BLmp1quTUVq7lY%3D&reserved=0 .

Best wishes,

- Edwin

p.s. I serve on the National Academies Committee for Astrobiology and Planetary Science, and can put you in touch with people who led National Academies reviews of various aspects of NASA planetary protection (e.g., https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fnap.nationalacademies.org%2Fread%2F9895%2Fchapter%2F1&data=05%7C01%7Cirene.cheng%40nih.gov%7C8a3d47518b5343c4705408da29325172%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C637867593329073473%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=%2Fyohw3BD8n3IdH8G0QGCCJubs0KilRZypbQLUI8J4wY%3D&reserved=0).

Submission Date: 4/27/22

Name: Marc Lipsitch

Name of Organization: Harvard University

Comment:

Thank you for the opportunity to provide written comments. I have attached them in the form of a letter to you. Please let me know if there are any concerns about the format.

Additional Comment (attachment):

HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH
Department of Epidemiology

April 27, 2022

Lyric Jorgenson, PhD
Acting Associate Director for Science Policy &
Acting Director of the Office of Science Policy
National Institutes of Health

Dear Dr. Jorgenson:

I regret that I am not able to attend the meeting today on the current oversight framework for research involving enhanced potential pandemic pathogens (ePPPs), for which I received two weeks' notice. In lieu of virtual attendance, I wish to offer the following written comments. I write in my capacity as a private citizen, epidemiologist, and Professor of Epidemiology at Harvard TH Chan School of Public Health.

In January 2020, Dr. Thomas Inglesby and I published in the American Society for Microbiology journal *mSphere* an article (freely available at https://journals.asm.org/doi/full/10.1128/mSphere.00990-19) entitled "Proposed Changes to U.S. Policy on Potential Pandemic Pathogen Oversight and Implementation." In it, we called for several changes to the policy related to transparency, a stated principle of the December 2017 guidance: "To the maximum extent possible, agencies' enhanced PPP review mechanisms should provide transparency to the public regarding funded projects involving the creation, transfer or use of enhanced PPPs." Specifically, we recommended for transparency and accountability:

- "the HHS review should make public who participates in the review, as well as the basis of the decision that the research is acceptable to fund, including the U.S. government's (USG's) calculation of the potential benefits and risks of the proposed enhanced PPP research."
- Ensuring that "the majority of the experts assembled for this work are free of institutional conflict of interest (e.g., employment by the funding agency or its parent or sister agencies), a goal most readily achieved by using experts from the academic or nonprofit sectors."
- "approval of state public health authorities (or local designates, as appropriate) should be required for enhanced PPP experiments"
- "the substance of the deliberations should also be public."
- "this kind of risk assessment, including any dissenting views, should be published in advance of the provision of any funding of the experiments."
- That HHS should "require a high-level official, such as the NIH director or HHS Secretary, to approve" ePPP research.

Center *for* Communicable Disease Dynamics

677 Huntington Avenue Boston, MA 02115 Tel: 617-432-7955 Fax: 617-566-7805

With respect to publication and resource sharing we recommended:

- "When enhanced PPP work is performed with USG funding, special consideration should be given to policies on resource sharing and related issues, to prevent the sharing of enhanced PPPs or the reagents to create them if such sharing could itself create an unacceptable biosafety or biosecurity risk. In cases of research approved under the HHS P3CO Framework, the presumption should be against resource sharing, in contrast to ordinary science where the presumption (or even requirement) is in the other direction."
- "Best-practice guidance should be developed to encourage responsible actions by non-USG funders and by publishers of scientific journals. Such best practices should be institutionalized, for example, according to the precedent of NIH recombinant DNA guidelines, which apply to research at institutions receiving federal funding for recombinant DNA work and their collaborators, regardless of the direct source of the funds for the specific research in question." Specific best practices are noted in the article.

With respect to international action, we recommended executing on the promise of the January 2017 document: "the US government should engage with other countries about policies concerning creation, transfer and use of enhanced PPP, encouraging the development of harmonized policy guidance."

Notwithstanding the disruption caused by the COVID-19 pandemic, which understandably diverted attention to other issues, these needs remain as pressing as ever. I note that many of them, and related ones, have been reiterated recently in a letter of April 19 to Secretary Becerra from the Ranking Members of the House Committee on Energy and Commerce, the Subcommittee on Health, and the Subcommittee on Oversight and investigations. These all remain my concerns as well.

In addition, since the writing of the article with Dr. Inglesby, several other concerns have arisen.

- First, it remains unclear what algorithm, checklist, or other procedure is used to flag proposals judged scientifically meritorious for P3CO review. It is stated at https://www.phe.gov/s3/dualuse/Pages/ResearchReview-PPP.aspx (dated September 27, 2021) that three proposals have been reviewed under P3CO. However I have been told in a private conversation by one investigator that they had had more than that number reviewed. Perhaps this was a misunderstanding, but I would ask if there is more than one level of review and perhaps the three are only those that have undergone "full" review.
- Second, the identity of reviewers and other details of the review has been withheld citing "personal security concerns, according to the a press release by House Republican members of the Energy and Commerce Committee, here: https://republicans-energycommerce.house.gov/news/ec-republicans-want-answers-on-secretive-nature-of-hhs-researchs-review-process/ . What is the basis of these concerns?
- Third, the process for initiating review in mid-funding cycle when unanticipated results or alterations to the planned research raise novel P3CO concerns has not been discussed, to my knowledge. While I have no well-formed view about whether such a procedure, if extant, would have been triggered for a recently publicized case, it is imperative that such a procedure should exist, as the nature of science is such that our view of the risks posed by studies will evolve as those studies produce results.

On a procedural note, I would urge that you do more than has been done for this meeting to provide early and widespread notice and to ensure the representation of a wide range of viewpoints among the speakers when a topic of this gravity is being discussed.

In summary, the events of the pandemic have put the spotlight on the disastrous consequences that an infectious disease can produce. This should only redouble our focus on ensuring that our regulatory framework maximizes opportunities to prevent accidental or deliberate release of an agent from a laboratory – both to protect the safety of the population and to inspire confidence that public support for science, critical for progress, is being used responsibly. I would urge the NIH and HHS to act on these recommendations without delay.

Sincerely,

Marc Lipsitch, DPhil
Professor of Epidemiology
Director, CCDD