Self-Assessment Worksheet for Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP)

Principal Investigator (PI)	
Date	
Funding information	

This worksheet is intended as a tool to help you assess your research according to the new U.S. Government Policy for Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential. Pages 2-4 are the worksheet. The remaining pages are appendices with additional information and lists of agents and toxins.

The DURC-PEPP policy requires PIs to self-assess research for potential DURC and PEPP in their research, and if identified, to notify the federal funding agency and the UW Institutional Review Entity (IRE).

Research involving infectious agents including Risk Group 3 and 4 microorganisms and all select agents and toxins (in any amount) are subject to review for potential DURC and PEPP by the UW IRE, a standing subcommittee of the UW Institutional Biosafety Committee (IBC). More information about UW IRE review processes including an IRE review flow chart are available on the EH&S DURC-PEPP webpage.

For help assessing your research, contact EH&S Biosafety at ehsbio@uw.edu or 206-221-7770. We can answer questions or schedule a meeting to assist you.

Instructions for using this worksheet:

1. Use Section A to assess for Category 2 (PEPP). More detailed PPP/PEPP information is in Appendix A.
2. Use Section B to assess for Category 1 (DURC). Appendix B has a list of biological agents and toxins subject to the policy, including Risk Group 3 agents excluded from the policy.
3. Use Section C to determine the overall research assessment and any required next steps.
4. Keep this assessment for future reference.
5. To request an IRE assessment, fill out a DURC-PEPP Application and submit to ehsbio@uw.edu

A. Category 2: Pathogen with Enhanced Pandemic Potential (PEPP) Assessment

Identify whether a pathogen with pandemic potential (PPP) will be involved at any point of the research lifecycle, regardless of its progenitor agent, including if an existing agent will be modified to become a PPP. A PPP is a "pathogen that is likely capable of wide and uncontrollable spread in a human population and would likely cause moderate to severe disease and/or mortality in humans." Refer to Appendix A for detailed information on assessing research for PPP/PEPP.

Involves or results in a PPP		
1.	Does the research **involve a PPP or is reasonably anticipated to result in a PPP**? • Any pathogen that is modified to result in a PPP • Use of an existing PPP: SARS-CoV, SARS-CoV-2, and Ebolaviruses • Generation, use, reconstitution, or transfer or an extinct/eradicated PPPs: Variola major, Variola minor, and 1918 influenza virus	☐ Yes ☐ No *If NO, skip to Question 3.*
Experimental outcomes		
2.	Is **the PPP involved being modified** in such a way that is reasonably anticipated to result in any of the following experimental outcomes?	
	a. **Enhance transmissibility of the pathogen in humans?** ▪ More transmissible than the wild-type pathogen such that it can spread widely and uncontrollably in the human population. ▪ Able to survive outside the host and/or withstand environmental conditions longer than the wild-type pathogen, facilitating transmission such that it can spread widely and uncontrollably in the human population. ▪ Altered tropism (i.e., tissue tropism or host range), changing 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. ▪ Increased transmissibility of an animal/zoonotic pathogen, such that it can utilize new non-human vectors/reservoirs to spread widely and uncontrollably in human population.	☐ Yes ☐ No
	b. **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 can cause moderate to severe disease in humans.	☐ Yes ☐ No
	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? ▪ Modifies a pathogen such that it can spread widely and uncontrollably in human population, and cause moderate to severe disease, despite existing population immunity to the wild-type pathogen.	☐ Yes ☐ No

3. Category 2 Assessment	
IF	**THEN** *(select outcome)*
NO to Question A.1	☐ Research DOES NOT meet Category 2 (PEPP) criteria.
YES to Question A.1 and NO to all Questions A.2.a-c	
YES to Question A.1. and YES to any Questions A.2.a-c	☐ **Research DOES MEET Category 2 (PEPP) criteria.**

Continue to Section B: Category 1: Dual Use Research of Concern (DURC) Assessment.

B. Category 1: Dual Use Research or Concern (DURC) Assessment

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

Biological agents and toxins used:		
1.	Does your research involve **one or more biological agents or toxins within the scope?** Refer to list of agents and toxins including excluded Risk Group 3 agents. ▪ Select agents and toxins, including toxins in any amount ▪ Risk Group 4 and a subset of Risk Group 3 pathogens per the NIH Guidelines ▪ Any biological agent affecting humans recommended to be handled at BSL-3 or BSL-4 per Biosafety in Microbiological and Biomedical Laboratories (BMBL)	☐ Yes ☐ No If NO, skip to Question 11.
Experimental outcomes for any above biological agents or toxins:		
2.	**Increase transmissibility of a pathogen within or between host species?** ▪ More transmissible than the wild-type pathogen such that it is able to transmit more efficiently in and among human, plant, or animal populations.	☐ Yes ☐ No
3.	**Increase the virulence of a pathogen or convey virulence to a non-pathogen?** ▪ More virulent than the wild-type pathogen, resulting in higher morbidity or mortality in human, plant, or animal populations.	☐ Yes ☐ No
4.	**Increase the toxicity of a known toxin or produce a novel toxin?** ▪ Causes morbidity or mortality comparable to its natural form at lower doses or 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.	☐ Yes ☐ No
5.	**Increase the stability of the pathogen or toxin in the environment, or increase the ability to disseminate a pathogen or toxin?** ▪ Ability to retain or increase its infectiousness or toxicity outside a living system. ▪ Can be more effectively delivered via aerosolization or enables novel aerosolization in a pathogen or toxin that typically transmits by other means. ▪ Enhances environmental stability of a pathogen or toxin, thereby increasing ease of transmissibility or capability to cause disease. ▪ Develops a method for producing/disseminating large quantities of a pathogen or toxin.	☐ Yes ☐ No
6.	**Alter the host range or tropism of the pathogen or toxin?** ▪ Alters the route of transmission of a pathogen or toxin to increase the ease and effectiveness by which it may be transmitted, thus having broad potential consequences to humans, animals, or plants. ▪ Alters the host range, which could put specific populations of humans, plants or animals that were not previously susceptible to the pathogen or toxin (e.g., making an avian pathogen infectious to and among mammals). ▪ Alters tissue tropism of a pathogen or toxin resulting in more severe disease manifestations in humans, plants or animals (e.g., a respiratory pathogen becoming neurotropic). ▪ Note: this 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.	☐ Yes ☐ No
7.	**Decrease the ability for a human or veterinary pathogen or toxin to be detected using standard diagnostic or analytical methods?** (Only applicable to human and veterinary Category 1 pathogens.) ▪ Make it undetectable by widely used diagnostic tests or detection methods. ▪ Alters the nucleic acid sequence in a way that preserves function but renders it no longer identifiable by screening mechanisms designed to detect nucleic acid sequences of concern.	☐ Yes ☐ No

8.	**Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions?** (Only applicable to human and veterinary Category 1 pathogens.) ▪ Causes disease which is not treatable or severely increases the failure risk with extant therapeutics. ▪ Modifies (i.e., a non-naturally occurring mutation) such that it becomes newly resistant to multiple antimicrobials, antivirals, or antitoxins. ▪ Exsiting prophylactic measures available to the general population, such as vaccines, are no longer effective at preventing disease or transmission.	☐ Yes ☐ No
9.	**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?** (Only applicable to human and veterinary Category 1 pathogens.) ▪ Modifies the antigenic profile 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.	☐ Yes ☐ No
10.	**Enhance the susceptibility of a host population to a pathogen or toxin?** ▪ An enhanced or a new ability to compromise immune responses of individuals or populations, thereby enabling the increased spread of disease. ▪ Suppresses the host's immune response, resulting in increased morbidity or mortality.	☐ Yes ☐ No

11. Category 1 Assessment:

IF	**THEN** *(select outcome)*
NO to Question B.1	☐ Research DOES NOT meet Category 1 (DURC) criteria.
YES to Question B.1 and NO to all Questions B.2-10	
YES to Question B.1. and YES to any Questions B.2-10	☐ **Research DOES meet Category 1 (DURC) criteria.**

Continue to Section C: Overall Research Assessment.

C. Overall Research Assessment

Use assessment information from Sections A and B:
1. If research <u>DOES NOT</u> meet the criteria for <u>both</u> Category 2 <u>and</u> Category 1 research: a. **An IRE Assessment is not required.** If filling out an eGC1, you can select NO for potential DURC-PEPP research. b. Experiments may proceed, pending any other required institutional or regulatory approvals (e.g., IBC or IACUC approval). c. Save this assessment for future use.
2. If research <u>DOES MEET</u> the criteria for <u>either</u> Category 2 or Category 1 research: a. **Research assessed as Category 2 or Category 1 cannot start, or if ongoing, must halt.** b. **Notify your federal funding agency about the results of this assessment.** c. **Notify the UW IRE at ehsbio@uw.edu.** d. The federal funding agency will review your assessment and grant materials and then request an IRE assessment. If an assessment is requested, submit a DURC-PEPP application to the UW IRE at ehsbio@uw.edu. We recommend that you keep this assessment worksheet and use it to fill out your DURC-PEPP application. A PI's assessment that their research is within scope of Category 1 or Category 2 does not necessarily mean the research is subject to Category 1 or Category 2 research oversight. It is the responsibility of the UW IRE to assess research referred by the PI to determine whether it meets the threshold to be designated as Category 1 or Category 2 research. The federal funding agency is responsible for evaluating and verifying the IRE's assessment.

Contact EH&S Biosafety at ehsbio@uw.edu for any questions.

Appendix A: Category 2 (PEPP) Assessment Detailed Information Return to Section A

PIs should identify whether a PPP will be involved at any point of the research lifecycle, regardless of its progenitor agent. In many cases, this includes consideration of the characteristics of the starting agent as well as those of the pathogen(s) anticipated to result from the proposed experiments. If an experimental outcome results in a non-PPP meeting the definition of a PPP, then the research is in scope of Category 2.

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

- 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.) and 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, environmental stability, respiratory route of transmission, and lack of availability of or access to non-medical and medical countermeasures (MCMs).
    - 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.
    - 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 can provide a high-level guideline to help assess which pathogens are included and excluded from the PPP definition.
    - Rt, CHR, and CFR 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. Other pathogen characteristics for determining disease potential may include types of symptoms, disease duration, or long-term symptoms that persist after infection.

A **pathogen with enhanced pandemic potential (PEPP)** 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. It may be a PPP in its wild-type form, or a pathogen that is not considered a PPP in its wild-type form, but when modified meets the definition of a PEPP.

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Appendix B: Biological Agents and Toxins within Scope of Category 1 (DURC) Return to Section B

Toxins	
☐	Abrin
☐	Botulinum neurotoxins
☐	Conotoxins (Short, paralytic alpha conotoxins containing the amino acid sequence $X_1CCX_2PACGX_3X_4X_5X_6CX^7$)
☐	Diacetoxyscirpenol
☐	Ricin
☐	Saxitoxin
☐	Staphylococcal enterotoxins (subtypes A,B,C,D,E)
☐	T-2 toxin
☐	Tetrodotoxin
Bacteria and Rickettsia	
☐	Bacillus anthracis
☐	Bacillus anthracis Pasteur strain
☐	Bacillus cereus Biovar anthracis
☐	Bartonella
☐	Botulinum neurotoxin producing species of Clostridium
☐	Brucella including B. abortus, B. canis, B. suis
☐	Burkholderia mallei
☐	Burkholderia pseudomallei
☐	Coxiella burnetti (except the Phase II, Nine Mile strain listed as Risk Group 2)
☐	Francisella tularensis (except strains listed as Risk Group 2)
☐	Mycoplasma capricolum
☐	Mycoplasma mycoides
☐	Orientia tsutsugamushi (formerly R. tsutsugamushi)
☐	Pasteurella multocida type B – “buffalo” and other virulent strains
☐	Ralstonia solanacearum
☐	Rathayibacter toxicus
☐	Rickettsia species: akari, australis, canada, conorii, prowazekii, rickettsii, siberica, typhi (mooseri)
☐	Rickettsia prowazekii
☐	Xanthomonas oryzae
☐	Yersinia pestis (except strains listed as Risk Group 2)
☐	Any other bacteria or rickettsia recommended to be handled at BSL-3 or BSL-4 per Biosafety in Microbiological and Biomedical Laboratories (BMBL)
Viruses	
☐	African swine fever virus
☐	Avian influenza virus
☐	Chapare virus
☐	Chikungunya virus (except the vaccine strain 181/25 listed as Risk Group 2)
☐	Classical swine fever virus
☐	Crimean-Congo hemorrhagic fever virus
☐	Eastern equine encephalitis virus
☐	Ebolaviruses
☐	Far Eastern subtype tick-borne encephalitis virus

☐	Flexal
☐	Foot-and-mouth disease virus
☐	Goat pox virus
☐	Guanarito virus
☐	Hantaviruses including Hantaan virus
☐	Hemorrhagic fever viruses as yet undefined
☐	Hendra virus (or Equine Morbillivirus)
☐	Herpesvirus simiae (Herpes B or Monkey B virus)
☐	Influenza viruses: ▪ 1918-1919 H1N1 (1918 H1N1) ▪ Reconstructed 1918 influenza virus (Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments) ▪ Human H2N2 (1957-1968) ▪ Avian influenza virus ▪ Highly pathogenic avian influenza H5N1 strains within the Goose/Guangdong/96-like H5 lineage
☐	Japanese encephalitis virus (except strains listed as Risk Group 2)
☐	Junin virus (except the candid #1 vaccine strain listed in as Risk Group 2)
☐	Lassa virus (or Lassa fever virus)
☐	Lujo virus
☐	Lumpy skin disease virus
☐	Lymphocytic choriomeningitis virus (LCMV) neurotropic strains (except lab-adapted strains)
☐	Machupo virus
☐	Marburg viruses
☐	Middle East respiratory syndrome coronavirus (MERS-CoV)
☐	Monkeypox virus (Clade I and Clade II containing nucleic acids coding for clade I MPVX virus virulence factors)
☐	Newcastle disease virus
☐	Nipah virus
☐	Peste des petits ruminants virus
☐	Rift Valley fever virus
☐	Rinderpest virus
☐	Sabia virus
☐	SARS-associated coronavirus (SARS-CoV)
☐	SARS-CoV/SARS-CoV-2 chimeric viruses resulting from any deliberate manipulation of SARS-CoV-2 to incorporate nucleic acids coding for SARS-CoV virulence factors
☐	Semliki Forest virus
☐	Sheep pox virus
☐	Siberian subtype tick-borne encephalitis virus
☐	St. Louis encephalitis virus (now Risk Group 2 but were Risk Group 3 when policy was published)
☐	Swine vesicular disease virus
☐	Tick-borne encephalitis virus complex including Absetterov, Central European encephalitis, Hanzalova, Hypr, Kumlinge, Kyasanur Forest disease, Omsk hemorrhagic fever, and Russian spring-summer encephalitis viruses
☐	Variola major virus (Smallpox virus)
☐	Variola minor virus (Alastrim)
☐	Venezuelan equine encephalitis virus (except the vaccine strains TC-83 and V3526)

☐	West Nile virus (now Risk Group 2 but were Risk Group 3 when policy was published)
☐	Yellow fever virus
☐	Any other virus recommended to be handled at BSL-3 or BSL-4 per Biosafety in Microbiological and Biomedical Laboratories (BMBL)
Fungi	
☐	Coniothyrium glycines (formerly Phoma glycinicola and Pyrenochaeta glycines)
☐	Sclerophthora rayssiae
☐	Synchytrium endobioticum
☐	Any other fungus recommended to be handled at BSL-3 or BSL-4 per Biosafety in Microbiological and Biomedical Laboratories (BMBL)
Prions	
☐	Transmissible spongiform encephalopathies (TSE) agents (Creutzfeldt-Jacob disease and kuru agents)
☐	Any other prion recommended to be handled at BSL-3 or BSL-4 per Biosafety in Microbiological and Biomedical Laboratories (BMBL)

Excluded Risk Group 3 Biological Agents These biological agents are excluded from the Category 1 biological agents in the DURC-PEPP policy.
Clade II of MPVX viruses (unless containing nucleic acids coding for clade I MPVX virus virulence factors)
Coccidioides immitis
Coccidioides posadasii
Histoplasma capsulatum
Histoplasma capsulatum var. duboisii
Human immunodeficiency virus (HIV) types 1 and 2
Human T cell lymphotropic virus (HTLV) types 1 and 2
Mycobacterium bovis
Mycobacterium tuberculosis
Simian immunodeficiency virus (SIV)
Vesicular stomatitis virus

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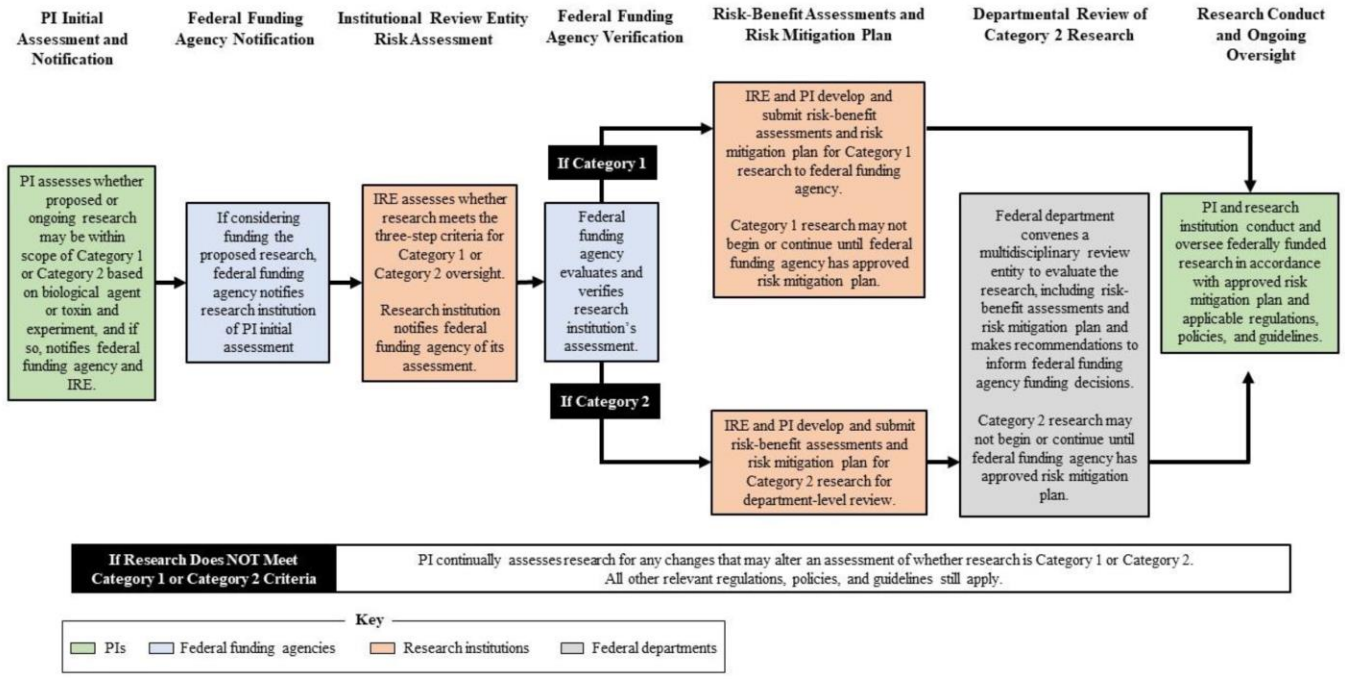
Appendix C: PI Assessment Overview Return to beginning of document

PIs should assess their research at the proposal stage and continuously throughout the entire course of research for its potential to be within scope of Category 1 or Category 2 research. If the PI self-assesses that research could be Category 1 or Category 2, the PI must notify the federal funding agency and UW Institutional Review Entity (IRE). Then the federal funding agency will notify the PI that an IRE assessment is required. The UW IRE will assess whether the research meets the thresholds to be designated Category 1 or Category 2 research The UW IRE is a standing subcommittee of the UW Institutional Biosafety Committee (IBC).

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).



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.

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