United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential

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Section 1. Introduction

1.1 Purpose

The United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential ("Policy") is a unified federal oversight framework for conducting and managing certain types of federally funded life sciences research on biological agents and toxins. This Policy addresses oversight of research on biological agents and toxins that, when enhanced, have the potential to pose risks to public health, agriculture, food security, economic security, or national security.[1] It supersedes the 2012 United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (Federal DURC Policy),[2] the 2014 United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (Institutional DURC Policy),[3] and the Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P3CO Framework).[4] This Policy is issued by the Office of Science and Technology Policy (OSTP) in accordance with the directives established by the 2022 National Biodefense Strategy and Implementation Plan,[5] as directed by National Security Memorandum 15,[6] to complete an interagency review of efforts to strengthen responsible conduct for biological research. This Policy has also been issued pursuant to Section 2315 of the Consolidated Appropriations Act, 2023 (42 U.S.C. § 6627) to achieve consistent review and oversight of life sciences research proposed for federal funding that may be reasonably anticipated to involve the creation, transfer, or use of pathogens with enhanced pandemic potential (PEPPs).[7]

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[1] Risks to national security can arise from, but are not limited to, risks posed to public health, agriculture, food security, or economic security.

[2] United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (2012), https://aspr.hhs.gov/S3/Documents/us-policy-durc-032812.pdf.

[3] United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (2014), https://aspr.hhs.gov/S3/Documents/durc-policy.pdf.

[4] Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (2017), https://aspr.hhs.gov/S3/Documents/P3CO-FinalGuidanceStatement.pdf.

[5] National Biodefense Strategy and Implementation Plan (2022), https://www.whitehouse.gov/wp-content/uploads/2022/10/National-Biodefense-Strategy-and-Implementation-Plan-Final.pdf.

[6] National Security Memorandum on Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security (2022), https://www.whitehouse.gov/briefing-room/presidential-actions/2022/10/18/national-security-memorandum-on-countering-biological-threats-enhancing-pandemic-preparedness-and-achieving-global-health-security/.

[7] Consistent with 42 U.S.C. § 6627, Category 2 research within this Policy is meant to provide additional oversight and risk mitigation for research with any pathogen that is reasonably anticipated to result in the development, use, or transfer of a PEPP, including the creation of new pathogens with pandemic potential (PPP) from non-PPPs as well as the enhancement of existing PPPs. The United States Government Policy for Oversight of Dual

The intent of this Policy is to strengthen oversight of life sciences research with biological agents and toxins throughout the research lifecycle by:

- Defining an expanded scope of biological agent and toxin research subject to additional oversight by the U.S. government;
- Providing a unified framework to support the consistent identification and oversight of research proposals subject to this Policy that accounts for safety, security, and ethical considerations; and
- Delineating the roles and responsibilities of principal investigators, research institutions, and federal departments and agencies that conduct, fund, or oversee research within the scope of this Policy, with an emphasis on institutional oversight and management of this research.

This Policy will take effect one year after its release date to provide a transition period for implementation. Federal departments and agencies will update, modernize, or promulgate applicable implementing guidance consistent with this Policy and 42 U.S.C § 6627(b)(1) by the effective date of this Policy.

OSTP is also releasing the *Implementation Guidance to the United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential* ("Implementation Guidance") to aid and assist in consistent implementation of this Policy.

1.2 Applicability of Policy

This Policy applies to federal departments and agencies that fund or sponsor intramural or extramural research at research institutions in the United States and internationally with biological agents or toxins where the research is within Category 1 or Category 2 under this Policy, as described in Section 4 ("federal funding agencies"). This includes research funded or sponsored by grants, contracts, cooperative agreements, and other agreements and transactions issued on or after the effective date of this Policy. This Policy covers the research proposal stage and the full life cycle of the research. Non-federally funded research at institutions that receive federal funding is addressed in Section 5.4 of this Policy. Research that

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Use Research of Concern and Pathogens with Enhanced Pandemic Potential ("Policy") addresses a key objective in the 2022 National Biodefense Strategy to "strengthen biosafety and biosecurity practices and oversight to prevent bioincidents and reduce biological risks associated with life sciences research and development and advances in biotechnology," the implementation of which was directed by the President in the National Security Memorandum on Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security (NSM 15). Affected departments and agencies concur with this Policy, and an appropriate official from each affected department or agency has committed the department or agency to fulfilling the responsibilities herein described to the extent consistent with applicable law.

is outside of the scope of this Policy but may benefit from voluntary risk assessment and mitigation is addressed in Section 6.

This Policy provides an oversight framework for research with biological agents or toxins that is within Category 1 or Category 2. It includes measures for federal funding agencies to establish and implement this research oversight framework, including in terms and conditions of funding documents for research institutions and principal investigators. Federal funding agencies should implement this Policy under statutory and regulatory authorities applicable to them, and should aim to develop and promote consistent processes across the agencies to the maximum extent appropriate.

1.3 Relationship to Statutes, Regulations, and Other Policies

This Policy complements existing federal statutes, regulations, other policies, and guidelines regarding biosafety and biosecurity oversight and the responsible conduct of research involving biological agents and toxins. Federal funding agencies should implement this Policy in a manner consistent with all applicable laws and regulations; all legally binding treaties, commitments, and United Nations Security Council resolutions prohibiting the development and use of pathogens and toxins as weapons; and all relevant Presidential Directives and Executive Orders. Nothing in this policy shall be construed to impair or otherwise affect the functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

Nothing in this Policy should be read as superseding any federal statutory authority, including those applicable to the Department of Health and Human Services, the Department of Agriculture, and any other federal department or agency, to regulate the possession, use, or transfer of biological select agents and toxins that have the potential to pose a severe risk to public, animal, or plant health, or to animal or plant products. Nothing in this Policy should be read as superseding any regulatory authority, including the Select Agent Regulations found at 42 CFR Part 73, 9 CFR Part 121, and 7 CFR Part 331; the export control regulations at 15 CFR Parts 730-774 (known as the "Export Administration Regulations" [EAR]); and 22 CFR Parts 120-130 (known as the "International Traffic in Arms Regulations" [ITAR]), among others.[8] The term "dual use" as used herein should not be interpreted to indicate which regulations govern the export of such items.

As stated above, this Policy supersedes the 2012 Federal DURC Policy, the 2014 Institutional DURC Policy, and the 2017 P3CO Framework.

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[8] If a Principal Investigator or research institution has a question about the relationship between the research oversight framework under this Policy and any other federal program, they may contact the federal funding agency under this Policy.

Section 2. Background, Policy Statement, and Guiding Principles

2.1 Background

Research involving biological agents and toxins is essential to the scientific advances that underpin improvements in the health and safety of the public, agricultural crops and other plants, animals, and the environment. While this research provides enormous benefits to society, there are risks associated with certain subsets of this work that require heightened biosafety and biosecurity practices, including appropriate risk assessment and risk mitigation strategies. The U.S. Government has existing statutes, regulations, policies, and guidelines that address potential biosafety and biosecurity risks, including those associated with research oversight and management.[9] Together, these authorities, policies, and guidelines provide a foundation for ensuring that scientific research is conducted safely and securely.

Research oversight is a critical component of effective biosafety and biosecurity practices and the responsible conduct of research involving biological agents and toxins. The intent of research oversight is to increase the awareness of researchers, research institutions, and federal funding agencies about the biosafety and biosecurity concerns associated with certain types of research and to ensure that appropriate risk mitigation measures are in place to prevent biosafety incidents (e.g., unintended personal exposure or release of an agent outside of containment) or biosecurity incidents (e.g., theft or intentional misuse of information, knowledge, products, or technology). The 2012 Federal DURC, the 2014 Institutional DURC, and the 2017 P3CO Framework policies have been key components of the federal oversight framework for research involving biological agents and toxins. Scientists, institutions, and federal funding agencies have gained valuable insight from implementing these policies over the past decade. Meanwhile, rapid advances in science and technology continue to provide societal benefits, while also posing new risks. Replacing these earlier policies with this Policy, aided by the Implementation Guidance, will enable the oversight system for research involving biological agents and toxins to better address these risks**.**

It is important to acknowledge that research within the scope of this Policy can increase our understanding of the biology of biological agents and toxins. This body of knowledge can support the development of new diagnostic, prevention, and treatment measures; improvements in public health and animal or plant disease surveillance; and enhancement of emergency preparedness and response efforts. Research designated within the scope of this

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[9] Examples include: federal select agents and toxins regulations (42 CFR Part 73, 9 CFR Part 121, and 7 CFR Part 331); *National Institutes of Health Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf); Biosafety in Microbiological and Biomedical Laboratories, 6th Edition (https://www.cdc.gov/labs/pdf/SF__19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf); and additional U.S. Laws, Regulations and Guidelines (https://aspr.hhs.gov/S3/Pages/default.aspx) .

Policy can also advance science and innovation and contribute to American research competitiveness. This Policy provides the necessary precautionary measures to ensure that potential biosafety and biosecurity risks are mitigated and research is carried out safely and securely. These measures should be applied in a manner commensurate with risk in order to minimize adverse impacts on legitimate research and preserve and foster the benefits of research.

2.2 Policy Statement

It is the policy of the U.S. Government that federally funded intramural or extramural research that meets the scope of Category 1 or Category 2 research within this Policy is subject to federal and institutional oversight. The purpose of this oversight is to preserve the benefits of such research while minimizing the biosafety and biosecurity risks, including risks that the knowledge, information, products, or technologies generated by the research could be used in a manner that results in harm to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

2.3 Guiding Principles

Federal funding agencies should follow these guiding principles, which informed development of this Policy:

A. Life sciences research facilitates advances in public health, agriculture, the environment, and other pertinent areas, and serves to strengthen national security. It is critical that such research be conducted ethically.

B. The goal of life sciences research is to produce beneficial knowledge, information, products, or technologies. Despite its value and benefits, some research may present biosafety and biosecurity risks, or provide knowledge, information, products, or technologies that could be misapplied to do harm with no, or only minor, modification to pose a significant threat with potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security. Therefore, to maintain the benefits of life sciences research, it is necessary to apply tools to assess risk and implement this Policy for the responsible oversight, conduct, and communication of such research.

C. Life sciences research is by nature dynamic and can produce unanticipated results. Therefore, both the nature of the experiment and the information and materials it generates must be evaluated throughout the research lifecycle for biosafety and biosecurity risks.

D. Oversight must recognize both the need for risk assessment and mitigation and the need to support the science that drives lifesaving technologies, enables medical

countermeasure development, and accelerates pandemic preparedness. As such, the degree of oversight should be commensurate with the identified biosafety and biosecurity risks.

E. Effective oversight helps maintain public trust in the life sciences research enterprise by demonstrating that the scientific community recognizes the potential implications of research and is acting responsibly to protect public welfare and preserve national security.

F. Federal agencies, other government entities, nongovernmental entities, and institutions that fund or conduct life science research have the shared responsibility of identifying and mitigating biosafety and biosecurity risks throughout the research life cycle and ensuring that effective oversight and risk mitigation is in place.

G. It is essential to have a common understanding of and consistent and effective implementation for research oversight across all institutions that support and conduct life sciences research.

H. Any research oversight process should be periodically evaluated for effectiveness, impact on the research enterprise, and ability to effectively address emerging risks emanating from advances in biotechnology and associated convergent and enabling fields.

I. The free, open, and responsible conduct and communication of federally funded life sciences research is vital to a robust scientific enterprise and will continue to be a goal of the U.S. government. It should also be a goal of all research institutions engaged in life sciences research. We collectively strive to pursue our open science goals in concert with our interests in national and economic security, research integrity, and public welfare — ensuring that knowledge is shared in a way that leads to responsible use.

J. Educating the scientific community, industry, emergency response officials, the broader public, and others about biosafety, biosecurity, and the dual use potential of life sciences research is essential for promoting responsible research behavior.

K. No policy or set of guidelines can anticipate every possible situation. Awareness of biosafety and biosecurity risks, dual use, and good judgment are necessary for objective and responsible risk assessment and conduct of responsible research. It is incumbent on those engaged in life sciences research to adhere to the intent of this Policy, the research oversight framework described herein, and other policies and regulations that promote responsible research.

Section 3. Definitions

For the purpose of this Policy, the following terms are defined:

A. "*Biological agents*" are any microorganism (including, but not limited to, bacteria, viruses, fungi, or protozoa), infectious material, or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infectious material, capable of causing:
   - Death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism;
   - Deterioration of food, water, equipment, supplies, or material of any kind; or
   - Deleterious alteration of the environment.

B. "*Biosafety*" is the application of practices, controls, and containment infrastructure that reduces the risk of unintentional exposure to, contamination with, release of, or harm from pathogens, toxins, and other associated biological materials.

C. "*Biosecurity*" is the application of security measures designed to prevent the loss, theft, misuse, diversion, unauthorized possession or material introduction, or intentional release of pathogens, toxins, biological materials, and related information and/or technology.

D. "*Dual use research*" is research conducted for legitimate purposes that generates knowledge, information, technologies, and/or products that can be utilized for benevolent or harmful purposes.

E. "*Dual use research of concern (DURC)*" is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be misapplied to do harm with no, or only minor, modification to pose a significant threat with potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

F. *"Federal funding agency*" is a federal department, agency, institute, center, or office that funds or sponsors intramural or extramural research at research institutions in the United States or internationally, with biological agents or toxins where the research is within Category 1 or Category 2 under this Policy, as described in Section 4.

G. "*Institutional Contact for Dual Use Research (ICDUR)*" is the official designated by the research institution to serve as an internal resource for application of this Policy as well as the liaison (as necessary) between the institution and the relevant federal funding agency.

H. "*Institutional review entity (IRE)*" is the entity established by the research institution to execute the institutional oversight responsibilities described in Section 5.2, with the attributes described in Section 5.2.B.

I. "*Life sciences*" is the study or use of living organisms, viruses, or their products, including all disciplines, methodologies, and applications of biology (including biotechnology, genomics, proteomics, bioinformatics, and pharmaceutical and biomedical research and techniques).

J. "*Pathogen with enhanced pandemic potential (PEPP)*" is a type of pathogen with pandemic potential (PPP) resulting from experiments that enhance a pathogen's transmissibility[10] or virulence, or disrupt the effectiveness of pre-existing immunity, regardless of its progenitor agent, such that it may pose a significant threat to public health, the capacity of health systems to function, or national security. Wild-type pathogens that are circulating in or have been recovered from nature are not PEPPs but may be considered PPPs because of their pandemic potential.

K. "*Pathogen with pandemic potential (PPP)*" is a pathogen that is likely capable of wide and uncontrollable spread in a human population and would likely cause moderate to severe disease and/or mortality in humans.[11]

L. "*Principal investigator*" (PI) is the senior/key person seeking or receiving federal research and development funding (i.e., extramural funding). This includes researchers at federal agency laboratories and facilities, as well as researchers at government-owned, contractor-operated laboratories and facilities (i.e., intramural researchers, whether or not federally employed). There may be more than one PI on a research grant or project within a single or multiple institution(s).

M. "*Reasonably anticipated*" describes an assessment of an outcome such that, generally, individuals with scientific expertise relevant to the research in question would expect this outcome to occur with a non-trivial likelihood. It does not require high confidence that the outcome will definitely occur but excludes experiments in which experts would anticipate the outcome to be technically possible, but highly unlikely.

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[10] Experiments that enhance a pathogen's transmissibility (as listed in Section 4.2.2.i) include those that enhance environmental stability of the pathogen or toxin or change the tropism or host range of the pathogen or toxin in a way that enables an increased ability to infect and transmit between humans, among others.

[11] Pathogens with pandemic potential are often those with little to no pre-existing immunity in the human population.

N. "*Research institution*" is any academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, government agency, or other legal entity that conducts life sciences research.

Section 4. Category 1 and Category 2 Research that is Subject to this Policy

To enable effective implementation, this Policy categorizes the research previously overseen by the 2012 Federal DURC, the 2014 Institutional DURC, and the 2017 P3CO Framework policies into Category 1 and Category 2 research. This Policy also expands the scope of research previously overseen by those policies. As outlined in more detail in Section 5, Category 1 research is subject to oversight by research institutions and federal funding agencies, and Category 2 research is subject to oversight by research institutions, federal funding agencies, and their federal department if applicable[12] due to heightened potential for biosafety and biosecurity risks.

Any research that meets the definition of both Category 1 and Category 2 research is designated as Category 2 research.

4.1 Category 1 Research

Category 1 research meets three criteria: (1) it involves one or more of the biological agents and toxins specified in Section 4.1.1; (2) it is reasonably anticipated to result, or does result, in one of the experimental outcomes specified in Section 4.1.2; and (3) based on current understanding, the research institution and/or federal funding agency assesses that the research constitutes DURC as specified in Section 4.1.3.

4.1.1 Biological Agents and Toxins within Scope of Category 1 Research[13]

- All Select Agents and Toxins listed in 9 CFR 121.3–121.4, 42 CFR 73.3–73.4, and 7 CFR 331.3 and regulated by USDA and/or HHS.[14]

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[12] In some cases, the federal funding agency and the department funding an in-scope research study are distinct (e.g., the National Institutes of Health and the Department of Health and Human Services). In other cases, they are the same (e.g., the National Science Foundation). Federal departments and agencies will implement this Policy based on their specific departmental structure.

[13] As of the time of release of this Policy, the Implementation Guidance provides a complete list of biological agents or toxins that may be within scope of Category 1 of this Policy. Beyond this list, as stated in Section 6.2, this Policy also provides voluntary guidance to PIs and research institutions for research that is outside of the scope of this Policy but that may pose potential risk and may warrant oversight and risk mitigation at the institutional level.

[14] The utilization of the Select Agents and Toxins lists to specify agents for Category 1 research does not indicate, suggest, or imply any regulatory link between the Federal Select Agent programs and this Policy, nor does it direct new authorities or activities for the Federal Select Agent Program.

- All Risk Group 4 pathogens listed in Appendix B of the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)* - Classification of Human Etiologic Agents on the Basis of Hazard.[15]
- A subset of Risk Group 3 pathogens[16] listed in Appendix B of the *NIH Guidelines* - Classification of Human Etiologic Agents on the Basis of Hazard.
- For biological agents affecting humans that have not been assigned a Risk Group in the *NIH Guidelines*, refer to the current edition of Biosafety in Microbiological and Biomedical Laboratories (BMBL).[17] In such cases, agents affecting humans that are recommended to be handled at Biosafety Level 3 (BSL-3) or Biosafety Level 4 (BSL-4) per the BMBL guidance are subject to this Policy.[18]
- Biological agents added during future updates to the Implementation Guidance as specified in Sections 7 and 8.

4.1.2 Category 1 Research Experimental Outcomes

Research within the scope of Category 1 are those experimental outcomes with a biological agent or toxin outlined in Section 4.1.1 that are reasonably anticipated to:

i. Increase transmissibility of a pathogen within or between host species;
ii. Increase the virulence[19] of a pathogen or convey virulence to a non-pathogen;
iii. Increase the toxicity of a known toxin or produce a novel toxin;
iv. Increase the stability of a pathogen or toxin in the environment, or increase the ability to disseminate a pathogen or toxin;[20]
v. Alter the host range or tropism of a pathogen or toxin;
vi. Decrease the ability for a human or veterinary pathogen or toxin to be detected using standard diagnostic or analytical methods;

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[15] *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*, (https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf).

[16] Note: As of the time of release of this Policy, this subset consists of all RG3 pathogens except HIV, HTLV, SIV, Mtb (including mycobacterium bovis), Clade II of MPVX viruses unless containing nucleic acids coding for clade I MPVX virus virulence factors, vesicular stomatitis virus, Coccidioides immitis, C. posadasii, Histoplasma capsulatum, and H. capsulatum var. duboisii. This list may be updated in the Implementation Guidance on a periodic basis.

[17] Biosafety in Microbiological and Biomedical Laboratories, 6th Edition (https://www.cdc.gov/labs/pdf/SF__19_308133-A_BMBL6_00-BOOK-WEB-final-3.pdf)

[18] Note: In the event no risk group or Biosafety Level has been assigned to an agent, for example in the case of a newly emerging pathogen or chimeric agent, the appropriate institutional body should perform a risk assessment to determine the appropriate Biosafety Level for handling the agent, given the experimental protocol being proposed. The assessment should take into account known properties of the agent and similarities to existing agents. Such agents requiring handling at BSL-3 or BSL-4 are biological agents under Section 4.1.1 of this Policy.

[19] E.g., the ability of a pathogen to cause disease.

[20] E.g., improving characteristics of the pathogen or toxin such as environmental stability and aerosolubility.

vii. Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions;[21]
viii. Alter a human or veterinary pathogen or toxin to disrupt the effectiveness of preexisting immunity, via immunization or natural infection, against the pathogen or toxin; or
ix. Enhance the susceptibility of a host population to a pathogen or toxin.

Illustrative examples of Category 1 research experiments that should require PI, IRE, and federal funding agency review and approval are presented in the Implementation Guidance.

4.1.3 Category 1 Risk Assessment

Based on current understanding, the research can be reasonably anticipated to provide, or does provide, knowledge, information, products, or technologies that could be misapplied to do harm with no — or only minor — modification to pose a significant threat with potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

As described further in Section 6, there may be additional types of life sciences research that do not involve biological agents or toxins in Section 4.1.1 or experiments in Section 4.1.2, yet pose DURC risks as described in Section 4.1.3. Principal Investigators and research institutions are encouraged to remain vigilant to such research, including work involving any other biological agent or toxin regardless of its Risk Group, and develop and apply appropriate risk mitigation measures.

See the Implementation Guidance for additional guidance on Category 1 research including illustrative examples.

4.2 Category 2 Research

Category 2 research meets three criteria: (1) it involves, or is reasonably anticipated to result in, a PPP as specified in Section 4.2.1; (2) it is reasonably anticipated to result in, or does result in, one or more of the experimental outcomes or actions specified in Section 4.2.2; and (3) based on current understanding, the research institution and/or federal funding agency assesses that the research is reasonably anticipated to result in the development, use, or transfer of a PEPP or an eradicated or extinct PPP that may pose a significant threat to public health, the capacity of health systems to function, or national security as specified in Section 4.2.3.

[21] E.g., antimicrobials, antivirals, antitoxins, vaccines.

4.2.1 Biological Agents within Scope of Category 2 Research[22]

A PPP, or any pathogen that will be modified in such a way that is reasonably anticipated to result in a PPP.

4.2.2 Category 2 Research Experimental Outcomes or Actions

Research within the scope of Category 2 are those experimental outcomes or actions with a pathogen outlined in Section 4.2.1 that are reasonably anticipated to:

i. Enhance transmissibility of the pathogen in humans;
ii. Enhance the virulence of the pathogen in humans;
iii. Enhance the immune evasion of the pathogen in humans such as by modifying the pathogen to disrupt the effectiveness of pre-existing immunity via immunization or natural infection; or
iv. Generate, use, reconstitute, or transfer an eradicated or extinct PPP, or a previously identified PEPP.

Illustrative examples of Category 2 Research Experiments that should require PI, IRE, and federal funding agency review and approval are presented in the Implementation Guidance.

4.2.3 Category 2 Risk Assessment

The research can be reasonably anticipated to result in the development, use, or transfer of a PEPP or an eradicated or extinct PPP[23] that may pose a significant threat to public health, the capacity of health systems to function, or national security. See the Implementation Guidance for additional guidance, including illustrative examples.

PIs and IREs should also assess Category 2 research for potential DURC risks as outlined in Section 4.1, and if applicable, include appropriate Category 1 risk mitigation in the draft mitigation plan as described in Section 5.

See the Implementation Guidance for additional guidance on Category 2 research including illustrative examples.

[22] The Implementation Guidance provides examples of the types of pathogens that, with enhancement, could potentially be considered Category 2 research.
[23] Current eradicated and extinct pathogens include Variola major, Variola minor, and 1918 H1N1 Influenza virus.

Section 5. Oversight Framework for Category 1 and Category 2 Research that is Subject to this Policy

This Section describes the organizational framework for research oversight and articulates the roles and responsibilities of entities that conduct research (e.g., PIs and research institutions) and entities that fund or sponsor research (e.g., federal funding agencies).

Generally, the process for the research oversight system described in this Policy is as follows:

A. The PI makes an initial assessment of whether their proposed or ongoing research may be within the scope of Section 4 based upon the biological agent or toxin and the experimental outcome or actions (as specified in Sections 4.1.1 and 4.1.2 for Category 1 research, and Sections 4.2.1 and 4.2.2 for Category 2 research, respectively). The research institution is responsible for ensuring that PIs are aware of and executing this responsibility appropriately.

B. The PI submits the research proposal to the federal funding agency including notification that the research may be within scope of Category 1 or Category 2 based on the biological agent or toxin and the experiment.

C. When the federal funding agency has completed merit review of the proposed research and if it is considering funding the proposed research, the federal funding agency notifies the research institution.

D. The research institution, through an IRE, reviews the PI's initial assessment and confirms whether proposed or ongoing research is within the scope of Category 1 or Category 2 research. If so, the IRE determines whether the research is Category 1 or Category 2, including based on a risk assessment under Section 4.1.3 (Category 1) or Section 4.2.3 (Category 2). The research institution notifies the federal funding agency of the results of its Category 1 or Category 2 research determination, and the federal funding agency evaluates and verifies the research institution's assessment. Examples of risk assessment methods are described in the Implementation Guidance.

E. If the research is assessed to be within scope of Category 1 or Category 2, the research institution, through an IRE, conducts risk-benefit assessments and develops a draft risk mitigation plan for the conduct and communication of research. The PI or research institution submits the risk-benefit assessment and a draft risk mitigation plan to the federal funding agency. Examples of risk mitigation approaches are described in the Implementation Guidance.

F. The federal funding agency reviews the risk-benefit assessment and draft risk mitigation plan as follows:

- For specific experiments within the research proposal determined to be within scope of Category 1, the federal funding agency evaluates the research institution's risk-benefit assessments and determines whether the potential benefits justify the potential risks prior to the funding decision. These specific experiments will not proceed until the federal funding agency approves the risk mitigation plan.
- For specific experiments within the research proposal determined to be within scope of Category 2, the federal funding agency refers the proposed research for department-level review.[24] Upon receipt of the Category 2 research proposal, the department convenes a multidisciplinary review entity to evaluate the research institution's risk-benefit assessments and risk mitigation plan prior to the federal funding agency making a funding decision on the research proposal. The multidisciplinary review entity will make recommendations to the federal funding agency regarding the risk-benefit assessments, risk mitigation plan, and research proposal funding. The specific experiments within the research proposal determined to be within scope of Category 2 will not proceed until the federal funding agency determines that the potential benefits justify the potential risks and approves the risk mitigation plan.

G. If research is identified as potentially within the scope of Category 1 or Category 2 research during the course of experimentation, the PI halts further work, notifies the federal funding agency and research institution, and contacts their IRE to conduct the required assessments consistent with the procedures in this Policy for assessing Category 1 or Category 2 research.

It is the responsibility of investigators and institutions to identify research that may fall within scope of Category 1 or Category 2 research. Federal funding agencies have the discretion to request additional information or review of individual research proposals or projects to determine whether they may fall within scope of Category 1 or Category 2 research.

5.1 Responsibilities of Principal Investigators

PIs should:

A. Be knowledgeable about and comply with or follow all applicable institutional and U.S.

[24] In some cases, the federal funding agency and the Department funding an in-scope research study are distinct (e.g., National Institutes of Health and the Department of Health and Human Services) and in other cases they are the same (e.g., National Science Foundation). Federal departments and agencies will implement this Policy based on their specific structure.

government policies, requirements, and regulations for oversight of biological agent and toxin research.

B. Assess their research at the proposal stage, and continuously throughout the research lifecycle, to identify whether there is research reasonably anticipated to be within scope of Category 1 (i.e., that (1) includes one or more of the agents specified in Section 4.1.1, and (2) is reasonably anticipated to result in one or more of the experimental outcomes specified in Section 4.1.2); or within scope of Category 2 (i.e., that (1) involves, or is reasonably anticipated to result in, a PPP as specified in Section 4.2.1, and (2) is reasonably anticipated to result in one or more of the experimental outcomes or actions specified in Section 4.2.2).

C. Following identification of potential Category 1 or Category 2 research, notify the federal funding agency and research institution, refer the research to an appropriate IRE, and be prepared to develop a risk-benefit assessment and a risk mitigation plan.

D. Work with the IRE to assess the risks and benefits of the proposed research and submit the risk-benefit assessments and draft risk mitigation plan for Category 1 or Category 2 research to the federal funding agency for review and approval when appropriate:

- If research is being proposed as part of a new funding proposal, submit the risk-benefit assessments and draft risk mitigation plan to the federal funding agency for review and approval following scientific merit review.
- If the research is being funded under an existing funding mechanism but has not yet been reviewed by the federal funding agency, then submit the risk-benefit assessments and draft risk mitigation plan to the federal funding agency for approval before conducting such work.
- If research is first identified as potentially within scope of Category 1 or Category 2 during the course of experimentation, halt further work and work with the IRE to develop the risk-benefit assessments and risk mitigation plan for submission to the federal funding agency for further review and approval to continue.

E. Conduct Category 1 and Category 2 research in accordance with the provisions identified in the risk mitigation plan approved by the federal funding agency.

F. Provide annual progress reports for Category 1 research and semiannual progress reports for Category 2 research, and as requested by the federal funding agency (e.g., as part of terms and conditions of award or risk mitigation plans), for review, evaluation, assessment, and, where necessary, clarification or confirmation.

G. Ensure that laboratory personnel conducting life sciences research within the scope of this Policy (i.e., those under the supervision of laboratory leadership including graduate

students, postdoctoral fellows, research technicians, laboratory staff, and visiting scientists) have received and maintain education and training on all research oversight policies and processes and demonstrated competency.

H. Communicate Category 1 and Category 2 research in a responsible manner. Communication of research and research findings is an essential activity for all researchers and occurs throughout the research process, not only at the point of publication. When researchers are planning to communicate Category 1 and Category 2 research results, it is their duty to ensure that it is done in a responsible manner, and follows any measures outlined in the risk mitigation plan approved by the federal funding agency.

5.2 Responsibilities of Research Institutions

Federally funded research institutions should:

A. Establish and implement internal policies and practices that provide for the identification and ongoing oversight of Category 1 and Category 2 research, and ensure Category 1 and Category 2 research is identified through appropriate PI and IRE review.

B. Establish an IRE to carry out the provisions in Section 5. A range of mechanisms for fulfilling the role of an IRE are acceptable as long as the review entity is appropriately constituted and authorized by the institution to conduct the review. Options include, but are not limited to:

- a committee established for research oversight review;
- an extant committee (such as an Institutional Biosafety Committee) whose constitution meets or could meet, with the addition of *ad hoc* members, the provisions below; or
- an externally administered committee (e.g., an Institutional Biosafety Committee or review entity at a neighboring or regional institution, or a commercial entity. The federal funding agency may provide this function in scenarios in which Section 5.3.G of this Policy applies).

Regardless of the mechanism selected to fulfill the institutional responsibility of reviewing research that may be within the scope of Section 4, the IRE should:

- Be composed of at least five members;
- Be sufficiently empowered by the research institution to ensure the research institution's research oversight policies are followed;
- Have sufficient breadth of expertise, to include biosafety and biocontainment expertise, to assess the applicability of Section 4 to the range of relevant life

sciences research conducted at a given research institution and understand biosafety and biosecurity implications of such research;

- Have knowledge of PPPs, PEPPs, dual use concerns, and related institutional and U.S. government policies;
- Understand risk assessment and risk management considerations, including awareness of a variety of risk mitigation measures and that designating research as Category 1 or Category 2 research does not necessarily mean the research should not be conducted or communicated;
- Make its procedures for reviewing life sciences research for Category 1 or Category 2 research accessible to the public. The publicly available policies of the institution should include an overview of the institution's procedures or review process, but need not include details of particular cases or the minutes of the IRE's proceedings, or specifics of the mitigation plan(s);
- On a case-by-case basis, recuse any member of an IRE who is involved in the research project in question or has a direct financial interest, except to provide specific information requested by the review entity;
- Engage in an ongoing dialogue with the PI of the research in question when developing appropriate risk mitigation plans; and
- Maintain records of institutional Category 1 and Category 2 research reviews and completed risk mitigation plans for at least three years after the completion of the funded project unless a longer period is required by law or regulation.

C. Certify at the time of seeking funding (e.g., by signing the face page of a grant application) that their research institution fully follows the research oversight framework under this Policy.

D. Conduct an institutional oversight process by an IRE when a PI makes an initial assessment that research may constitute Category 1 or Category 2. The IRE:

- Assesses whether the research is within scope of Category 1 or Category 2 by determining:
  - For Category 1, whether the research (1) includes one or more of the agents specified in Section 4.1.1; (2) is reasonably anticipated to result in one or more of the experimental outcomes specified in Section 4.1.2; and (3) constitutes DURC as specified in Section 4.1.3; and
  - For Category 2, whether the research (1) involves, or is reasonably anticipated to result in, a PPP as specified in Section 4.2.1; (2) is reasonably anticipated to result in one or more of the experimental outcomes or actions specified in Section 4.2.2; and, (3) is reasonably anticipated to result in the development, use, or transfer of a PEPP or an eradicated or extinct PPP that may pose a significant threat to public health or the capacity of health systems to function, as specified in Section 4.2.3.

If the IRE determines that the research in question does not meet the definition of Category 1 or Category 2 research, the IRE should communicate this determination to the federal funding agency. This research is not subject to additional review or oversight under this Policy, unless the federal funding agency, while reviewing the IRE's determination, determines otherwise. In these cases, the research should continue to be managed throughout the research life cycle under Section 5 of this Policy;

- Works with the PI to conduct a risk-benefit assessment and develop a risk mitigation plan for Category 1 or Category 2 research, as necessary;
- Ensures that the federal funding agency is notified and a risk mitigation plan is reviewed, approved, and implemented prior to the initiation of the proposed Category 1 or Category 2 research;
- Assists with and oversees the implementation of the risk mitigation plan. The research should be conducted in accordance with the approved risk mitigation plan and should be periodically reviewed by the research institution to determine if additional modifications to the risk mitigation plan are appropriate;
- Evaluates risk mitigation plans at least annually (a shorter mitigation plan review cycle may be elected, especially for Category 2 research) and modifies them as necessary for the duration of the research. Institutions are responsible for ensuring that the research is conducted in accordance with the risk mitigation plan. Research evaluated prior to this Policy and determined to be within scope of Category 1 and Category 2, and for which a risk mitigation plan has already been developed, does not need a new risk mitigation plan, but the extant risk mitigation plan will be subject to ongoing review and modification based on the recommended periodicity, as necessary, by the research institution;
- Within 30 calendar days of the institutional review, notifies the federal funding agency of any research within the scope of Section 4, including whether it meets or does not meet the definition of Category 1 or Category 2 research; and
- Within 90 calendar days from the time that the research institution determines the research to be Category 1 or Category 2 research, provides a copy of the risk mitigation plan to the federal funding agency for review.

E. Ensure that internal policies establish a mechanism for the PI to refer an existing project to the IRE if, at any time, the research uses a biological agent or toxin as described in Sections 4.1.1 or 4.2.1 and can be reasonably anticipated to produce one or more of the outcomes or actions listed in Sections 4.1.2 or 4.2.2, or if the PI otherwise believes the project should undergo IRE review.

F. Designate an ICDUR to serve as an internal resource regarding oversight of Category 1 or Category 2 research. If questions arise regarding implementation of this Policy, or when guidance is needed about identifying Category 1 or Category 2 research or developing risk mitigation plans, the ICDUR serves as the liaison (as necessary) between the research

institution and the federal funding agency.

G. Provide education and training on research oversight for Category 1 or Category 2 research for individuals conducting life sciences research that may be within the scope of this Policy. Institutions should also address Category 1 or Category 2 research in existing courses on research ethics and/or the responsible conduct of research.

H. Maintain records of personnel training on research oversight for at least three years after the completion of the funded project, unless a longer period is required by law or regulation.

I. Maintain appropriate records of IRE reviews and completed risk mitigation plans for the term of the research grant, contract, cooperative agreement, or other agreement or transaction, plus three years after its completion, unless a longer period is required by law or regulation.

J. Establish a mechanism to ensure that the resulting biological agent or toxin from Category 1 and Category 2 research are properly accounted for and destroyed when no longer needed if not already required to do so by existing law and regulation.

K. Report instances of failure to follow this Policy, as well as mitigation measures undertaken by the research institution to prevent recurrences of similar failures, within 30 calendar days of research institution awareness or research institution receipt of notification of a failure to the federal funding agency.

L. As necessary, assist the PIs of life sciences research when questions arise about whether their research may entail further review or oversight.

M. Establish an internal mechanism for PIs to appeal institutional decisions regarding research that is determined by the IRE to meet the definition of Category 1 or Category 2 research.

N. On an annual basis, provide a formal assurance to relevant federal funding agencies that the research institution is operating consistent with this Policy.

O. Make relevant information available to local authorities on Category 1 and Category 2 research, as appropriate.

PIs and IREs are encouraged to remain vigilant to additional types of research including work involving any biological agent or toxin, regardless of its Risk Group, that is outside the scope of this Policy, but where the research poses risks such that it meets the definition of DURC and apply appropriate risk mitigation measures.

This Policy also recognizes that there will be situations where elements of potential Category 1 or Category 2 research are being carried out at multiple research institutions through a subaward with a primary institution that directly receives an award from the federal funding agency. In cases of such collaborations involving multiple institutions via a subaward, the primary institution is considered the research institution in this Policy and is responsible for notifying the federal funding agency of research determined to be Category 1 or Category 2, providing copies of each institution's risk mitigation plan, or a single plan with relevant components. Furthermore, any sub awardees participating in the collaboration should follow with the oversight framework under this Policy, and the primary institution should ensure that Category 1 or Category 2 research oversight is consistently applied by all entities participating in the collaboration, e.g., through inclusion of appropriate requirements in the terms of the subaward.

5.3 Responsibilities of Federal Funding Agencies

Federal funding agencies that fund research subject to this Policy will, consistent with applicable law:

A. As a condition of funding, require all research institutions that they fund to fully follow this Policy. One mechanism for doing so is through a term and condition of award.

B. Respond to questions from research institutions regarding the federal funding agency's oversight of research as defined in this Policy and provide guidance to research institutions regarding this Policy.

C. For proposed and funded research determined to meet the definition of Category 1 or Category 2 research, review projects on an ongoing basis and:

- Notify the research institution of the federal funding agency's determination of whether the research is within scope of Category 1 or Category 2;
- Review and approve institutional risk-benefit assessments and risk mitigation plans and notify the research institution of any concerns, disagreements, or proposed modifications with the assessments or plans;
- Determine that the potential benefits of the research justify the potential risks and approve the risk mitigation plan before notifying the research institution and PI that the experiments identified as Category 1 or Category 2 may proceed; and
- Prior to reaching the final determination to fund, or continue to fund, the research, consult with the research institution to address any disagreements identified.

D. For research designated within scope of Category 1, refer the research and associated risk-benefit assessments and risk mitigation plan to the federal funding agency review

entity. The federal funding agency-level review entity will, consistent with applicable law:

- Have the following expertise represented: scientific research, biosafety, biosecurity and national security, ethics, as well as other relevant areas, as determined by the federal funding agency.
- Provide federal law enforcement, intelligence components, and the State Department (for research conducted overseas) an opportunity to share information that is potentially relevant to risk-benefit assessments.
- Review the risk-benefit assessments and risk mitigation plan in concert with funding decisions.

E. For research designated within scope of Category 2, refer the research and associated risk-benefit assessments and risk mitigation plan to the federal funding agency's department-level review entity.[25] The department-level review entity will, consistent with applicable law:

- Be comprised of officials established in offices that do not have a direct reporting line to the head of the agency component that may fund the proposed research and have effective procedures in place to address potential conflicts of interest.
- Have the following expertise represented: scientific research, biosafety, biosecurity, medical countermeasure (MCM) development and availability, law enforcement and national security, ethics, public health preparedness and response, biodefense, Select Agent Regulations, public health policy, as well as other relevant areas, as determined by the department.
- In assessing the potential risks associated with Category 2 research, the federal funding agency will, consistent with applicable law, provide relevant agencies in the federal law enforcement, intelligence components, and the State Department (for research conducted overseas) an opportunity to share information that is potentially relevant to risk-benefit assessments.
- Include non-voting ex officio and/or ad hoc members from other federal departments and agencies as deemed appropriate by the chair of the review entity.
- Evaluate the proposed research including the risk-benefit assessments and draft risk mitigation plan. The proposed research will satisfy the following criteria:

[25] The Centers for Disease Control and Prevention (CDC) is one of only two World Health Organization (WHO) Collaborating Centers approved for Variola virus research in the world. All research using Variola virus at CDC is overseen by the WHO and required by the World Health Assembly resolution 52.10 to have immediate public health impact. The WHO Advisory Committee on Variola Virus Research reviews all research that is proposed by CDC each year. This review and risk assessment may be deemed by HHS as satisfying the review requirements outlined in the Policy for Category 2 research with Variola virus.

- It has been evaluated by an independent scientific merit review process (whether internal or external) through already established federal funding agency review processes and has been determined to be scientifically sound and of merit;
- It has undergone an assessment of the overall potential risks and benefits associated with the research, which determines that the potential benefits to society justify the potential risks;
- There are no feasible, equally efficacious alternative methods to address the same research question in a manner that poses less risk than does the proposed approach;
- The PI and the research institution where the research would be carried out have the demonstrated capability 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;
- Its 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;
- It will be supported through mechanisms that allow for appropriate management of risks and ongoing U.S. government and/or institutional oversight of all aspects of the research throughout the course of the project; and
- It 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 the department-level multidisciplinary review entity.

F. Respond to reports of concerns about implementation of this Policy and work with research institutions to address such concerns.

G. If a research institution outside of the United States is unable to meet one or more of the criteria in Section 5.2.B but the federal funding agency nevertheless determines that it remains in the best scientific interest to fund the research, the federal funding agency will serve as the implementing IRE or take other steps it determines are needed to ensure adequate biosafety and biosecurity oversight of Category 1 and Category 2 research.

H. Implement this Policy in accordance with the federal funding agency's relevant and applicable authorities, regulations, and statutes.

I. To the extent practicable, complete the review process within 90 calendar days of receiving the risk-benefit assessments and draft risk mitigation plan for Category 1 or Category 2 research.

J. To align with the scope of this new Policy, federal departments and agencies will take a phased approach to support the conduct of in-person inspections or site visits, or review evidence of in-person inspections or site visits carried out by an appropriate inspection entity (e.g., an existing regulatory authority such as the Federal Select Agent Program, other appropriate federal or state authority, or institutional or external entity/body/official), to ensure adequate biosafety and biosecurity measures and risk mitigation for funded Category 1 and Category 2 research, subject to appropriations and authorities.

K. As necessary, request additional information or review of individual research proposals or projects to determine whether they may fall within scope of Category 1 or Category 2 research.

L. Develop review processes for Category 1 and Category 2 research under this Policy. Federal departments and funding agencies are structured differently. Review processes including department-level review for Category 2 research may therefore vary. Final decisions on whether to fund Category 1 research will be made at a level no lower than the Senior Executive Service level by the federal funding agency (or equivalent), or by a senior official with the statutory responsibility to make final decisions regarding funding of awards. Final decisions on whether to recommend and fund Category 2 research will be made by a senior official at a level no lower than Assistant Secretary (or equivalent) or with the statutory responsibility to make final decisions regarding funding of awards, or their designee.[26]

M. In addition to performing the oversight responsibilities described above, aid in implementation of this Policy through efforts such as:

- Develop risk-benefit assessments and training tools and materials for use by the agency and by institutions implementing this Policy and Implementation Guidance.
- Develop appropriate funding application forms and instructions to aid in PI and research institution identification and attestation of Category 1 and Category 2 research.
- Provide education and outreach to research institutions, funding agencies, and other affected stakeholders about research oversight policies and issues.
- Provide guidance to research institutions on the conduct, communication of research and research findings, and distribution of Category 1 or Category 2 research products and on the communication of such research.
- Ensure clear, effective, and efficient implementation of this Policy through regular

[26] Any such designee must serve at a level no lower than the Deputy Assistant Secretary (or equivalent) level.

engagement with interested communities, including scientists, research administrators, security experts, scientific journals and publication outlets, and public health officials domestically and internationally.
- Routinely coordinate with other federal funding agencies that fund research within scope of this Policy to facilitate consistent implementation.
- Engage with overseas partners, as appropriate, regarding policies relating to research oversight of Category 1 or Category 2 research, and encourage the development of harmonized policy guidance.

There may be cases in which a federal department or agency simply passes through funding from another federal department or agency to support life sciences research at an institution that conducts or sponsors research involving Category 1 or Category 2 research. In this instance, the federal department or agency originally providing the funding is considered the federal funding agency, and the ultimate recipient of the funds is considered the research institution, and they respectively carry out the roles of each under this Policy. Pass-through agencies should be made aware of this Policy and associated requirements, and support the federal funding agency if requested.

5.4 Non-Federally Funded Research

Where a federal department or agency is authorized to establish oversight requirements on non-federally funded life sciences research as a condition of receiving federal funding, the federal department or agency should establish that U.S. research institutions attest to the federal government that they are implementing oversight of non-federally funded Category 1 and Category 2 research in accordance with the research oversight framework under this Policy. Such oversight should include a process managed by an IRE to: identify Category 1 and Category 2 research; conduct risk-benefit assessments before proceeding with Category 1 and Category 2 research; and implement a risk mitigation plan for Category 1 and Category 2 research, consistent with the principles described in this Policy and Implementation Guidance. Such authorities should also be exercised to establish that these institutions annually report the number of studies receiving Category 1 and Category 2 oversight.

5.5 Waiver for Urgent Research and Response

The Secretary of any federal department[27] that funds research covered under Category 1 or Category 2 may issue a waiver temporarily exempting all research proposals on a designated biological agent or toxin from the oversight process established in this Policy, if the Secretary determines that: (1) such research is urgently required to respond to a declared or potential Public Health Emergency or other emergency, including agricultural emergencies, related to a

[27] For federal funding agencies that are not under a department, the head of the federal funding agency may issue this waiver.

biological incident; (2) temporarily suspending the research oversight framework under this Policy is necessary to facilitate an effective response to such an emergency; and, (3) the benefits of such a waiver exceed the potential risks. Such a waiver will expire after 180 days, but may be renewed by the Secretary as needed. Such a waiver may apply to Category 1 oversight, Category 2 oversight, or both, as determined by the Secretary, and does not supersede other existing statutes, regulations, or policies that may apply to the research and the institution's responsibility to ensure biosafety and biosecurity practices during the conduct of research.

5.6 Failure to Follow the Research Oversight Framework

For PIs and research institutions, failure to follow the research oversight framework under this Policy may result in suspension, limitation, or termination of federal funding and loss of future federal funding opportunities for the research proposal and for other life sciences research at the research institution, as imposed by the federal funding agency. Federal funding agencies will consider relevant statutory and regulatory authorities when considering appropriate actions.

5.7 Reporting by Federal Departments and Agencies

To the extent practicable, to facilitate awareness about implementation of this Policy, federal funding agencies that fund research within scope of this Policy should take the following actions:

A. Submit annual reports on research designated within scope of Section 4 to the Assistant to the President for National Security Affairs, the Director of OSTP, and the Director of the Office of Pandemic Preparedness and Response Policy (OPPR). These reports should summarize information about federal funding agency and department decisions on Category 1 or Category 2 research that was funded, including risk-benefit assessments and risk mitigation measures put in place. OSTP, federal departments, and federal funding agencies may periodically review a subset of studies considered for Category 2 review at the federal funding agency level, and the determinations as to whether to designate those as Category 2, to assess consistency in implementation across funding agencies.

B. Make general information about the review process and approaches taken to mitigate risks for research determined to be Category 1 and Category 2 research available to the public, including state and local officials, to the extent feasible and allowed by law.

C. After consultation with relevant interagency partners, as consistent with applicable law and policy and without releasing information that could compromise national security, the safety and security of such research activities, confidential business

information, or any identifiable, sensitive information of relevant individuals:

- Publicly share information on the types of expertise represented on their Category 2 department-level review committees.
- Generate a joint public, aggregate, annual report across federal departments and agencies describing the types of Category 2 experiments that received funding and the types of anticipated benefits, potential risks, and risk mitigation measures in place.

Federal funding agencies should not publicly disclose risk-related information obtained from other federal departments and agencies without the consent of those departments and agencies.

Section 6. Research Outside of Policy Scope

All research should be conducted and communicated safely, securely, and responsibly, to protect the health and safety of the public, plants, animals, and the environment, and minimize the risk of potential misuse of information, products, and technologies. Research institutions are encouraged to be mindful that research outside of Category 1 and Category 2 articulated in Section 4 of this Policy may also benefit from the institutional and federal research oversight framework under Section 5. Research institutions are encouraged to expand their oversight and apply these mechanisms for other life sciences research, and research in which other fields converge with biology, when appropriate; however, any such expansion would not be subject to oversight requirements as articulated in this Policy.

6.1 Types of Research Typically Not Within Scope of Category 2 Research

The following types of experiments are not typically within scope of Category 2 research because the outcomes or actions typically do not result in the enhancement of a pathogen's transmissibility or virulence or a disruption of the effectiveness of pre-existing immunity resulting in a PEPP as outlined in Section 4.2. However, researchers are expected to exhibit vigilance and evaluate research in case unexpected results warrant Category 2 review for the development, use, or transfer of a PEPP.

A. Surveillance activities, including collection of diagnostic and clinical specimens, sampling, sequencing, and basic viral characterization, in which the pathogen is not modified via genetic manipulation or laboratory adaptation to enhance transmissibility or virulence in humans.[28]

[28] Basic viral characterization studies that would not be subject to departmental review include pseudo-type virus studies with proteins from lab-adapted strains, human receptor binding, animal model susceptibility studies that do not involve transmission, and in vitro experiments with human cell lines or primary cells that do not involve serial passage, beyond what is required for viral isolation and characterization.

B. Research on evaluating, testing, and/or producing vaccines and related biologics such as immunoglobulins and the generation of high-growth strains.

C. Experiments focused on evaluating and developing antivirals, including monoclonal antibodies, for treatment or prevention of disease caused by circulating human viruses.

6.2 Voluntary Guidance for Other Types of Research that May Pose Biosafety or Biosecurity Risks

This subsection provides voluntary guidance to PIs and research institutions for research that is outside of the scope of this Policy but that may pose potential risk and may warrant oversight and risk mitigation at the institutional level.

6.2.1 Research with Other Human and Zoonotic Biological Agents and Toxins

This Policy encourages research institutions to oversee any research with biological agents and toxins outside of the scope outlined in Section 4, regardless of funding source. This oversight should involve assessment of biosafety and biosecurity risks, including dual use potential of knowledge, information, products, or technologies, and the development of a risk mitigation plan that includes the need to update the appropriate federal funding agency if unexpected Category 1 or Category 2 research is identified during experimentation.

6.2.2 Research involving *In Silico* Models and Computational Approaches

This Policy recognizes the rapidly evolving nature of computational biology and the increasing use of computational models and approaches, including the use of artificial intelligence, that potentially contributes to the production of dual-use biological knowledge, information, technologies, and products. This Policy encourages institutional oversight of *in silico* research, regardless of funding source, that could result in the development of potential dual-use computational models directly enabling the design of a PEPP or a novel biological agent or toxin. This oversight should involve an assessment of the benefits and risks, including the dual use potential of the *in silico* research to determine if the research should be conducted, and as appropriate, the development of a risk mitigation plan that considers how to responsibly share and communicate research results and datasets related to the biological agents or toxins under study.

6.3 Entities that Do Not Receive Federal Funding

Research institutions that do not receive any federal funds for life sciences research, but that nevertheless conduct life sciences research with identifiable biosafety or biosecurity risks, are strongly encouraged to implement oversight procedures consistent with the culture of shared responsibility underpinning this Policy. The U.S. government will consider additional

approaches outside of this Policy for promoting use of these or similar oversight procedures by research institutions that conduct life sciences research and do not receive federal funding.

Section 7. Additional Resources

To aid in the implementation of this Policy, the following resources are available for use:

A. Guidance for Category 1 and Category 2 research oversight. OSTP, in consultation with relevant federal departments and agencies, is releasing Implementation Guidance to assist investigators and research institutions in the implementation of this Policy. This document will aid in understanding and identifying research that raises significant biosafety or biosecurity concerns, developing risk-benefit assessments and risk mitigation plans, responsibly communicating research, and educating individuals and institutions on research oversight. The Implementation Guidance may be updated on a more frequent basis than the Policy itself and, therefore, it is advisable for entities subject to this Policy to regularly consult the Implementation Guidance.

B. Consultation with the federal funding agencies. Institutions may seek advice from federal funding agencies on matters related to research oversight. Such consultations should involve the ICDUR and are not mandatory or intended as a substitute for institutional review or reporting. Such consultations may be particularly helpful when:

    - The IRE seeks guidance on developing a risk mitigation plan commensurate to the assessed risks;
    - The IRE considers the only viable risk mitigation measure to be not conducting or not communicating the research in question;
    - The PI does not agree with the finding of the IRE and so would like to request outside technical advice;
    - The research in question represents a particularly complex case or appears to be outside the scope of the current definition of Category 1 or Category 2 research, but presents significant concerns; or
    - Guidance is beneficial to ensure a clear understanding of how the U.S. government interprets the definition of Category 1 or Category 2 research and related terms.

Section 8. Policy Review and Revision

At least every four years, OSTP, in consultation with relevant federal departments and agencies, will review this Policy and update it as necessary and appropriate, to ensure that it adequately considers risks from DURC and research that may be reasonably anticipated to involve the creation, transfer, or use of PEPPs. This review will take into consideration the benefits of such research and the mitigation of risks, consistent with 42 U.S.C. § 6627 (a)(1)(B).

At least every two years, OSTP, in consultation with relevant federal departments and agencies, may review the Implementation Guidance to this Policy including the associated lists of biological agents and toxins and update it as needed. Reviews of this Policy and/or its Implementation Guidance will consider benefits and risks arising from emerging scientific and technological advances and any implementation challenges. Future revisions of this Policy and/or its Implementation Guidance may be informed by inputs from interested communities, including scientists; national security officials; public health officials; state, local, tribal, and territorial officials; global health specialists; and the general public, as well as engagement with international partners, as appropriate. Following the release of this policy, OSTP will work with relevant federal departments and agencies to develop additional policy guidance on mechanisms and tools to help ensure federally funded research institutions are implementing appropriate biosafety, biosecurity, and mitigation mechanisms.[29]

[29] As part of this effort, OSTP and National Security Council staff, in consultation with relevant departments and agencies, will coordinate a process for identifying countries posing risks in which the U.S. government should not fund Category 1 and Category 2 research.