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

Key Responsibilities for Principal Investigators, Institutions and National Funding Agencies (Excerpted Directly from the Updated Policy)

Responsibilities of Principal Investigators

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

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.

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:

• 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 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.