B.1 Definition and Scope of Category 1 Oversight

B.1.1 Definition: Dual Use Research of Concern

Dual use research of concern (DURC) as defined in the Policy 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."

B.1.2 Research Subject to Category 1 Oversight

Research that is subject to Category 1 oversight must meet the following three criteria:

- Involves one or more of the biological agents or toxins within scope of Section 4.1.1 of the Policy;

- Is reasonably anticipated to result, or does result, in one or more of the experimental outcomes listed in Section 4.1.2 of the Policy; and

- Based on current understanding, the research institution and/or federal funding agency assesses that the research constitutes DURC, as specified in Section 4.1.3 of the Policy.

The Policy supersedes the Federal DURC Policy and Institutional DURC Policy, expands the scope of biological agents and toxins, and refines the list of experimental outcomes. The expanded scope of biological agents and toxins is based upon the recognition that additional biological agents and toxins, when manipulated in certain ways, have the potential to negatively impact public health, agriculture, food security, economic security, or national security.

This *Implementation Guidance* includes a checklist of all biological agents and toxins outlined in Section 4.1.1 of the Policy as of the time of the release of the Policy (see Appendix C) to assist with identifying those studies most likely to require enhanced oversight. However, the U.S. government also recognizes that it is difficult to anticipate all possible DURC that requires enhanced oversight, and there may be additional types of research that do not involve the biological agents or toxins or experiments outlined in Section 4.1.1 and Section 4.1.2 of the Policy that could constitute DURC.

PIs and IREs are encouraged to remain vigilant to additional types of research with any biological agent or toxin, regardless of its Risk Group, where the biological agent or toxin is experimentally manipulated in a way that could meet the definition of DURC, and to develop and apply appropriate risk mitigation measures. The PI and IRE are best positioned to assess whether studies on biological agents or toxins beyond this list should be considered for additional risk mitigation measures because of the dual use risks they may pose. Advances in science and technology have the potential to present situations that are not anticipated in this *Implementation Guidance* and PIs and IREs are encouraged to seek additional guidance from federal funding agencies, as needed. PIs, IREs, and research institutions are encouraged

to voluntarily conduct analogous risk assessment and develop risk mitigation measures when designing and developing engineered biological systems for other applications, even though such mitigation measures are outside the scope of the Policy.

Table 2 provides examples of risks posed by each type of Category 1 research experimental outcome listed in Section 4.1.2 of the Policy that, when involving biological agents and toxins listed in Section 4.1.1 of the Policy, may meet the threshold for Category 1 research oversight. These examples are provided to illustrate the types of risks associated with each experimental outcome and may not represent the full range of possible risks.

Table 2. Examples of Potential Risks Posed by Category 1 Experimental Outcomes

Category 1 Experimental Outcomes	**Examples of Associated Risks**
i. Increase transmissibility of a pathogen within or between host species	• 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.
ii. Increase the virulence of a pathogen or convey virulence (i.e., the ability of a pathogen to cause disease) to a non-pathogen	• Creates a pathogen more virulent than the wild-type pathogen, resulting in higher morbidity or mortality in human, plant, or animal populations.
iii. Increase the toxicity of a known toxin or produce a novel toxin	• 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.
iv. Increase the stability of a pathogen or toxin in the environment, or increase the ability to disseminate a pathogen or toxin (e.g., improving characteristics of the pathogen or toxin such as environmental stability and ability to be aerosolized)	• 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.

Category 1 Experimental Outcomes	Examples of Associated Risks
	• Enhances the environmental stability of a pathogen or toxin, thereby increasing ease of transmissibility or capability to cause disease. • Develops a method for producing or disseminating large quantities of a pathogen or toxin.
v. Alter the host range or tropism of a pathogen or toxin	• 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). • Alters tissue tropism of a pathogen or toxin resulting in more severe disease manifestation in humans, plants, or animals (e.g., a respiratory pathogen's ability to become neurotropic). Note: Importantly, this type of experimental 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.
vi. Decrease the ability for a human or veterinary pathogen or toxin to be detected using standard diagnostic or analytical methods	• Alters a pathogen or toxin such that it is no longer identifiable by widely used diagnostic tests or other detection modalities. • Alters the nucleic acid sequence of a pathogen or toxin in a way that preserves function but renders the pathogen or toxin no longer identifiable by screening

Category 1 Experimental Outcomes	Examples of Associated Risks
	mechanisms designed to detect nucleic acid sequences of concern.[6] Note: This type of experimental outcome is only applicable for human and veterinary Category 1 pathogens.
vii. Increase resistance of a pathogen or toxin to clinical and/or veterinary prophylactic or therapeutic interventions (e.g., antimicrobials, antivirals, antitoxins, vaccines)	• Alters a pathogen or toxin such that it causes disease which is not treatable, or severely increases the failure risk with extant therapeutics. • Modifies (i.e., a non-naturally occurring mutation) a pathogen or toxin such that it becomes newly resistant to multiple antimicrobials, antivirals, or antitoxins. • Creates a pathogen or toxin for which existing prophylactic measures available to the general population, such as vaccines, are no longer effective at preventing disease or transmission. Note: This type of experimental outcome is only applicable for human and veterinary Category 1 pathogens.
viii. 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	• Modifies the antigenic profile of a pathogen or toxin 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. Note: This type of experimental outcome is only applicable for human and veterinary Category 1 pathogens.
ix. Enhance the susceptibility of a host population to a pathogen or toxin	• Generates a pathogen or toxin with an enhanced or a new ability to compromise immune responses of

[6] Sequences of concern are defined in "Screening Framework Guidance for Providers and Users of Synthetic Nucleic Acids," October 2023. https://aspr.hhs.gov/legal/synna/Documents/SynNA-Guidance-2023.pdf; and "Framework for Nucleic Acid Synthesis Screening," April 2024. https://www.whitehouse.gov/wp-content/uploads/2024/04/Nucleic-Acid_Synthesis_Screening_Framework.pdf.

Category 1 Experimental Outcomes	Examples of Associated Risks
	individuals or populations, thereby enabling the increased spread of disease. • Creates a pathogen or toxin that suppresses the host's immune response, resulting in increased morbidity or mortality.