Caltech Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern

Purpose

The purpose of this Policy is to strengthen regular institutional review and oversight of certain life sciences research with high-consequence pathogens and toxins in order to identify potential Dual Use Research of Concern (DURC) and mitigate risks where appropriate. This Policy delineates the roles and responsibilities of Researchers and the Institute, and establishes requirements and performance standards for review of research, identification of potential DURC, and development and implementation of risk mitigation measures for DURC, where applicable. In so doing, the Policy seeks to preserve the benefits of 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, or national security.

Definitions

For the purpose of this Policy the following terms are defined:

A. "Dual use research" is research conducted for legitimate purposes that generates knowledge, information, technologies, and/or products that can be utilized for benevolent or harmful purposes.

B. "Dual use research of concern," or "DURC," 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, material, or national security.

C. "Institutional Contact for Dual Use Research," or "ICDUR," is designated by the Institute to serve as an internal resource for issues 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 Federal funding agency. The Institute ICDUR shall be the Director of Research Compliance.

D. "Institutional review entity" is established by the institution to execute the requirements in Section 7.2.B.i-7.2.B.v of the US Government Policy for Institutional Oversight of Life Sciences Dual Use Research (USG Policy) and meets the requirements prescribed in Section 7.2.E of the USG Policy.

E. "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 agricultural science, plant science, animal science, bioinformatics, genomics, proteomics, synthetic 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.

F. "National Science Advisory Board for Biosecurity" (NSABB) is a Federal advisory committee established to advise the USG on dual use research issues.

G. "USG Policy" refers to the US Government Policy for Institutional Oversight of Life Sciences Dual Use Research published September 2014 and the US Government Policy for the Oversight of Life Sciences Dual Use Research of Concern published March 2012.

Applicability of this Policy and Scope of Oversight of DURC

Applicability

Pursuant to USG Policy, this Policy and its oversight requirements apply to all research within the scope identified below, which is conducted at the Institute or its Jet Propulsion Laboratory, regardless of source of funding.

Non-compliance with this Policy may result in suspension, limitation, or termination of Federal funding, or loss of future Federal funding opportunities for the non-compliant Federally-funded research project and of Federal funds for other life sciences research at the Institute.

Scope of Oversight Required Under this Policy

Under this Policy, all life sciences research that uses one or more of the agents or toxins listed in Sections 6.2.1 and Section III.1 of the USG Policy, and produces, aims to produce, or can be reasonably anticipated to produce one or more of the effects listed in Sections 6.2.2 or III.2 of the USG Policy will be evaluated for DURC potential. For reference, the current Sections 6.2.1/III.1 and 6.2.2/III.2 are listed below; however, these are subject to change and should be reviewed on a regular basis[1].

[1] PROVIDE LINK TO LIST(S) http://www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf; http://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf

Current (September 2015) Agents and Toxins pursuant to USG Policy Section 6.2.1. [2]

a) Avian influenza virus (highly pathogenic)
b) *Bacillus anthracis*
c) Botulinum neurotoxin[3]
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*

Current (September 2015) Categories of Experiments pursuant to USG Policy Section 6.2.2.

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, above.

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[2] These agents and toxins are regulated by the Select Agent Program under Federal law (7 C.F.R. part 331, 9 C.F.R. part 121, 42 C.F.R. part 73), and have the potential to pose a severe threat to human, animal, or plant health, or to animal and plant products.

[3] For the purposes of this Policy, there are no exempt quantities of toxin. Research involving any quantity of Botulinum neurotoxin should be evaluated for DURC potential.

Framework for Oversight of DURC

The framework for the oversight of DURC and the roles and responsibilities of Principal Investigators (PIs), the Institute, Federal funding agencies and the US Government under this Policy are as follows:

A. The PI shall identify his/her own life sciences research utilizing any of the Agents and Toxins within the scope of DURC, pursuant to 6.2.1/III.1 of the USG Policy (see above) and notify the Administrative Committee on Biosafety in its capacity of the Institutional Review Entity (IRE) of the intent to use such agents or toxins;

B. An Institutional review process will be performed by the IRE. The IRE which will assess whether the research produces, aims to produce, or is reasonably anticipated to produce one or more of the effects listed in Section 6.2.2/III.2 of the USG Policy (see above), and if so, determine whether the research meets the definition of Dual Use Research of Concern, or "DURC":

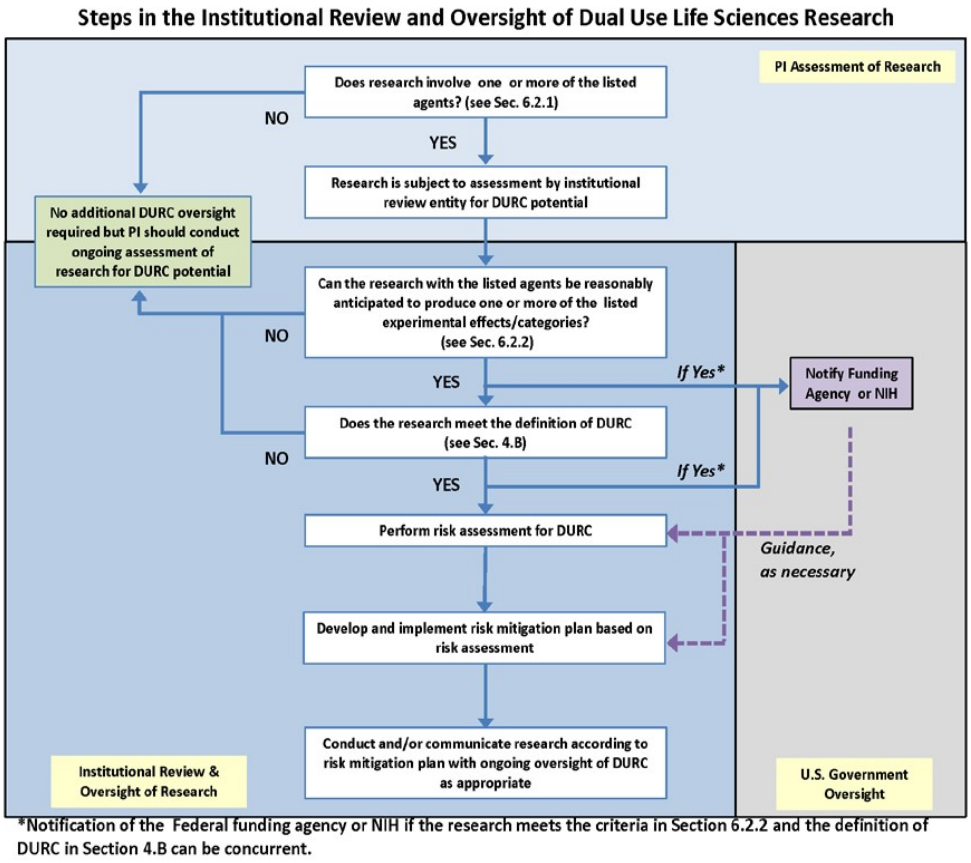
> *DURC is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.*

Should the research be determined to be DURC, the IRE review will also include assessing the benefits and risks associated with the conduct and communication of the DURC, developing a plan for mitigating identified risks, and ensuring that research is conducted in accordance with a risk mitigation plan compliant with USG Policy;

C. The ICDUR is responsible communicating the results of the IRE review process and providing the risk mitigation plan from the Institute to the Federal funding agency or, for non-Federally funded research, to the National Institutes of Health (NIH) (which will receive for administrative purposes on behalf of all of the Institute's Federal funders) and provision of an annual assurance of compliance with the USG Policy; and

D. The Federal funding agencies and the USG are responsible for additional oversight as articulated in the USG Policy.

Figure 1 provides an overview of the institutional oversight process.



Responsibilities of Principal Investigators of Research that is Subject to Institutional DURC Oversight

PIs shall:

A. Identify his or her research involving one or more of the agents or toxins listed in USG Policy Section 6.2.1/III.1 (see above). If a PI determines that his or her research does not utilize any of the agents or toxins listed in USG Policy Sections 6.2.1/III.1, no further action by the PI is needed in terms of DURC oversight.
   i. The research should be identified at the time of the proposal preparation /submission. Such research should be indicated on the Division Authorization Form (DAF).
   ii. A copy of the proposal and DAF will be communicated as soon as possible from the Division to the Institute IBC (ibc@caltech.edu) for referral to the IRE.
   iii. The PI will be required to complete an application to the IBC, completing the IRE questions. The PI may be asked to draft a risk mitigation plan to be provided to the IRE as well.
   iv. If, at any time, a PI determines that his or her research with one or more of the agents or toxins listed in USG Policy Sections 6.2.1/III.1 also produces or

can be reasonably anticipated to produce one or more of the 7 effects listed in USG Policy Section 6.2.2/III.2, or may meet the definition of DURC, he or she must immediately notify the IBC (ibc@caltech.edu) and complete a new application or amend an existing IBC protocol to include answers to the IRE sections.

B. Work with the IRE to complete and implement a risk mitigation plan as required.

C. Conduct DURC in accordance with the provisions in the IRE approved risk mitigation plan.

D. Be knowledgeable about and comply with all Institute and Federal policies and requirements for oversight of DURC.

E. Ensure that all 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 that is deemed DURC) have received education and training on DURC.

F. 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 simply at the point of publication. When researchers are planning to communicate DURC, it is their duty to ensure that it is done in a responsible manner, and in compliance with any risk mitigation plan stipulated by the IRE.

Responsibilities of the Institute when Conducting Research that is Subject to Institutional DURC Oversight

The Institute shall:

A. Implement and maintain this Policy regarding DURC. Internal practices will be established that provide for the identification and effective oversight of DURC.

B. Designate the Institutional Contact for Dual Use Research (ICDUR) to serve as an internal resource for issues regarding compliance with and implementation of the requirements for the oversight of research that falls within the scope of the USG Policy and/or meets the definition of DURC.
   i. The Director of Research Compliance will be the designated ICDUR.

ii. The ICDUR serves as the liaison (as necessary) between the Institute and the relevant program officers at the Federal funding agencies, or for non-Federally funded research, between the Institute and NIH who is responsible for addressing questions arising regarding compliance, implementation of USG Policy, or providing guidance about identifying DURC or developing risk mitigation plans.

iii. The ICDUR reports instances of noncompliance with this Policy, as well as mitigation measures undertaken by the Institute to prevent recurrences of similar noncompliance, within 30 calendar days to the Federal funding agency or, for non-Federally funded research, to NIH (which will receive for administrative purposes on behalf of all of the institution's Federal funders).

C. Establish an institutional review entity (IRE) to execute the review and mitigation as required by the USG Policy. The Administrative Committee on Biosafety will serve as the Institute IRE. Minutes from IRE meetings shall be prepared and kept separate from the minutes of the Institutional Biosafety Committee.

The IRE shall:

i. Be sufficiently empowered by the Institute to ensure compliance with this Policy and the related USG Policy.

ii. Have sufficient breadth of expertise to assess the dual use potential of the range of relevant life sciences research conducted at the Institute and shall have knowledge of dual use issues, concerns, and related institutional and Federal policies and understand risk assessment and risk management considerations. The IRE will be aware that a variety of risk mitigation measures are available and that designating research as DURC does not necessarily mean that the research should not be conducted or communicated.

iii. Provide DURC review and oversight as prescribed by this Policy.

iv. Make this policy available to the public.

v. On a case by case basis, recuse any member of the IRE who is involved in the research project in question or has a direct financial interest, except to provide specific information requested by the IRE.

vi. Engage in an ongoing dialogue with the PI of the research in question when developing appropriate risk mitigation plans.

vii. Provide education and training on DURC for individuals conducting life sciences research that falls within the scope of this Policy.

viii. 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.

ix. As necessary, assist the PIs of life sciences research when questions arise about whether their research may require further review or oversight.

x. On an annual basis, provide a formal assurance to the Federal funding agencies that the institution is in compliance with all aspects of this Policy.

D. Implement the following process for DURC review:

DURC review by the IRE is required when:

(1) research is identified by a PI as utilizing one of the agents or toxins listed in USG Policy Sections 6.2.1/III.1 or

(2) a PI notifies the IBC that his/her research using one or more of the agents or toxins listed in USG Policy Sections 6.2.1/III.1 also produces or can be reasonably anticipated to produce one or more of the 7 effects listed in USG Policy Section 6.2.2/III.2,

If DURC review is required, the IBC will receive a copy of the proposed research and an IBC protocol with a completed IRE section. The copy of the proposal and the IBC application will be communicated to the IRE. The IRE will initiate its institutional oversight process. The IRE, through its oversight process, will:

i. Verify that research utilizes one or more of the agents or toxins listed in USG Policy Section 6.2.1/III.1;

ii. Determine whether the research produces, aims to produce, or is reasonably anticipated to produce one or more of the effects listed in USG Policy Section 6.2.2/III.2;

iii. Determine whether the research meets the DURC definition and is therefore DURC.

   a. If the IRE determines that the research in question does not fall within the scope of Section 6.2.2/III.2 or does not meet the definition of DURC, the research can continue without additional DURC oversight; however, IBC approval is still required.

   b. Should the IRE determine that research is DURC but the PI feels that his/her research does not meet the definition of DURC, he/she may appeal in writing to the IRE and the Vice Provost for Research.

iv. Asses the dual use risks and the benefits of the research;

v. Work with the PI to develop a risk mitigation plan for DURC, as necessary;

vi. Work with the PI to implement the risk mitigation plan. After a risk mitigation plan is developed, the research must be conducted in accordance with that plan and must be periodically reviewed by the IRE to determine if additional modifications to the risk mitigation plan are appropriate. For research that has been proposed but not yet initiated, the DURC component of the project should not be initiated until a risk mitigation plan is implemented;

vii. Coordinate with the IBC review of the work to ensure continuity between the IBC, the IRE and the researchers;

viii. Consult with the Federal Funding Agency, as necessary. The IRE, through the ICDUR, may consult with the Federal department or agency that is funding the research in question for advice on matters related to DURC. The funding agency program officers can provide guidance on DURC issues. Questions regarding non-Federally funded research can be directed to the NIH or to the Federal funding agency to which NIH refers the Institute based on the nature of the research in question. Consultation with the funding agency is not mandatory or intended as a substitute for the Institute's dual use review or the reporting requirement, below.

ix. Within 30 calendar days of the IRE review of the research for DURC potential, the ICDUR will notify the Federal funding agency of any research that falls within the scope of USG Policy, including whether it meets or does not meet the definition of DURC. For non-Federally funded research, notification may be made to NIH (who may in turn notify the appropriate Federal funding agency, based upon the nature of the research); and

x. Within 90 calendar days from the time that the IRE determined the research to be DURC, the ICDUR will provide a copy of the risk mitigation plan to the funding agency for review – or for non-Federally funded research, provision of the plan to NIH for review (or referral to the appropriate funding agency).