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Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

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March 30, 2023

Lawrence A. Tabak, D.D.S., PhD.
Senior Official Performing the Duties of the NIH Director
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

Dr. Tabak,

Having not received a formal response to our letter dated October 31, 2022, and pursuant to Rules X and Xl of the U.S. House of Representatives, we request documents and information related to research that involves a project on monkeypox virus enhancement planned and/or conducted at the National Institute of Allergy and Infectious Diseases (NIAID). The National Institutes of Health (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.[2] 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

[1] 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.

[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.

> 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.
>
> 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.[3]

According to the *Department of Health and Human Services (HHS) Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens (HHS P3CO),* a potential pandemic pathogen (PPP) is defined as "a pathogen that satisfies both of the following: (1) It is likely highly transmissible and likely capable of wide and uncontrollable spread in human populations; and (2) It is likely highly virulent and likely to cause significant morbidity and/or mortality in humans."[4] An enhanced PPP is defined as "a PPP resulting from the enhancement of the transmissibility and/or virulence of a pathogen."[5] Enhanced PPPs do not include naturally occurring pathogens that are circulating in or have been recovered from nature, regardless of their pandemic potential."[6] The HHS P3CO is "intended to guide HHS funding decisions on individual proposed research that is reasonably anticipated to create, transfer, or use enhanced PPPs," and "ensures a multidisciplinary, department-level pre-funding review and evaluation of proposed research meeting the scope outlined herein to help inform funding agency decisions."[7]

Based on the available information, it appears 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. Accordingly, this experiment would seem to involve risks reasonably anticipated to create, transfer, or use PPPs resulting from the enhancement of a pathogen's transmissibility or virulence in humans. Thus, under the circumstances, we are interested in learning whether this experiment was reviewed under the

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[3] 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

[4] HHS Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens, 2017, https://www.phe.gov/s3/dualuse/Documents/P3CO.pdf.

[5] *Id.*

[6] *Id.*

[7] *Id.*

HHS P3CO framework used to review research proposals posing significant biosafety or biosecurity risks.

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.[8] 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.[9] 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.[10] 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 Centers for Disease Control and Prevention's (CDC's) Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC).[11]

In light of these concerns over the adequacy of NIH's oversight of research posing a significant risk of biosafety and biosecurity risks, and involving a federal select agent, please provide the following by April 13, 2023:

1. All proposals and progress reports discussing the clade 1 monkeypox virus experiment (clade 1 study).
2. All documents related to the planning of the clade 1 experiment.
3. All documents related to NIH award 1ZIAAI000979.
4. The date that the clade 1 experiment was proposed. If not available, why was the experiment planned per Dr. Moss' comments and then dropped? When was the plan or conduct of the clade I experiment discontinued? If the experiment proceeded, when did the experiment start?
5. Is the clade 1 experiment ongoing? If not, when did it stop? If ongoing, what is the status of the experiment? All documents relating to the discontinuation of the clade 1 experiment.

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[8] 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

[9] Select agents are biological agents and toxins that have been determined to have the potential to pose a severe threat to public health and safety, to animal and plant health, or to animal or plant products. *See* 42 C.F.R. Part 73, https://www.ecfr.gov/current/title-42/chapter-I/subchapter-F/part-73. Monkeypox virus is listed as an HHS select agent and toxin. 42 C.F.R. §73.3.

[10] 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

[11] "The entity's Responsible Official (RO) should submit any request to conduct a restricted experiment through eFSAP. FSAP will review the request. HHS only 42 CFR § 73.3 or overlap 42 CFR § 73.4 and 9 CFR § 121.4 select agents may be further reviewed by CDC's Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC)." 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

6. What review did this research proposal undergo at the NIH? Who reviewed the research proposal? What was the basis of the review decision?
7. What are the risks from this research?
8. What are the benefits from this research?
9. What is the potential benefit to human health from this research? Is there an aim to find a treatment or vaccine?
10. All documents related to whether the clade 1 study should be referred to P3CO review.
11. Was the clade 1 study referred for P3CO review? If not, why not?
12. 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? If not, why not?
13. Why must clade 1 genes be transferred to clade 2 genes? Why not delete the genes from Clade 1 to determine effects on virulence?
14. A copy of the submission on the clade 1 study sent to the NIAID Institutional Biosafety Committee (IBC) or to an NIH IBC.
15. All documents related to NIH DURC review process for the clade 1 experiment.
16. All documents related to the CDC's ISTATTAC review and approval process for the clade 1 experiment.

In addition, the Committee believes testimony from NIH officials and employees about these, and related matters will be necessary. Please contact Committee staff to identify appropriate personnel and schedule videotaped, transcribed interviews.

Finally, this letter serves as a formal request to preserve all existing and future records and materials in NIH's possession relating to the topics addressed in this letter. You should construe this preservation notice as an instruction to take all reasonable steps to prevent the destruction or alteration, whether intentionally or negligently, of all documents, communications, and other information, including electronic information and metadata, that are or may be responsive to this congressional inquiry. This instruction includes all electronic messages sent using official and personal accounts or devices, including records created using text messages, phone-based message applications, or encryption software.

An attachment to this letter provides additional instructions for responding to the Committee's request.

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

Sincerely,

Cathy McMorris Rodgers
Chair
Energy and Commerce Committee

Brett Guthrie
Chair
Subcommittee on Health

H. Morgan Griffith
Chair
Subcommittee on Oversight and Investigations

cc: Frank Pallone Jr., Ranking Member, Energy and Commerce Committee
Anna Eshoo, Ranking Member, Subcommittee on Health
Kathy Castor, Ranking Member, Subcommittee on Oversight and Investigations