Compliance Overview:

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

Oversight of DURC and PEPP

This training outlines responsibilities for compliance with the *United States Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP)* – *subsequently known as "USG Policy"* – as well as the associated SLU policy.

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

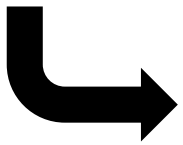
The USG Policy:

- provides a unified oversight framework for DURC and PEPP
- goes into effect May 2025
- supersedes previous USG oversight policies for DURC and PPP

USG 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.
- Applies to federally funded research (however, the ***SLU policy*** applies to all research, regardless of funding source).
- Identifies responsibilities for each party, including the PI, the entity, and the federal government.
  - "The PI makes an initial assessment of whether their proposed or ongoing research may be within the scope" of this policy.

    and
  - "The research institution is responsible for ensuring that PIs are aware of and executing this responsibility appropriately."



TRAINING

What is DURC & PEPP (USG Policy definitions)

- **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.

- **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.

- **Pathogen with enhanced pandemic potential (PEPP)** is a type of pathogen with pandemic potential (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.

Major PI Responsibilities

1) Understand both the USG Policy and SLU Policy
2) Assess whether proposed *or ongoing research* may be within scope of Category 1 (DURC) or Category 2 (PEPP) based on the:
    1) biological agent or toxin,
    2) experiment and expected outcome, AND
    3) risk assessment.

    This assessment does not need to be recorded or shared with the IRE at the time of proposal submission unless the research involves DURC/PEPP.
3) For any research potentially falling into scope, the PI must notify the Institutional Review Entity (IRE) and federal funding agency *(detailed further in later slides).*

Category 1 Research meets all 3 criteria:

It involves one or more of the biological agents and toxins:

- Any select agent or toxin
  - Includes select agent toxins in permissible amounts, such as tetrodotoxin.
- Nearly all Risk Group 3 agents
  - exceptions include Mtb, HIV, clade II MPOX and others.

It is *reasonably anticipated* to result in one or more of the following experimental outcomes:

1. **Increase transmissibility** of a pathogen within or between host species
2. **Increase the virulence** of a pathogen or convey virulence to a non-pathogen
3. **Increase the toxicity** of a known toxin or produce a novel toxin
4. **Increase the stability** of a pathogen or toxin in the environment, or **increase the ability to disseminate** a pathogen or toxin
5. **Alter the host range or tropism** of a pathogen or toxin
6. **Decrease the ability** for a human or veterinary pathogen or toxin **to be detected** using standard diagnostic or analytical methods
7. **Increase resistance** of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions
8. 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
9. **Enhance the susceptibility of a host population** to a pathogen or toxin

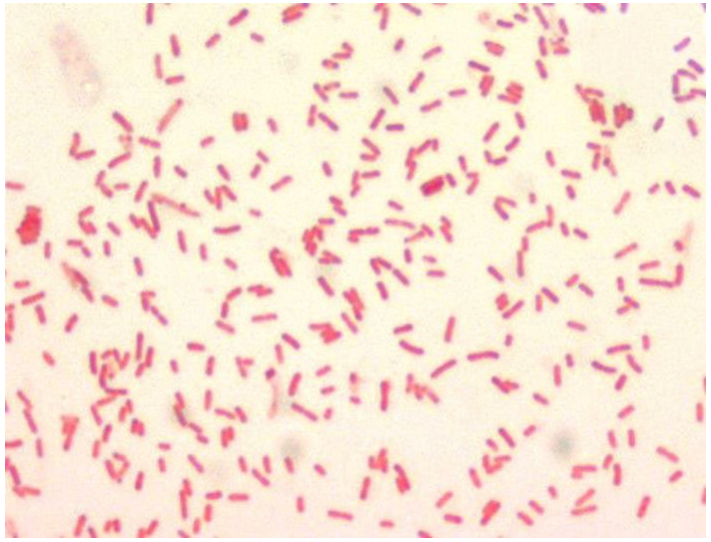
Risk assessment:

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.

DURC

Example of Category 1 Research

- Researchers plan to generate *Yersinia pestis* strains to differentially express biofilm-forming genes.
- They hypothesize that the modified *Y. pestis* strains will produce biofilms faster and increase the transmission in rodents.



Yersinia pestis bacilli @1000x (CDC)

<u>Assessment</u>:

1. *Y. pestis* is a select agent.
2. The study is *reasonably anticipated* to result in an experimental outcome outlined in the policy →*increased transmissibility*
3. Based on risk assessment, this would be defined as DURC.

See USG Policy and USG Policy Implementation Guidance for additional examples and more information.

Category 2 Research meets all 3 criteria:

It involves one, or is reasonably anticipated to result in, a PPP:

A pathogen with pandemic potential (PPP) as defined in the USG 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*."

- sustained human-to-human transmission (Rt>1)
- high hospitalization and/or case fatality rates

It is *reasonably anticipated* to result in one or more of the following experimental outcomes:

1. **Enhance transmissibility** of the pathogen **in humans**;
2. **Enhance the virulence** of the pathogen **in humans**;
3. **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
4. **Generate, use, reconstitute, or transfer an eradicated or extinct PPP, or a previously identified PEPP**
   - examples, influenza A 1918 H1N1 and 1957-1968 H2N2

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.

PEPP

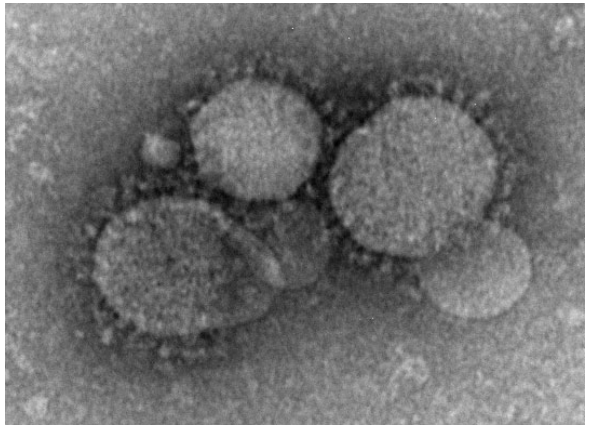
Note: Research meeting the definitions of both Category 1 and Category 2 research is designated as Category 2 research.

Example of Category 2 Research

- Researchers plan to mutate MERS-CoV viral proteins and assess the impact on viral replication and transmission. Growth kinetics will be evaluated in vitro and in vivo, using models of transmissibility.
- The PI hypothesizes that these mutations may enhance transmissibility.
- The goal is to identify MERS-CoV amino acids associated with transmissibility to better understand the transmissibility potential of other zoonotic merbecoviruses.

<u>Assessment</u>:

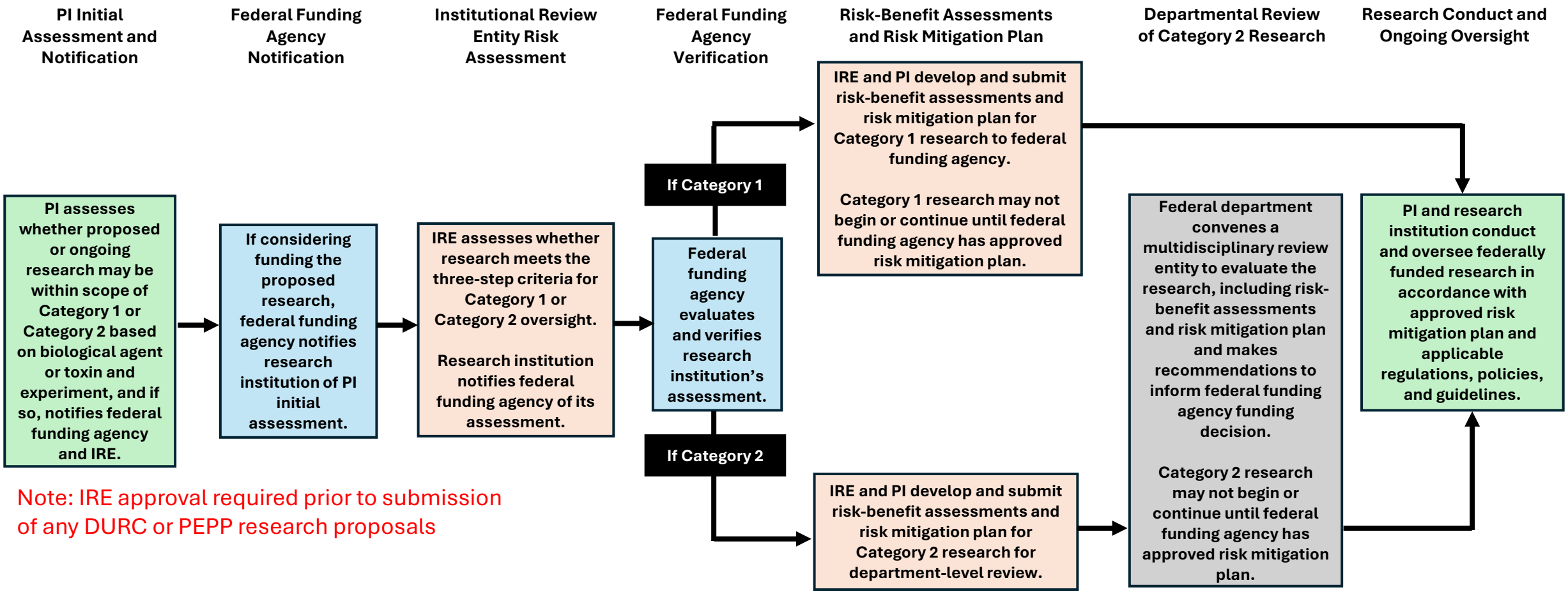
1. MERS-CoV would be considered a PPP.
2. The study is *reasonably anticipated* to result in an experimental outcome outlined in the policy
   →*increased transmissibility*
3. The research is *reasonably anticipated* to yield a PEPP.



MERS-CoV (negative stain electron microscopy; CDC)

See USG Policy and USG Policy Implementation Guidance for additional examples and more information.

Process overview



Note: IRE approval required prior to submission of any DURC or PEPP research proposals

If Research Does NOT Meet Category 1 or Category 2 Criteria

PI continually assesses research for any changes that may alter an assessment of whether research is Category 1 or Category 2. All other relevant regulations, policies, and guidelines still apply.

Key

PIs | Federal funding agencies | Research institutions | Federal departments

Expected Funding Requirement

- Regardless of the type of research, this policy *may* require the entity to provide documentation of the IRE's review and confirmation of the PI's assessment of their research for DURC/PEPP prior to release of funding.
- **The turnaround times for Just-in-Time (JIT) requests are short, and the IRE will not be able to review the research in a compressed timeline.**
- Therefore, it is highly recommended that PIs submit a completed DURC/PEPP assessment form to the IRE if they anticipate funding (e.g. – high review score).
- For research falling within scope of the USG Policy, the PI must also provide a risk-benefit assessment and risk mitigation plan and obtain IRE approval.
- This will allow the IRE to complete their review and confirm the PI's assessment prior to the JIT request.

Major PI Responsibilities – Revisited

1) Understand the USG and SLU Policies
2) Assess whether proposed *or ongoing research* may be within scope of Category 1 (DURC) or Category 2 (PEPP) based on the:
    1) biological agent or toxin,
    2) experiment and expected outcome, AND
    3) risk assessment.
3) If any research potentially falls into scope, PIs must:
    - immediately notify the Institutional Contact for Dual Use Research (ICDUR) and obtain Institutional Review Entity (IRE) approval *prior to submission* of the research proposal.
        - *SLU's ICDUR is the Biological Safety Officer.*
    - work with the IRE to develop a risk-benefit assessment and risk mitigation plan.
    - notify the federal funding agency through the ICDUR.
    - conduct and communicate results of such research as specified in the plans.
    - provide annual progress reports to the IRE and federal funding agency.
    - ensure that all personnel are adequately trained.

Entity Responsibilities

- Must ensure that PIs are knowledgeable about the USG Policy
- Shall establish an IRE and make procedures for reviewing Category 1 and Category 2 research available to the public.
  - At SLU, the IRE is a subcommittee of the Institutional Biosafety Committee (IBC)
  - IRE procedures are detailed in the IBC Policy companion document "*Institutional Biosafety Committee (IBC) Procedures and Principal Investigator Responsibilities*"
- Additional responsibilities specific for Category 1 and Category 2 research are outlined in the USG Policy

SAINT LOUIS UNIVERSITY

Summary and Contact Information

- The USG Policy superseding previous policies on DURC and PPP go into effect on May 6, 2025.
- SLU PIs must be compliant with the USG Policy as well as the SLU IBC Policy for compliance with DURC and PEPP.
- PIs must assess their research *beginning at the proposal stage* for Category 1 and Category 2 research.
- For any research meeting Category 1 or Category 2 definitions, contact the ICDUR (BSO) at SLU as soon as possible and obtain IRE approval and notify the federal funding agency at the time of submission. Further, if at any time PIs identify their research as Category 1 or 2, they should notify the SLU ICDUR immediately.
- PIs should submit a DURC/PEPP assessment form to the IRE if they anticipate funding.
- For any questions, please contact:

Chris Eickhoff
Biological Safety Officer
Institutional Contact for Dual Use Research (ICDUR)
Christopher.Eickhoff@health.slu.edu

References

- United States Government **Policy** for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential (“USG Policy”) https://aspr.hhs.gov/S3/Documents/USG-Policy-for-Oversight-of-DURC-and-PEPP-May2024-508.pdf
- **Implementation Guidance** for the United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential https://aspr.hhs.gov/S3/Documents/USG-DURC-PEPP-Implementation-Guidance-May2024-508.pdf
- SLU Institutional Biosafety Committee **(IBC) Policy** – updates to be effective May 6, 2025 https://slu.policystat.com/policy/token_access/c7a0fe32-84f7-49c1-b90e-6a54401c436a/
- SLU Institutional Biosafety Committee **(IBC) Procedures** and Principal Investigator Responsibilities – *contains IRE Procedures for reviewing DURC and PEPP research* (attached to IBC Policy)

Documentation of Training

Please complete the following form to document your training:

PI Training Acknowledgement: SLU DURC/PEPP Training