Appendix A: Research Subject to Category 1 Oversight

This information is adapted from Section B.1 *Definition and Scope of Category 1 Oversight* of the USG Policy Implementation Guide.

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.

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

Research Subject to Category 1 Oversight

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

1. Involves one or more of the biological agents or toxins within scope of Section 4.1.1 of the USG Policy (see the List of Agents and Toxins that follows);
2. Is reasonably anticipated to result, or does result, in one or more of the experimental outcomes listed in Section 4.1.2 of the USG Policy stated below;
    i. Increase transmissibility of a pathogen within or between host species
    ii. Increase the virulence of a pathogen or convey virulence (i.e., the ability of a pathogen to cause disease) to a nonpathogen
    iii. Increase the toxicity of a known toxin or produce a novel toxin (i.e., decreases dose or increases morbidity or mortality at a similar dose)
    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, ability to be aerosolized, or spread by additional means)
    v. Alter the host range or tropism of a pathogen or toxin (includes tissue tropism)
        - 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
        - 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)
        - E.g. Resulting morbidity or mortality is not treatable or severely increases treatment failure rates with existing therapeutics and prophylactics
        - 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

- E.g. Alterations to the antigen profile such that pre-existing immunity is less efficient or no longer exists.
- 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
- E.g. Enhanced or a new ability to compromise immune responses or creates a pathogen or toxin that suppresses the host's immune response.

3. 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 USG Policy.

List of Agents and Toxins

The ABSA Risk Group Database is a great quick reference for risk groups and containment levels but is not the equivalent to the list of references linked in the top matter of this document under Category 1.

HHS Select Agents and Toxins

- Abrin
- *Bacillus cereus* Biovar *anthracis*
- Botulinum neurotoxins
- Botulinum neurotoxin producing species of *Clostridium*
- Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence $X_1CCX_2PACGX_3X_4X_5X_6CX_7$)
- *Coxiella burnetii*
- Crimean-Congo haemorrhagic fever virus
- Diacetoxyscirpenol
- Eastern Equine Encephalitis virus
- Ebola virus
- *Francisella tularensis*
- Lassa fever virus
- Lujo virus
- Marburg virus
- Mpox virus
- 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)
- Ricin
- *Rickettsia prowazekii*
- 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
- Saxitoxin
- South American Haemorrhagic Fever viruses:
  - Chapare
  - Guanarito
  - Junín
  - Machupo
  - Sabia
- Staphylococcal enterotoxins (subtypes A,B,C,D,E)
- T-2 toxin

- Tetrodotoxin
- Tick-borne encephalitis complex (flavi) viruses:
  - Far Eastern subtype
  - Siberian subtype
- Kyasanur Forest disease virus
- Omsk hemorrhagic fever virus
- Variola major virus (Smallpox virus)
- Variola minor virus (Alastrim)
- *Yersinia pestis*

Overlap Select Agents and Toxins

- *Bacillus anthracis*
- *Bacillus anthracis* Pasteur strain
- *Burkholderia mallei*
- *Burkholderia pseudomallei*
- Hendra virus
- Nipah virus
- Rift Valley fever virus
- Venezuelan equine encephalitis virus

USDA Veterinary Services (VS) Select Agents and Toxins

- African swine fever virus
- Avian influenza virus
- Classical swine fever virus
- Foot-and-mouth disease virus
- Goat pox virus
- Lumpy skin disease virus
- *Mycoplasma capricolum*
- *Mycoplasma mycoides*
- Newcastle disease virus
- Peste des petits ruminants virus
- Rinderpest virus
- Sheep pox virus
- Swine vesicular disease virus

USDA Plant Protection And Quarantine (PPQ) Select Agents and Toxins

- *Coniothyrium glycines* (formerly *Phoma glycinicola* and *Pyrenochaeta glycines*)
- *Ralstonia solanacearum*
- *Rathayibacter toxicus*
- *Sclerophthora rayssiae*
- *Synchytrium endobioticum*
- *Xanthomonas oryzae*

NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules
Appendix B, Risk Group 4 and subset of Risk Group 3
https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf

Risk Group 4 (RG4) - Bacterial Agents
None

Risk Group 4 (RG4) - Fungal Agents
None

Risk Group 4 (RG4) - Parasitic Agents
None

Risk Group 4 (RG4) - Viral Agents

- *Arenaviruses*
  - Guanarito virus
  - Lassa virus
  - Machupo virus
  - Sabia
  - Junin virus
    - (except the candid #1 vaccine strain listed in Appendix B-II-D Risk Group2 (RG2) – Viruses)
- *Bunyaviruses* (Nairovirus)
  - Crimean-Congo hemorrhagic fever virus
- *Filoviruses*
  - Ebola viruses
  - Marburg viruses
- *Flaviruses* - Group B Arboviruses
  - 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
- *Herpesviruses* (alpha)
  - Herpesvirus simiae (Herpes B or Monkey B virus)
- *Paramyxoviruses*
  - Equine Morbillivirus (Hendra virus)
- Hemorrhagic fever viruses as yet undefined

Risk Group 3 (RG3) - Bacterial Agents Including Rickettsia*

- *Bartonella*
- *Brucella* - including *B. abortus, B. canis, B. suis*
- *Burkholderia* (*Pseudomonas*) *mallei* and *B. pseudomallei*
- *Coxiella burnetii*
  - (except the Phase II, Nine Mile strain listed in Appendix B-II-A, Risk Group 2 (RG2) - Bacterial Agents Including Chlamydia)
- *Francisella tularensis*
  - (except those strains listed in Appendix B-II-A, Risk Group 2 (RG2) – Bacterial Agents Including Chlamydia)
- *Orientia tsutsugamushi* (was *R. tsutsugamushi*)
- *Pasteurella multocida* type B -"buffalo" and other virulent strains
- *Rickettsia akari*, *R. australis*, *R. canada*, *R. conorii*, *R. prowazekii*, *R. rickettsii*, *R. siberica*, R. *typhi* (*R. mooseri*)
- *Yersinia pestis*
  - (except those strains listed in Appendix B-II-A, Risk Group 2 (RG2) - Bacterial Agents Including Chlamydia)

Risk Group 3 (RG3) - Fungal Agents*
None

Risk Group 3 (RG3) - Parasitic Agents
None

Risk Group 3 (RG3) - Viruses and Prions*

- *Alphaviruses (Togaviruses) - Group A Arboviruses*
  - Chikungunya virus
    - (except the vaccine strain 181/25 listed in Appendix B-II-D Risk Group2 (RG2) – Viruses)
  - Semliki Forest virus
  - Venezuelan equine encephalomyelitis virus
    - (except the vaccine strains TC-83 and V3526, see Appendix B-II-D (RG2) – Viruses)
  - Other viruses as listed in the reference source (see Section V-C, Footnotes and References of Sections I through IV)
- *Arenaviruses*
  - Flexal
  - Lymphocytic choriomeningitis virus (LCM) (neurotropic strains)
- *Bunyaviruses*
  - Hantaviruses including Hantaan virus
  - Rift Valley fever virus
- *Coronaviruses*
  - SARS-associated coronavirus (SARS-CoV)
  - Middle East respiratory syndrome coronavirus (MERS-CoV)
- *Flaviviruses - Group B Arboviruses*
  - Japanese encephalitis virus (except those strains listed in Appendix B-II-D Risk Group 2 (RG2) - Viruses)
  - Yellow fever virus (Except for vaccine strain 17D)
  - Other viruses as listed in the reference source (see Section V-C, Footnotes and References of Sections I through IV)
- *Orthomyxoviruses*
  - Influenza viruses 1918-1919 H1N1 (1918 H1N1), human H2N2 (1957-1968), and highly pathogenic avian influenza H5N1 strains within the Goose/Guangdong/96-like H5 lineage (HPAI H5N1).
- *Poxviruses*
  - Monkeypox virus (Clade I & Clade II containing nucleic acids coding for clade I MPVX virus virulence factors)
- Prions
  - Transmissible spongiform encephalopathies (TSE) agents (Creutzfeldt-Jacob disease and Kuru agents) (see Section V-C, Footnotes and References of Sections I through IV, for containment instruction)

EXCLUDED RG3 Agents:

- Human immunodeficiency virus (HIV) types 1 and 2
- Human T cell lymphotropic virus (HTLV) types 1 and 2
- Simian immunodeficiency virus (SIV)
- *Mycobacterium tuberculosis, Mycobacterium bovis*
- Clade II of MPVX viruses unless containing nucleic acids coding for clade I MPVX virus virulence factors
- Vesicular stomatitis virus

- *Coccidioides immitis* (sporulating cultures; contaminated soil)
- *Histoplasma capsulatum, H. capsulatum* var. *duboisii*

Other RG3 Agents:

- 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.

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)

Select Agents and Toxins List

Select Agents and Toxins Exclusions (not excluded from this policy)

NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules

Biosafety in Microbiological and Biomedical Laboratories, 6th Edition