

Approved by Office of the Provost – September 14, 2015

**POLICY FOR LIFE SCIENCES DUAL USE RESEARCH OF CONCERN
YALE UNIVERSITY**

I. PURPOSE

The purpose of this Policy is to strengthen the institutional review and oversight by Yale University (“Yale” or the “University”) of certain research to identify potential Dual Use Research of Concern (DURC) and to develop and implement risk mitigation where appropriate. In so doing, this Policy seeks to preserve the benefits of life sciences DURC research while minimizing the risk that the output of such research would be used for harmful purposes.

This Policy sets the rules for the individuals and committees at Yale who are responsible for the implementation of the University’s requirements with respect to DURC.

All research conducted at the University involving DURC Agents (as defined below) is subject to this Policy, regardless of the source of funding.

II. DEFINITIONS

BSC: The Yale University Biosafety Committee, which also serves as Yale’s Institutional Biosafety Committee (“IBC”)

Dual Use Research: research conducted for legitimate purposes that can be utilized for both benevolent and harmful purposes

DURC: Dual Use Research of Concern, meaning 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

DURC Agents: the following 15 agents and toxins referred to in the United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (the “2014 Policy”):

1. Avian influenza virus (highly pathogenic)
2. *Bacillus anthracis*

3. Botulinum neurotoxin (For purposes of this Policy, there are no exempt quantities of botulinum neurotoxin. Research involving any quantity of botulinum neurotoxin should be evaluated for DURC potential.)
4. *Burkholderia mallei*
5. *Burkholderia pseudomallei*
6. Ebola virus
7. Foot-and-mouth disease virus
8. *Francisella tularensis*
9. Marburg virus
10. Reconstructed 1918 Influenza virus
11. Rinderpest virus
12. Toxin-producing strains of *Clostridium botulinum*
13. Variola major virus
14. Variola minor virus
15. *Yersinia pestis*

Experimental Effects of Concern: the following 7 categories of experiments referred to in the 2014 Policy:

1. Enhances the harmful consequences of the agent or toxin
2. Disrupts immunity or effectiveness of an immunization against the agent or toxin without clinical and/or agricultural justification
3. 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
4. Increases the stability, transmissibility or the ability to disseminate the agent or toxin.
5. Alters the host range or tropism of the agent or toxin
6. Enhances the susceptibility of a host population to the agent or toxin
7. Generates or reconstitutes an eradicated or extinct agent or toxin listed in the definition of DURC Agents above.

ICDUR: Institutional Contact for Dual Use Research, who is the individual designated by the University to be the institutional point of contact for questions relating to compliance with this Policy and the liaison with the relevant US Government funding agencies. The University has designated the Director of Environmental Health and Safety as the ICDUR.

IRE: Institutional Review Entity.

USG: US Government.

US Funding Agency: the USG agency that is funding the subject research or, if the research is not USG-funded, the USG agency designated by the NIH, based on the nature of the research. If a federal department or agency simply passes through funding from another federal department or agency to support life sciences research involving one or more of the DURC Agents, the agency originally providing the funding shall be considered the US Funding Agency.

III. REQUIREMENTS FOR PRINCIPAL INVESTIGATORS

A Principal Investigator (“PI”) must submit for institutional review any anticipated or proposed research that meets any of the following criteria:

- the research directly involves nonattenuated forms of one or more of the DURC Agents;
- the research with nonattenuated forms of one of more of the DURC Agents produces, aims to produce or can reasonably be anticipated to produce one or more Experimental Effects of Concern; or
- the PI concludes that his/her research may meet the definition of DURC.

If a PI’s research meets any of the foregoing criteria, he/she will promptly notify the IRE by contacting EHS with the relevant information, including the PI’s assessment as to whether the research produces, aims to produce or is reasonably anticipated to produce one of more of the Experimental Effects of Concern and provide documentation indicating the reasons for his/her conclusion. EHS will provide a form for this notification. ***The research may not proceed without IRE approval, either through a determination that it is not DURC subject to this Policy, or because an approved mitigation plan has been implemented.***

Yale’s process for identifying possible DURC also includes

- queries on EHS/BSC forms for reviewing research EHS, including DURC questions on the Yale IBC Registration of Recombinant DNA Research, the Yale EHS Request to Use Infections Agents Registration and the Yale EHS FORM 01 Biological Materials Registration.
- the restricted items list though SciQuest, which triggers for DURC agents.
- EHS Safety Advisors, who check for new pathogen and high risk toxin research at least annually during their biosafety inspections

IV. POLICY REQUIREMENTS FOR INSTITUTIONAL REVIEW

The 2014 Policy requires an institution to designate an IRE to execute the institutional review of potential DURC Research. The Yale IRE is made up of the members of the Yale BSC. On a case-by-case basis, the IRE will recuse any member who is involved in the research project in question or has a direct financial interest, except to provide specific information requested by the IRE.

A. Review by the IRE for DURC Agents and Experimental Effects

The first step of the IRE review process is to verify that the subject research directly involves nonattenuated forms of one or more of the DURC Agents based on the materials provided by the PI and any other relevant materials. The USG also deems any of the following need not be reviewed under the 2014 Policy:

- The use of any of the DURC Agents in attenuated forms (unless the experiment will reconstitute a virulent agent);
- The use of the genes from any of the DURC Agents;
- *In silico* experiments (e.g., modeling experiments, bioinformatics approaches) involving the biology of the DURC Agents); or
- Research relating to the public, animal and agricultural health impact of any of the DURC Agents (e.g., modeling the effects of a toxin, developing new methods to deliver a vaccine, developing surveillance mechanisms for a DURC Agent).

The IRE will notify the PI in writing that the research may proceed, provided all other requirements are met, if it concludes that the research does not involve one or more DURC Agents or is not intended for review under the above criteria.

If the IRE concludes that the research does involve one or more DURC Agents, it will assess whether the research produces, aims to produce or is reasonably anticipated to produce one of more of the Experimental Effects of Concern based on review of the assessment and materials provided by the PI and any other relevant materials.

Based on the foregoing, if the IRE concludes that the research does not involve Experimental Effects of Concern and is therefore not subject to additional DURC oversight, it will notify the PI in writing that the research may proceed if all other requirements are met.

B. Review for DURC

If the IRE concludes that the research does involve one or more DURC Agents and Experimental Effects of Concern, the IRE will assess the risks of the research and determine whether the research is DURC. In so doing, it should examine descriptions of the research, the PI's assessments and other relevant information such as the project proposal, any project reports, any previous outcomes of Dual Use reviews and examples of similar research in the literature.

Guidance on points to consider while making this assessment can be found in Section C.2 of the Companion Guide¹. The applicable US Funding Agency may be consulted for advice.

If the IRE determines that the subject research does not meet the definition of DURC, it is not subject to additional institutional oversight and the IRE will promptly so notify the PI and, within 30 days, the applicable US Funding Agency. The IRE will inform the PI that the research may proceed if other requirements are met. The IRE and/or the ICDUR may consult with the US Funding Agency with respect to the Committee's determination.

C. Development of Mitigation Plan

If the IRE concludes that the subject research does meet the definition of DURC, it will promptly so notify the PI and within 30 calendar days, the applicable US Funding Agency, and shall proceed to develop a risk mitigation plan. The IRE will inform the PI that the research may not proceed without implementation of the risk mitigation plan as approved by the IRE.

In order to determine the acceptable level of risk associated with the DURC and the best mitigation strategies, the IRE will assess the potential benefits of the Research, with input from the PI, and then weigh the risks and benefits. Guidance on points to consider in making this assessment can be found in Section C.2 of the Companion Guide.

The IRE will then develop a draft risk mitigation plan (the "Risk Mitigation Plan") in consultation with the PI. The Plan should indicate the DURC associated risks, the specific risk mitigation measure to be employed and how these measure address the identified risks. Strategies for mitigating risks include:

- Applying additional biosafety or biosecurity measures
- Modifying the experimental design or methodology
- Planning for medical countermeasures

¹ Tools for the Identification, Assessment, Management, and Responsible Communication of Dual Use Research of Concern (the "Companion Guide") <https://www.phe.gov/s3/dualuse/Documents/durc-companion-guide.pdf>.

- Determining a plan for responsibly communicating the research findings
- Educating and training research staff
- Developing a specific monitoring plan
- Not conducting certain aspects of the research.

Guidance on points to consider in drafting a Risk Mitigation Plan and in creating a responsible communication plan can be found in Sections D and F of the Companion Guide. The applicable US Funding Agency may also be consulted for advice.

At the conclusion of its review, the IRE will submit its findings and its recommendations as to the elements of the draft Risk Mitigation Plan to the Office of the Provost. The

Deputy Provost, or his designee, will decide whether or not to act on the recommendations of the IRE as to whether the research constitutes DURC and the adequacy of the IRE's draft Risk Mitigation Plan and may require revisions to the draft Plan.

The Deputy Provost's decision and any other institutional decision regarding DURC may be appealed by the affected PI to the Provost. The Provost will have the final word as to all institutional decisions regarding DURC that have been appealed.

D. Notification to the US Funding Agency and Finalization of the Risk Mitigation Plan

Within 90 calendar days following the final institutional approval of the draft Risk Mitigation Plan by the cognizant Deputy Provost (or the Provost), the ICDUR shall submit such draft Plan to the applicable USG Funding Agency for final review and approval. The USG Funding Agency must provide an initial response within 30 calendar days following receipt of the draft Plan. The ICDUR and the PI will work with the USG Funding Agency to respond to any questions or concerns it may have regarding the draft Risk Mitigation Plan. The USG Funding Agency must finalize the Plan within 60 days following receipt of the draft Plan. The cognizant Deputy Provost must also approve the final Risk Mitigation Plan. Upon approval by both the USG Funding Agency and the Deputy Provost, the IRE will notify the PI that the research may proceed according to the Risk Mitigation Plan, provided other requirements are met.

E. Sub-awards

If elements of a potential DURC Research project are being carried out at multiple institutions through a subaward with a primary institution that directly receives the grant or contract from the US Funding Agency (the "Prime Institution"), the Prime Institution will be responsible for notifying the applicable US Funding Agency of research that may constitute DURC and if such research is determined to be DURC, providing copies of each institution's Risk Mitigation Plan. The Prime Institution should also ensure that DURC oversight is consistently applied by all entities participating in the collaboration.

If Yale is not the Prime Institution, and the Prime Institution's procedures or standards are less rigorous than Yale's, Yale reserves the right to apply more rigorous procedures or standards.

V. ONGOING INSTITUTIONAL RESPONSIBILITIES

1. Responsibilities of the PI

The PI will:

- Conduct DURC Research in accordance with the final Risk Mitigation Plan;
- Notify the ICDUR of the addition of any DURC Agents or Experimental Effects of Concern, or any other substantive change in the conduct of the DURC Research;
- Notify EHS if for whatever reason (e.g., changes in the research, new discoveries), he/she feels that the research should be reconsidered by the IRE because it might constitute DURC, or is no longer DURC; and
- 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 research with one or more of DURC Agents have received EHS-approved education and training on DURC.

2. Responsibilities of the ICDUR

The ICDUR shall:

- Ensure that the IRE reviews each DURC Research Risk Mitigation Plan annually;
- Provide education and training on DURC for individuals conducting research with one or more of the DURC Agents and maintain records of such education and training for the term of the research grant or contract plus three years after its completion;
- Maintain records of institutional DURC reviews and completed Risk Mitigation Plans for no less than eight years, unless a shorter period is required by law or regulation;
- Notify the applicable US Funding Agency within 30 calendar days of any change in the status of any DURC, including whether such research has been determined by the IRE to no longer meet the definition of DURC. The notification should include details of any changes to an approved Risk Mitigation Plan, which must be approved by the US Funding Agency; and
- Report within 30 calendar days to the applicable US Funding Agency instances of noncompliance with this Policy, as well as mitigation measures undertaken by the University to prevent recurrences of similar noncompliance.

3. Responsibilities of the IRE

The IRE shall review, at least annually, all active Risk Mitigation Plans at the University.

In reviewing such Plans, the IRE will follow the same procedures as are described in this Policy.

Guidance on points to consider while conducting this review may be found in the Companion Guide, Section E. If the research in question still constitutes DURC, the IRE, working with the PI, should modify the applicable Risk Mitigation Plan as needed to ensure that the Plan still adequately mitigates the risks associated with the DURC.