Oklahoma State University
Institutional Biosafety Committee
Review of Research with Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential

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

I. Purpose

This policy outlines the Oklahoma State University (OSU) institutional review and oversight process for research involving certain high-consequence pathogens and toxins in order to identify dual use research of concern (DURC), pathogens with enhanced pandemic potential, and mitigate associated risks.

II. Scope

All research directly involving the biological agents and toxins listed below is subject to additional review and oversight. Principal investigators (PI) are ultimately responsible for ensuring that all research involving these agents is submitted to the Institutional Biosafety Committee (IBC) for review.

III. Definitions

Dual Use Research: Research conducted for legitimate purposes that generates knowledge, information, technologies, and/or products that could be utilized for both benevolent and harmful purposes.

Dual Use Research of Concern (DURC): Life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

Pathogen with Pandemic Potential (PPP): A pathogen that is likely capable of wide and uncontrollable spread in a human population and would likely cause moderate to severe disease or mortality in humans.

Pathogen with Enhanced Pandemic Potential (PEPP): 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.

Institutional Contact for Dual Use Research (ICDUR): An individual designated by the institution to serve as an institutional point of contact for questions regarding compliance with the implementation of the

requirements for the oversight of DURC/PEPP as well as the liaison between the institution and relevant federal funding agencies. **At OSU, the Biosafety Officer (BSO) is the ICDUR.**

Institutional Review Entity (IRE): A committee established by the institution to review all research with dual use potential or pathogens with enhanced pandemic potential. **At OSU, the IBC will serve as the IRE.**

Life Sciences: Sciences which pertain to living organisms (e.g., microbes, human beings, animals, and plants) and their products, including all disciplines and methodologies of biology such as aerobiology, agricultural science, plant science, animal science, bioinformatics, genomics, proteomics, microbiology, synthetic biology, virology, molecular biology, environmental science, public health, modeling, engineering of living systems, and all applications of the biological sciences.

Principal Investigator (PI): An individual who is designated by OSU to direct a project or program and who is responsible for the scientific and technical direction of that project or program.

IV. Research Requiring Review & Oversight

Per the United States Government Policy for Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential, two research categories are used to further define DURC/PEPP and identify the research subject to this policy:

Category 1: research categorized as DURC
Category 2: research categorized as PEPP

Category 1 research meets these three criteria:

1. It involves one or more of the specified biological agents and toxins in the following categories.
    a. All Federally Regulated Select Agents and Toxins including those at amounts below the Permissible Toxin Amounts.
    b. All Risk Group 4 pathogens listed in Appendix B of the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines).
    c. A subset of Risk Group 3 pathogens listed in Appendix B of the NIH Guidelines.
    d. For biological agents affecting humans that have not been assigned a Risk Group in the NIH Guidelines, agents affecting humans that are recommended to be handled at BSL3 or BSL4 per the BMBL guidance are subject to the USG DURC-PEPP Policy.

2. It is reasonably anticipated to result, or does result, in one of the experimental outcomes specified below:
    a. Increase transmissibility of a pathogen within or between host species;
    b. Increase the virulence (e.g. ability to cause disease) of a pathogen or convey virulence to a non-pathogen;
    c. Increase the toxicity of a known toxin or produce a novel toxin;
    d. Increase the stability of a pathogen or toxin in the environment, or increase the ability to disseminate a pathogen or toxin (e.g. environmental stability or aerosolubility);

e. Alter the host range or tropism of a pathogen or toxin;
f. Decrease the ability for a human or veterinary pathogen or toxin to be detected using standard diagnostic or analytical methods;
g. Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions (e.g., antimicrobials, antivirals, antitoxins, vaccines);
h. 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
i. Enhance the susceptibility of a host population to a pathogen or toxin.

3. 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.

Category 2 research meets these three criteria:

1. It involves, or is reasonably anticipated to result in, a pathogen with pandemic potential (PPP), or any pathogen that will be modified in such a way that is reasonably anticipated to result in a PPP.

2. It is reasonably anticipated to result in, or does result in, one or more of the experimental outcomes or actions specified here:
    a. Enhance transmissibility of the pathogen in humans;
    b. Enhance the virulence of the pathogen in humans;
    c. 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
    d. Generate, use, reconstitute, or transfer an eradicated or extinct PPP, or a previously identified PEPP.

3. 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.

V. Responsibilities

Principal Investigators (PIs)

A. All OSU Principal Investigators (PIs) proposing or conducting research involving biological agents and toxins must assess whether or not their research potentially falls under the USG DURC-PEPP Policy.
    1) Specifically, PIs proposing to work with and/or generate any agents that fall under the scope of Category 1 or Category 2 as described above must complete the initial DURC-PEPP Self-Assessment questionnaire at the proposal stage when seeking funding and/or in OneAegis during their initial IBC protocol submission.

2) If DURC-PEPP research is identified, the PI must work with the OSU Institutional Review Entity (IRE) to develop a risk-benefit assessment and risk mitigation plan that must be approved by the funding agency before the work can begin.

3) PIs are to notify the Institutional Contact for Dual Use Research (ICDUR) if at any time before or during the project they identify potential Category 1 or Category 2 research.

B. If identification occurs at the proposal stage, the PI should notify the federal funding agency when they submit the proposal. The ICDUR will follow up with next steps if potential DURC-PEPP research has been identified.

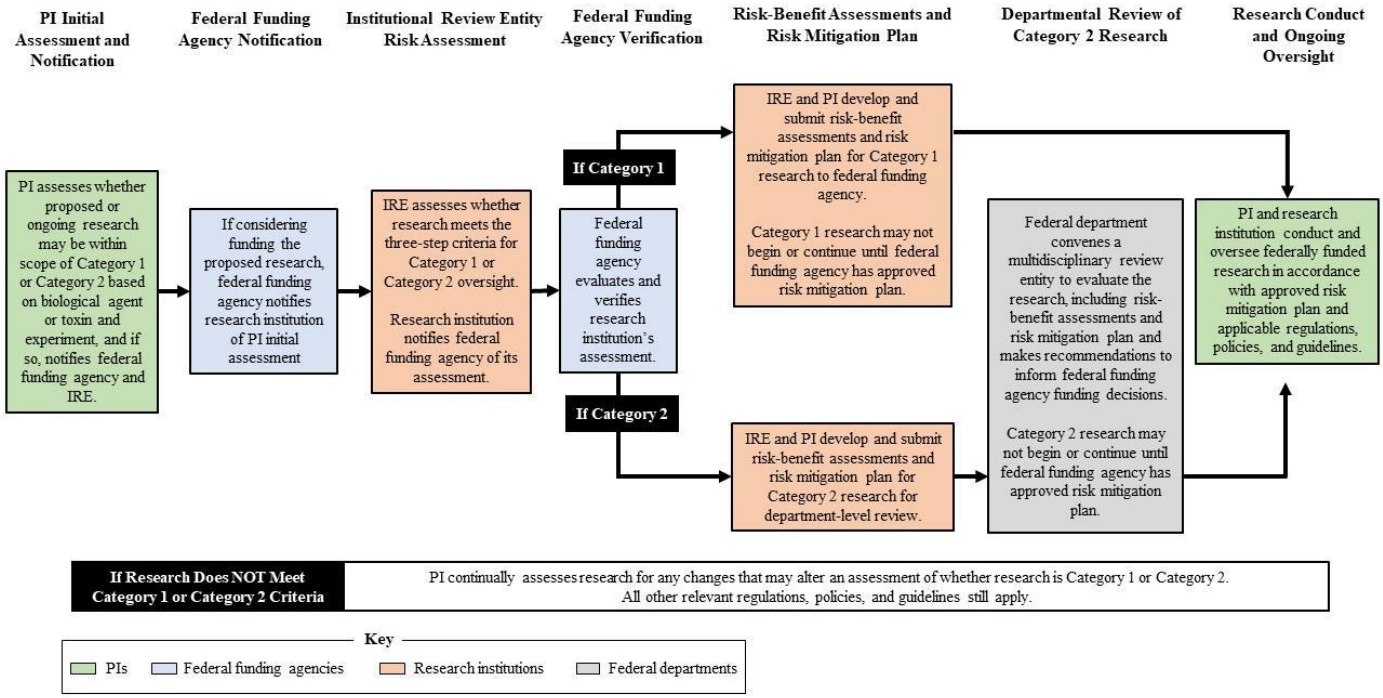
If identification of potential DURC-PEPP work occurs during the course of experimentation, the PI must halt further work, notify the federal funding agency, and contact the OSU Institutional Review Entity (IRE) to conduct the required assessments consistent with the procedures in the USG DURC-PEPP Policy for assessing Category 1 or Category 2 research.

IRE

A. Establish and implement internal policies and practices that provide for the identification and oversight of DURC-PEPP.
B. When research is identified by a PI as utilizing agents that fall under the scope of Category 1 or Category 2, initiate an institutional review and oversight process that includes the following steps, as applicable.
    1) Verification that the research identified by the PI utilizes one or more of the listed agents or toxins.
    2) Review of the PI's assessment of whether the research produces, aims to produce, or is reasonably anticipated to produce one or more of the listed experimental effects.
    3) If the research has been assessed to meet the scope of the USG Policy for Institutional Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential, determination of whether the research meets the DURC and/or PEPP definition.
    4) Within 30 calendar days of the institutional review of the research for DURC-PEPP potential, notification to the funding agency of any research that involves one or more of the identified agents and one or more of the listed experimental effects, including whether it meets or does not meet the definition of DURC-PEPP.

VI. Review Process

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).



PIs proposing to work with and/or generate any agents that fall under the scope of Category 1 or Category 2 as described above must complete the initial DURC-PEPP Self-Assessment questionnaire at the proposal stage when seeking funding and/or in OneAegis during their initial IBC protocol submission.

This review process will allow the IRE to assess the potential that the information, technology, or products generated by the proposed research could be misused to harm public health, agriculture, or national security. In making a determination, the IRE will consider the following.

- The types of knowledge, information, technology, or products anticipated to be generated through the research.
- How the results or product of the research will be shared or distributed.
- The novelty of the information provided by the research or of the research methods.
- Whether the products of the research are applicable to other pathogenic organisms or agents.
- Whether the research highlights vulnerabilities in existing public health or agricultural infrastructure.
- The expertise and/or resources that would be required to apply the knowledge, information, technology, or product for malevolent purposes.

- Whether the products of the research could be directly misused to pose a threat to public health and safety, agriculture, plants, animals, the environment, materiel, or national security.
- How readily the knowledge, information, technology, or products from the research could be used to threaten public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.
- The nature of the potential consequences (e.g., harm to the economy, the environment, agriculture, or public health) that could result from misuse of the research results.

If the IRE determines that the research **does not** meet the definition of DURC-PEPP, the research is not subject to additional institutional DURC-PEPP oversight. However, if the IRE determines that the research **does** meet the definition of DURC-PEPP, the PI will be notified, and a draft risk mitigation plan will be prepared.

The ICDUR will inform the appropriate federal funding agency of the IRE's assessment of the DURC potential of the project within 30 days of the determination.

VII. Risk Mitigation Plan

If the IRE finds that the proposed research meets the definition of DURC, the committee will work with the PI to develop a draft risk mitigation plan based on an assessment of the risks and benefits associated with the research. The plan will be specifically tailored to the research in question and will outline the strategies that will be used to mitigate all identified risks. Possible risk mitigation measures may include the application of additional biosafety or biosecurity measures, modification of the experimental design or methodology, and/or the application of medical countermeasures. Additionally, the plan may include information regarding the responsible communication of DURC-PEPP findings.

This draft plan will be submitted to the federal funding agency within 90 days of the IRE's determination that the research in question is DURC-PEPP. To the extent practicable, the agency review entities should complete the review process within 90 calendar days of receiving the risk-benefit assessments and draft risk mitigation plan for Category 1 or Category 2 research from the research institution. The project may not be initiated until an approved risk mitigation plan is received from the federal funding agency.

VIII. Ongoing Review of DURC

The IRE will review all DURC-PEPP protocols and associated risk mitigation plans on an annual basis. The federal funding agency will be notified of any modifications or updates to DURC-PEPP research protocols or risk mitigation plans within 30 days.

IX. Training

All PIs and laboratory personnel (i.e., those under the supervision of laboratory leadership, including graduate students, postdoctoral fellows, research technicians, laboratory staff, and visiting scientists) who will conduct research with one or more of the applicable agents or toxins must complete training

on DURC at the time that the indicated protocol is submitted for IBC review or when he or she is added to the protocol via modification.

X. References

Oklahoma State University Policy 4-0301, Institutional Biosafety Policy.

United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential. Available from: USG-Policy-for-Oversight-of-DURC-and-PEPP.pdf

Implementation Guidance for the United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential. Available from: USG-DURC-PEPP-Implementation-Guidance.pdf