CASE WESTERN RESERVE UNIVERSITY
INSTITUTIONAL REVIEW ENTITY
PROCEDURES FOR THE REVIEW AND USE OF
DUAL USE RESEARCH OF CONCERN

I. References

A. *United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (USG Policy)*, September 2015. The *USG Policy* is available at https://osp.od.nih.gov/biotechnology/dual-use-research-of-concern/

B. For further clarification of the regulations, Principal Investigators ("Investigators") should refer to the full text of the *USG Policy*.

II. Purpose

The purpose of these procedures is twofold. The first purpose is to lend guidance to Case Western Reserve University ("CWRU;" "University") and its Investigators for the institutional review and oversight of research within the life sciences for a well-defined subset of research that involves fifteen agents and toxins and seven categories of experiments. These experiments are those with high-consequence pathogens and toxins which require review to identify potential dual use research of concern (DURC) and mitigate risks, where appropriate. This procedure delineates the roles and responsibilities of CWRU and its Investigators. It contains regulatory requirements as set out by the United States Government (USG) as well as University policy promulgated for the review and conduct of potential DURC research. The second purpose is to preserve the benefits of life sciences DURC while minimizing the risk that the knowledge, information, products, or technologies generated from such research could be used in a manner that results in harm to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security in compliance with the *USG Policy*.

III. Definitions and Abbreviations

A. BSO: Biological Safety Officer

B. Co-Investigator: Faculty or non-faculty researchers who are not principal investigators.

C. Dual use research: Research conducted for legitimate purposes that generates knowledge, information, technologies, and/or products that could be utilized for both benevolent and harmful purposes.

D. DURC: Dual use research of concern is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat

with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

E. EHS: Environmental Health and Safety Office.

F. IBC: Institutional Biosafety Committee is a committee that meets the requirements for membership specified *National Institutes of Health Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)* and reviews, approves, and oversees projects which fall under the *NIH Guidelines*.

G. Institution: For the purpose of these procedures the "Institution" shall be Case Western Reserve University.

H. Institutional Contact for Dual Use Research: The ICDUR is an individual designated by the institution to serve as an institutional point of contact for questions regarding compliance with

and implementation of the requirements for the oversight of DURC as well as the liaison (as necessary) between the institution and the relevant USG funding agency.

I. IRE: Institutional Review Entity is a committee established by the institution as described in Section 7.2.E and empowered to execute the requirements in Section 7.2.B.i- iii, v, and viii of *USG Policy*.

J. Life Sciences: Life sciences pertains to living organisms (e.g., microbes, human beings, animals, and plants) and their products, including all disciplines and methodologies of biology such as aerobiology, agricultural science, plant science, animal science, bioinformatics, genomics, proteomics, microbiology, synthetic biology, virology, molecular biology, environmental science, public health, modeling, engineering of living systems, and all applications of the biological sciences. The term is meant to encompass the diverse approaches to understanding life at the level of ecosystems, populations, organisms, organs, tissues, cells, and molecules.

K. NIH: The National Institutes of Health

L. ORC: The "Office of Research Compliance" at Case Western Reserve University

M. Principal Investigator: The investigator who is primarily responsible for the conduct of the reach. Only faculty members may be Principal Investigators. All non-faculty researchers are properly characterized as Co-Investigators.

N. USG: United States Government.

IV. Policy and Applicability

Life sciences research that meets the scope specified in Section 6.2 of the *USG Policy* is subject to USG as well as institutional oversight. The purpose of this oversight is to preserve the benefits of such research while minimizing the risk that the knowledge, information, products, or technologies generated by DURC could be used in a manner that results in harm to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

Oversight includes the identification of life sciences research that raises dual use concerns as well as the implementation of measures to mitigate the risk that DURC is used in a manner that results in harm. Measures that mitigate the risks of DURC should be applied in a manner that minimizes, to the extent possible, adverse impact on legitimate research, is commensurate with the risk, includes flexible approaches that leverage existing processes, and endeavors to preserve and foster the benefits of research.

USG Policy applies to the following entities:

A. USG departments and agencies that fund or conduct life science research.

B. Institutions within the United States that both:
   a. Receive USG funds to conduct or sponsor life sciences research; and
   b. Conduct or sponsor research that involves one or more of the 15 agents or toxins listed in Section 6.2.1, even if the research is not supported by USG funds.

C. Institutions outside of the United States that receive USG funds to conduct or sponsor research that involves one or more of the 15 agents or toxins listed in Section 6.2.1.

Non-compliance with *USG Policy* may result in suspension, limitation, or termination of USG funding, or loss of future USG funding opportunities for the non-compliant USG- funded research project and of USG funds for other life sciences research at the institution, consistent with existing regulations and policies governing USG funded research, and may subject the

institution to other potential penalties under applicable laws and regulations. (See *USG Policy* for additional details.)

V. Agents and Toxins and Categories of Experiments

Research conducted at or sponsored by CWRU, or research conducted by CWRU faculty members or students on the main campus of CWRU, must be evaluated for DURC potential if 1) it uses one or more of the agents or toxins listed in Section 6.2.1, and 2) produces, aims to produce, or can be reasonably anticipated to produce one or more of the effects listed in Section 6.2.2.

As detailed in Section 6.2.1 of *USG Policy*, the fifteen (15) agents and toxins covered by this procedure. Note: There are no exempt quantities of botulinum neurotoxin. Research involving any quantity of botulinum neurotoxin should be evaluated for DURC potential.

A. Agents and Toxins
   a. Avian influenza virus (highly pathogenic)
   b. *Bacillus anthracis*
   c. Botulinum neurotoxin
   d. *Burkholderia mallei*
   e. *Burkholderia pseudomallei*
   f. Ebola virus
   g. Foot-and-mouth disease virus
   h. *Francisella tularensis*
   i. Marburg virus
   j. Reconstructed 1918 Influenza virus
   k. Rinderpest virus
   l. Toxin-producing strains of *Clostridium botulinum*
   m. Variola major virus
   n. Variola minor virus
   o. *Yersinia pestis*

As detailed in Section 6.2.2 of *USG Policy,* if research with the 15 agents and toxins is planned, evaluation for DURC potential is required if research produces, aims to produce, or can be reasonably anticipated to produce one or more of the effects under the listed categories of experiments.

B. Categories of experiments
   a. Enhances the harmful consequences of the agent or toxin.
   b. Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical and/or agricultural justification.
   c. Confers to the agent or toxin resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates their ability to evade detection methodologies.
   d. Increases the stability, transmissibility, or the ability to disseminate the agent or toxin.
   e. Alters the host range or tropism of the agent or toxin.
   f. Enhances the susceptibility of a host population to the agent or toxin.

g. Generates or reconstitutes an eradicated or extinct agent or toxin listed in 6.2.1 and above.

VI. Organizational Structure and Responsibilities

A. The University

The University's duties include, but are not be limited to:

a. The responsibility for compliance with applicable regulations DURC used in research rests under the auspices of the Vice President for Research and Technology Management. The IRE and EHS shall serve as the immediate point of contact with Investigators to receive and review research projects proposing use DURC.

b. Establish and implement policies that provide for the review, identification and safe conduct of DURC research and that ensure compliance with the *USG Policy* for research that uses one or more of the agents or toxins listed in Section 6.2.1 also produces, aims to produce, or is reasonably anticipated to produce one or more of the effects listed in Section 6.2.2.

c. When research is identified by a Principal Investigator as utilizing one of the agents or toxins listed in Section 6.2.1, initiate an institutional review and oversight process, as applicable. Note: Research that has already been determined to be DURC under the *March 2012 DURC Policy,* and for which a risk mitigation plan has already been developed, is not required to re-review, but may be subject to updates (see *USG Policy*).

d. Ensure that internal policies establish a mechanism for the Principal Investigator to immediately refer a project to the IRE as soon as potential research needing DURC review is identified.

e. Designate an Institutional Contact for Dual Use Research (ICDUR) to serve as an institutional point of contact for questions regarding compliance with and implementation of the requirements for the oversight of research that falls within the scope of Section 6.2 and/or meets the definition of DURC.

f. Establish an IRE to execute the requirements for DURC review. At CWRU, the IRE which will function as a separate *ad hoc* review board of the CWRU IBC and review DURC for investigators on the physical campus of CWRU. The IRE membership will be comprised of CWRU IBC members, with additional expertise added as required by the review of planned uses of agents/toxins requiring a mitigation plan and required registrations, in accord with the requirements of *USG Policy* (see below).

g. Support the IRE, in the administration of its responsibilities, as per *USG Policy* and detailed below.

B. The Institutional Review Entity (IRE)

The IREs duties include, but are not be limited to:

a. In accordance with *USG Policy* and University procedures, the IRE shall review research that falls within the scope of Section 6.2.1.

b. The IRE will be composed of at least five members and be sufficiently empowered by the institution to ensure it can execute the requirements of *USG Policy*. The IRE will include persons with 1) sufficient breadth of expertise to assess the dual use potential of the range of relevant life sciences research conducted at a given research facility; 2) knowledge of relevant USG policies and understanding of risk assessment and risk management considerations, including biosafety and biosecurity; 3) may also include, or have available as

consultants, at least one person knowledgeable in the institution's commitments, policies, and standard operating procedures.

c. No member of the IRE may be involved in the review or approval of a project in which he/she is, has been, or expects to be engaged or has a conflict of interest, except to provide specific information requested by the IRE.
d. Maintain records of institutional DURC reviews and completed risk mitigation plans for the term of the research grant or contract plus three years after its completion, but no less than eight years, unless a shorter period is required by law or regulation.
e. Provide education and training on DURC for individuals conducting life sciences research with one or more of the agents listed in Section 6.2.1 of the *USG Policy*, and maintain records of such education and training for the term of the research grant or contract plus three years after its completion. Institutions may also wish to address dual use topics in existing courses on research ethics or the responsible conduct of research. Institutions may require additional record keeping and should designate an individual responsible for maintaining documentation.
f. Ensure compliance with *USG Policy* and with approved risk mitigation plans.
g. Report instances of noncompliance with this Policy, as well as mitigation measures undertaken by the institution to prevent recurrences of similar noncompliance, within 30 calendar days to the USG funding agency. In the case of non-USG funded research, reports should be made to the USG agency designated by NIH (per Section 7.E of *USG Policy*).
h. Engage in an ongoing dialogue with the PI of the research in question when conducting a risk assessment and developing a risk mitigation plan.
i. As necessary, assist the PIs conducting life sciences research when questions arise about whether their research may require further review or oversight.
j. Establish an internal mechanism for PIs to appeal institutional decisions regarding research that is determined by the IRE to meet the definition of DURC.
k. Make information about the process for review of research subject to the Policy available upon request, as consistent with applicable law.
l. When applying for or accepting USG funds for life sciences research, as applicable, certify that the institution will be or is in compliance with all aspects of *USG Policy*.

C. Principal Investigator

a. Eligibility: Only faculty members are eligible to be Principal Investigators and submit applications to the IRE. All non-faculty researchers and students are properly characterized as Co-Investigators for purposes of conducting DURC research sponsored by and conducted at the main campus of the University. On behalf of the institution, the Principal Investigator is responsible for full compliance with the *USG Policy* in the conduct of DURC research.
b. General Responsibilities: As part of this general responsibility, the Principal Investigator *shall* notify the Institutional Review Entity (IRE) using the CWRU IRE DURC Review Form as soon as any DURC research is identified and prior to the initiation of any research with any of the covered agents and toxins. The form includes the following information regarding the planned research: 1) research involves one or more of the agents or toxins listed in Section 6.2.1; and/or 2) research with one or more of the agents or toxins listed in Section 6.2.1 also produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven effects listed in Section 6.2.2; and/or 3) research that is within the scope of Section 6.2 may meet the definition of DURC. The notification must include the

PI's assessment of whether any research involving these agents or toxins produces, aims to produce, or is reasonably anticipated to produce one or more of the effects listed in Section 6.2.2.

c. Work with the IRE to assess the dual use risks and benefits of the DURC and to develop risk mitigation measures.
d. Conduct DURC in accordance with the provisions in the risk mitigation plan.
e. Be knowledgeable about and comply with all institutional and USG policies and requirements for oversight of DURC.
f. Ensure that laboratory personnel (i.e., those under the supervision of laboratory leadership, including graduate students, postdoctoral fellows, research technicians, laboratory staff, and visiting scientists) conducting life sciences research with one or more of the agents listed in Section 6.2.1 of *USG Policy* have received education and training on DURC.
g. Communicate DURC in a responsible manner. Communication of research and research findings is an essential activity for all researchers, and occurs throughout the research process, not only at the point of publication. Researchers planning to communicate DURC should do so in compliance with the approved risk mitigation plan developed by the IRE and in compliance with per Section 7.2.B.vii of *USG Policy*.

VII. Additional Resources and Forms

CWRU IRE DURC Review Form August 7, 2017

National Institutes of Health Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), April 2016. The *NIH Guidelines* are available at http://osp.od.nih.gov/office-biotechnology-activities/biosafety/nih-guidelines

CWRU Export Control
http://www.case.edu/compliance/exportcontrol/

CWRU Export Control---Shipping Guidance
http://www.case.edu/compliance/exportcontrol/shipping-abroad/

CWRU Environmental Health & Safety
https://www.case.edu/ehs/