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ONE HUNDRED SEVENTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

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October 31, 2022

Lawrence A. Tabak, D.D.S., PhD.
Acting Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

Dr. Tabak,

As Republican leaders on the committee in the U.S. House of Representatives with jurisdiction over public health, we write regarding concerns related to research that involves a project on monkeypox virus enhancement conducted at the National Institute of Allergy and Infectious Diseases (NIAID). The NIH project number that includes this experiment appears to be *Poxvirus Host Interactions, pathogenesis and immunity*, 1ZIAAI000979.[1] The Principal Investigator of this project is Dr. Bernard Moss of NIAID.

The project involves transferring genes from "clade 1" or Congo Basin clade monkeypox virus (a rare version of monkeypox virus that is 1,000 times more lethal in mice than the version currently circulating in humans) into "clade 2" or West African clade monkeypox virus (the version currently circulating in humans). Information about the specific experiments became known in a September 2022 SCIENCE article on NIAID work on monkeypox. In particular, the article detailed the following about the project:

> Evolutionary virologists have instead concentrated on the influenza virus, HIV, and other small viruses whose genomes consist of RNA. Poxviruses, by contrast, are made of DNA, and are much larger and more complex. With roughly 200,000 nucleotides and 200 genes, the monkeypox genome is more than 20 times the size of HIV's. It's not clear what many of those genes do, [Dr. Bernard] Moss says, let alone how they interact with each other or how changes in any of them might affect their impact on humans.

[1] NIH RePORTER, Project Details, *Poxvirus Host Interactions, pathogenesis and immunity*, 1ZIAAI000979, https://reporter nih.gov/search/Dm7t3Wqn0k-MLTGNZf3t2g/project-details/10482754. The specific experiments to transfer genes from clade 2 monkeypox to clade-1 monkeypox virus are not mentioned in the abstract, being one of many specific experiments being performed in a large project with a 30-line project summary.

> Moss has been trying for years to figure out the crucial difference between two variants of monkeypox virus: clade 2, which until recently was found only in West Africa and is now causing the global outbreak, and clade 1, believed to be much deadlier, which has caused outbreaks in the Democratic Republic of Congo for many decades. He's found that clade 1 virus can kill a mouse at levels 1000 times lower than those needed with clade 2. To find out why, Moss and his colleagues swapped dozens of clade 2 genes, one at a time, into clade 1 virus, hoping to see it become less deadly, but with no luck so far. Now, they are planning to try the opposite, endowing clade 2 virus with genes from its deadlier relative.[2]

It appears that the project is reasonably anticipated to yield a lab-generated monkeypox virus that is 1,000 times more lethal in mice than the monkeypox virus currently circulating in humans and that transmits as efficiently as the monkeypox virus currently circulating in humans. The risk-benefit ratio indicates potentially serious risks without clear civilian practical applications. Based on available information, this experiment would seem to involve risks reasonably anticipated to create, transfer, or use potential pandemic pathogens (PPPs) resulting from the enhancement of a pathogen's transmissibility or virulence in humans (enhanced PPPs). Under the circumstances, we are interested in learning whether this experiment was reviewed under the HHS P3CO (Potential Pandemic Pathogens) framework used to review risky research proposals. We recently received a letter from HHS implicitly confirming that the HHS P3CO review committee has been inactive since 2019, without any indication that the Biden administration is reactivating this committee. (See attachment). Nevertheless, it is important to know whether NIAID itself conducted any internal review on this issue.

Further, human disease associated with clade 2 or West African monkeypox virus infection is less severe and is associated with less than one percent mortality, whereas clade 1 or Congo Basin monkeypox infection has a 10 percent case fatality rate in unvaccinated persons.[3] Because of its significantly greater lethality, Clade 1 or Congo Basin clade monkeypox viruses are regulated as select agents by the Federal Select Agents Program. Entities that possess, use, or transfer this agent must comply with the HHS Select Agent and Toxin Regulations unless there is an applicable exemption or exclusion.[4] Thus, under these regulations, it would appear the clade 1 monkeypox virus experiment is a restricted experiment that must be reviewed by the Federal Select Agent Program, and may be further reviewed by the CDC's Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC).[5]

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[2] Kai Kupferschmidt, *Moving Target: The global monkeypox outbreak is the virus an unprecedented opportunity to adapt to humans. Will it change for the worse?* SCIENCE (September 16, 2022), https://www.science.org/content/article/will-monkeypox-virus-become-more-dangerous

[3] Christina L. Hutson, *et al*, *Dosage Comparison of Congo Basin and West African Strains of Monkeypox Virus using a Prairie Dog Animal Model of Systemic Orthopoxvirus Disease*, 402 VIROLOGY 72-82 (2010). https://www.sciencedirect.com/science/article/pii/S0042682210001650?via%3Dihub

[4] Federal Select Agents Program, Select Agents and Toxins. In 42 CFR Part 73, 42 CFR § 73 United States Department of Health and Human Services, Ed. 2005. *See also* C.D.C./U.S.D.A. Federal Select Agent Program, *SA Grams: Monkeypox Reporting Requirements*, (October 4, 2022) https://selectagents.gov/resources/sagrams/2022.htm

[5] C.D.C./U.S.D.A., Federal Select Agent Program, *Restricted Experiments Guidance: Request to Conduct a Restricted Experiment*, (last reviewed August 27, 2020), https://www.selectagents.gov/compliance/guidance/restricted/conduct.htm

In light of these concerns over the adequacy of NIH's oversight of risky research involving a federal select agent, please provide the following by November 14, 2022:

1. All proposals and progress reports discussing the clade 1 monkeypox virus experiment (clade 1 study).
2. For NIH award 1ZIAAI000979, please provide a copy of the grant terms.
3. When did the clade 1 experiment start? Is the experiment ongoing? If not, when did it stop? If ongoing, what is the status of the experiment?
4. What review did this research undergo at NIH? Who reviewed the research proposal? What was the basis of the review decision?
5. What are the risks from this research?
6. What are the benefits from this research?
7. What is the potential benefit to human health from this research? Is there an aim to find a treatment or vaccine?
8. Any correspondence related to whether the clade 1 study should be referred to P3CO review.
9. Was the clade 1 study referred for P3CO review? If not, why not?
10. Was the clade 1 study referred to the Federal Select Agent Program for review? If not, why not? If so, was the clade 1 study further reviewed by the ISATTAC?
11. Why must clade 1 genes be transferred to clade 2 genes? Why not delete the genes from Clade 1 to determine effects on virulence?
12. A copy of the submission on the clade 1 study sent to the NIAID Institutional Biosafety Committee (IBC) or to an NIH IBC.
13. What is the biosafety level of the facility being used for the clade 1 experiment? What biocontainment measures are being taken with this experiment?

If you have questions about this correspondence, please contact Alan Slobodin of the Minority Committee Staff at 202-225-3641.

Sincerely,

Cathy McMorris Rodgers
Republican Leader
House Committee on Energy and Commerce

Brett Guthrie
Republican Leader
Subcommittee on Health

H. Morgan Griffith
Republican Leader
Subcommittee on Oversight and
Investigations

CC: The Honorable Frank Pallone, Chair, House Energy and Commerce Committee
The Honorable Anna Eshoo, Chair, Subcommittee on Health
The Honorable Diana DeGette, Chair, Subcommittee on Oversight and Investigations

DEPARTMENT OF HEALTH & HUMAN SERVICES

Administration for Strategic Preparedness and Response

Assistant Secretary for Preparedness and Response
Washington, D.C. 20201

The Honorable Cathy McMorris Rodgers
Ranking Member
Committee on Energy and Commerce
2322 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Brett Guthrie
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2322 Rayburn House Office Building
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The Honorable H. Morgan Griffith
Ranking Member
Subcommittee on Oversight and Investigations
2322 Rayburn House Office Building
Washington, D.C. 20515

Dear Ranking Members Rodgers, Guthrie, and Griffith:

Thank you for your letter regarding the U.S. Department of Health and Human Services' (HHS) Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (P3CO Framework). We appreciated the opportunity to brief your staff on this framework as well as your continued interest in this issue.

The HHS P3CO Framework (accessible via https://www.phe.gov/s3/dualuse/Documents/P3CO.pdf) is intended to guide funding decisions on proposed research that is reasonably anticipated to create, transfer, or use enhanced potential pandemic pathogens (PPP). The HHS P3CO Framework is responsive to and in accordance with the Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/p3cofinalguidancestatement.pdf) issued by the White House Office of Science and Technology Policy (OSTP P3CO Policy Guidance). The framework outlines a strategy for a layered review to be performed on enhanced PPP research both at the funding-agency and the department-level. The framework describes a robust multidisciplinary, pre-funding review process that considers the potential scientific and public health benefits, biosafety and biosecurity risks, and appropriate risk mitigation strategies to help inform agency decisions.

Per the HHS P3CO Framework, HHS is to periodically re-evaluate and modify the P3CO review process, as necessary, to reflect scientific advances and changes to the regulatory landscape. To help inform such evaluations, and to enhance transparency and public engagement in the review and oversight process for enhanced PPP research, HHS has convened the National Science Advisory Board for Biosecurity (NSABB), a federal advisory

committee that provides expert advice, guidance, and recommendations to the U.S. Government (USG) on biosecurity oversight of dual use research, to conduct such a review (note that the list of NSABB voting members is available at https://osp.od.nih.gov/biotechnology/national-science-advisory-board-for-biosecuritynsabb/#members). The Board provides broad and diverse expertise, and its deliberations and recommendations have informed the USG's policy development on biosecurity for more than 15 years. The NSABB was first charged in January 2020 with providing recommendations on balancing security and public transparency when sharing information about enhanced PPP research, but due to the rapid escalation of the COVID-19 pandemic, the activities of the NSABB were paused to allow members to prioritize COVID-19 research response activities at their home institutions. The NSABB was re-engaged in February 2022 and, as part of its current charge, is evaluating the scope and effectiveness of the current oversight framework for research involving enhanced PPPs, including the OSTP P3CO Policy Guidance and the HHS P3CO Framework.

Under the HHS P3CO Framework, proposed research that is being considered for funding by the HHS funding agency, is deemed to be scientifically meritorious by an independent internal or external review process and has been determined by the funding agency to be reasonably anticipated to create, transfer, or use enhanced PPPs must be referred for HHS department-level review. This review is carried out by a group ("HHS P3CO Review Group") comprised of individuals who represent key federal agencies and Departments. Members of the HHS P3CO Review Group leverage multidisciplinary expertise and perspectives from across the U.S. government to review proposed research that meets the scope of enhanced PPP research. Department-level review is specified to be multi-disciplinary and pre-funding, and accordingly disciplines represented on the panel include scientific research, biosafety and biosecurity, medical countermeasures, public health preparedness and response, public health policy, law, and ethics. All HHS P3CO Review Group members serve as subject matter experts (SMEs) in an advisory capacity to provide information and perspectives to the committee to assist HHS in its deliberations. Some members of the review group will change in order to have the best SMEs for a given topical area under consideration. In order to provide transparency regarding members, HHS provided the names of the HHS employees on the HHS P3CO Review Group to the House Energy and Commerce Committee on January 14, 2022. Names were provided to staff for review in camera due to security concerns surrounding the release of member names. Notably, the ethics expert on the latest review group was not from HHS, and, as such, did not appear in that list.

To date, the HHS P3CO Review Group has reviewed three different research proposals. Information about the reviews can be found on HHS's Sciences, Safety, and Security website at https://www.phe.gov/s3/dualuse/Pages/ResearchReview-PPP.aspx. Information about all NIHfunded research projects is available on the NIH Reporter at https://reporter.nih.gov, an electronic tool that allows users to search a repository of

NIH-funded research projects. For each of these reviews, the individuals asked to serve as SMEs on the HHS P3CO Review Group has varied depending on the proposal under review.

Thank you for your interest and questions on the HHS P3CO process and overall investments in research to support pandemic preparedness and response. Please let me or my staff know if further information is needed related to the HHS P3CO review process.

Sincerely,

Dawn O'Connell