University of Utah
Institutional Biosafety Committee
Standard Operating Procedure

Subject Dual Use Research of Concern Policy and Pathogens with Enhanced Pandemic Potential

SOP Number 15_02_01

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University of Utah SOP to address the federal Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential Policy

A. The purpose of this SOP is identify procedures to meet the United States Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP), which went into effect May 6, 2025 (United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential (May 2024)). This 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. It supersedes the 2012 United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (Federal DURC Policy), the 2014 United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (Institutional DURC Policy), and the Recommended Policy Guidance for Departmental Development of Review Mechanisms for Potential Pandemic Pathogen Care and Oversight (P3CO Framework). This SOP supersedes the document that was developed in response to the earlier policies and delineates the roles and responsibilities of the University of Utah and its investigators, the identification of potential DURC and PEPP, and the development and implementation of risk mitigation measures, where applicable.

B. To enable effective implementation, the 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 below, 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, 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.

(i) Category 1 Research:

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

(a) **Biological Agents and Toxins within Scope of Category 1 Research**

- 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 the USDA and/or HHS.
- All Risk Group 4 (RG4) pathogens listed in Appendix B of the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*.
- A subset of Risk Group 3 pathogens* listed in Appendix B of the *NIH Guidelines*.
- 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). 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.[#]
- Biological agents added during future updates to the Policy.

*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 on a periodic basis.

[#]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 University of Utah Institutional Review Entity (IRE) will perform a risk assessment to determine the appropriate Biosafety Level for handling the agent, given the experimental protocol being proposed. The assessment will consider 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 B.(i).(a) of this Policy.

(b) **Category 1 Research Experimental Outcomes**

Research within the scope of Category 1 are those experimental outcomes with a biological agent or toxin outlined Section B.(i).(a) that are reasonably anticipated to:

i Increase transmissibility of a pathogen within or between host species;
ii Increase the virulence 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;
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;
vii Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions;
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.

(c) **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.

(d) **Examples of Potential Risks Posed by Category 1 Experimental Outcomes**

Appendix 1 provides examples of risks posed by each type of Category 1 research experimental outcome listed in Section B.(i).(b) of the Policy that, when involving biological agents and toxins listed in Section B.(i).(a) of the Policy, may meet the threshold for Category 1 research oversight.

(ii) Category 2 Research:

Category 2 research meets three criteria: (1) it involves, or is reasonably anticipated to result in, a pandemic potential (PPP), as specified in Section B.(ii).(a); (2) it is reasonably anticipated to result in, or does result in, one or more of the experimental outcomes or actions specified in Section B.(ii).(b); 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 B.(ii).(c).

(a) **Biological Agents and Toxins within Scope of Category 2 Research**

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

A PPP as defined in the Policy 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."

A pathogen's capability for "wide and uncontrollable spread in a human population" is a function of the pathogen's ability to spread in a human population through an efficient means of transmission (e.g., via aerosol, respiratory droplets, direct contact, fomites, etc.). As a general benchmark, "wide and uncontrollable spread" typically refers to pathogens expected to exhibit sustained human-to-human transmission in a population under specific conditions, or an effective reproductive number (Rt) greater than one. Conditions that aid wide and uncontrollable spread include a relative lack of pre-existing population immunity to the pathogen, environmental stability of the pathogen, respiratory route of transmission, and lack of availability of or access to non-medical and medical countermeasures (MCMs) to contain the pathogen. Once a population has been exposed to a pathogen over multiple years or seasonal cycles, the ability for that pathogen to spread disease throughout the human population and cause moderate to severe disease in humans may diminish. However, the absence of one of these conditions alone is insufficient to rule out pandemic potential. For example, Influenza A virus subtype H1N1 (1918) is considered to have pandemic potential because it may be able to spread widely in a population despite the existence of MCMs.

A pathogen's capability to cause "moderate to severe disease and/or mortality in humans" may be estimated by comparing case hospitalization rate (CHR) and/or case fatality rates (CFR). These comparisons may not be clear-cut or relevant in every

circumstance, but rather can provide a high-level guideline to help PIs, IREs, and federal funding agencies assess which pathogens are included and excluded from the PPP definition.

While R_t, CHR, and CFR are key tools for determining whether a pathogen is a PPP, it is important to note that these metrics can vary widely based on a range of factors (e.g., levels of population immunity, access to health care, community behaviors, etc.), and relevant data on these metrics may not be available for many pathogens under study in the laboratory. Other pathogen characteristics for determining moderate to severe disease potential may include types of symptoms, duration of disease, or long-term symptoms that persist after infection.

Classification of a pathogen as a PPP can evolve over time, including during the course of a pandemic, due to changing levels of population immunity, development of MCMs, and emergence of variants with differing levels of transmissibility and pathogenicity. Cumulatively, these metrics are meant to help broadly establish a reference class of pathogens that fit in the PPP definition, to help PIs, IREs, and federal funding agencies determine whether a particular pathogen fits the PPP definition based on what is known about the transmissibility and disease characteristics of that pathogen.

A pathogen with enhanced pandemic potential (PEPP) as defined in the Policy is "a type of PPP resulting from experiments that enhance a pathogen's transmissibility 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."

"Progenitor agent" within the PEPP definition refers to the starting pathogen of the proposed experiment, which may be a PPP in its wild-type form or a pathogen that is not considered a PPP in its wild-type form, but that when modified meets the definition of a PEPP.

Category 2 oversight is also required for experiments that generate, use, reconstitute, or transfer an eradicated or extinct PPP that may pose a significant threat to public health, the capacity of health systems to function, or national security, regardless of whether the experiment enhances the PPP. Current eradicated and extinct PPPs include Variola major and minor,[#] and Influenza A virus subtypes H1N1 (1918) and H2N2 (1957-1968). Any research with these PPPs is considered Category 2 because of the heightened consequences of biosafety or biosecurity incidents that could occur from directly handling or possessing such pathogens,

even without any enhancement to virulence or transmissibility.

[#]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.

Pathogens that may be subject to Category 2 oversight are described in Appendix 2.

(b) **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 B.(ii).a 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.

(c) 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 that may pose a significant threat to public health, the capacity of health systems to function, or national security.

PIs and IREs should also assess Category 2 research for potential DURC risks as outlined in Section B.(a), and if applicable, include appropriate Category 1 risk mitigation in the draft mitigation plan as described in Appendices 5 and 6.

(d) Examples of Potential Risks Posed by Category 2 Experimental Outcomes

Appendix 3 provides examples of risks posed by each type of Category 2 research experimental outcome listed in Section B.(ii).b of the Policy that, when conducted with

pathogens described in Section B.(ii).a of the Policy, may be assessed as being 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.

C.(i). 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).

A general overview of the Policy oversight Framework is provided in Appendix 4. In brief, the process for the research oversight system described in this Policy is as follows:

a. The Principal Investigator (PI) makes an initial assessment of whether their proposed or ongoing research may be within the scope of Section B. based upon the biological agent or toxin and the experimental outcome or actions (as specified in Sections B.(i).(a) 4.1.1 and B.(i).(b) for Category 1 research, and Sections B.(ii).(a) and B.(ii).(b) 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 B.(i).(c) (Category 1) or Section B.(ii).(c) (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 Policy Implementation Guidance.

e. If the research is assessed to be within scope of Category 1 or Category 2, the research institution, through an Institutional Review Entity (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 Policy 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. 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.

If the research falls outside of the scope of the Federal Policy, for example because the research is not federally funded, the University of Utah will implement similar requirements for the establishment and implementation of Risk Mitigation strategies and annual reporting to the Institutional Biosafety Committee (IBC), as described below.

C.(ii). Responsibilities of Principal Investigators

PIs must:

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. They must review the US Government Policy document and are advised to use the Policy Implementation Guidance to assist in their determination since this provides detailed guidance for the responsibilities of PIs.

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

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.

i. For research that is not federally funded and, therefore falls outside of the scope of the federal Policy, the PI will develop similar approaches with regard to risk-benefit analyses, risk assessments, risk mitigation strategies, annual reporting and education and training, for approval by the University of Utah IBC as part of their IBC registration.

C.(iii). Responsibilities of Research Institutions

C.(iii).(a). The University of Utah will establish an Institutional Review Entity (IRE) to execute the review requirements described below. The Associate Vice President of Research Integrity and Compliance (AVPRIC) has authorized the University of Utah Institutional Biosafety Committee (IBC) to serve as the IRE.

To meet the requirements of the federal policy, the Institution will ensure that the IRE will:

- 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 B 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 the 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.(iii).(b). The Office of Sponsored Projects will 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.

C.(iii).(c). The IRE will conduct an institutional oversight process when a PI makes an initial assessment that research may constitute Category 1 or Category 2 and the federal funding agency notifies the institution that the project has the scientific merit to be funded. The IRE:

- Assess 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 B.(i).(a); (2) is reasonably anticipated to result in one or more of the experimental outcomes specified in Section B.(i).(b); and (3) constitutes DURC as

specified in Section B.(i).(c); and

- For Category 2, whether the research (1) involves, or is reasonably anticipated to result in, a PPP as specified in Section B.(ii).(a); (2) is reasonably anticipated to result in one or more of the experimental outcomes or actions specified in Section B.(ii).(b); 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 B.(ii).(c).

If the IRE determines that the research in question does not meet the definition of Category 1 or Category 2 research, the IRE will 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 C 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 B, 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.

For research that is not federally funded and, therefore falls outside of the scope of the federal Policy, the University of Utah IBC will serve the same role of the IRE and work with the PI to develop similar approaches with regard to risk-benefit analyses, risk assessments, risk mitigation strategies, annual reporting and education and training.

C.(iii).(d). The AVPRIC ensures 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 B.(i).(a) or B.(ii).(a) and can be reasonably anticipated to produce one or more of the outcomes or actions listed in Sections B.(i).(b) or B.(ii).(b), or if the PI otherwise believes the project should undergo IRE review.

C.(iii).(e). The Institution will designate an Institutional Contact for Dual Use Research (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.

- For the University of Utah, the Biosafety Officer (BSO) is designated the ICDUR to serve as the institutional point of contact for questions regarding compliance with and implementation of the requirements for the oversight of research that falls within the scope of Section B.

C.(iii).(f). The BSO will 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.

- Classes will be available through Bridge and will be required to be taken annually by any PIs working with agents a biological agent or toxin described in Sections B.(i).(a) or B.(ii).(a)

C.(iii).(g). The BSO will 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.

C.(iii).(h). The BSO will 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.

C.(iii).(i). The BSO will 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.

C.(iii).(j). The AVPRIC will 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.

C.(iii).(k). As necessary, the BSO will assist the PIs of life sciences research when questions arise about whether their research may entail further review or oversight.

C.(iii).(l). The AVPRIC will 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.

C.(iii).(m). On an annual basis, the AVPRIC will provide a formal assurance to relevant federal funding agencies that the research institution is operating consistent with this Policy.

C.(iii).(n). The AVPRIC will make relevant information available to local authorities on Category 1 and Category 2 research, as appropriate.

PIs and the IRE must 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.

In 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.

Detailed Guidance for IRE role in the review process is provided in Appendix 5.

C.(iv). Responsibilities of Federal Funding Agencies

The responsibilities of funding agencies are described in detail in the United States Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP). For proposed and funded research determined to meet the definition of Category 1 or Category 2 research, the funding agency will 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.

C.(v). 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.

Appendix 1.

Table 1 provides examples of risks posed by each type of Category 1 research experimental outcome listed in Section B.(i).(b) of the Policy that, when involving biological agents and toxins listed in Section B.(i).(a) of the Policy, may meet the threshold for Category 1 research oversight. These examples are provided to illustrate the types of risks associated with each experimental outcome and may not represent the full range of possible risks. Example scenarios are described in the Policy Implementation Guidance.

Table 1. Examples of Potential Risks Posed by Category 1 Experimental Outcomes

Category 1 Experimental Outcomes	**Examples of Associated Risks**
i. Increase transmissibility of a pathogen within or between host species	• Creates a pathogen more transmissible than the wild-type pathogen such that it is able to transmit more efficiently in and among human, plant, or animal populations.
ii. Increase the virulence of a pathogen or convey virulence (i.e., the ability of a pathogen to cause disease) to a non-pathogen	• Creates a pathogen more virulent than the wild-type pathogen, resulting in higher morbidity or mortality in human, plant, or animal populations.
iii. Increase the toxicity of a known toxin or produce a novel toxin	• Creates a toxin that causes morbidity or mortality comparable to its natural form at lower doses or creates a toxin that causes higher morbidity or mortality at similar doses comparable to its natural form. • Creates a new toxin, not found in nature, for which there is limited knowledge on how to detect, mitigate, or respond.
iv. Increase the stability of a pathogen or toxin in the environment, or increase the	• Renders a pathogen or toxin with the ability to retain or increase its infectiousness or toxicity outside a living system.

ability to disseminate a pathogen or toxin (e.g., improving characteristics of the pathogen or toxin such as environmental stability and ability to be aerosolized)	• Creates a pathogen or toxin that can be more effectively delivered via aerosolization, or enables novel aerosolization in a pathogen or toxin that typically transmits by other means. • Enhances the environmental stability of a pathogen or toxin, thereby increasing ease of transmissibility or capability to cause disease. • Develops a method for producing or disseminating large quantities of a pathogen or toxin.
v. Alter the host range or tropism of a pathogen or toxin	• Alters the route of transmission of a pathogen or toxin to increase the ease and effectiveness by which a pathogen or toxin may be transmitted, thus having broad potential consequences to humans, animals, or plants. • Alters the host range of a pathogen or toxin, which could put specific populations of humans, plants or animals at risk that were not previously susceptible to a given pathogen or toxin (e.g., makes an avian pathogen infectious to and among mammals). • Alters tissue tropism of a pathogen or toxin resulting in more severe disease manifestation in humans, plants, or animals (e.g., a respiratory pathogen's ability to become neurotropic). Note: Importantly, this type of experimental outcome is specifically for modifications to the pathogen or toxin and does not include the use of model systems in which there is broader or ubiquitous infection due to overexpression or differential expression of the cellular receptor.

vi. Decrease the ability for a human or veterinary pathogen or toxin to be detected using standard diagnostic or analytical methods	• Alters a pathogen or toxin such that it is no longer identifiable by widely used diagnostic tests or other detection modalities. • Alters the nucleic acid sequence of a pathogen or toxin in a way that preserves function but renders the pathogen or toxin no longer identifiable by screening mechanisms designed to detect nucleic acid sequences of concern.* Note: This type of experimental outcome is only applicable for human and veterinary Category 1 pathogens.
vii. Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions (e.g., antimicrobials, antivirals, antitoxins, vaccines)	• Alters a pathogen or toxin such that it causes disease which is not treatable, or severely increases the failure risk with extant therapeutics. • Modifies (i.e., a non-naturally occurring mutation) a pathogen or toxin such that it becomes newly resistant to multiple antimicrobials, antivirals, or antitoxins. • Creates a pathogen or toxin for which existing prophylactic measures available to the general population, such as vaccines, are no longer effective at preventing disease or transmission. Note: This type of experimental outcome is only applicable for human and veterinary Category 1 pathogens.
viii. Alter a human or veterinary pathogen or toxin to disrupt the effectiveness of pre-existing immunity, via immunization or natural infection, against the pathogen or toxin	• Modifies the antigenic profile of a pathogen or toxin such that it is less efficiently or no longer recognized via pre-existing immunity, thereby rendering humans or animals vulnerable to diseases from which they might otherwise have been protected. Note: This type of experimental outcome is only applicable for human and veterinary Category 1 pathogens.

ix. Enhance the susceptibility of a host population to a pathogen or toxin	• Generates a pathogen or toxin with an enhanced or a new ability to compromise immune responses of individuals or populations, thereby enabling the increased spread of disease. • Creates a pathogen or toxin that suppresses the host's immune response, resulting in increased morbidity or mortality.

*Sequences of concern are defined in "Screening Framework Guidance for Providers and Users of Synthetic Nucleic Acids," October 2023. https://aspr.hhs.gov/legal/synna/Documents/SynNA-Guidance-2023.pdf; and "Framework for Nucleic Acid Synthesis Screening," April 2024. https://www.whitehouse.gov/wp- content/uploads/2024/04/Nucleic-Acid_Synthesis_Screening_Framework.pdf.

Appendix 2: Pathogens that May be Subject to Category 2 Oversight

Category 2 oversight may be required in three cases:

A) When the starting agent is a PPP and the research is reasonably anticipated to result in one of the experimental outcomes to produce a modified pathogen that meets the definition of a PEPP;

B) When the starting agent is a not a PPP and the research is reasonably anticipated to result in one of the experimental outcomes to produce a modified pathogen that meets the definition of a PEPP;*

C) When one transfers, generates, uses, or reconstitutes an extinct or eradicated PPP, regardless of whether the extinct or eradicated pathogen will be enhanced relative to its wild-type form.

The paragraphs below provide high-level rationale for why certain pathogens are considered PPPs in their wild-type form and others are only considered PPPs after experimental modification. These examples are intended to assist PIs and IREs in their determination of whether their research involves, or is reasonably anticipated to involve, a PPP, and may be reasonably anticipated to result in a PEPP due to expected experimental outcomes. The paragraphs below illustrate some of the considerations that may be considered when determining if the pathogen and proposed research should be included in Category 2 research assessment. The rationales in this part of the *Implementation Guidance* are not fully comprehensive but can provide general guidelines for how available quantitative metrics can, on a case-by-case basis, help inform the assessments.

*The assessment of whether modification of a starting agent that is not a PPP would be reasonably anticipated to result in a PEPP relies on the specific traits of the pathogen and on the type and degree of enhancement being made. For example, enhancing only the virulence of a pathogen that is already highly virulent, but retains limited transmissibility abilities, would not be expected to meet the definition of PEPP and thus not require Category 2 oversight.

Examples of Pathogens with Pandemic Potential (PPP) in wild-type form

SARS-CoV: SARS-CoV is the etiological agent that causes severe acute respiratory syndrome (SARS). It is an RNA virus transmitted person-to-person most readily through respiratory droplets. During the 2003 outbreak, its basic reproduction rate (R0) was estimated to be about 3 in the absence of controlling measures, giving it potential for wide and uncontrollable spread. However, the lack of transmission before symptom onset allowed for effective implementation of non-pharmaceutical interventions (NPI) to disrupt disease transmission in humans. SARS-CoV is characterized to cause severe disease, given its outbreak case-fatality rate (CFR) was estimated near 10%, with two-thirds of probable cases in the U.S. resulting in hospitalization. While the general population did not have immunity to SARS-CoV, NPIs prevented the 2003 outbreak from reaching pandemic levels. Generally, modifications to SARS-CoV that increase its virulence, transmissibility, or disrupt the effectiveness of pre-existing immunity in humans may be reasonably anticipated to result in a PEPP.

SARS-CoV-2, ancestral lineage, in the absence of population immunity and Medical Countermeasures (MCMs): SARS- CoV-2 is the etiological agent that causes coronavirus disease 2019 (COVID-19). It is an RNA virus transmitted person-to-person most readily through respiratory route, with the capability of spreading from infected persons without symptoms. During its emergence in humans in early 2020, the R0 of SARS-CoV-2 was heterogeneous and context dependent, but was greater than 1 and resulted in wide and uncontrollable spread globally. During that time of the pandemic (i.e., January to May 2020), the population had little to no pre-existing immunity and effective countermeasures were not available. The ancestral lineage of SARS- CoV-2 caused moderate to severe disease in individuals at that time: for example, among laboratory-confirmed infections with case reports submitted to CDC between January and May 2020, the case hospitalization rate was estimated at 14% and the CFR at 5.4%. Additionally, pre-symptomatic and asymptomatic transmission dynamics and a range of virulence from asymptomatic to lethal disease contributed to wide and uncontrollable spread on a global level significantly impacting public health, the capacity of health systems to function, and national security. Within the context of early 2020, the ancestral lineage of SARS-CoV-2, or emerging pathogens with comparable characteristics, would be characterized as a PPP due to lack of population immunity and effective medical countermeasures. As of May 2024, SARS-CoV-2 would not be considered a PPP because of the development of vaccines and other effective medial countermeasures, as well as the rise of population immunity. If SARS-CoV-2, regardless of lineage, were genetically modified to enhance transmissibility, virulence, and disrupt effectiveness of pre-existing immunity in humans, it could still be anticipated to result in a PEPP.

Examples of non-PPPs that could result in a PEPP *after modification via listed experimental outcome*

Ebola virus: Ebola is a term commonly used for disease caused by filoviruses in the genus *Orthoebolavirus*, including most prominently Ebola virus (*Orthoebolavirus zairense*) as well as several other species. These RNA viruses are transmitted person-to-person most readily through direct contact with blood or body fluids from symptomatic infected persons rather than through respiratory route. One review of published estimates proposed a pooled mean R0 for the two most common species of about 2, with high heterogeneity and variability across countries, while acknowledging its R_t can be affected by other characteristics modifying population susceptibility. Ebola virus causes severe disease. CDC lists outbreaks with estimates of CFR typically greater than 30% and sometimes greater than 80% depending on the outbreak, and essentially all diagnosed illnesses result in hospitalization. Ebola viruses have also caused reoccurring outbreaks since the first recognized cases in 1976, with the largest in 2014-2016 totaling about 28,000 cases and 11,000 deaths. None of these outbreaks progressed to pandemic-level spread, even though specific MCMs were generally not available and resources for implementing NPIs were often limited. Some preventive and therapeutic countermeasures for *Orthoebolavirus zairense* have been approved in recent years that might further help with containment of outbreaks. Based on historical experience with the nature and extent of spread and on the potential for improved control measures, the wild-type Ebola virus is not considered a PPP; however, significant modification to the virus, particularly enhancing transmissibility or disrupting the effectiveness of pre-existing immunity, may result in an Ebolavirus with enhanced pandemic potential, i.e., a PEPP.

SARS-CoV-2, Omicron lineage, given population immunity as of May 2024: SARS-CoV-2 is the etiological agent that causes COVID-19. The omicron lineage of SARS-CoV-2 became dominant in late 2021 and has spread widely and uncontrollably, with some R0 estimations around 10, but an Rt ranging from 10 to less than 1 depending on levels of pre-existing immunity and other factors. Given population immunity as of May 2024, its CFR is generally considered to be less than 0.5% and it generally is not considered to cause moderate to severe disease in most of the human population. Due to MCMs, including approved vaccines and therapeutics, and the existing population immunity, the circulating omicron lineage of SARS-CoV-2 is currently not considered to pose a significant threat to the capacity for health systems to function or national security. Experiments that are reasonably anticipated to enhance the virulence of or evade pre-existing immunity to the omicron lineage SARS-CoV-2, or other emerging variants with similar characteristics, may result in a PEPP.

Highly Pathogenic Avian Influenza A(H5) and A(H7) subtypes: Avian influenza A viruses may cause severe (highly pathogenic avian influenza, HPAI) or mild/inapparent (low pathogenic avian influenza, LPAI) infections in poultry, can infect and be transmitted by wild birds, and

occasionally spill over to result in sporadic mammalian, including human, infections. Either HPAI or LPAI can cause either mild or severe infections in humans. Particular concern has been raised regarding the potential for severe and fatal human infections with H7N9 and H5N1, with estimated CFRs of about 40-50% of detected cases, although the completeness of detection is unclear and milder cases have also been reported. However, human-to-human transmission has been rare and non-sustained. There are several MCMs or candidate MCMs that might also help to limit transmission depending on specific circumstances. Because A(H5) and A(H7) viruses do not transmit efficiently in humans, they are not considered PPPs in their wild-type state. However, because they can cause moderate to severe disease in humans, modification of A(H5) and A(H7) viruses that facilitate enhanced human-to-human transmission compared to their parental strains could reasonably be anticipated to pose a significant threat to public health, the capacity of health systems to function, or national security, and result in a PEPP. This type of research would be considered Category 2 and necessitate department-level review before the research commences or proceeds.

Note: Research that is reasonably anticipated to result in one or more of the experimental outcomes listed in Section B.(i).(b) of the Policy on an HPAI virus such as A(H5) or A(H7), if not designated as Category 2 research, may be considered Category 1 research due to the viruses' potential to pose a significant threat to animals.

Appendix 3

Table 2 provides examples of risks posed by each type of Category 2 research experimental outcome listed in Section B.(ii).b of the Policy that, when conducted with pathogens described in Section B.(ii).a of the Policy, may be assessed as being 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. These examples are provided to illustrate the types of risks associated with each experimental outcome and may not represent the full range of possible risks. Example scenarios are described in the Policy Implementation Guidance.

Table 2. Examples of Potential Risks Posed by Category 2 Experimental Outcomes

Category 2 Experimental Outcomes	**Examples of Associated Risks**
i. Enhance transmissibility of the pathogen in humans	• Creates a pathogen more transmissible than the wild-type pathogen such that it is able to spread widely and uncontrollably in the human population. • Creates a pathogen able to survive outside the host and/or withstand environmental conditions longer than the wild-type pathogen, facilitating transmission such that it is able to spread widely and uncontrollably in the human population. • Creates a pathogen with altered tropism (i.e., tissue tropism or host range), that could change the route of transmission, resulting in increased transmissibility relative to the wild-type pathogen such that it is able to spread widely and uncontrollably in the human population. • Increases transmissibility of an animal or zoonotic pathogen, such that it can now utilize new non-human vectors or reservoirs to spread widely and

	uncontrollably in the human population.
ii. Enhance the virulence of the pathogen in humans	• Creates a pathogen more virulent than the wild-type pathogen (i.e., resulting in higher morbidity or mortality) such that it is able to cause moderate to severe disease 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	• Modifies a pathogen such that it is able to spread widely and uncontrollably in the human population, and cause moderate to severe disease, despite existing population immunity against the wild-type pathogen.
iv. Generate, use, reconstitute, or transfer an eradicated or extinct PPP, or a previously identified PEPP	• Reconstitutes or creates a pathogen for which little or no natural immunity exists. • Transfers a reconstructed eradicated or extinct PPP or a previously identified PEPP to another laboratory with or without further experimentation.

Experiments that May be Subject to Category 2 Oversight

Examples of experiments that could be reasonably anticipated to result in creation of a PEPP, include but are not limited to:

- Certain serial passaging experiments to select for increased virulence and/or transmissibility in animal models and/or cell and organoid systems that are designed to model human pathogenesis or transmission
    a. Examples of serial passaging experiments that could fall under Category 2 oversight include:
        i. Serial passaging a respiratory pathogen that replicates in ferrets to select for increased transmissibility between animals, as ferrets have a similar lower and upper respiratory tract as humans and are often used as human surrogates for

transmission studies.

ii. Serial passaging experiments in primary human cells or human organoid systems that are reasonably anticipated to select for increased virulence or transmissibility in humans.

b. Examples of serial passaging experiments that are not included in Category 2 oversight:

i. A mouse model designed to overexpress a human receptor to study viral infection that result in abnormal pathogenesis (e.g., encephalitis). Increased virulence in the mouse model does not necessarily represent increased virulence in humans due to differences in receptor expression compared to humans.

ii. Serial passaging in animal models to adapt the virus to that system in order to develop a model for pathogenesis often results in mutations that improve replication for that species and diverge away from infecting humans.

- Experiments deliberately generating PPP strains that are resistant to FDA-approved, cleared, or licensed Medical Countermeasures (MCMs), when such resistance trait(s) are not known to occur naturally and such resistance trait(s) could compromise the ability to control the morbidity, mortality, or spread in humans.
- Modifying the host range of highly virulent animal pathogens (e.g., avian influenza) to increase transmission between humans or animal reservoirs and humans.
- Creating a chimera from two PPPs such that the resulting pathogen could have enhanced transmission or virulence as compared to at least one of the progenitor pathogens.
- Assembling and rescuing infectious 1918 pandemic influenza virus through a reverse genetics protocol.

Appendix 4. General Overview of the Policy Oversight Framework

This Appendix describes the organizational framework for research oversight and broadly articulates the roles and responsibilities of entities that conduct research (i.e., PIs and research institutions) and entities that fund or sponsor research (i.e., federal funding agencies). The framework will be implemented by federal funding agencies in compliance with applicable laws, regulations, and policies, such as through the development of terms and conditions for funding awards. See Figure 1 for a graphic representation of the workflow. Generally, the process for the research oversight system described in the Policy is as follows:

1. The PI makes an initial assessment of whether their proposed or ongoing research may be within scope of Category 1 and/or Category 2 based upon i) the biological agent or toxin and ii) the experimental outcome or actions (as specified in the Policy in Section B).

    i. PIs and IREs are reminded to also assess Category 2 research for potential DURC risks. The research institution is responsible for ensuring that PIs are aware of and executing this responsibility appropriately.

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

3. 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.

4. The IRE reviews the PI's initial assessment and confirms whether proposed or ongoing research is within the scope of Category 1 and/or Category 2 research. If so, the IRE determines whether the research is Category 1 or Category 2, based on a risk assessment under Section B of the Policy. The research institution notifies the federal funding agency of the results of its determination, and the federal funding agency evaluates and verifies the research institution's assessment. Examples of risk assessment measures are described in Appendix 5.

    Note: Any research that meets the definition of both Category 1 and Category 2 research is designated as Category 2 research and must proceed through Category 2 assessment and risk mitigation.

5. If the research is assessed to be Category 1 or Category 2, the IRE will conduct a risk-benefit assessment and develop a draft risk mitigation plan for the conduct and communication of the research. The PI or research institution submits the risk-benefit assessments and a risk mitigation plan to the federal funding agency. Examples of risk mitigation approaches are described in Appendix 6.

6. The federal funding agency reviews the risk-benefit assessments and risk mitigation

plan as follows:

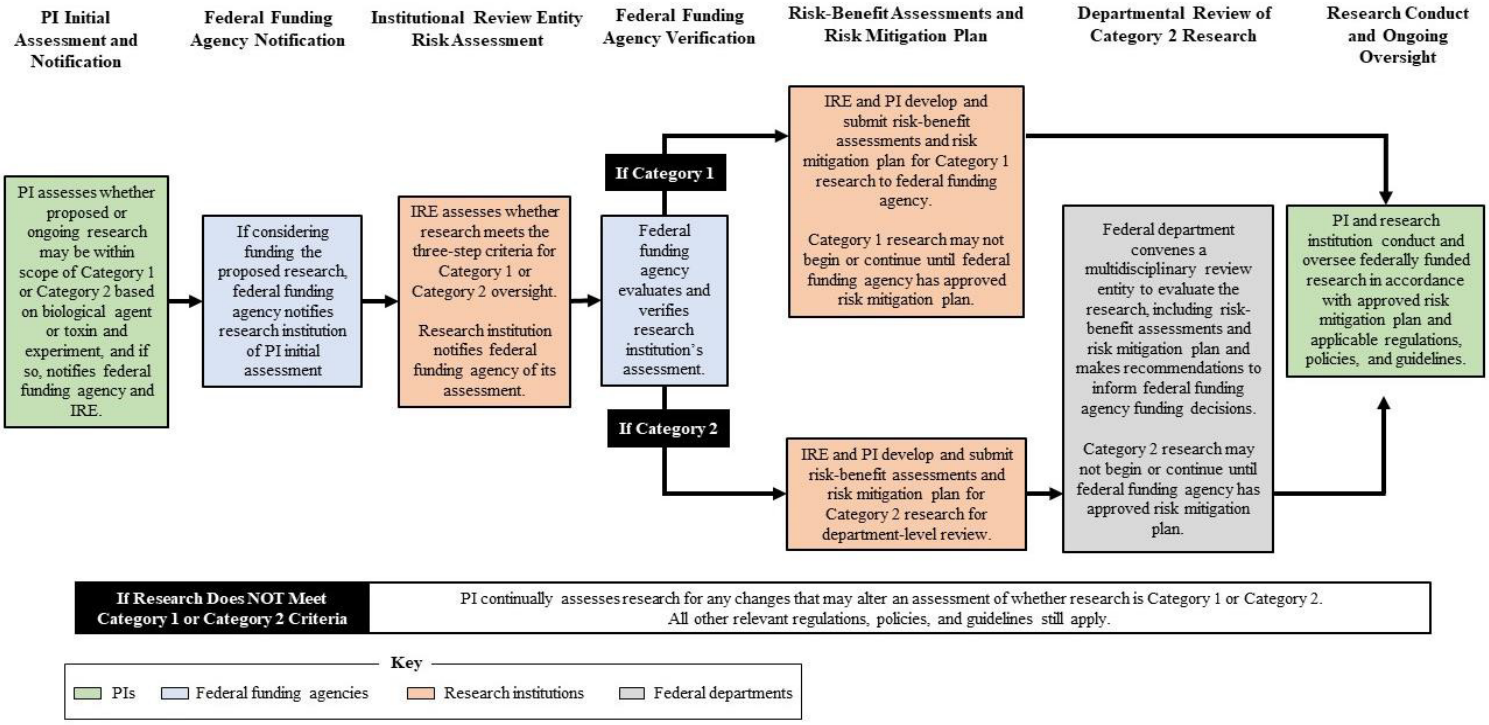
- For specific experiments within the research proposal determined to be Category 1, the federal funding agency evaluates the research institution's risk-benefit assessments and determines whether the potential benefits justify the potential risks prior to the funding decision. These specific experiments will not proceed until the federal funding agency approves the risk mitigation plan.

- For specific experiments within the research proposal determined to be Category 2, the federal funding agency refers the proposed research for department-level review. 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 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.

7. If research is identified as potentially within the scope of Category 1 or Category 2 research during the course of experimentation, the PI should halt further work, notify the federal funding agency, and contact their IRE to conduct the required assessments consistent with the procedures in the Policy for assessing Category 1 or Category 2 research.

It is the responsibility of PIs and research institutions to identify research that may fall within scope of Category 1 and/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. PIs should also 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

Figure 1. Overview of Review Process for Category 1 or Category 2 Research. Depicts the general workflow for review and assessment of research under to the Policy involving PIs (green boxes), research institutions (peach boxes), federal funding agencies (blue boxes), and federal departments (gray box).



Appendix 5: Guidance for the IRE Review Process

A summary of the key actions and responsibilities for IREs during the review and assessment of research is provided below. As a reminder, the IRE is not required to review the research for Category 1 or Category 2 designation until after the federal funding agency has determined that the research is eligible for federal funding based on a scientific merit review. It is recommended that IREs begin their processes by considering whether the proposed studies fall under Category 2 research first, and then considering Category 1 research as described below in 1 and 2, respectively. These key actions and responsibilities are not necessarily recommended to be implemented sequentially 1 through 11. Depending on the outcome at key steps, indicators in the details below can help guide workflow order. See Figure 2 for a graphic representation of the workflow.

Note: Any research that meets the definition of both Category 1 and Category 2 research is designated as Category 2 research and must proceed through Category 2 assessment and risk mitigation.

1. Assess for Category 2 Research

Step 1: Confirm that the research involves, or is reasonably anticipated to result in, a PPP.

To determine whether research should be designated as Category 2, the IRE should assess and confirm the PI's assessment that the research involves, or is reasonably anticipated to result in, a PPP, as specified in B.(ii).(a) of the Policy. More information on how to assess this is included in Part B.2 of this *Implementation Guidance*.

- If the research involves a PPP or is reasonably anticipated to result in a PPP, including the generation, use, reconstitution, or transfer of an eradicated, extinct, or existing PPP, proceed to Step 2.

- If the research is NOT found to involve a PPP and is NOT reasonably anticipated to result in a PPP, including generation, use, reconstitution, or transfer an eradicated, extinct, or existing PPP, proceed to Step 4.

Step 2: Confirm that the research is reasonably anticipated to result in, or does result in, one or more of a listed experimental outcomes or actions in scope of Category 2 research.

To determine whether research should be designated as Category 2, the IRE should assess and confirm the PI's assessment that the research is reasonably anticipated to result in, or does result in, one or more of a listed experimental outcomes or actions, listed in Section B.(ii).(b)

of the Policy.

- If the research is reasonably anticipated to result in, or does result in, one or more of the listed experimental outcomes or actions as described in Section B.(ii).(b) of the Policy, proceed to Step 3.

- If the research is NOT reasonably anticipated to result in one or more of the listed experimental outcomes or actions as described in Section B.(ii).(b) of the Policy, proceed to Step 4.

Step 3: Assess risks of potential Category 2 research and determine whether research should be designated as Category 2.

To determine if research should be designated as Category 2, the IRE should assess the research for biosafety and biosecurity risks. In performing the risk assessment, the IRE should examine descriptions of the research in question, the PI's assessment of the applicability of the pathogen (Step 1) and categories of experimental outcome or action (Step 2), and other relevant information. In designating research as Category 2, the IRE is required to determine whether the research can be 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 outlined in Section B.(ii).(c) of the Policy.

Key to this Category 2 determination is an assessment of whether the research involves a pathogen that, through one or more of the listed experimental outcomes, *may pose a significant threat to public health, the capacity of health systems to function, or national security*. Research involving PPPs, whether eradicated, extinct, or existing, may not always rise to the level of posing this type of significant threat as indicated above. In such cases, the research would not be considered to reasonably result in the development, use, or transfer of a PEPP or extinct or eradicated PPP needing Category 2 oversight. Factors that could be useful in determining these types of significant threats include the pathogen's cumulative capability for wide and uncontrollable spread, extent of disease, the degree of pre-existing population immunity, and the availability of Medical Countermeasures (MCMs) to provide preventative and treatment interventions, and other public health and social considerations. For example, if upon exposure or misuse of the pathogen the nation's hospital systems were to become inundated with patients infected with a pathogen causing moderate to severe disease morbidity and/or mortality, it would pose a significant threat to public health, the capacity of health systems to function, or national security.

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Examples of materials to consider during this risk assessment include the project proposal, any project reports, and examples of similar research in the literature. Biosafety and

biosecurity assessments should also identify hazardous potential of the pathogen or information as a result of identified experimental outcome(s), actions that can reasonably result in exposure to or misuse of the potential PEPP or information, likelihood that such exposure or misuse will occur, and potential consequences of such an exposure or misuse. Established risk assessment models such as those described in the Biosafety in Microbiological Biomedical Laboratories (BMBL) or *NIH Guidelines* can help guide these assessments. IREs are encouraged to consult with their relevant institutional, local, or state security offices and departments, as appropriate, for any additional factors that may be helpful to consider when conducting assessments related to public health, the capacity of health care systems to function, or of a significant threat to national security.

There are two potential outcomes following the risk assessment:

- If the research can be reasonably anticipated to result in the development, use, or transfer of a PEPP or an eradicated or extinct PPP that poses a significant threat to public health, the capacity of health systems to function, or national security, designate the research as Category 2 research. The IRE should proceed to Step 6a to assess the Category 2 research for potential DURC risks, and then notify the funding agency of the Category 2 designation (Step 7).

- If the research is NOT reasonably anticipated to result in the development, use, or transfer of a PEPP or an eradicated or extinct PPP that poses a significant threat to public health, the capacity of health systems to function, or national security, the research does not meet the scope of Category 2 research and the IRE does not need to proceed with Category 2 assessment and risk mitigation. The IRE should proceed to Step 4 to evaluate the research for Category 1 designation. However, the PI should be informed that if at any time the reviewed research may meet the scope of Category 1 or Category 2 research, the PI should halt further work, refer the research again to the IRE for review, and notify the funding agency.

2. Assess for Category 1 Research

Step 4: Confirm that the research involves one or more of the listed biological agents or toxins.

To determine whether research should be designated as Category 1, the IRE should assess and confirm that the PI's assessment that the research directly involves one or more of the biological agents or toxins listed described in Section B.(i).(a) of the Policy. A checklist of these biological agents and toxins is included in Appendix C of this *Implementation Guidance*.

i. If the research involves one or more of the biological agents or toxins listed in Section B.(i).(a) of the Policy, the IRE should proceed to Step 5.

ii. If the research does NOT involve one or more of the biological agents listed in Section B.(i).(a) of the Policy, the research should not be designated as Category 1 research and the IRE does not need to continue with the Category 1 assessment and risk mitigation. However, the IRE must still proceed to Step 7 to notify the appropriate federal funding agency of its findings. The PI should be informed that if at any time the reviewed research may meet the definition of Category 1 or Category 2 research, the PI should halt further work, refer the research again to the IRE for review, and notify the federal funding agency.

Step 5: Confirm that the research is reasonably anticipated to result, or does result, in one or more of the listed experimental outcomes in scope of Category 1 research.

To determine whether research should be designated as Category 1, the IREs should assess and verify the PI's assessment of whether the research is reasonably anticipated to result, or does result, in one or more of the listed experimental outcomes listed in Section B.(i).(b) of the Policy.

The IRE should examine descriptions of the research in question, the PI's assessment of the applicability of the categories of experiments, and other relevant information, as warranted. Examples of materials to consider include the project proposal, any project reports, any previous outcomes of dual use reviews, and examples of similar research in the literature.

- If the research is reasonably anticipated to result, or does result, in one or more of the listed experimental outcomes on a designated biological agent or toxin identified in Step 4, proceed to Step 6 to assess dual use risks and determine whether the research should be designated as Category 1 research.

- If NONE of the listed experimental outcomes applies, the research should not be designated as Category 1 research and the IRE does not need to continue with the Category 1 assessment and risk mitigation. However, the IRE must proceed to Step 7 to notify the appropriate federal funding agency of its findings. The PI should be informed that if at any time in the future if the reviewed research may meet the definition of Category 1 or Category 2 research, the PI should halt further work, and refers the research again to the IRE for review, and notify the federal funding agency.

Step 6: Assess the dual use risk associated with the research and determine whether research should be designated Category 1 (if applicable).

Step 6a: Assess the dual use risk associated with the research.

Research already designated as Category 2, or research being assessed as potential Category 1,

should next be assessed for risks associated with DURC.

DURC is defined as "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."

When considering whether the research in question meets the definition of DURC, the IRE should identify the risks associated with the potential misuse of the information, technologies, or products that may be generated. Although risk assessments may be either quantitative or qualitative, the assessment process outlined below is qualitative in nature and requires the consideration and judgment of the IRE on the following:

A) The ways in which knowledge, information, technologies, or products from the research could be misused to harm public health and safety, agriculture, plants, animals, the environment, materiel, or national security.

B) The ease with which the knowledge, information, technologies, or products might be misused and the feasibility of such misuse.

C) The magnitude, nature, and scope of the potential consequences of misuse.

The IRE should consider the points in Box 1 below to assess the potential risks associated with conducting the research in question or communicating its results at any time during the lifecycle of the project. These points address some of the aspects of potential DURC that could be considered, but they are not exhaustive – IREs should augment these points to fit their needs and the research under consideration. This risk assessment is intended to assist IREs in determining whether the research in question meets the definition of DURC. In cases where the research is determined to be DURC, this assessment will also inform the subsequent process of identifying strategies for mitigating those risks.

Box 1: Points to Consider in Assessing Research for its Dual Use Potential
• Type of Misuse: In what ways could the knowledge, information, products, or technologies from the research be misused? The risk of misuse may be higher for research that can be directly misused than for research that requires significant additional scientific advances to facilitate its misapplication.   ○ What types of knowledge, information, products, or technologies are anticipated to be generated through the research?

- Can the knowledge, information, products, or technologies from the research be misapplied with no, or only minor, modification to cause harm?
    - If so, how?
    - If not, do the outcomes of the research need to be combined with other knowledge, information, products, or technologies in order to pose a threat? If so, is the other knowledge, information, products, or technologies already or readily available?
- Is there concern about immediate or near-future potential misuse, or is the concern about misuse in the distant future? Consider the time frame in which information from the research might be misused. Information that can be misused in the near term may be of greater concern.

- Ease of Misuse: How easily could the knowledge, information, products, or technologies be misapplied to do harm with no, or only minor, modification? Consider the technical expertise and/or physical resources that would be required to apply the knowledge, information, products, or technologies for malevolent purposes. The risk of misuse may be lower for knowledge, information, products, or technologies that would be expensive, difficult to procure, or that require a high degree of technical skill to facilitate such misuse.
    - Would misuse of the knowledge, information, products, or technologies require a low or high degree of technical skill and sophistication to use the information from dual use research for harmful purposes? Alternatively, would it make achieving the harmful outcome easier for an unsophisticated actor?
    - Would misuse of the knowledge, information, products, or technologies require materials, equipment, or reagents that are expensive or difficult to procure?
- Dissemination: How will the knowledge, information, products, or technologies of the research in question be shared or distributed? Knowledge, information, products, or technologies that are freely available and widely distributed may be more easily accessed by individuals with harmful intent.
    - Who will have access to the knowledge, information, products, or technologies?
    - Will the knowledge, information, products, or technologies be shared openly or remain within the laboratory?
- Information Risks: What is the novelty of the information provided by the research or

research methods? Research that adds novel information or consolidates information in novel ways may be of greater concern than information that is already widely available.

  - Have the results of similar research been previously described or shared? If so, at what venues and in what detail? How readily available are these results?

- Potential Vulnerabilities: Does the research highlight vulnerabilities or consolidate existing information in ways that highlight vulnerabilities in existing MCMs, public health approaches, or agricultural infrastructure? Research that highlights vulnerabilities could impede our ability to prepare for and respond to disease outbreaks that could impact public health, agriculture, food security, economic security, or national security.

- Potential Consequences: Given your responses to the preceding questions, how readily could the knowledge, information, products, or technologies from the research be used to threaten public health, agriculture, food security, economic security, or national security?

  When considering the potential consequences of the misuse of knowledge, information, technology, or products obtained from research, think broadly about the potential impacts on public health, agriculture, food security, economic security, or national security from the intentional misapplication of the results from the research in question. In general, information that could be misused to harm large populations of humans, plants, or animals; cause public panic; or require costly response efforts would be considered a greater risk.

  - Consider the nature of the potential consequences (e.g., harm to public health, agriculture, food security, economic security, or national security) that might result from misuse of the research results in question. Information that could be misused to harm numerous sectors of society or the environment may be of greater concern.

  - Consider the scope and magnitude of the potential consequences. Research or research information that could be misused to cause severe harm, disease, or consequences is generally considered to be of greater concern. Could the impact on people, animals, and/or plants be considered minor, moderate, or major?

  - Consider the availability and efficacy of MCMs. Sufficient and efficacious MCMs could decrease concern about the consequences of misuse. MCMs may include

drugs, biological products, public health practices, pesticides, or devices intended for diagnosis, detection, mitigation, prevention, or treatment.

- Are there currently any MCMs to help mitigate the potential consequences of misuse?
- Are the MCMs readily and widely available?
- What are the impacts on the healthcare system when it comes to administering the MCMs?

Note: IRE and PIs are expected to be well-positioned to make technical assessments about how readily and in what ways certain knowledge, information, products, or technologies obtained from research might be misused.

Step 6b: Determine whether research should be designated Category 1.

To determine whether research should be designated as Category 1, IREs should assess whether the research, based on current understanding, constitutes DURC, as specified in Section B.(i).(c) of the Policy. Careful consideration of the dual use risks associated with the research should underpin the determination of whether the research in question meets the definition of DURC.

- If the research is already considered Category 2 research, it is not Category 1 research. Dual use risk mitigation such as responsible research communication still applies and should be incorporated into the risk mitigation plan developed for the Category 2 research, as appropriate. Proceed to Step 7 to notify the federal funding agency of Category determination.
- Based on the dual use risk assessment, if the research meets the definition of DURC, and is not already considered Category 2 research, designate the research as Category 1 and proceed to Step 7 to notify the federal funding agency of Category determination.
- Based on the risk assessment carried out in Step 6a, if the research does NOT meet the definition of DURC, and is not designated as Category 2 research, then the research is not subject to additional institutional oversight and the IRE does not need to continue with the review. However, the IRE must proceed to Step 7 to notify the appropriate federal funding agency of its findings. The PI should be informed that if at any time the reviewed research may meet the definition of Category 1 or Category 2 research, the PI should halt further work, refer the research again to the IRE for Category 1 or Category 2 review, and notify the federal funding agency.

3. Risk-Benefit Assessments, Risk Mitigation Plan, and Oversight of Category 1 or Category 2 Research

Step 7: Notify federal funding agency of Category determination.

- If the IRE determines that the research meets Category 1 or Category 2 designation, the IRE should inform the PI, and funding includes drafting of risk-benefit assessments (proceed to Step 8 and Step 9) and a risk mitigation plan (Step 10).

- If the IRE determines that the research does NOT meet Category 1 or Category 2 designation, the IRE must still inform the PI and the federal funding agency of these findings. However, no further actions are needed.

It is the responsibility of PIs and research 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.

The research institution should notify the appropriate federal funding agency of the IRE's findings as soon as possible and no later than within 30 calendar days after the of the IRE's determination.

If significant concerns about Category designation remain, the Institutional Contact for Dual Use Research (ICDUR) should be informed. The ICDUR and the IRE may choose to consult with a representative of the federal funding agency.

Step 8: Assess the potential benefit

In order to determine the acceptable level of risk associated with Category 1 and Category 2 research and the best mitigation strategies, the research should be assessed for its potential benefits. There are many benefits inherent to scientific research, but it must be performed safely and securely. Such benefits may impact various sectors of society and be realized over different time frames. The points in Box 2 below address some aspects of the research that could be considered, but they are not exhaustive. IREs should augment these points to fit their needs and the research under consideration.

Box 2: Points to Consider in Assessing the Benefits of the Category 1 and Category 2 Research
• What are the potential benefits to public health, agriculture, food security, economic security, or national security from the research? • What potential solution(s) does the research offer to an identified problem or vulnerability?

- How would the research be useful to the scientific, public health, national security, or agriculture communities?
- How will the knowledge, information, technology, or products generated from the research be broadly applicable (e.g., to human health, multiple scientific fields, populations of organisms)?
- If a benefit has been identified, in what time frame (e.g., immediate, near future, years from now) might this research benefit public health, agriculture, food security, economic security, or national security?

Step 9: Develop risk-benefit assessments.

IREs should produce a risk-benefit assessment that assesses the potential benefits and the potential risks of the proposed research in a clear and thorough manner. Weighing the risks and benefits of Category 1 and Category 2 research can be challenging because risks and benefits are not always easily quantified in ways that are comparable.

The process of weighing the risks and benefits of Category 1 and Category 2 research is an exercise in making rational assessments, despite uncertainty. Uncertainty can best be managed by ensuring that the process draws on the expertise and perspectives of a group of individuals of diverse backgrounds and experience. Discussion and debate within such a group can help to (a) identify and mitigate the biases that individuals may inevitably bring to the challenges of this sort, (b) uncover assumptions in arguments, (c) scrutinize and test the basis for judgments, and (d) yield conclusions that represent a consensus and are optimally defensible.

In assessing risks, some assessments will entail judgments of feasibility that may be expressed in such phrases as “highly likely” or “less likely” rather than with quantitative measures (e.g., 90 percent or 10 percent). Others will be expressed in such phrases as “readily” or “very easily,” or “with difficulty” or “with great difficulty.” With still other assessments, the aim will be to project the possible consequences of the misuse of Category 1 and Category 2 research knowledge, information, products, or technologies and to describe the magnitude of these consequences (e.g., projected rates of morbidity and mortality —– in humans, animals, or plants —– due to infection with or exposure to biological agents or toxins). Such projections will often be based on or extrapolated from limited data and thus will be associated with varying degrees of uncertainty. In assessing the benefits, similar challenges will be encountered. It will be difficult to identify with precision the concrete benefits that can be reasonably expected to accrue from a particular body of Category 1 and Category 2 research and to project, with accuracy, the time frame within which those benefits could be realized. Judgments may also be

expressed in qualitative rather than quantitative terms. They may be tempered with some degree of uncertainty.

Box 3 provides examples of several questions that can be posed with respect to most Category 1 and Category 2 research that undergoes this process of risk-benefit assessment. The answers to these questions will inform the development of a risk mitigation plan.

Box 3: Points to Consider for Weighing the Risks and Benefits of Category 1 and Category 2 research
• Are there other ways in which the potential benefits of the research could be achieved that would reduce the anticipated risks? • Could the knowledge, information, products, or technologies of concern be more readily applied to improvements in surveillance, development of MCMs, or other beneficial purposes than to malevolent applications? What reasons or evidence support the answer to this question? • What is the time frame in which potential benefits might be realized? Does it rely on other research endeavors? • How might the potential benefits and the anticipated risks be distributed across different human, animal, and plant communities? Who or what will be the likely beneficiaries of the potential benefits? Who or what will bear the anticipated risks? Is it likely that one or more specific populations will bear the burden of the anticipated risks? • Considering the anticipated risks along with potential benefits, are the risks of such a feasibility and magnitude that they warrant proceeding after developing and implementing a risk mitigation plan? Are the potential benefits of significant magnitude to warrant proceeding despite the risks? • What is the most responsible way to proceed? Do measures in the risk mitigation plan effectively and measurably reduce the anticipated risk?

Step 10: Develop a draft risk mitigation plan.

The risk-benefit assessments will be used by the PI and IRE to develop a draft risk mitigation plan. Both the risk-benefit assessments and the draft mitigation plan should be provided to the federal funding agency for review and approval within 90 calendar days from the IRE determination.

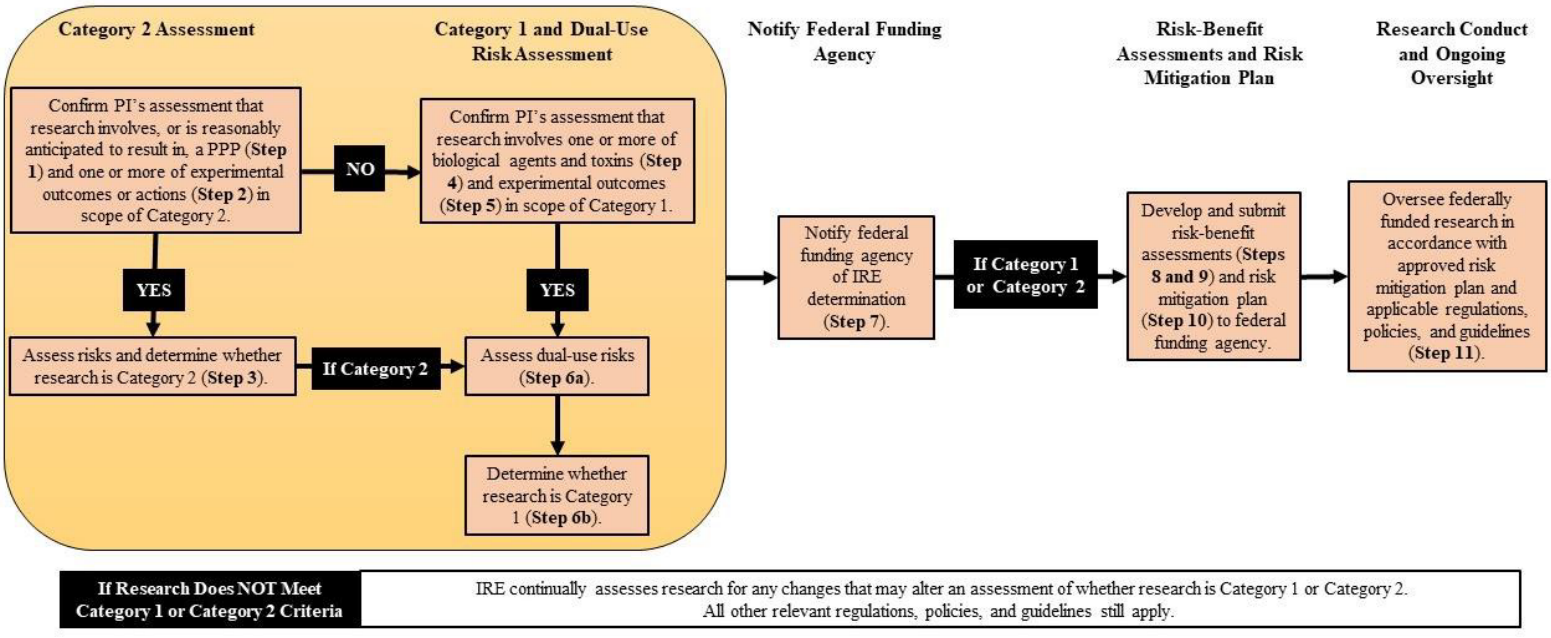
The IRE, along with the PI, should draft a risk mitigation plan and determine if additional measures are needed to mitigate risks associated with Category 1 or Category 2 research. Guidance for developing this risk mitigation plan is provided in Part F of this *Implementation Guidance*.

Step 11: Oversee the research.

Following approval of risk-benefit assessments and the risk mitigation plan by the federal funding agency, the IRE assists with and oversees the implementation of the risk mitigation plan. This includes ensuring that the research is conducted in accordance with the approved risk mitigation plan and is periodically reviewed by the research institution to determine if additional modifications to the risk mitigation plan are appropriate.

The IRE should also evaluate the risk mitigation plan at least annually and, working with the funding agency as appropriate, modify the plan as necessary for the duration of the research.

Figure 2. IRE Review Process for Category 1 or Category 2 Research. Depicts the IRE workflow for review and assessment of research that might be subject to the Policy.



Appendix 6: Guidance for Drafting a Risk Mitigation Plan

1. Strategies for Developing a Draft Risk Mitigation Plan

It is important to consider the nature of the risks associated with Category 1 and Category 2 research prior to identifying strategies for mitigating those risks. Although risk assessments may be quantitative or qualitative, the assessment process outlined in Appendix 5 is, for the most part, qualitative in nature and requires consideration and judgment.

Some of the identified risks may be addressed by risk mitigation measures already in place. For example, some of the listed agents are regulated under the Federal Select Agent Program (FSAP), which requires appropriate biosafety and biosecurity oversight of specific biological agents and toxins that have the potential to pose a severe threat to human, animal, or plant health, or to animal and plant products. The *NIH Guidelines* and *BMBL* also contain biosafety and physical security provisions that may be applicable to research within scope of the Policy.

The biological agents generated by the Category 1 or Category 2 research being reviewed should have a designated management plan for their full life-cycle: from the time of creation, appropriate inventory and access controls, tracking (if transferred to or shared with third parties), and ultimate safe destruction.

For each project containing research identified as Category 1 or Category 2 research, the Policy requires that where necessary, additional risk mitigation measures be proposed and instituted. The IRE should consider the strategies outlined in Box 4 to determine the most appropriate risk mitigation measures that are tailored specifically to the research in question. These strategies are neither comprehensive nor mutually exclusive and may be used in combination. More than one strategy may be applicable for addressing a given risk.

Box 4: Menu of Risk Mitigation Measures that May Be Applicable to Your Research
Risk Mitigation Measures Already in Place at Your Institution Use all applicable measures from this menu in your draft risk mitigation plan to summarize the risk mitigation measures that the IRE and/or PIs have identified as already in place and address the risks associated with the Category 1 and Category 2 research in question. Specify any others that are not listed. • The research is being conducted in compliance with the select agent regulations (42 CFR part 73, 9 CFR part 121) biosafety and biosecurity requirements.

- The researchers are required by the terms and conditions of the grant or contract to adhere to the well-established biosafety and containment practices and procedures in the *NIH Guidelines*.
- The researchers are required by the terms and conditions of the grant or contract to adhere to the well-established biosafety and containment practices and procedures in BMBL.
- The researchers are required by the terms and conditions of the grant or contract to conduct the research at the appropriate BSL (and attest, with documentation if available, that the BSL facility is certified against appropriate standards to the appropriate level of containment, if not registered with the FSAP).
- The *NIH Guidelines* require that the biosafety aspects of the research be reviewed and approved (where appropriate) by an Institutional Biosafety Committee.
- The research has been reviewed for its Category 1 or Category 2 potential by an appropriately constituted IRE.
- The PI and researchers are required by the terms and conditions of the grant or contract to undergo training in the safe conduct of research with the biological agent(s) or toxin(s) in question.
- The researchers have a designated management plan for the full life-cycle a biological agent(s) or toxin(s) generated from the research; from time of creation, appropriate inventory and access controls, tracking (if transferred to or shared with third parties), and ultimate safe destruction.
- The researchers are required by the terms and conditions of the grant or contract to undergo training in the responsible conduct of research and/or research ethics as required by the institution and federal guidelines.
- The researchers are required by the terms and conditions of the grant or contract to be enrolled in an occupational health surveillance program, when appropriate.

Supplementary Risk Mitigation Measures that Could be Newly Implemented for Your Research:

Select all applicable additional measures from this menu to summarize the risk mitigation measures that the IRE, or PIs, have identified as additional measures necessary to mitigate the risks associated with the Category 1 or Category 2 research in question. Specify any others that are not listed. These measures may be in place or

proposed:

- Modify the design or conduct of the research to mitigate potential risks while achieving the benefits of the proposed research.
- Apply specific or enhanced biosafety and biosecurity measures.
- Evaluate MCM efficacy against biological agents or toxins resulting from Category 1 and/or Category 2 research prior to initiating research. Where effective MCMs exist and are readily and widely available, it may be useful to include that information in publications.
- Refer the institution to available educational tools for assessing and mitigating potential risks of the research.
- Regularly review, at the institutional level, emerging research findings for additional Category 1 and Category 2 research.
- Request that institutions notify federal funding agencies if additional Category 1 or Category 2 research is identified, and propose modifications to the risk mitigation plan, as needed.
- Determine the venue and mode of communication (addressing content, timing, and possibly the extent of distribution of the information) to communicate the research responsibly.
- Review annual progress reports from PIs to determine if Category 1 and Category 2 research results have been generated, and if so, flag them for institutional attention and additional mitigation measures as described above, as necessary. Progress reports may be required and reviewed with greater frequency, as commensurate with risk assessments.
- Develop a plan and methodologies for responsibly communicating the findings of the research, any time during the lifecycle of the project, including voluntary redaction of the research publications or communications.

If the risks posed by the project cannot be adequately mitigated with these measures, federal funding agencies should consider whether it is appropriate to:

- Request voluntary redaction of publications or communications resulting from the project.

- Terminate or do not provide funding.

2. Elements of a Risk Mitigation Plan

Risk mitigation plans should provide sufficient details on the research subject to the Policy to enable the federal funding agency to adequately assess the research institution's plan for managing the risks associated with Category 1 and/or Category 2 research identified by the IRE.

Risk mitigation plans should include the following:

- The name and contact information for the PI(s).
- The name and contact information for the authorized institutional official – sometimes known as "the Responsible Official" when research involves biological select agents and toxins (BSAT).
- The name of the ICDUR (if different from the authorized institutional official).
- The dates and details of the reviews and assessments of the research by the IRE.
- The dates and details of the PI's initial review or ongoing assessment of the research.
- Identification of whether the research has been identified as Category 1 and/or Category 2 under the Policy.
- Details of the risks identified by the IRE in its review of the research, and an explanation of the risk mitigation strategy or strategies that are being implemented by the institution to address those risks.
- Other materials, such as proposals and progress reports related to the research, that may be requested by the federal government.