Dual Use Research of Concern (DURC)

Pathogens with Enhanced Pandemic Potential (PEPP)

Training for Principal Investigators / Researchers

UTHealth® Houston

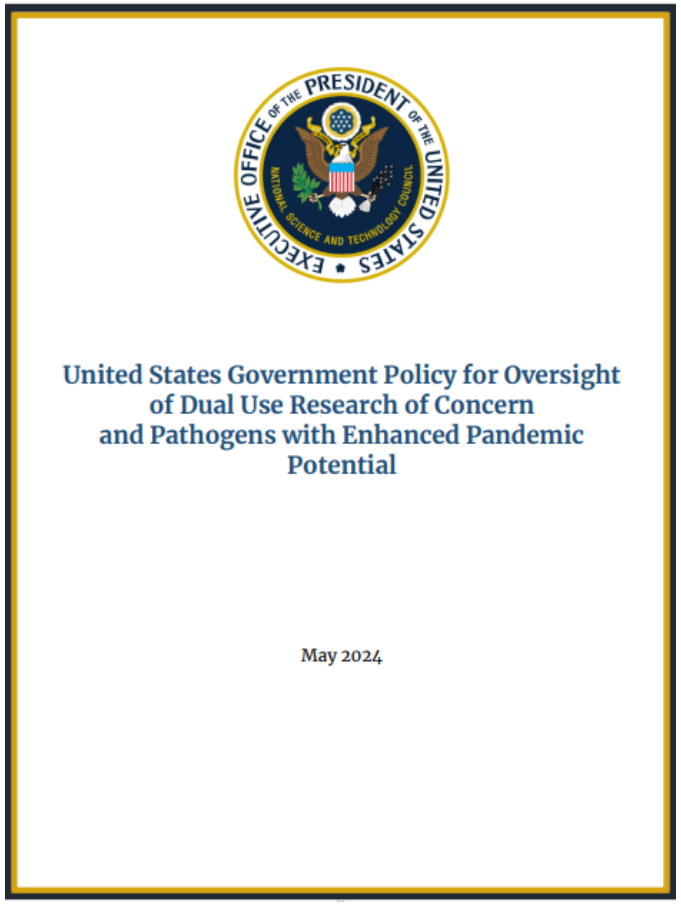
Objectives

After review of these slides, researchers should have an understanding of…

- UTHealth Houston's implementation of United States Government Policy for Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential (2025)
- Definitions associated with United States Government Policy for Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential (2025)
- Principal Investigator role of United States Government Policy for Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential (2025)
- Assessment of criteria

United States Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential - May 2025

- Released May 2024
- **Effective date May 6, 2025**
- Unified federal oversight framework for certain types of federally funded life sciences 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
- Includes research funded or sponsored by grants, contracts, cooperative agreements
- Supersedes 2012 Federal DURC policy, 2014 Institutional DURC Policy and 2017 P3CO Framework



United States Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential - May 2025

- *Dual use research* is research conducted for legitimate purposes that generates knowledge, information, technologies, and/or products that can be utilized for benevolent or harmful purposes

- *Dual use research of concern (DURC)* is research that 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, the environment, materiel, or national security.

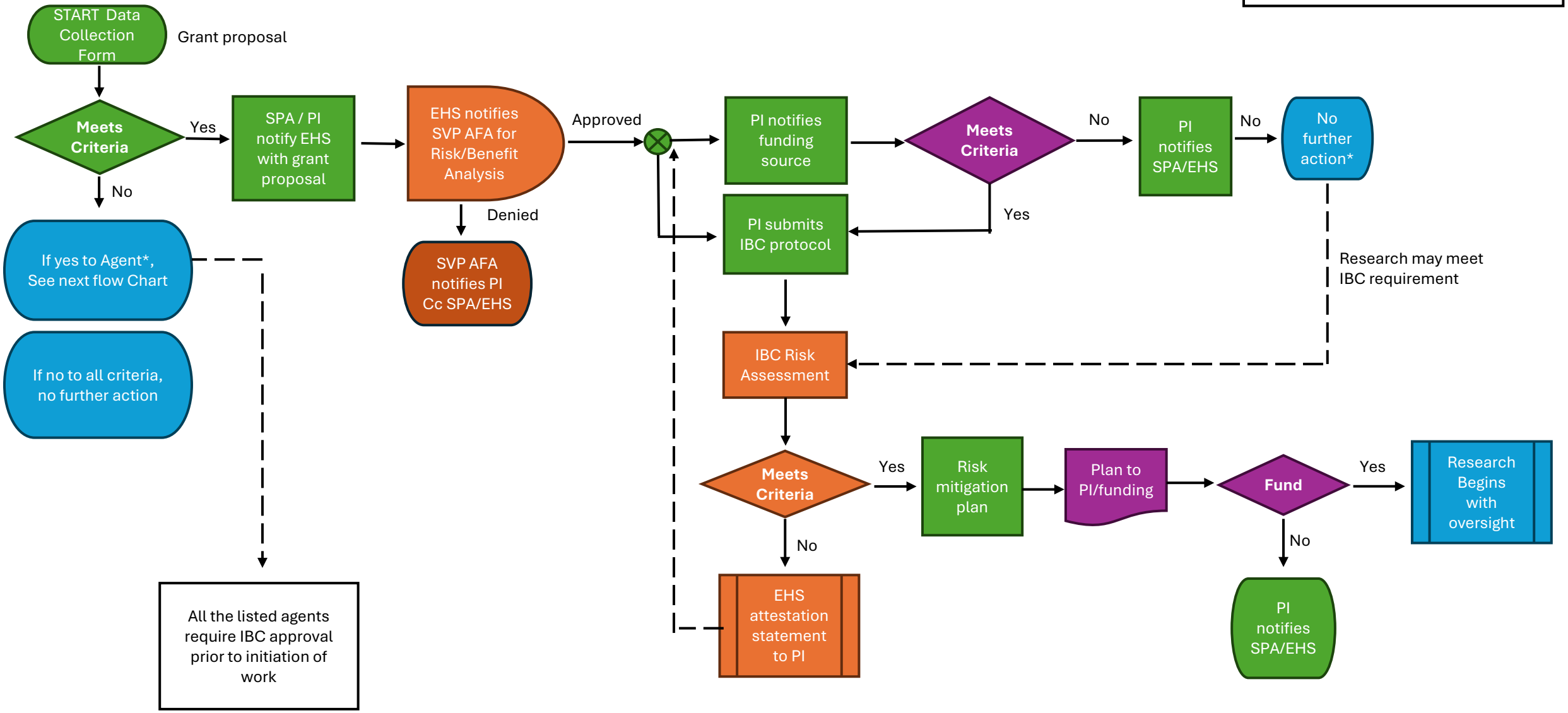
United States Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential - May 2025

- *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

UTHealth Houston DURC/PEPP Review Process

SPA (Sponsored Projects Administration)
PI (Principal Investigator)
EHS (specifically Biological Safety)
(SVP AFA) Senior Vice President, Academic and Faculty Affairs



Category 1 research meets all three criteria:

(1) The research involving one or more of the biological agents and toxins below:

a. 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 USDA and/or HHS
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) - Classification of Human Etiologic Agents on the Basis of Hazard
c. A subset of Risk Group 3 pathogens listed in Appendix B of the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) - Classification of Human Etiologic Agents on the Basis of Hazard.
d. All Risk Group 4 pathogens listed in Appendix B of the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines) - Classification of Human Etiologic Agents on the Basis of Hazard
e. Biological agents affecting humans that have not been assigned a Risk Group in the NIH Guidelines

Refer to Appendix A

(2) The research is reasonably anticipated to result, or does result, in one of the experimental outcomes below:

a. Increase transmissibility of a pathogen within or between host species
b. Increase the virulence19 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. 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
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
i. Enhance the susceptibility of a host population to a pathogen or toxin.

Refer to the Implementation Guidance

(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.

Does your research involve meet all three criteria for Category 1 (DURC) research? Yes or No (dropdown box)

Biological Select Agent and Toxin

HHS Select Agents and Toxins			
☐	Abrin	☐	Severe acute respiratory coronavirus (SARS-CoV)
☐	*Bacillus cereus Biovar anthracis*	☐	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
☐	Botulinum neurotoxins	☐	Saxitoxin
☐	*Clostridium botulinum* and neurotoxin-producing species of *Clostridia*	☐	Chapare virus
☐	Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence X1CCX2PACGX3X4X5X6CX7)	☐	Guanarito virus
☐	*Coxiella burnetii*	☐	Junín virus
☐	Crimean-Congo hemorrhagic fever virus	☐	Machupo virus
☐	Diacetoxyscirpenol	☐	Sabía virus
☐	Eastern equine encephalitis virus	☐	Staphylococcal enterotoxins (subtypes A, B, C, D, E)
☐	*Ebolavirus*	☐	T-2 toxin
☐	*Francisella tularensis*	☐	Tetrodotoxin
☐	Lassa fever virus	☐	Tick-borne encephalitis complex virus: Far Eastern subtype
☐	Lujo virus	☐	Tick-borne encephalitis complex virus: Siberian subtype
☐	Marburg virus	☐	Kyasanur Forest disease virus
☐	Mpox virus Clade I	☐	Omsk hemorrhagic fever virus
☐	1918-1919 H1N1 including reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 Influenza virus)	☐	Variola major virus (Smallpox virus)
☐	Ricin	☐	Variola minor virus (Alastrim)
☐	*Rickettsia prowazekii*	☐	Yersinia pestis

Biological Select Agent and Toxin

Overlap Select Agents and Toxins			
☐	*Bacillus anthracis*	☐	Hendra virus
☐	*Bacillus anthracis Pasteur strain*	☐	Nipah virus
☐	*Burkholderia mallei*	☐	Rift Valley fever virus
☐	Burkholderia pseudomallei	☐	Venezuelan equine encephalitis virus
USDA Veterinary Services (VS) Select Agents and Toxins			
☐	African swine fever virus	☐	*Mycoplasma mycoides*
☐	Avian influenza virus [this is included here as a veterinary select agent in 9 CFR 121.3. Low pathogenicity strains are excluded.]	☐	Newcastle disease virus
☐	Classical swine fever virus	☐	Peste des petits ruminants virus
☐	Foot-and-mouth disease virus	☐	Rinderpest virus
☐	Goat pox virus	☐	Sheep pox virus
☐	Lumpy skin disease virus	☐	Swine vesicular disease virus
☐	*Mycoplasma capricolum*		
USDA Plant Protection and Quarantine PPQ) Select Agents and Toxins			
☐	*Coniothyrium glycines*	☐	*Sclerophthora rayssiae*
☐	*Ralstonia solanacearum*	☐	*Synchytrium endobioticum*
☐	*Rathayibacter toxicus*	☐	*Xanthomonas oryzae*

Other Risk Group 4 Pathogens

Other Risk Group 4 Pathogens			
☐	Tick-borne encephalitis virus complex including Absetterov, Central European encephalitis, Hanzalova, Hypr, and Kumlinge	☐	Hemorrhagic fever agents and viruses as yet undefined
☐	Herpesvirus simiae (herpes B or monkey B virus)		

Other Risk Group 3 Pathogens

Other Risk Group 3 Pathogens			
☐	*Bartonella*	☐	Hantaviruses, including Hantaan virus
☐	Brucella	☐	Middle East respiratory syndrome coronavirus (MERS-CoV)
☐	*Orientia tsutsugamushi*	☐	Severe acute respiratory coronavirus 2 (SARS-CoV-2)
☐	*Pasteurella multocida* type B -"buffalo" and other virulent strains	☐	Japanese encephalitis virus except strain SA 14-14-2
☐	*Rickettsia akari, R. australis, R. canada, R. conorii, R. rickettsii, R, siberica, R. typhi (R. mooseri)*	☐	Yellow fever virus
☐	Chikungunya virus except the vaccine strain 181/25	☐	Human influenza A virus H2N2 (1957-1968)
☐	Semliki Forest virus	☐	Highly pathogenic avian influenza A virus H5Nx strains within the Goose/Guangdong/96-like H5 lineage (e.g., H5N1, H5N6, H5N8 etc.)
☐	Flexal virus	☐	Transmissible spongiform encephalopathy (TSE) agents (e.g., Creutzfeldt-Jacob disease and kuru agents)
☐	Lymphocytic choriomeningitis virus (LCM) (neurotropic strains)		
Other			
☐	Any attenuated pathogen or vaccine strain that is currently excluded from the Select Agent Regulations that exhibits the recovery of virulence at or near the wild-type	☐	Mpox virus clade I/II chimeric viruses resulting from any deliberate manipulation of clade II to incorporate nucleic acids coding for clade I virulence factors

Examples of Category 1 DURC

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.

Creates a pathogen more virulent than the wild-type pathogen, resulting in higher morbidity or mortality in human, plant, or animal populations.

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.

Renders a pathogen or toxin with the ability to retain or increase its infectiousness or toxicity outside a living system.

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.

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).

Examples of Category 1 DURC

Examine a ***Y. pestis*** gene that is hypothesized to be involved with biofilm production. The researchers hypothesize that some of the genetic changes observed on the gene potentially contribute to the increased transmission of *Y. pestis* to rodent hosts.

They will generate *Y. pestis* strains that differentially express this gene and test each strain's ability to form biofilms in flea guts and to transmit the pathogen to a rodent host. They hypothesize that strains overexpressing this gene will produce biofilm faster and more effectively, thereby increasing *Y. pestis* transmission in rodents.

PI creates a novel expression system using a native *Clostridium* spp host to recombinantly express a new **botulinum neurotoxin (BoNT**) serotype for the purpose of toxin purification and full characterization.

The virulence and susceptibility to countermeasures of the newly expressed BoNT serotype has not yet been fully characterized, but preliminary experiments indicate that the newly expressed BoNT serotype is likely more toxic due to changes in post- translational modifications observed in other more toxic serotypes.

Category 2 research meets all three criteria:

(1) The research involves, or is reasonably anticipated to result in, a PPP
   a. A PPP, or any pathogen that will be modified in such a way that is reasonably anticipated to result in a PPP

(2) The research is reasonably anticipated to result in, or does result in, one or more of the experimental outcomes or actions specified below
   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
   d. Generate, use, reconstitute, or transfer an eradicated or extinct PPP, or a previously identified PEPP

Refer to the Implementation Guidance

(3) The research can be reasonably anticipated to result in the development, use, or transfer of a PEPP or an eradicated or extinct PPP23 that may pose a significant threat to public health, the capacity of health systems to function, or national security.

Does your research involve meet all three criteria for Category 2 (PEPP) research? Yes or No (dropdown box)

Examples of Category 2 PEPP

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.

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.

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.

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.

Examples of Category 2 PEPP

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.

Highly Pathogenic Avian Influenza A(H5) and A(H7) subtypes

Because A(H5) and A(H7) viruses do not transmit efficiently in humans, they are not considered PPPs in their wild-type state.18 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

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.

Experiments that are Not Typically Subject to Category 2 Oversight

Surveillance activities, including collection of diagnostic and clinical specimens, sampling and sequencing, and basic viral characterization, in which the pathogen or toxin is not modified via genetic manipulation or laboratory adaptation to enhance transmissibility or virulence in humans such that it can spread uncontrollably in human population and cause moderate to severe disease.

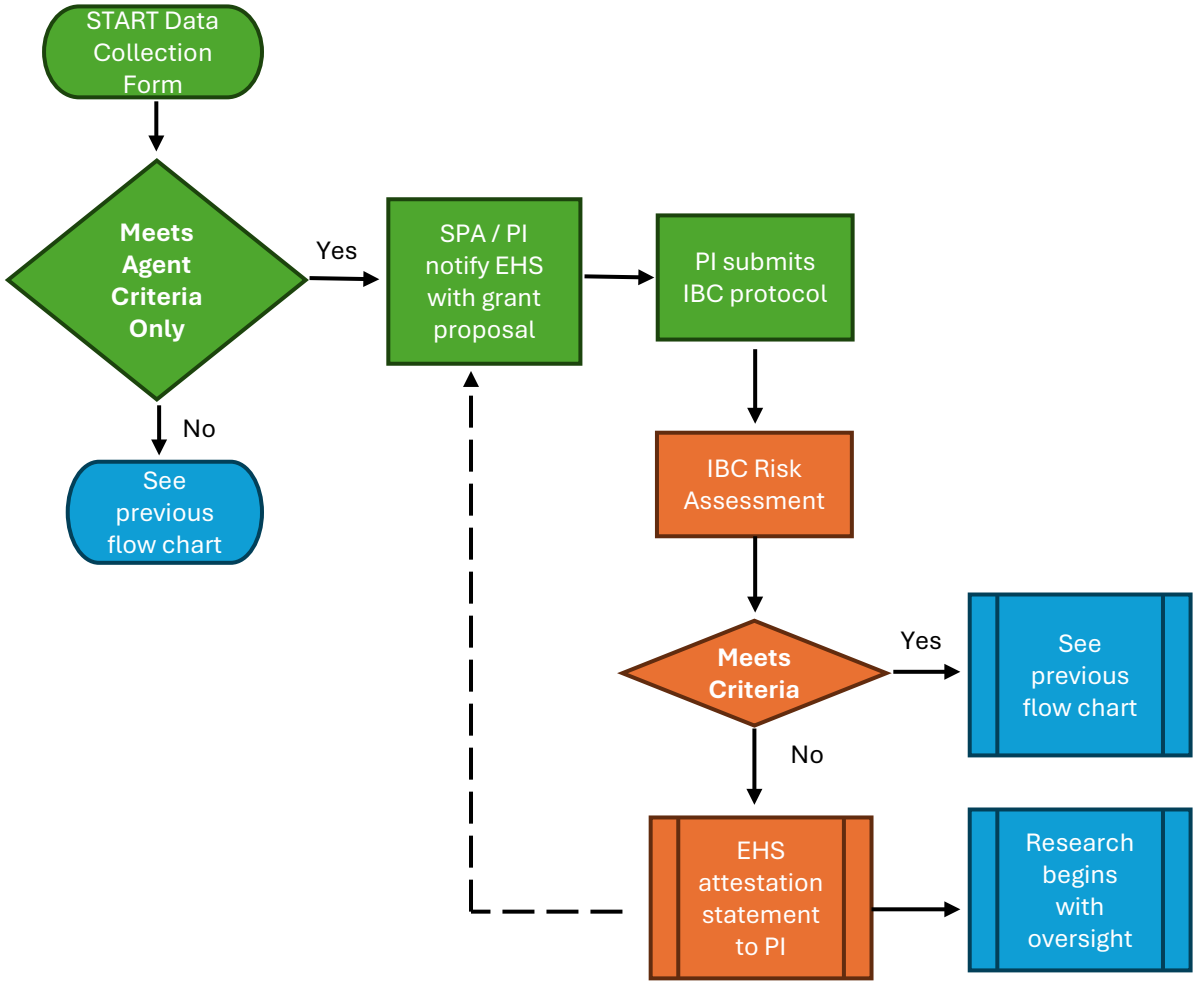
Research on evaluating, testing, and/or producing vaccines and related biologics such as immunoglobulins and the generation of high-growth strains, with the attenuation of virulence and transmissibility below wild-type levels.

Experiments focused on evaluating and developing antivirals for the treatment or prevention of disease caused by circulating human viruses, when generation of antiviral resistant strains are not reasonably anticipated to result in a PEPP.

Basic viral characterization studies, including but not limited to, pseudotype virus studies with proteins from laboratory-adapted strains, human receptor binding studies, animal model susceptibility studies that do not involve serial transmission, and *in vitro* experiments with human cell lines or primary human cells that do not involve certain types of serial passage that would be considered higher risk.

UTHealth Houston DURC/PEPP Review Process

SPA (Sponsored Projects Administration)
PI (Principal Investigator)
EHS (specifically Biological Safety)
(SVP AFA) Senior Vice President, Academic and Faculty Affairs



PI Responsibility

- Initial assessment of whether their proposed or ongoing research may be within the scope of this policy
- Submit the research proposal to the federal funding agency including notification that the research may be within the scope of this policy
- Work with the IBC to develop a risk mitigation plan
- Conducting approved work associated with this policy only after approval by the federal funding agency, the IBC and in accordance with the risk mitigation plan
- Being knowledgeable about this policy and educate lab personnel accordingly
- Provide annual progress reports for Category 1 and semiannual progress reports for Category 2 to the federal funding agency for review, evaluation, assessment, clarification or confirmation
- Communication of research and research findings associated with this policy in a responsible manner

Research Institution Responsibility

- Establish and implement internal policies and practices for research under this policy.
- Ensure PIs are aware of and executing the initial assessment of their research regarding this policy
- Establish an Institutional Review Entity (IRE)
  - UTHealth Houston IBC will fulfill the role of the IRE
- Engage in an ongoing dialogue with the PI of the research in question when developing appropriate risk mitigation plans
- 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
- 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
- Conduct an institutional oversight process by an IRE when a PI makes an initial assessment that research may constitute Category 1 or Category 2

Research Institution Responsibility

- Works with the PI to conduct a risk-benefit assessment and develop a risk mitigation plan for Category 1 or Category 2 research
- 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
- Evaluates risk mitigation plans at least annually
- Within 30 calendar days of the institutional review, notify the federal funding agency of any research, whether it meets or does not meet the definition of Category 1 or Category 2 research
- 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.

Research Institution Responsibility

- Designate an ICDUR to serve as an internal resource regarding oversight of Category 1 or Category 2 research.
- 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.
- 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.
- 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
- 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.

Research Institution Responsibility

- 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
- 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.
- On an annual basis, provide a formal assurance to relevant federal funding agencies that the research institution is operating consistent with this Policy.

Federal Funding Agency Responsibility

- Complete a merit review of the proposed research and if it is considering funding the proposed research, notify the research institution
- 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
- Prior to reaching the final determination to fund, or continue to fund, the research, consult with the research institution to address any disagreements identified

Resources:

[U.S. Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP)]

[NIH Implementation of the U.S. Government Policy for Oversight of Dual Use Research of Concern (DURC) and Pathogens with Enhanced Pandemic Potential (PEPP)]

[UTHealth Houston Biological Safety Program]

IBC Policies

Trainings