Determining Applicability of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP)

This checklist assists Principal Investigators (PIs) in identifying when proposed or ongoing research may be subject to the DURC/PEPP Policy and outlines PI responsibilities for this research. Harvard University requires institutional evaluation of research described under the Policy regardless of funding source. Sponsored research requires additional review steps under the Policy.

DURC or PEPP apply if both an agent to be used in the research and a listed potential experimental outcome of the research are applicable. For example, a checkbox marked in **both** Section A and Section B under Category 1 would require an assessment for DURC, but a single checkbox in either Section would **NOT** require an assessment for DURC. For research meeting criteria of both Category 1 and 2, Category 2 requirements apply.

Please check all that apply to your study.

IMPORTANT NOTE: Policies, actions, and definitions in this Executive Order supersede implementation of the DURC/PEPP Policy, which will be replaced or revised by September 2025. Research meeting the definition of "dangerous gain-of-function research" is paused. Updates will be made to this checklist upon publication of the new policy.

- Implementation Update: Improving the Safety and Security of Biological Research Notice Number: NOT-OD-25-112

Category 1 Research –DURC

A. Biological Agents and Toxins Within Scope

- ☐ All Select Agents and Toxins listed in 9 CFR 121.3–121.4, 42 CFR 73.3–73.4, and 7 CFR 331.3 (including non-regulated quantities of toxins)
- ☐ All Risk Group 4 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.
  - Note: This subset currently 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 (VSV), *Coccidioides immitis, C. posadasii*, *Histoplasma capsulatum*, and *H. capsulatum* var. duboisii. This list may be updated in the Implementation Guidance on a periodic basis.
- ☐ 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 specifically mentioned in the Implementation Guidance.

B. Potential Experimental Outcomes

- ☐ Increase transmissibility of a pathogen within or between host species;
- ☐ Increase the virulence of a pathogen or convey virulence to a non-pathogen;
- ☐ Increase the toxicity of a known toxin or produce a novel toxin;
- ☐ Increase the stability of a pathogen or toxin in the environment, or increase the ability to disseminate a pathogen or toxin;
- ☐ Alter the host range or tropism of a pathogen or toxin;
- ☐ Decrease the ability for a human or veterinary pathogen or toxin to be detected using standard diagnostic or analytical methods;
- ☐ Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions;
- ☐ 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
- ☐ Enhance the susceptibility of a host population to a pathogen or toxin.

Category 2 Research –PEPP

A. Biological Agents Within Scope

- ☐ A potential pandemic pathogen (PPP), or any pathogen that will be modified in such a way that is reasonably anticipated to result in a PPP.
    - PPP is defined as: 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*.
    - Special consideration should be given to pathogens with previously declared pandemics
    - **Example:** To understand which genes are involved in transmissibility, researchers intend to introduce mutations in viral proteins of a replication-competent, wild-type MERS-CoV and assess the impact on viral replication and transmission. They anticipate mutating certain regions of the viral genome is reasonably anticipated to enhance transmissibility relative to wild-type MERS-CoV.

B. Potential Experimental Outcomes

- ☐ Enhance transmissibility of the pathogen in humans
- ☐ Enhance the virulence of the pathogen in humans
- ☐ 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
- ☐ Generate, use, reconstitute, or transfer an eradicated or extinct PPP, or a previously identified PEPP

If you have checked boxes under both sections in the same Category, please reach out to your Biosafety Officer to submit for review of your research.

PI Responsibilities: Category 1 and Category 2 Research

- ☐ Be knowledgeable about and comply with or follow all applicable institutional and U.S. government policies, requirements, and regulations for oversight of biological agents
- ☐ Assess research at the proposal stage, and continuously throughout the research lifecycle, to identify whether there is research reasonably anticipated to be within scope Category 1 or 2
- ☐ Notify the appropriate funding agency/IRE and submit information for review
- ☐ 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
- ☐ Conduct Category 1 and Category 2 research in accordance with the risk mitigation plan approved by the federal funding agency
- ☐ 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
- ☐ Ensure that laboratory personnel conducting life sciences research within the scope of this Policy are trained in its oversight
- ☐ Communicate Category 1 and Category 2 research in a responsible manner—throughout the research process, not only at the point of publication—and follow any measures outlined in the risk mitigation plan approved by the federal funding agency