

Update on Federal Policy Development for Gain-of- Function Research

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Certain Gain-of-Function Studies Raise Safety and Security Concerns

The debate regarding gain-of-function (GOF) research has centered around **a specific subset of GOF studies** that involve the **generation of pathogens with pandemic potential**.

- **Dual use/biosecurity issues:** Do the studies generate information that could be utilized to create a potentially human-transmissible virus that, in the wrong hands, could be intentionally released to threaten public health and security?
- **Biosafety issues:** Could the engineered pathogens accidentally infect a lab worker or be released into the environment?

Policy questions

- *Should such research findings be communicated? If so, how can they be responsibly communicated?*
- *Under what conditions can these studies be safely conducted?*
- *Should this type of research be conducted at all?*

Gain-of-Function Deliberative Process

NSABB led a **deliberative process to reassess the potential risks and benefits associated with GOF research** and developed recommendations for the evaluation and oversight of GOF research involving pathogens with pandemic potential.

NSABB Report (May 2016)

- Central finding: Studies anticipated to enhance pathogens with pandemic potential have potential public health benefits but also entail significant potential risks
- Recommended additional, multidisciplinary Department-level evaluation prior to funding decision, and appropriate ongoing oversight if funded



U.S. Government Policy Guidance for Oversight of Enhanced PPP Research

OSTP Recommended Policy Guidance for Departmental Development of Review Mechanisms for PPP Care and Oversight (January 2017) directs federal departments and agencies considering funding projects anticipated to involve the creation, transfer, or use of enhanced PPP to adopt a department-level, multidisciplinary, pre-funding review mechanism that considers:

- Potential risks and benefits
- Alternative approaches
- Capacity of the investigators and institution to conduct the work safely and mitigate potential risks
- Ongoing oversight throughout research conduct and communication of results
- Ethical issues

Oversight of Enhanced PPP Research

– Scope

Scope of review: Federally funded projects anticipated to involve the **creation, transfer, or use of enhanced potential pandemic pathogens**

A **potential pandemic pathogen (PPP)** is one 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.

An **enhanced PPP** is a PPP resulting from the enhancement of a pathogen's transmissibility and/or virulence.

Oversight of Enhanced PPP Research

– Scope

- Wild-type pathogens that are circulating in or have been recovered from nature are not enhanced PPPs, regardless of their pandemic potential
- To the extent that transmissibility and/or virulence of PPPs are modified in the following categories of studies the resulting pathogens are not considered to be enhanced PPPs
 - Surveillance activities, including sampling and sequencing; and
 - Activities associated with developing and producing vaccines, such as generation of high growth strains

Oversight of Enhanced PPP Research – Review Principles

8 Principles to be considered

1. The proposal or plan for such a project has been evaluated by an independent expert review process (whether internal or external) and has been determined to be scientifically sound;
2. The pathogen that is anticipated to be generated by the project must be reasonably judged to be a credible source of a potential future human pandemic;
3. An assessment of the overall potential risks and benefits associated with the project determines that the potential risks as compared to the potential benefits to society are justified;

Oversight of Enhanced PPP Research – Review Principles

8 Principles to be considered

4. There are no feasible, equally efficacious alternative methods to address the same question in a manner that poses less risk than does the proposed approach;
5. The investigator and the institution where the project would be carried out have the demonstrated capacity and commitment to conduct it safely and securely, and have the ability to respond rapidly, mitigate potential risks and take corrective actions in response to laboratory accidents, lapses in protocol and procedures, and potential security breaches;
6. The project's results are anticipated to be responsibly communicated, in compliance with applicable laws, regulations, and policies, and any terms and conditions of funding, in order to realize their potential benefit;

Oversight of Enhanced PPP Research – Review Principles

8 Principles to be considered

7. The project will be supported through funding mechanisms that allow for appropriate management of risks and ongoing Federal and institutional oversight of all aspects of the research throughout the course of the project;
8. The project is ethically justifiable. Non-maleficence, beneficence, justice, respect for persons, scientific freedom, and responsible stewardship are among the ethical values that should be considered by a multidisciplinary review process making decisions about whether to fund research involving PPPs.

New HHS Framework for Oversight of Enhanced PPP Research

Adoption of a review mechanism in accordance with the OSTP recommended policy guidance will be considered sufficient for lifting the funding pause.

Department of Health and Human Services (HHS) is considering a framework for the pre-funding review and oversight of enhanced PPP research in line with OSTP guidance.

- Enhanced PPP research paused during the GOF funding pause would be evaluated using the new proposed review mechanism.
- Projects determined suitable to proceed would do so with appropriate risk mitigation measures in place.

Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P3CO)

Section 1. Introduction

- 1.1. Federal departments and agencies ("agencies") conducting, supporting, or planning to conduct or support the creation, transfer, or use of enhanced pathogens of pandemic potential should develop review mechanisms that are generally aligned with the approach recommended by the National Science Advisory Board for Biosecurity (NSABB) in its May 2016 report [Recommendations for the Evaluation and Oversight of Proposed Gain-of-Function Research](#) (NSABB Recommendations).
- 1.2. The intent of this document is to recommend consistent and appropriate Federal agency review and reporting processes for the enhanced oversight of Federally funded research that is anticipated to create, transfer, or use enhanced pathogens with pandemic potential.
- 1.3. In areas that are not specified in this recommended policy guidance, agencies should use discretion, although they are urged to consider the [NSABB Recommendations](#) and to consult with other agencies in formulating their review mechanisms.
- 1.4. Agencies that adopt a review mechanism consistent with the provisions specified below will have satisfied the requirements for lifting that agency's moratorium on certain gain-of-function research consistent with the October 17, 2014 statement "U.S. Government Gain-of-Function Deliberative Process and Research Funding Pause on Selected Gain-of-Function Research Involving Influenza, MERS, and SARS Viruses."

Section 2. Scope and Definitions

- 2.1. Agency review mechanisms pursuant to this recommended policy guidance should govern creation, transfer, and use of enhanced potential pandemic pathogens, defined below in a way that is meant to capture the activities that were addressed in the [NSABB Recommendations](#) as "gain-of-function research of concern."
- 2.2. A potential pandemic pathogen (PPP) is one that satisfies both of the following:
 - 2.2.1. It is likely highly transmissible and likely capable of wide and uncontrollable spread in human populations, and
 - 2.2.2. It is likely highly virulent and likely to cause significant morbidity and/or mortality in humans.
- 2.3. An enhanced PPP is a PPP resulting from the enhancement of a pathogen's transmissibility and/or virulence. Wild-type pathogens that are circulating in or have

Resources

❖ NSABB

- Public comments to NSABB: nsabb@od.nih.gov
- Website: <http://osp.od.nih.gov/office-biotechnology-activities/biosecurity/nsabb>



❖ Science, Safety, Security (S3)

- <http://www.phe.gov/s3/Pages/default.aspx>



❖ NIH Office of Science Policy

- Website: <http://osp.od.nih.gov/>
- Blog: <http://osp.od.nih.gov/under-the-poliscope>
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