U.S. Department of Health and Human Services

Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens

2017

Department of Health and Human Services Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens

Section I. Purpose and Principles

Research involving potential pandemic pathogens (PPPs) is essential to protecting global health and security. However, there are biosafety and biosecurity risks associated with undertaking such research that must be adequately considered and appropriately mitigated in order to help safely realize the potential benefits. The *HHS Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens* (*HHS P3CO Framework*) is intended to guide HHS funding decisions on individual proposed research that is reasonably anticipated to create, transfer, or use enhanced PPPs. This *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* issued by OSTP on January 9, 2017[1] and supersedes the previous *Framework for Guiding Department of Health and Human Services Funding Decisions about Research Proposals with the Potential for Generating Highly Pathogenic Avian Influenza H5N1 Viruses that are Transmissible among Mammals by Respiratory Droplets*[2]. The *HHS P3CO Framework* ensures a multidisciplinary, department-level pre-funding review and evaluation of proposed research meeting the scope outlined herein to help inform funding agency decisions. In so doing, the *HHS P3CO Framework* seeks to preserve the benefits of life sciences research involving enhanced PPPs while minimizing potential biosafety and biosecurity risks.

Section II. Scope and Definitions

For the purposes of this *HHS P3CO Framework*:

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

B. An **enhanced PPP** is defined as a PPP resulting from the enhancement of the transmissibility and/or virulence of a pathogen. Enhanced PPPs do not include naturally occurring pathogens that are circulating in or have been recovered from nature, regardless of their pandemic potential.

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[1] Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight. U.S. Government, January 2017.

[2] Framework for Guiding Department of Health and Human Services Funding Decisions about Research Proposals with the Potential for Generating Highly Pathogenic Avian Influenza H5N1 Viruses that are Transmissible among Mammals by Respiratory Droplets. U.S. Government, February 2013.

C. 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 for the purposes of this Framework[3]:

   1. Surveillance activities, including sampling and sequencing; and

   2. Activities associated with developing and producing vaccines, such as generation of high growth strains.

D. Proposed intramural and extramural life sciences research that is being considered for funding and that has been determined by the funding agency as reasonably anticipated to create, transfer, or use enhanced PPPs is subject to additional HHS department-level review as outlined herein.

E. A pathogen previously considered by an agency to be an enhanced PPP should no longer be so considered if the HHS and the White House Office of Science and Technology Policy, in consultation with the Departments of Defense, Homeland Security, Agriculture, and Justice, generally acting through the Federal Bureau of Investigation, jointly determine, on the basis of additional information that has been developed about the risks or the benefits of that pathogen's creation, transfer, or use, that the department-level review processes outlined in this framework are no longer appropriate.

[3] For additional guidance and examples of activities that would and would not be considered to involve enhanced PPP see *Recommendations for the Evaluation and Oversight of Proposed Gain-of-Function Research.* National Science Advisory Board for Biosecurity, May 2016.

Box 1. Criteria for guiding HHS funding decisions on proposed research that involves, or is reasonably anticipated to involve, creation, transfer, or use of enhanced PPPs.

Department-level review of proposed research reasonably anticipated to create, transfer, or use enhanced PPPs will be based on the following criteria:

1) The research 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 created, transferred, or used by the research 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 research determines that the potential risks as compared to the potential benefits to society are justified;
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 research 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 research'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;
7) The research 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 research; and
8) The research 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 in making decisions about whether to fund research involving PPPs.

Section III. Review and Oversight Framework

A. The identification, review, and oversight of research subject to department-level review will require responsibilities (Figure 1) of the:

- Funding agency considering funding the proposed research; and
- HHS.

Figure 1: Overview of Responsibilities under the HHS P3CO Framework

Entity	Responsibilities
Funding agency	• Conduct standard scientific merit review; • Refer proposed research that is reasonably anticipated to create, transfer, or use enhanced PPPs for departmental-level review; • Provide relevant information necessary for departmental-level review; • Participate in departmental-level review process, as requested; • Consider the recommendations resulting from the departmental-level review; • Make a funding decision, stipulating terms and conditions of award including additional risk mitigation measures if appropriate; • Report relevant information on funding decisions to HHS and OSTP; • Ensure implementation of and adherence to required risk mitigation procedures and other terms/conditions of award, if funded.
HHS	• Convene a multidisciplinary group to review proposed research that has been determined by the funding agency as being reasonably anticipated to create, transfer, or use enhanced PPPs; • Critically evaluate the proposed research including the risk/benefit assessment and proposed risk mitigation plan; • Consider the eight criteria for guiding HHS funding decisions (Box 1) and additional relevant factors and information; • Develop recommendations on acceptability for HHS funding, including suggestions for additional risk mitigation measures and/or terms and conditions of award, if funded.

B. The HHS department-level review will evaluate proposed research referred by the funding agency that meets the scope outlined in Section II. This review and evaluation will be guided by the criteria listed in Box 1. The evaluation will include consideration of a:

   - Risk/benefit analysis of the proposed research;
   - Risk mitigation plan; and
   - Additional relevant factors.

C. A department-level review will result in recommendations to the funding agency on whether the proposed research is acceptable for HHS funding and what, if any, additional risk mitigation measures should be incorporated into the terms and conditions of award, if funded.

D. If funded, research that is reasonably anticipated to create, transfer, or use an enhanced PPP may require additional risk mitigation strategies which may include, but are not limited to:

   - Modification of the design or conduct of the research;
   - Application of specific or enhanced biosecurity or biosafety and biocontainment measures;

- Evaluation of existing evidence of medical countermeasures (MCM) efficacy, or experiments conducted to determine MCM efficacy against agents or toxins resulting from the research; and
- Methodologies for responsible communication of results.

Section IV. HHS Department-level Review

A. 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.

B. The purpose of the department-level review is to provide a multidisciplinary, pre-funding review and evaluation of proposed research that meets the scope outlined in Section II to recommend whether HHS funding is appropriate, and if so, to help identify the appropriate risk mitigation strategies. The following disciplines should be represented during the department-level review: scientific research, biosafety, biosecurity, MCM development and availability, law, ethics, public health preparedness and response, biodefense, select agent regulations, and public health policy, as well as the funding agency perspectives and other relevant areas. The HHS department-level review group may include non-voting *ex officio* and/or *ad hoc* members from HHS and other federal departments and agencies as deemed appropriate by the Review Group Chair.

C. Extra care in the department-level review should be given to proposed research that is reasonably anticipated to:

- Enhance the harmful consequences of the pathogen;
- Disrupt immunity or the effectiveness of an immunization against the pathogen without clinical or agricultural justification;
- Confer to the pathogen resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that pathogen or facilitate the pathogen's ability to evade detection methodologies;
- Increase the stability, transmissibility, or the ability to disseminate the pathogen;
- Alter the host range or tropism of the pathogen;
- Enhance the susceptibility of a host population to the pathogen; or
- Generate or reconstitute an eradicated or extinct pathogen.

D. The HHS department-level review may result in the following recommendations:

- Research is acceptable for HHS funding;
- Research is not acceptable for HHS funding;
- Research is acceptable for HHS funding on the condition that certain experiments are modified;

- Research is acceptable for HHS funding on the condition that certain risk mitigation measures are employed at the federal and/or institutional level; or
- Other recommendations, as deemed appropriate.

For research determined to be not in accordance with all of the criteria for guiding HHS funding decisions on proposed research reasonably anticipated to create, transfer, or use enhanced PPPs, a recommendation will be that the research is not acceptable for HHS funding.

Section V. Evaluation of the HHS P3CO Review Process

HHS will periodically re-evaluate and modify this 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 will periodically ask the National Science Advisory Board for Biosecurity to review the process described herein.