Appendix B: Pathogens that May be Subject to Category 2 Oversight

This information is taken from the USG Policy Implementation Guide. Please see Section B.2 *Definitions and Scope of Category 2 Oversight* for additional discussion and examples of experiments that may require Category 2 Oversight.

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 or mortality in humans."

PEPP is a type of PPP that results 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."

It is important to note that wild-type pathogens from nature are not PEPPs but may be considered PPPs because of their pandemic potential. Additionally, the wild-type pathogen (not enhanced) also does not necessarily need to begin as a PPP to result in a PEPP.

A pathogen's capability for "wide and uncontrollable spread in a human population" is a function of

1) Efficient transmission (i.e., via aerosol, respiratory droplets, direct contact, fomites, etc.)
    a. The agent is expected to exhibit sustained human-to-human transmission in a population under specific conditions, or an effective reproductive number (Rt) greater than one.
    b. The agent is expected to survive outside the host and/or withstand environmental conditions longer than the wild-type pathogen.
    c. The agent has an 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.
    d. An animal or zoonotic pathogen has increased transmissibility, such that it can now utilize new non-human vectors or reservoirs to spread.
    e. Lack of availability or access to non-medical and medical countermeasures (MCMs) to contain the pathogen.

2) Virulence
    a. Exposure is expected to result in higher morbidity or mortality in comparison to the wild-type and results in moderate to severe disease in humans.
        - Resistant to FDA-approved, cleared, or licensed MCMs, when such resistance trait(s) are not known to occur naturally and such resistance trait(s) could compromise the ability to control the morbidity, mortality, or spread in humans

3) Population Immunity
    a. A lack of or disruption to the of effectiveness of pre-existing immunity
    b. Altered immune evasion of the pathogen ,

Category 2 oversight may be required when:

1) When the starting agent is a PPP *and* the research is reasonably anticipated to result in one of the experimental outcomes to produce a modified pathogen that meets the definition of a

PEPP;

2) When the starting agent is a not a PPP *and* the research is reasonably anticipated to result in one of the experimental outcomes to produce a modified pathogen that meets the definition of a PEP;

3) When one transfers, generates, uses, or reconstitutes an extinct or eradicated PPP, regardless of whether the extinct or eradicated pathogen will be enhanced relative to its wild-type form.

Experiments that are Not Typically Subject to Category 2 Oversight

PIs are expected to exhibit vigilance and evaluate (and reevaluate) research in case unexpected results warrant Category 2 review.

For further examples on how to identify and assess Category 2 research, refer to Appendix D of the Implementation Guide.

- 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.

References

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

IMPLEMENTATION GUIDANCE for the United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential (Implementation Guide)