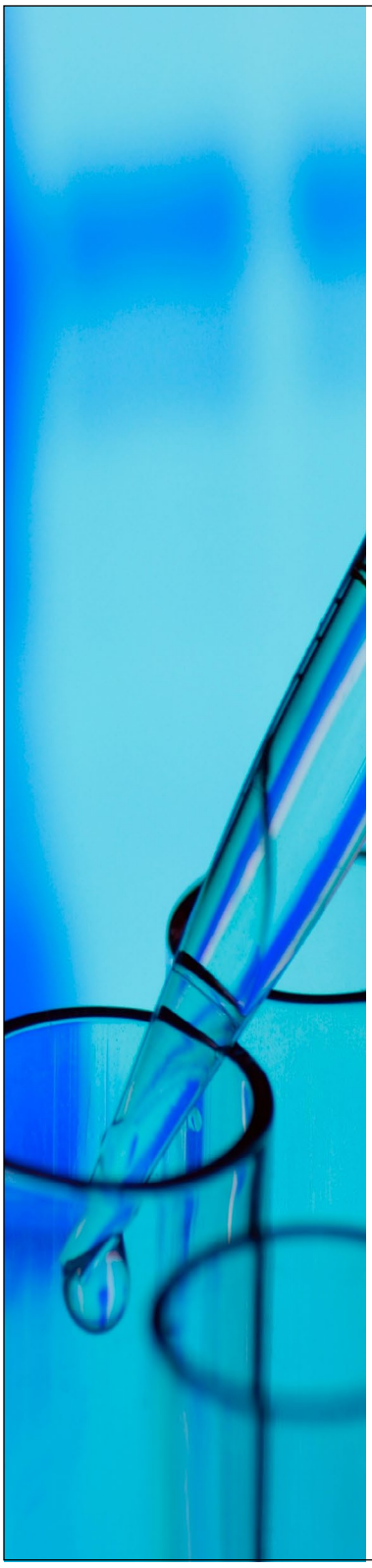

Tools for the Identification, Assessment, Management, and Responsible Communication of

Dual Use Research of Concern

A Companion Guide

to the United States Government Policies for Oversight of Life Sciences Dual Use Research of Concern

Prepared by the National Institutes of Health
on behalf of the United States Government

SEPTEMBER 2014

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List of Terms & Abbreviations

Companion Guide	*Tools for the Identification, Assessment, Management, and Responsible Communication of Dual Use Research of Concern: A Companion Guide to the U.S. Government Policies for Oversight of Life Sciences Dual Use Research of Concern*
DURC	Dual use research of concern
DURC policies	Collectively, the *United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (Policy for Institutional DURC Oversight)* and the *United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (March 2012 DURC Policy)*
EAR	Export Administration Regulations
HHS	U.S. Department of Health and Human Services
IBC	Institutional biosafety committee
ICDUR	Institutional contact for dual use research
IRE	Institutional review entity
Listed agents	The 15 agents and toxins listed in Section 6.2.1 of the *Policy for Institutional DURC Oversight* and Section III.1 of the *March 2012 DURC Policy*.
March 2012 DURC Policy	*United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern*
NSABB	National Science Advisory Board for Biosecurity
Policy for Institutional DURC Oversight	*United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*
PI	Principal investigator
SAR	Select Agents Regulations
USDA	U.S. Department of Agriculture
USG	United States Government

Introduction to the Companion Guide

The USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (Policy for Institutional DURC Oversight) and the *USG Policy for Oversight of Life Sciences Dual Use Research of Concern (March 2012 DURC Policy)* apply to the oversight of life sciences DURC that is either funded by the U.S. Government (USG) or taking place at institutions receiving funding from the USG for life sciences research.

- The *March 2012 DURC Policy* sets forth a process of regular Federal review of USG-funded or USG-conducted research and requires Federal agencies that fund or sponsor life sciences research to identify DURC and evaluate this research for possible risks, as well as benefits, and to ensure that risks are appropriately managed and benefits realized.
- The *Policy for Institutional DURC Oversight* complements the *March 2012 DURC Policy* by establishing review procedures and oversight requirements for the same scope of research at the institutions that receive Federal funds for life sciences research.

Together, these two policies work to engage the life sciences research community and the Federal departments and agencies that fund such research in a shared commitment to address the risk that knowledge, information, products, or technologies generated from life sciences research could be used for harm. In addition, the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy* emphasize a culture of responsibility by reminding all involved parties of the shared duty to uphold the integrity of science and prevent its misuse.

This *Companion Guide* comprises a set of tools designed for institutions, principal investigators (PIs), and institutional review entities (IREs) implementing the *Policy for Institutional DURC Oversight*. However, it is anticipated that much of the guidance embedded in these tools, such as the identification of DURC, risk-benefit assessments, and developing risk mitigation strategies, may also be helpful for Federal agencies in the implementation of the *March 2012 DURC Policy*. Such guidance may also be applied more broadly to research that is not within the scope of these policies but that may warrant review for dual use potential and special oversight, and it may be used by others within the scientific community (e.g., journal editors) that are not subject to these policies.

As shown in the box below, sections of the *Companion Guide* are intended for different audiences, depending on who is involved at different stages in the process for institutional review and oversight of DURC.

Section	Title	Intended Audience(s)
A	Qs & As on the U.S. Government Policies for Oversight of Life Sciences Dual Use Research of Concern	All
B	Identification and Assessment of Research That Requires Institutional Review: Guidance for Principal Investigators and Institutions	PIs, institutions, ICDURs
C	Framework for Institutional Review: Guidance for Institutions and Institutional Review Entities	Institutions, IREs, ICDURs
D	Developing a Draft Risk Mitigation Plan: Guidance for Institutional Review Entities	Institutions, IREs, ICDURs
E	Review of Risk Mitigation Plans: Guidance for Institutional Review Entities	Institutions, IREs, ICDURs
F	Guidance for Responsible Communication of DURC Findings	All
Appendix	**Title**	**Relevant Section(s) of *Companion Guide***
1	Definitions to Assist in the Consideration of the Categories of Experimental Effects	All
2	Template for Notifying the IRE of Research That Requires Institutional Review	B
3	Template for Assessment by the IRE of Research for DURC Potential	C
4	Template for 30-Day Reporting of Research That Meets the Scope of the *Policy for Institutional DURC Oversight*	C
5	Export Controls and DURC – Guidance for Institutions and Principal Investigators	General Applicability

The Process for DURC Oversight

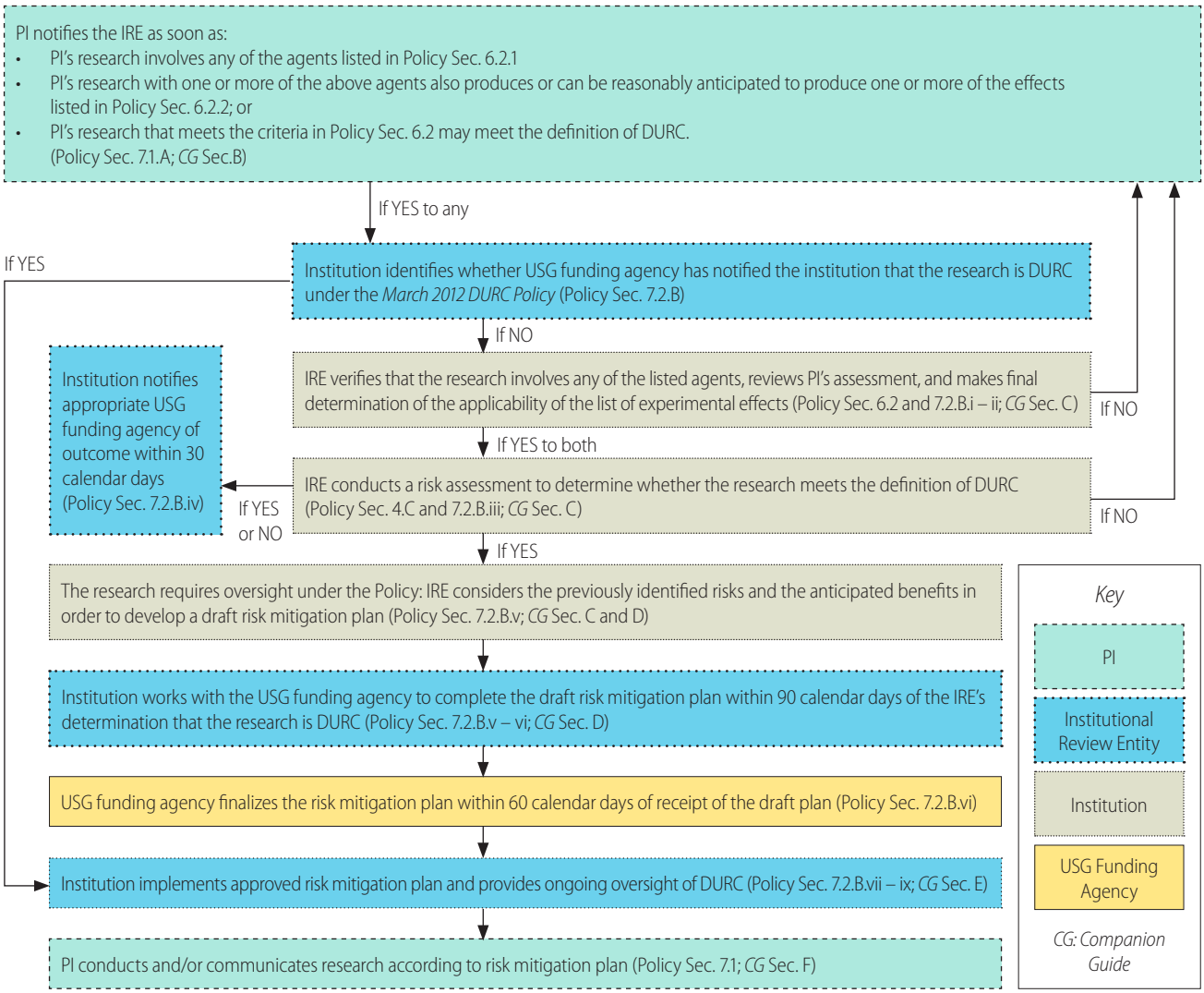
The effective oversight of DURC is based on identifying DURC and its associated risks, then devising ways to mitigate these risks. Under both USG policies on DURC, this process begins with the identification of research that directly involves 1 or more of the 15 listed agents. Any such research that is identified must then be assessed for whether the research produces, aims to produce, or can be reasonably anticipated to produce one or more of seven listed experimental effects. The two policies differ on the entity responsible for the identification and review of research that falls within this scope: Under the *March 2012 DURC Policy*, this is the responsibility of Federal funding agencies; under the *Policy for Institutional DURC Oversight*, this is the responsibility of research institutions, which includes PIs and IREs.

The overall process for review and oversight of DURC under the *Policy for Institutional DURC Oversight* is summarized by the flowchart below. To help with the implementation of this review framework, the USG has also developed a series of case studies that demonstrate the types of analysis that should be brought to bear during institutional review and also highlight important administrative steps throughout the review process. These case studies can be found at http://www.phe.gov/s3/dualuse.

Under the *Policy for Institutional DURC Oversight,* the identification of DURC-related risks and the management of those risks begin with the identification, by PIs, of research that directly involves nonattenuated[1] forms of 1 or more of the 15 listed agents. As mentioned above, any such research that is identified must then be assessed for whether the research produces, aims to produce, or can be reasonably anticipated to produce one or more of seven listed experimental effects. **Section B** of the *Companion Guide* is intended to assist PIs in fulfilling the

[1] The 15 agents and toxins listed in this Policy are subject to the select agent regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121), which set forth the requirements for possession, use, and transfer of select agents and toxins, and have the potential to pose a severe threat to human, animal, or plant health, or to animal or plant products. It is important to note, however, that the Federal Select Agent Program does not oversee the implementation of this Policy or the March 2012 DURC Policy.

Process for Institutional Review of Life Sciences Research within the Scope of the Policy



requirements for the identification and assessment of research that requires institutional review. The next step in the oversight process is institutional review. **Section C** of the *Companion Guide* is intended to assist institutions in establishing an IRE and implementing the institutional review and oversight requirements of the *Policy for Institutional DURC Oversight*. Of note, **Section C** provides institutions and IREs with a framework to assist in the identification and assessment of life sciences DURC. Specifically, this section outlines a multistep process for reviewing a PI's assessment of research that may have DURC potential, determining whether this research meets the definition of DURC, and, if so, evaluating the risks and benefits of the DURC.

Risk identification and assessment is also addressed in **Section C** of this *Companion Guide*. The framework for risk assessment and mitigation follows a multistep process:

Step 1: Verify that the research directly involves nonattenuated forms of one or more of the listed agents.

Step 2: Assess whether the research produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects.

Step 3: Assess the risks of dual use and determine whether the research is DURC.

For research determined by the IRE to be DURC:

Step 4: Assess the potential benefits of the DURC.

Step 5: Weigh the risks and benefits of the DURC.

Step 6: Develop a draft risk mitigation plan for conducting the DURC and communicating its findings.

The final step of the institutional review process, developing a draft risk mitigation plan, is covered in detail in **Section D** of the *Companion Guide*. Both risk assessment and risk mitigation pose unique challenges:

- Risks can often be reduced but are rarely eliminated.
- Assessing risks requires speculation on the ways that information from research may be misused.
- In order to determine the level of acceptable risk and the best mitigation strategy, it is also important to identify the likely benefits of the research, which may not be apparent early on.
- The individuals that constitute an IRE may be more accustomed to assessing the benefits of scientific research than its risks.

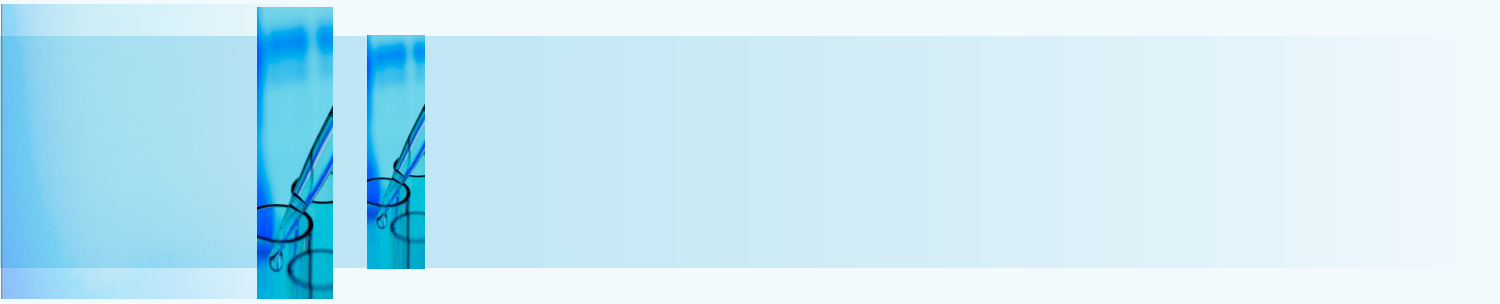
Importantly, it is anticipated that risks associated with the majority of DURC can be mitigated appropriately and that the research will still be conducted. The goal of the risk-benefit assessment process is to promote the responsible conduct and communication of DURC, not to restrict such research.

Section E provides IREs with guidance on the assessment of any extant, active risk mitigation plans at an institution (i.e., risk mitigation plans already implemented under the *March 2012 DURC Policy* or the *Policy for Institutional DURC Oversight*). Risk mitigation plans should be revised as needed based on changes in the research plan, new and/or unexpected research findings, or technological developments.

Section F, "Guidance for Responsible Communication of DURC Findings," is a tool intended to guide institutions, IREs, and individuals in identifying and assessing the risks and benefits of communicating information from research that poses concerns about dual use. It includes a series of questions that can be considered as well as options for the communication of information from research judged to be of dual use concern.

The *Companion Guide's* appendices are intended to assist institutions and others in understanding DURC and the DURC oversight policies more fully, as well as to assist in the implementation of different requirements of the policies. Use of the templates provided in the appendices is completely optional and, if they are used, institutions may edit and amend the templates to fit their needs.

This *Companion Guide* will be revised as warranted.



A. Qs & As on the U.S. Government Policies for Oversight of Life Sciences Dual Use Research of Concern

A. Qs & As on the U.S. Government Policies for Oversight of Life Sciences Dual Use Research of Concern

1. What are "dual use research" and "dual use research of concern (DURC)"?

Dual use research is research conducted for legitimate purposes that generates knowledge, information, technologies, and/or products that can be utilized for both benevolent and harmful purposes. Conceivably, much of life sciences research could be considered dual use—that is, most of the information it generates has some potential to be misused. Thus, both DURC policies focus on "dual use research of concern," or "DURC," which is defined as:

> *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.*

2. Does the designation of DURC mean the research should not be published or conducted?

No. A determination that research is DURC, in and of itself, does not mean that the research should not be published or conducted. Research that is categorized as DURC is often vitally important to science, public health, and agriculture, and its findings contribute to the broader base of knowledge that advances science and public health objectives. Upon identifying research as DURC, institutions should give careful thought to the ways in which the research or its results might be misused and the mitigation measures that can be put in place to minimize the possibility of misuse.

3. Why is the Federal Government issuing the *U.S. Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern?*

The potential for dual use of certain life sciences research has been recognized as an important biosecurity issue for a number of years. The Federal agencies sponsoring research have an important responsibility to address this issue, which was formalized in the *U.S. Government Policy for Oversight of Life Sciences Dual Use Research of Concern* (*March 2012 DURC Policy*). However, it is vitally important that researchers and their institutions are also vigilant with respect to the potential for dual use of life sciences research that they carry out. The *Policy for Institutional DURC Oversight* articulates and formalizes the roles and responsibilities of institutions and investigators when they are conducting certain types of research supported by the Federal Government. Investigators, in particular, are often best positioned to understand the implications for dual use of the information, technologies, and products emanating from their research and to propose and implement strategies to mitigate the possibility that the results of their research will be misused to do harm.

In short, the *Policy for Institutional DURC Oversight* aims to preserve the benefits of life sciences research while minimizing the risk that the knowledge, information, products, or technologies generated by such research could be used in a manner that results in harm.

4. How does the *Policy for Institutional DURC Oversight*relate to the *March 2012 DURC Policy*?

The *March 2012 DURC Policy* requires Federal agencies to periodically review their life sciences research portfolios to identify DURC, evaluate this research for possible risks, as well as benefits, and ensure that risks are appropriately managed and benefits realized. The *Policy for Institutional DURC Oversight* complements the *March 2012 DURC Policy* by establishing review procedures and oversight requirements for the same scope of research at the institutions that receive Federal funds for life sciences research. Together, the two DURC policies work to engage the life sciences research community and the Federal departments and agencies that fund such research in a shared commitment to address the risk that knowledge, information, products, or technologies generated from life sciences research could be used for harm. In addition, the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy* emphasize a culture of responsibility by reminding all involved parties of their shared duty to uphold the integrity of science and prevent its misuse.

5. Why is the scope of the *Policy for Institutional DURC Oversight*and the *March 2012 DURC Policy* limited to research with the 15 listed agents and 7 categories of experiments?

Because oversight of DURC will be a new undertaking for many institutions, the USG has limited the scope of the DURC policies to a subset of life sciences research involving 7 categories of experiments and 15 agents that poses the greatest risk of deliberate misuse with the most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence. The USG will solicit feedback on the experience of institutions in implementing the *Policy for Institutional DURC Oversight*. Once there is sufficient experience with oversight based on this scope, the USG will assess the benefits and risks of expanding the scope of the *Policy for Institutional DURC Oversight* to encompass additional agents and/or categories of experiments and will update it as warranted.

6. Can institutions review more than just the 15 listed agents and 7 categories of experiments for the research's potential to be DURC?

Yes, but it is not required. Research institutions are encouraged to be mindful that research outside the scope articulated in the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy* may also constitute DURC. Institutions have the discretion to consider other categories of research for their DURC potential and may expand their internal oversight to other types of life sciences research as they deem appropriate, but such expansion would not be subject to oversight as articulated in either policy.

7. Does the scope of the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy* apply to attenuated forms of the listed agents?

No. The *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy* apply to research that directly involves nonattenuated forms of the listed agents. The only forms of the agents or toxins listed in these policies that are considered by the USG to be attenuated and therefore not subject to the requirements of these policies can be found in the Select Agent and Toxin Exclusions list under "Attenuated Strains of HHS and USDA Select Agents and Toxins" at http://go.usa.gov/8rwQ. However, if an attenuated form of any of the 15 listed agents is subjected to any manipulation that restores or enhances its virulence or toxic activity, the resulting agent or toxin will be subject to the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy*.

8. What is meant by "direct involvement" of forms of the listed agents in the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy*?

While life sciences research is broadly defined in both DURC policies to include all disciplines and methodologies of biology (including bioinformatics, genomics, proteomics, and modeling), the review and oversight requirements of both DURC policies do not apply to research that involves the use of the genes from any of the listed agents; *in silico* experiments (e.g., modeling experiments, bioinformatics approaches) involving the biology of the listed agents; or research related to the public, animal, or agricultural health impact of any of the listed agents (e.g., modeling the effects of a toxin, developing new methods to deliver a vaccine, developing surveillance mechanisms for a listed agent).

9. What types of institutions are subject to the *Policy for Institutional DURC Oversight*?

The *Policy for Institutional DURC Oversight* applies to all those institutions (and their investigators) receiving Federal funding for life sciences research that are also conducting research (funded by *any* source; see Question 10) involving any of the 15 agents listed in the Policy. Note that the *Policy for Institutional DURC Oversight* defines an institution as any government agency (Federal, state, tribal, or local), academic institution, corporation, company, partnership, society, association, firm, sole proprietorship, or other legal entity conducting research, except that Federal departments and agencies receiving funding from another Federal department or agency to conduct or sponsor intramural or extramural life sciences research will not be considered an "institution" for the purposes of this Policy.

10. Does the *Policy for Institutional Oversight of Life Sciences DURC* apply only to federally funded research, or does it apply more broadly?

If an institution (a) receives any Federal funding for any life sciences research and (b) is conducting work with 1 or more of the 15 agents and toxins listed in the Policy, then any research conducted at that institution with those 15 agents and toxins – regardless of the source of funding – must comply with the requirements articulated in the Policy.

11. How do the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy* relate to the Select Agent Regulations (SAR)?

The *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy* apply to a subset of life sciences research that involves 1 or more of 15 listed agents and toxins. Each of these 15 agents and toxins is also regulated by the U.S. Department of Health and Human Services (HHS) and U.S. Department of Agriculture (USDA) Select Agent Program. Select Agent Regulations (www.selectagents.gov/Regulations.html) apply to research involving any of the biological agents and toxins included in the Select Agents and Toxins List (www.selectagents.gov/Select Agents and Toxins List.html).

Select Agent Regulations require that individuals working with any of those agents undergo electronic records checks and that their institutions put into place biosafety and physical security measures to avoid accidents or deliberate misuse of the agents. These physical biosafety and biosecurity measures are critical to promoting the biosecurity of life sciences research, but they do not directly address the dual use issue. In particular, SAR does not apply to research information; the *Policy for Institutional DURC Oversight* and *March 2012 DURC Policy* both address this important facet of biosecurity.

12. If an institution already has a risk mitigation plan in place per the *March 2012 DURC Policy*, is the research still subject to institutional review? Does the institution need to draft a new risk mitigation plan?

No. Institutions undertaking 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, are *not* required to review the research (as described in Sections 7.2.B.i – vii of the *Policy for Institutional DURC Oversight*) or develop and submit a new risk mitigation plan under the *Policy for Institutional DURC Oversight*.

However, the institution is required to have its IRE review all risk mitigation plans (regardless of the policy under which the risk mitigation plan was developed) and notify the USG of any change in status of the DURC, per Sections 7.2.B.viii – ix of the *Policy for Institutional DURC Oversight*.

13. Where can institutions and investigators find more information about DURC and the *Policy for Institutional DURC Oversight*?

For information about the requirements at your institution, consult your institution's IRE or the institutional contact for dual use research (ICDUR). Information about dual use research in the life sciences in general, as well as specific details on the *Policy for Institutional DURC Oversight*, is available on the U.S. Government Science, Safety, Security (S3) website: http://www.phe.gov/s3/dualuse.

14. Is there a specific point of contact at the Federal funding agencies that can assist with questions related to the review of research and oversight of DURC or receive reports of this research?

Questions regarding whether a particular project may constitute DURC generally should first be addressed to the program officer at the funding agency supporting the project. The program officer will know who else to consult within the government for additional perspective.

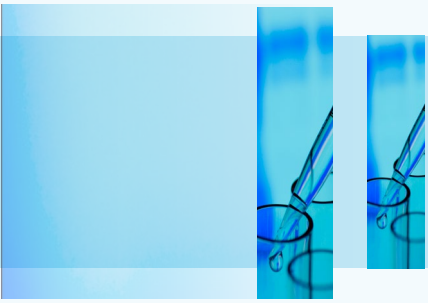
In many cases, the research requiring review under the *Policy for Institutional DURC Oversight* will be USG-funded, and thus the submission of notifications and risk mitigation plans (if needed) should be made directly to the USG funding agency. When IREs are determining whether research meets the definition of DURC (see Section 7.2.B.iii of the *Policy for Institutional DURC Oversight*), they may identify research that, while taking place at an institution subject to the Policy, is not directly funded by a USG funding agency. For such non-USG-funded research, the initial 30-day notification to the USG should be made to the National Institutes of Health (NIH; DURC@od.nih.gov; include "DURC Notification" in the subject line), which will in turn refer the notification to an appropriate USG funding agency based upon the nature of the research.

15. What are export controls and how do they apply to research subject to the U.S. Government DURC oversight policies?

Export controls are a mechanism by which the U.S. Government regulates the export of controlled goods and activities to ensure consistency with U.S. foreign policy and national security interests, U.S. law, and its international commitments. There are generally two types of export transactions: (1) transferring controlled material or technology outside the United States; and (2) transferring controlled technology to non-U.S. persons who are within the United States, which is considered a "deemed export." A DURC designation does not automatically subject the research to export controls, but some DURC may be subject to these controls. It is expected that most DURC that would be subject to export controls would be controlled for export under the Export Administration Regulations (EAR) administered by the Department of Commerce, Bureau of Industry and Security. The fifteen agents listed in the USG DURC oversight policies are all included in the EAR control list (for the complete list, see Part 774 of the EAR available under the "Regulations" tab on the Bureau of Industry and Security homep-age at www.bis.doc.gov). This means that transfers of these materials, and/or information or technology related to their development, production, or manipulation, are subject to the EAR and may require an export license or a deemed export license. See **Appendix 5** of the *Companion Guide* for more information on export control regulations and how they may apply to your research.

16. Is there a specific point of contact within the U.S. Government for addressing questions about the *Policy for Institutional DURC Oversight*?

Individuals with questions about interpreting or implementing the Policy may send queries to DURC@ostp.gov. Questions about the possible DURC nature of particular projects of research should be addressed to the pro-gram official at the pertinent funding agency, unless the project is not federally funded, in which case questions can be sent to: DURC@od.nih.gov.



B. Identification and Assessment of Research That Requires Institutional Review: Guidance for Principal Investigators and Institutions

B. Identification and Assessment of Research That Requires Institutional Review: Guidance for Principal Investigators and Institutions

This section of the *Companion Guide* is intended to assist **principal investigators (PIs)** and their institutions in fulfilling requirements under the *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*[2] (*Policy for Institutional DURC Oversight*) for the identification and assessment of research that requires institutional review for DURC potential.

- **Part 1** of this section details the **PI's responsibilities** as described in the ***Policy for Institutional DURC Oversight***.
- **Part 2** of this section provides **guidance** to PIs on the identification and assessment of research that requires institutional review.

The use of the guidance in this section is optional.

1. Policy Requirements for the Identification and Assessment by PIs of Research That Requires Institutional Review

The *Policy for Institutional DURC Oversight* requires **PIs** at institutions subject to this Policy[3] to notify the institutional review entity (IRE) as soon as any of the following three criteria are met:[4]

A. The PI's research directly involves nonattenuated[5] forms of one or more of the listed agents;

B. The PI's research with nonattenuated forms of one or more of the listed agents also produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects; or

C. The PI concludes that his or her research with nonattenuated forms of one or more of the listed agents that also produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects *may* meet the definition of DURC and should be considered (or reconsidered) by the IRE for its DURC potential.

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[2] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*, September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx.

[3] The *Policy for Institutional DURC Oversight* and its oversight requirements apply to the following institutions: (1) USG departments and agencies that fund or conduct life sciences research, (2) institutions within the United States that receive USG funds to conduct or sponsor life sciences research and conduct or sponsor research, regardless of source of funding, that involves 1 or more of the 15 agents or toxins listed in the Policy, and (3) institutions outside the United States that receive USG funds to conduct or sponsor research that involves 1 or more of the 15 agents or toxins listed in the Policy.

[4] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*, September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx., Section 7.1.A.

[5] The 15 agents and toxins listed in this Policy are subject to the select agent regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121), which set forth the requirements for possession, use, and transfer of select agents and toxins, and have the potential to pose a severe threat to human, animal, or plant health, or to animal or plant products. It is important to note, however, that the Federal Select Agent Program does not oversee the implementation of this Policy or the March 2012 DURC Policy.

The PI's identification of research that meets one or more of these three criteria initiates an IRE review of the research. The PI should consider these three "triggers" for IRE review throughout the conduct of the research, including the submission of progress reports and at points when research findings are communicated. As soon as the PI identifies research that meets one of the above three criteria, he or she is to immediately refer the research to the IRE.

Section 7.2 of the *Policy for Institutional DURC Oversight* also requires that **institutions** subject to this Policy:

- Establish and implement internal policies and practices that provide for the identification and effective oversight of DURC;
- Initiate an institutional review and oversight process when a PI identifies research that involves one of the listed agents; and
- Ensure that internal policies establish a mechanism for the PI to immediately refer a project to the IRE as soon as any of the above-listed three criteria are met.

2. Identification and Assessment by PIs of Research That Requires Institutional Review

As noted above, PIs are required to submit research for IRE review as soon as any of the following three criteria are met:

A. The PI's research directly involves nonattenuated forms of one or more of the listed agents; or

B. The PI's research with nonattenuated forms of one or more of the listed agents also produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects; or

C. The PI concludes that his or her research with nonattenuated forms of one or more of the listed agents that also produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects *may* meet the definition of DURC and should be considered (or reconsidered) by the IRE for its DURC potential.

The three subsections below describe each of these criteria in more detail.

A. Research Involving the Listed Agents

To initiate the institutional review process, PIs are to notify the IRE if they are conducting research that directly uses nonattenuated forms of one or more of the following agents:

Avian influenza virus (highly pathogenic)
Bacillus anthracis
Botulinum neurotoxin (in any quantity)
Burkholderia mallei
Burkholderia pseudomallei
Ebola virus
Foot-and-mouth disease virus
Francisella tularensis
Marburg virus
Reconstructed 1918 influenza virus
Rinderpest virus
Toxin-producing strains of *Clostridium botulinum*
Variola major virus
Variola minor virus
Yersinia pestis

Research identified under criterion A would include current projects at the time the institution becomes subject to or implements the *Policy for Institutional DURC Oversight*, as well as future projects at the time they are initiated.

When a PI determines that his or her research does directly involve nonattenuated forms of one or more of these listed agents, he or she must *also* assess whether the research produces, aims to produce, or is reasonably anticipated to produce one or more of the experimental effects listed below, and this assessment should be provided to the IRE for its consideration during the review of the research.

The categories of experimental effects are as follows:

- Enhances the harmful consequences of the agent or toxin;
- Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical and/or agricultural justification;
- 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;
- Increases the stability, transmissibility, or the ability to disseminate the agent or toxin;
- Alters the host range or tropism of the agent or toxin;
- Enhances the susceptibility of a host population to the agent or toxin; and
- Generates or reconstitutes an eradicated or extinct listed agent or toxin.

The IRE will consider the PI's assessment of the applicability of the categories of experimental effects as part of its review of the research. Therefore, the PI's assessment should be documented in a format that can be easily supplied to the IRE when needed. An optional reporting template (**Appendix 2**) is provided to assist PIs in notifying the IRE of research that requires institutional review. **Section C** of this *Companion Guide* includes more detail on the IRE and its institutional review process. The *Companion Guide's* **Appendix 1**, "Definitions to Assist in the Consideration of the Categories of Experimental Effects," may also be useful.

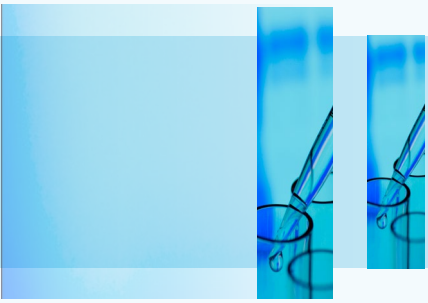
B. Research Involving a Listed Agent That Also Produces, Aims to Produce, or Can Be Reasonably Anticipated to Produce One or More of the Listed Experimental Effects

There may be instances in which a project is referred to the IRE for review (e.g., the research involves one of the agents listed above), but the research is determined by the IRE not to involve any of the seven experimental effects. In these instances the research does not require further review. However, if there is a change in this research such that it produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects, the PI should then notify the IRE and supply a revised assessment of the applicability of the listed categories of experimental effects.

C. Research That the PI Thinks May Meet the Definition of DURC

There may also be instances in which an IRE determines that the research (a) directly involves nonattenuated forms of one or more of the listed agents, and (b) produces, aims to produce, or is reasonably anticipated to produce one or more of the listed experimental effects but the IRE's final determination is that the research in question does not meet the definition of DURC (and is therefore not subject to additional oversight). Because there are no further oversight requirements for such research, the PI should notify the IRE in the future if, for whatever

reason (e.g., changes in the research, new discoveries), he or she feels that the research should be reconsidered by the IRE because it may now meet the definition of DURC. The IRE will review the research, including any new information, and determine whether the research is DURC.



C. Framework for Institutional Review: Guidance for Institutions and Institutional Review Entities

C. Framework for Institutional Review: Guidance for Institutions and Institutional Review Entities

This section of the *Companion Guide* is intended to assist institutions in establishing an **institutional review entity (IRE)** and implementing the **institutional review and oversight** requirements of the *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*[6] (*Policy for Institutional DURC Oversight*).

- **Part 1** of this section reiterates the **Policy requirements** related to the institutional review of life sciences research that meets the scope of the Policy, including the requirements for establishing an IRE.

- **Part 2** of this section **provides institutions and IREs with a framework** to assist in the identification and assessment of life sciences dual use research of concern (DURC). Specifically, this section outlines a multistep process for reviewing a principal investigator's (PI's) assessment of research that may have DURC potential, determining whether this research meets the definition of DURC, and, if so, evaluating the risks and benefits of the DURC. The final step of the process, developing a draft risk mitigation plan, is covered in detail in **Section D** of this *Companion Guide*.

The use of the framework provided in this section is optional.

1. Policy Requirements for Institutional Review of Life Sciences Research for DURC Potential

The *Policy for Institutional DURC Oversight* requires that institutions meet the following requirements:[7]

- Have policies and practices in place that enable PIs to identify and refer to an IRE any life sciences research that requires institutional review. (The process for PI identification and assessment of research that requires institutional review is described in **Section B** of the *Companion Guide*.)

- Establish an IRE to execute the institutional review of research for DURC potential. The IRE and its review requirements are addressed in this section of the *Companion Guide*.

- Have policies and practices in place for **institutional review and oversight of research**. The process for institutional review is detailed in Part 2 of this section of the *Companion Guide*.

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[6] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern,* September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx

[7] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern,* September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx, Section 7.2.

Requirements for Institutional Review Entities

The *Policy for Institutional DURC Oversight* describes a range of mechanisms and options for fulfilling the requirement for an IRE:

- Setting up a new committee at the institution for the sole purpose of conducting reviews of research for dual use potential;
- Using an extant committee, such as an institutional biosafety committee (IBC); or
- Using an externally administered committee, such as an IBC or review entity at a neighboring or regional institution, or a commercial entity.

Regardless of how the requirement for establishing an IRE is fulfilled, the IRE must meet the following criteria:

- Be composed of at least five members;
- Be sufficiently empowered by the institution to ensure it can execute the relevant requirements in Section 7.2.B of the *Policy for Institutional DURC Oversight*;
- Have sufficient breadth of expertise to assess the dual use potential of the range of relevant life sciences research conducted at a given research facility;
- Include persons with knowledge of relevant USG policies and understanding of risk assessment and risk management considerations, including biosafety and biosecurity. The review entity may also include, or have available as consultants, at least one person knowledgeable in the institution's commitments, policies, and standard operating procedures;
- On a case-by-case basis, recuse any member of an IRE who is involved in the research project in question or has a direct financial interest, except to provide specific information requested by the review entity; and
- Engage in an ongoing dialogue with the PI of the research in question when conducting a risk assessment and developing a risk mitigation plan.

Requirements for the IRE Review Process

The *Policy for Institutional DURC Oversight* requires the IRE to undertake the following steps in its review of research:[8]

- **Verify** that the research identified by the PI directly utilizes nonattenuated[9] forms of one or more of the listed agents.
- **Review the PI's assessment** of whether the research produces, aims to produce, or is reasonably anticipated to produce one or more of the listed experimental effects and the final determination of whether the research meets the scope of the *Policy for Institutional DURC Oversight*.

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[8] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*, September 24,2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx, Section 7.2.B

[9] The 15 agents and toxins listed in this Policy are subject to the select agent regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121), which set forth the requirements for possession, use, and transfer of select agents and toxins, and have the potential to pose a severe threat to human, animal, or plant health, or to animal or plant products. It is important to note, however, that the Federal Select Agent Program does not oversee the implementation of this Policy or the March 2012 DURC Policy.

- For research that the IRE determines meets the scope of the *Policy for Institutional DURC Oversight,* **conduct a risk assessment and determine whether the research meets the definition of DURC.** This assessment should involve the PI, as appropriate.
- **Assess the benefits of the DURC** while also considering the risks identified in the previous step.
- **Develop a *draft* risk mitigation plan** for the identified DURC. This plan should be based on the assessment of the risks and benefits performed in the previous step. More information on drafting risk mitigation plans can be found in **Section D** of the *Companion Guide*.
- **Review, at least annually, *all* active risk mitigation plans at the institution.** If the research in question still constitutes DURC, the IRE should modify the plan as needed. More information on the annual review of active risk mitigation plans can be found in **Section E** of the *Companion Guide*.

2. Framework for IRE Review of Research

This section provides IREs with a framework to assist in the process of identifying and assessing life sciences research for DURC. An optional template (**Appendix 3**) is provided to assist IREs in the assessment of research for DURC potential. In addition, a second optional template (**Appendix 4**) is provided to assist institutions in reporting research that meets the scope of the *Policy for Institutional DURC Oversight* to the appropriate USG funding agency within 30 calendar days of completing the institutional review.

The effective oversight of DURC is based on identifying and managing the risks associated with the potential that the information, technology, or products generated by life sciences research could be misused to harm public health, agriculture, or national security. Risk mitigation is a process in which risks are identified and assessed, and measures are put in place to address the identified risks. Together, risk assessment and risk mitigation pose unique challenges:

- Risks can often be reduced but are rarely eliminated.
- Assessing risks requires speculation on the ways that information derived from research may be misused.
- In order to determine the level of acceptable risk and the best mitigation strategy, it is also important to identify the likely benefits of the research, which may not be apparent early on.
- The individuals that constitute an IRE may be more accustomed to assessing the benefits of scientific research than its risks.

Although risk assessments may be either quantitative or qualitative, this framework is geared toward a qualitative assessment, which will require consideration and judgment by the IRE. In addition, because it is assumed that members of the IRE may already be accustomed to assessing the benefits of the research, the questions posed in **Section C** for identifying DURC-associated risks (Step 3) are more detailed than those that assess the potential benefits (Step 4).

The framework for risk assessment and risk mitigation follows a multistep process:

Step 1: Verify that the research directly involves nonattenuated forms of one or more of the listed agents.

Step 2: Assess whether the research produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects.

Step 3: Assess the risks of dual use and determine whether the research is DURC.

For research determined by the IRE to be DURC:

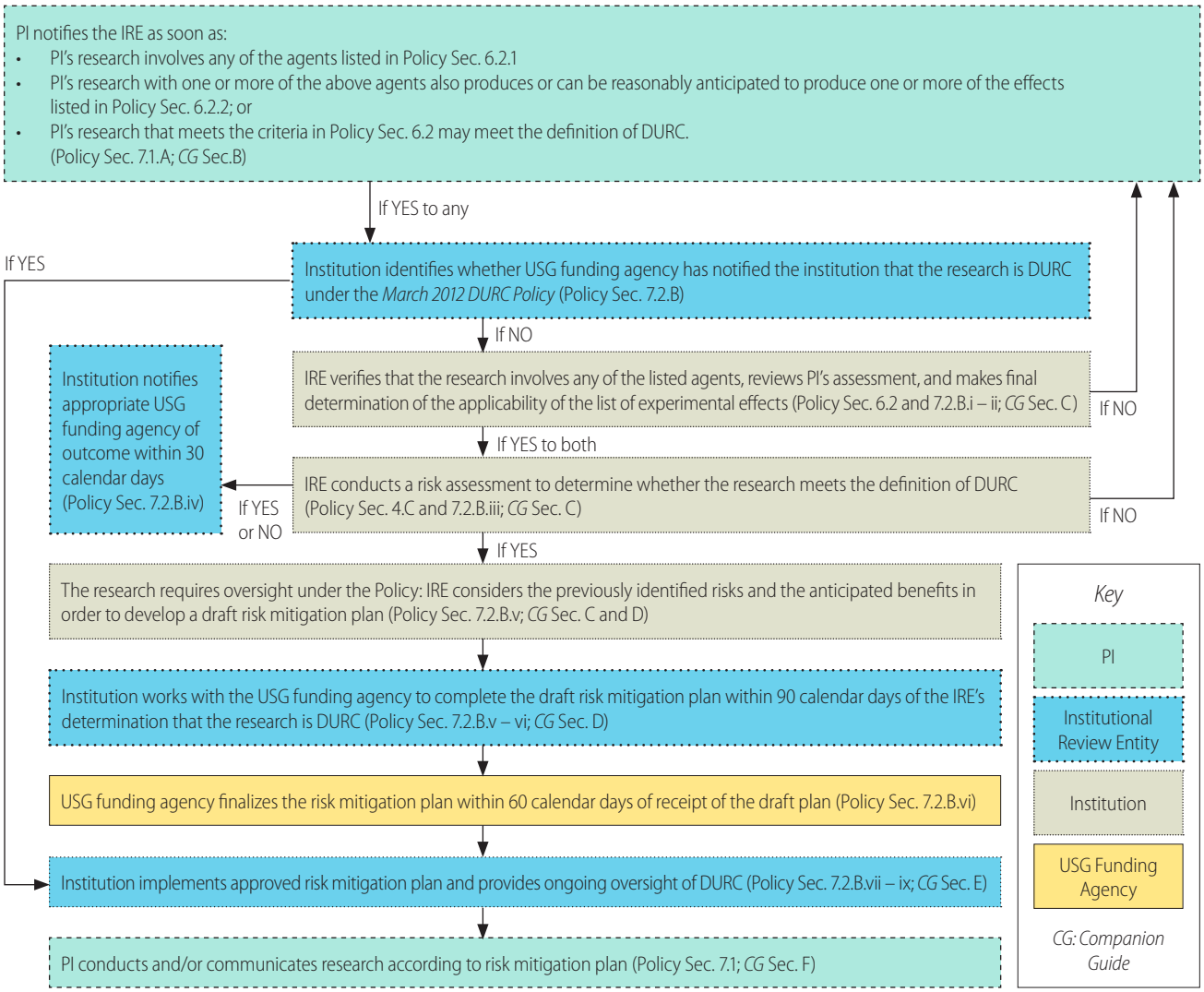
Step 4: Assess the potential benefits of the DURC.

Step 5: Weigh the risks and benefits of the DURC.

Step 6: Develop a draft risk mitigation plan for conducting the DURC and communicating its findings (described in detail in **Section D** of the *Companion Guide*).

It is anticipated that this review process will be conducted entirely by the IRE. However, situations may arise that require additional consultation with the Federal funding agency. Institutions may consult with the USG department or agency that is funding the research in question for advice on the review of research for DURC

Process for Institutional Review of Life Sciences Research within the Scope of the Policy



potential.[10] Such consultations should involve the institutional contact for dual use research (ICDUR), an individual designated by the institution to serve as a point of contact for questions regarding compliance with and implementation of the requirements for the oversight of DURC and to liaise (as necessary) between the institution and the relevant USG funding agency. The funding agency program officers can provide guidance on DURC issues. Such consultations may be appropriate when, for example, the following conditions are present:

- The PI does not agree with the finding of the IRE and the institution would like to request outside advice;
- The research in question represents a particularly complex case or appears to fall outside the scope of the *Policy for Institutional DURC Oversight* but still seems to present significant concerns; or
- Guidance is required to ensure a clear understanding of how the USG interprets the definition of DURC and related terms.

Step 1: Verify that the research directly involves nonattenuated forms of one or more of the listed agents.

The first step of the IRE review process is to verify that the research indeed directly involves nonattenuated forms of 1 or more of the 15 agents listed in Section 6.2.1 of the *Policy for Institutional DURC Oversight*. The IRE should review the available descriptions of the research and its findings from, for example, grant proposals, project reports, and other materials supplied by the PI before addressing whether the research directly involves nonattenuated forms of the listed agents. Research involving any of the following is not currently intended for review under the *Policy for Institutional DURC Oversight*:

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

If the IRE answers "*No*" in Step 1, the research is not subject to additional institutional DURC oversight, and the entity does not need to continue with the assessment. The PI should be informed that, if at some future point his or her research does involve nonattenuated forms of any of the above-listed agents, he or she will need to notify the appropriate institutional authorities (e.g., the IRE, the ICDUR) per the policy of the institution.

Step 2: Assess whether the research produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects.

In Step 2 of the institutional review process, IREs are required to assess whether the research in question produces, aims to produce, or is reasonably anticipated to produce one or more of the experimental effects listed in Section 6.2.2 of the *Policy for Institutional DURC Oversight*.

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[10] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern,* September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx Section 8.B

The IRE should examine descriptions of the research in question, the PI's assessment of the applicability of the categories of experiments, and other relevant information, as warranted. Examples of materials to consider include the project proposal, any project reports, any previous outcomes of dual use reviews, and examples of similar research in the literature. The *Companion Guide's* **Appendix 1**, "Definitions to Assist in the Consideration of the Categories of Experimental Effects," may also be useful.

If *none* of the listed experimental effects applies, the research *does not* meet the scope of the *Policy for Institutional DURC Oversight* and the IRE does not need to continue with the review. However, the PI should be informed that if at any time the reviewed research produces or can be reasonably anticipated to produce one or more of the listed experimental effects, or if the reviewed research may meet the definition of DURC (see Step 3), he or she must refer it again to the IRE for review.

Step 3: Assess the risks of dual use and determine whether the research is DURC.

Careful consideration of the risks of dual use associated with the research should underpin the determination of whether the research in question meets the definition of DURC: *"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."*

Step 3a: Assess the risks of dual use associated with the research

When considering whether the research in question meets the definition above, the IRE should first identify the risks associated with the potential misuse of the information, technologies, or products that may be generated. Although risk assessments may be either quantitative or qualitative, the assessment process outlined below is qualitative in nature and requires the consideration and judgment of the IRE on the following:

- The *ways* in which knowledge, information, technologies, or products from the research could be misused to harm public health and safety, agriculture, plants, animals, the environment, materiel, or national security.
- The *ease with which* the knowledge, information, technologies, or products might be misused and the feasibility of such misuse.
- The *magnitude, nature, and scope* of the potential consequences of misuse.

Consider the points below to assess the potential risks associated with conducting the research in question or communicating its results. These points address some of the aspects of potential DURC that could be considered, but they are not exhaustive – IREs should augment these points to fit their needs and the research under consideration. This risk assessment is intended to assist IREs in determining whether the research in question meets the definition of DURC. In cases where the research is determined to be DURC, this assessment will also inform the subsequent process of identifying strategies for mitigating those risks.

Points to Consider in Assessing Research for Its Dual Use Potential

1. **The ways in which knowledge, information, technologies, or products from the research could be misused.** Address the following questions and considerations regarding the nature and disposition of the knowledge, information, technology, or products that could be generated by the research under consideration:

Points to Consider in Assessing Research for Its Dual Use Potential (cont.)

a. What types of knowledge, information, technology, or products are anticipated to be generated through the research?

b. How will the results or products of the research in question be shared or distributed? *Knowledge, information, technology, or products that are freely available and widely distributed may be more easily accessed by individuals with harmful intent.*

   – Who will have access to the knowledge, information, technology, or final products?

   – Will it be shared openly or remain within the laboratory?

c. What is the novelty of the information provided by the research or of the research methods? *Research that adds novel information or consolidates information in novel ways may be of greater concern, whereas information that is already widely available is generally of lower concern.*

   – Have the results of the research been previously described or shared?

   – If so, at what venues and in what detail?

   – How readily available are these results?

d. Are the products of the research under consideration applicable to other more common or less pathogenic organisms or agents? *Knowledge, information, technology, or products generated from research that could be applied to more commonly available organisms to increase their associated risks may be of greater concern.*

e. Does the research highlight vulnerabilities in existing countermeasures or public health or agricultural infrastructure?

   – Does the research highlight weaknesses in the ability to prepare for and respond to disease outbreaks that could impact public, agricultural, or environmental health?

   – Does the research consolidate existing information in ways that highlight vulnerabilities in public health and/or safety preparedness?

2. The ease with which the knowledge, information, technologies, or products might be directly misused and the feasibility of such misuse. IRE members are not expected to have expertise in national security, but IRE members and investigators in general are in a good position to make technical assessments about how readily and in what ways certain knowledge, information, technologies, or products obtained from research might be misused. Address the following questions and considerations regarding factors that impact the likelihood of misuse, including technical feasibility, level of expertise, necessary reagents, or the need for additional scientific advances or technologies.

a. Consider the technical expertise and/or physical resources that would be needed to apply the knowledge, information, technology, or product for malevolent purposes. *The risk of misuse may be lower for knowledge, information, technologies, or products that would be expensive, difficult to procure, or that require a high degree of technical skill to facilitate such misuse.*

   – Would it require a low or high degree of technical skill and sophistication to use the information from dual use research for harmful purposes?

Points to Consider in Assessing Research for Its Dual Use Potential (cont.)

- Would its misuse require materials, equipment, or reagents that are expensive or difficult to procure?

b. Consider whether the products of the research in question could be directly misused to pose a threat to public health and safety, agriculture, plants, animals, the environment, materiel, or national security. *The risk of misuse may be higher for research information that can be directly misused than for research information that requires significant additional scientific advances to facilitate its misapplication.*

- Can the products, information, or technologies generated from the research be directly misapplied? If so, how?
- If not, do these outcomes of the research need to be combined with other knowledge, information, technology, or products in order to pose a threat? If so, is that other information already available?

c. Consider the time frame in which information from the research might be misused. *Information that can be misused in the near term may be of greater concern.*

- Is there concern about immediate or near-future potential use, or is the concern about misuse in the distant future?

d. Given your responses to the preceding questions, how readily could the knowledge, information, technology, or products from the research be used to threaten public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security?

3. Potential consequences of misuse. When considering the potential consequences of the misuse of scientific knowledge, information, technology, or products obtained from research, think broadly about the potential impacts on public health, agriculture, the environment, and/or the economy from the intentional misapplication of the results from the research in question. In general, information that could be misused to harm large populations of humans, plants, or animals; cause public panic; or require costly response efforts would be considered a greater risk.

a. Consider the nature of the potential consequences (e.g., harm to the economy, the environment, agriculture, or public health; public terror) that might result from misuse of the research results in question. *Information that could be misused to harm numerous sectors of society or the environment may be of greater concern.*

b. Consider the scope and magnitude of the potential consequences. *Research or research information that could be misused to cause severe harm, disease, or consequences is generally considered to be of greater concern.*

- Could the impact on people, plants, and/or animals be considered minor, moderate, or major?

c. Consider the available countermeasures. *Adequate countermeasures may help to decrease concern about the consequences of misuse. Countermeasures may include drugs, biological products, public health practices, pesticides, or devices intended for diagnosis, detection, mitigation, prevention, or treatment.*

- Are there currently any countermeasures to help mitigate the potential consequences?
- Are they readily available?

Step 3b: Apply the definition of DURC

The IRE should consider the identified risks in determining whether the research in question meets the definition of dual use research of concern (DURC): *"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."*

If the IRE determines that the research *does not* meet the DURC definition, the research is not subject to additional institutional DURC oversight. However, the institution must still notify the appropriate USG funding agency of the findings of the institutional review. If significant concerns about dual use remain, the ICDUR should be informed. The ICDUR and the IRE may choose to consult with a representative of the USG department or agency that is funding the research in question.

If the IRE determines that the research *does* meet the DURC definition, the research is DURC, as defined in the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy*, and is subject to additional DURC oversight. The IRE should inform the PI of its findings and proceed with the review process, which includes the development of a draft risk mitigation plan (see Steps 4-6, below). The institution must notify the appropriate USG funding agency of the IRE's findings within 30 calendar days of review.

Step 4: Assess the potential benefits of the DURC.

In order to determine the acceptable level of risk associated with DURC and the best mitigation strategies, the research in question should be assessed for its potential benefits. The benefits inherent to scientific research are many. Such benefits may impact various sectors of society and be realized over different time frames. The points in the box below address some of the aspects of the research that could be considered, but they are not exhaustive – IREs should augment these points to fit their needs and the research under consideration.

Points to Consider in Assessing the Benefits of the DURC

a. Are there potential benefits to public health and/or public safety from the research?

b. Are there potential benefits of the research for agriculture, plants, animals, the environment, materiel, or national security?

   – What potential solution does it offer to an identified problem or vulnerability?

c. Will this research be useful to the scientific, public health, or public safety communities? If so, how?

d. Because scientific research can have broad impacts, it is important to consider the scope of the potential benefits.

   – Will the knowledge, information, or technology generated from the research be broadly applicable (e.g., to human health, multiple scientific fields, populations of organisms)?

   – What populations of plants or animals might be positively affected?

e. If a benefit has been identified, in what time frame (e.g., immediate, near future, years from now) might this research benefit science, public health, agriculture, plants, animals, the environment, materiel, or national security?

Step 5: Weigh the risks and benefits of the DURC.

This can be the most challenging step in the risk-benefit assessment; it is often described as a step that entails "weighing" or "balancing" the risks with or against the benefits of DURC. This language, however, suggests that risks and benefits can be quantified and that they are commensurable. This is rarely, if ever, the case.

The process of weighing the risks and benefits of DURC is an exercise in making defensible, rational judgments in the midst of unavoidable uncertainty. Uncertainty can best be managed by ensuring that the process draws on the expertise and perspectives of a group of individuals of diverse backgrounds and experience. Discussion and debate within such a group can help to (a) identify and mitigate the biases that individuals inevitably bring to the challenges of this sort, (b) uncover often implicit assumptions in arguments, (c) scrutinize and test the basis for judgments, and (d) yield conclusions that represent a consensus (literally, "a thinking together") and are optimally defensible.

In assessing the risks, some assessments will entail judgments of feasibility that will be best expressed in such phrases as "highly likely" or "less likely" rather than with quantitative measures (e.g., 90 percent or 10 percent). Others will be expressed in such phrases as "readily" or "very easily," or "with difficulty" or "with great difficulty." With still other assessments, the aim will be to project the possible consequences of the misuse of DURC information and to describe the magnitude of these consequences (e.g., projected rates of morbidity and mortality – in humans or animals – due to infection with a pathogen). Such projections will often be based on (and perhaps extrapolated from) limited data and thus will be associated with varying degrees of uncertainty.

In assessing the benefits, similar challenges will be encountered. It will be difficult to identify with precision the concrete benefits that can be reasonably expected to accrue from a particular body of DURC and to project, with accuracy, the time frame within which those benefits could be realized. Here, too, the judgments will be expressed in qualitative rather than quantitative terms. They will, as well, be tempered with some degree of uncertainty. There are several questions that can be posed with respect to most any body of DURC that undergoes this process of risk-benefit assessment. The answers to these questions will inform the development of a risk mitigation plan (see Step 6 and **Section D** of the *Companion Guide*).

Points to Consider for Weighing The Risks and Benefits of the DURC

a. Could the information of concern be more readily applied to improvements in surveillance or to the development of countermeasures than to malevolent applications? What reasons or evidence support the answer to this question?

b. What is the time frame in which potential benefits might be realized?

c. How might the potential benefits and the anticipated risks be distributed across different populations (humans and animals)?

   – Who or what will be the likely beneficiaries of the potential benefits? Will the potential benefits be distributed equally or disproportionately across different populations? *Here, it will be helpful to keep in mind that, for example, human populations may differ in terms of size: The potential benefits may accrue to a large or, alternatively, to a small number of individuals. Or, human populations may differ along socioeconomic or cultural lines: The potential benefits may accrue to or have little impact on a vulnerable or low-resourced population versus a well-resourced population.*

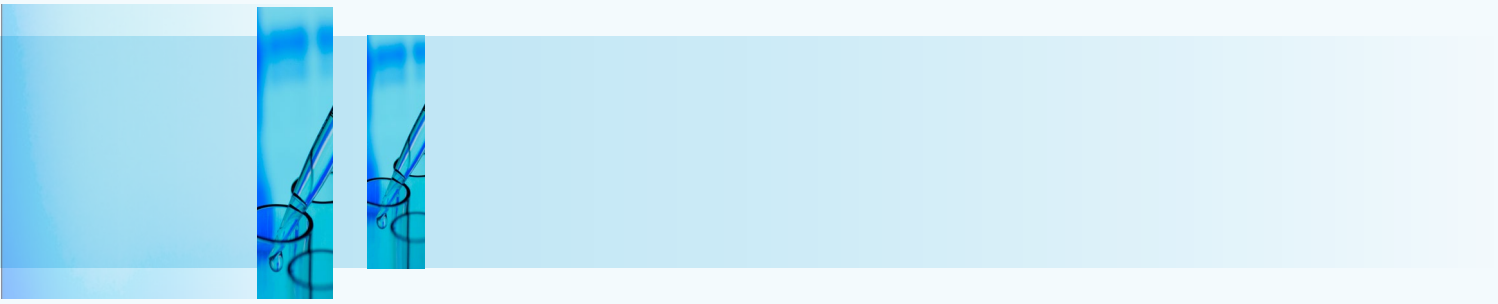
Points to Consider for Weighing Risks and Benefits of the DURC (cont.)

- Who or what will bear the anticipated risks? Is it likely that one or more specific populations will bear the burden of the anticipated risks?
- Is it likely that the distribution of the anticipated risks and the potential benefits will be fair or just?

d. Considering the anticipated risks in tandem with the potential benefits, are the risks of such a feasibility and magnitude that they warrant proceeding after developing and implementing a risk mitigation plan? Are the potential benefits of significant magnitude to warrant proceeding despite the risks? What is the most responsible way to proceed? For the vast majority of cases of DURC, an appropriate risk mitigation plan can be developed and effectively implemented.

Step 6: Develop a draft risk mitigation plan for conducting the DURC and communicating its findings.

The final step of the process, developing a draft risk mitigation plan, is covered in detail in **Section D** of the *Companion Guide*.



D. Developing a Draft Risk Mitigation Plan: Guidance for Institutional Review Entities

D. Developing a Draft Risk Mitigation Plan: Guidance for Institutional Review Entities

This section provides guidance for institutional review entities (IREs) in developing a draft risk mitigation plan for conducting DURC and communicating its results.

IREs should conclude their assessments of the risks and benefits of DURC by developing a draft risk mitigation plan, based on the identified risks, considering the strategies outlined below. Note, however, that no risk mitigation strategy (or combination of strategies) can reduce risks to zero: the aim should be to minimize potential risks to the extent possible to ensure that risks are appropriately managed and benefits realized.

- **Part 1** of this section details the **Policy requirements** for developing a draft risk mitigation plan, as described in the *USG Policy for Insitutional Oversight of Life Sciences Dual Use Research of Concern* (*Policy for Institutional DURC Oversight)*[11] and the *USG Policy for Overisight of Life Sciences Dual Use Research of Concern (March 2012 DURC Policy.)*[12]
- **Part 2** of this section provides guidance that outlines several **strategies the IRE should consider to mitigate the DURC-associated risks identified.** These strategies may be used in combination, and the specific risk mitigation measures employed should be tailored to the research in question.

The use of the guidance provided in this section is optional.

1. Policy Requirements for Development of a Draft Risk Mitigation Plan

The *Policy for Institutional DURC Oversight* requires that IREs **develop a *draft* risk mitigation plan** for any DURC identified by the IRE.[13] This plan should be based on the assessment of the risks and benefits, as described in **Section C** of the *Companion Guide*.

Once DURC has been identified, institutions should do the following:

- Work with the USG funding agency (or, for nonfederally funded DURC, the NIH-designated USG agency) to **develop the *draft* risk mitigation plan**.
- **Submit a copy of the *draft* risk mitigation plan within 90 calendar days of an IRE's determination that the research is DURC** to the USG funding agency (or, for nonfederally funded DURC, the NIH-desig-

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[11] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern,* September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx.

[12] *USG Policy for Oversight of Life Sciences Dual Use Research of Concern*, March 29, 2012, www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf.

[13] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern,* September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx. Section 7.2.B.

nated USG agency) for review and final approval. USG agencies are required to provide an initial response to institutions within 30 calendar days and should finalize the plan within 60 calendar days of receipt of the draft plan.

In addition, the *March 2012 DURC Policy* requires USG departments and agencies to collaborate with institutions or researchers in the development of a risk mitigation plan that applies any necessary and appropriate risk mitigation measures.[14]

Note that a final, USG-approved risk mitigation plan will fulfill the requirements of both DURC policies.

2. Developing a Draft Risk Mitigation Plan

IREs should conclude their risk-benefit assessment of DURC by developing a draft risk mitigation plan. The plan should indicate the DURC-associated risks identified by the IRE, the specific risk mitigation measures to be employed, and how these measures address the identified risks.

The IRE should consider the strategies outlined below to determine the most effective risk mitigation measures that are tailored specifically to the research in question. These strategies are not mutually exclusive and may be used in combination. More than one strategy may be applicable for addressing a given risk. Also, the same strategy may be appropriate for addressing more than one risk. Lastly, the risk mitigation strategies provided in this section are general in nature; the list is not meant to be exhaustive. IREs are encouraged to consider additional strategies for mitigating the concerns about dual use raised by the research in question. Note, however, that no risk mitigation strategy (or combination thereof) can reduce risks to zero; the aim should be to adequately and appropriately manage the identified risks.

Of note, although it is the responsibility of the IRE to develop the draft risk mitigation plan, there may be situations that require consultation with the Federal funding agency. Such consultations may be appropriate when, for example:

- The IRE requires guidance on developing an adequate risk mitigation plan in cases where the potential risks are perceived as particularly high;
- The IRE considers the only viable risk mitigation measures to be not conducting the research in question or not communicating its results.

The IRE should work with the USG funding agency to finalize the risk mitigation plan.

Strategies for Mitigating DURC-Associated Risks

Determine whether existing biosafety and biosecurity measures are adequate

After considering the proposed biosafety and biosecurity measures under which the DURC will be conducted, the IRE may determine that the specific risks associated with the DURC (a) are adequately mitigated, or (b) warrant additional biosafety and biosecurity measures.

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[14] *USG Policy for Oversight of Life Sciences Dual Use Research of Concern*, March 29, 2012, www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf, Section IV.1.e.

Possible risk mitigation measures:

- Apply specific additional biosafety or biosecurity measures to more effectively mitigate the identified risk(s).
- Modify the experimental design or methodology. This might include utilizing an attenuated strain or employing other molecular/genetic containment measures that limit a strain's ability to proliferate outside a laboratory environment or within different hosts (e.g., humans). The IRE should carefully consider whether the proposed modifications could affect the ability to achieve the scientific aims.

Evaluate applicability of existing countermeasures

The IRE should consider how the existence or absence of countermeasures should inform the design of the DURC and communication of its results. The existence of countermeasures may help to decrease concern about the consequences of misuse. Countermeasures may include drugs, biological products, public health practices, pesticides, or devices intended for diagnosis, detection, mitigation, prevention, or treatment.

Possible risk mitigation measures:

- Evaluate the efficacy of medical countermeasures against agents or toxins resulting from DURC. Where efficacious countermeasures exist, include this information in communications. If no efficacious countermeasures exist, consult with the IRE and, as necessary, the USG funding agency about how to proceed with the conduct of research and the communication of its results.
- For DURC involving an agent for which there are no existing countermeasures, consider whether the research aims could be met by utilizing a strain or toxin that is sensitive to countermeasures.

Develop a plan for responsibly communicating the findings of DURC

The IRE should consider how the concerns about dual use associated with the research in question may be mitigated by developing a plan for responsible communication of its findings. In general, the results of life sciences should be communicated openly and to the fullest extent possible. Any restriction of scientific communication should be the rare exception rather than the rule. However, if the communication of the results of DURC could pose potential security risks, the logical next step is a risk-benefit analysis of communicating the information.

The *Guidance for Responsible Communication of DURC Findings* (**Section F** of the *Companion Guide*) can be used to facilitate consideration of the risks and benefits of communicating the findings of DURC and to develop a responsible communication plan. Note particularly the following:

- The decision regarding communication is not necessarily a binary (yes/no) one. Rather, a range of options for communication should be identified and considered.
- Research findings are communicated at many points throughout the research process. The responsible communication of DURC findings should be considered at each point.

It is the expectation of the USG that the vast majority of DURC findings will be communicated. The goal of the risk mitigation process is to promote the responsible conduct of DURC and communication of its results, not the restriction of such research. In cases in which the IRE considers the most appropriate risk mitigation measure to be either to redact specific information or to not communicate the research findings at all, consider consulting the USG funding agency.

Possible risk mitigation measures:

- Consider changing the timing, mode, or venue of communication for the DURC in question.
- Establish a mechanism for prepublication or precommunication review by the institution and/or the appropriate USG funding agency.
- Consider the need to redact specific information in light of security concerns.
- When communicating the DURC, emphasize the biosafety and biosecurity measures that were in place throughout the course of the research.
- Emphasize the public health or broader significance of the DURC. For example, describe specifically how the findings may inform the development of countermeasures, disease surveillance, preparedness, and response efforts.

Educate and train research staff using available DURC educational tools

All research staff should receive training and education related to DURC and the DURC oversight policies. IREs may also consider whether additional training is required to address specific concerns about dual use raised by the research in question. The USG and individual Federal funding agencies have developed training and education resources, which will be made available on the U.S. Government Science, Safety, Security (S3) website, www.phe.gov/s3/dualuse/.

Training tools or modules developed by nonfederal entities or organizations such as the National Science Advisory Board for Biosecurity, the Southeast Regional Center of Excellence for Emerging Infections and Biodefence, the Federation of American Scientists, and the University of Bradford (United Kingdom) may also be useful in providing additional education or training.

Possible risk mitigation measures:

- Provide additional training that addresses risks or concerns that are unique to the DURC in question.
- Require that research staff receive refresher training on a more frequent basis.

Develop a plan for monitoring the DURC

It may be possible to mitigate concerns about dual use research through increased monitoring of the DURC in a manner that helps to ensure that the risks of dual use are adequately and appropriately managed over time. Risks may change over time based on new research findings or technological developments. For example, research that may at one time have been considered to be of concern may be of less concern if new countermeasures become available. On the other hand, new technologies may increase the feasibility for misuse, which over time may change the perceived risks associated with a certain line of research. In addition, under the *Policy for Institutional DURC Oversight*, the IRE is required to review all risk mitigation plans at least annually and to modify plans as warranted. Increased monitoring of the DURC may result in more frequent updates to risk mitigation plans.

Possible risk mitigation measures:

- Review the DURC in question at more frequent time intervals.
- Identify certain experimental outcomes that require the research to be reviewed again by the IRE prior to proceeding further.

Do not conduct certain aspects of the DURC

It is the expectation of the USG that the vast majority of DURC will be conducted. The goal of the risk mitigation process is to promote the responsible conduct of DURC and communication of its results, not the restriction of such research. In some very rare cases, however, the risks associated with the DURC may be so significant that no amount of potential benefits can outweigh the risks. In these instances, the most appropriate option may be to not conduct certain aspects of the research.

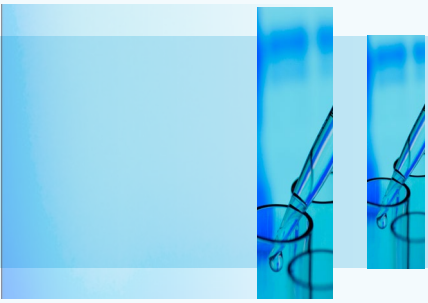
Consultation with the USG funding agency is encouraged in situations where the IRE considers the only appropriate risk mitigation measure to be not conducting the research in question. The funding agency can provide input on the IRE's risk-benefit assessment. As needed, the USG funding agency could consult with other relevant subject matter experts, and it can explore whether classification is an appropriate option to proceed with the research.

3. Elements of a Draft Risk Mitigation Plan

Risk mitigation plans should provide sufficient details on the research in question to enable the USG funding agency to adequately assess the institution's plan for managing the risks associated with DURC identified by the IRE.

Risk mitigation plans should include the following:

- The name and contact information for the PI(s).
- The name and contact information for the authorized institutional official.
- The name of the ICDUR (if different from the authorized institutional official).
- The dates and details of the reviews and assessments of the research by the IRE.
- The dates and details of the PI's initial review or ongoing assessment of the research.
- Identification of whether the research has been identified as DURC under the *March 2012 DURC Policy*.
- Details of the risks identified by the IRE in its review of the research, and an explanation of the risk mitigation strategy or strategies that are being implemented by the institution to address those risks.
- Other materials, such as proposals and progress reports related to the research, that may be requested by the USG agency.



E. Review of Risk Mitigation Plans: Guidance for Institutional Review Entities

E. Review of Risk Mitigation Plans: Guidance for Institutional Review Entities

This section provides institutional review entities (IREs) with guidance on the **assessment of a risk mitigation plan**. These plans should be revised as needed based on changes in the research plan, new and/or unexpected research findings, or technological developments.

- **Part 1** of this section details the **institutional and IRE responsibilities** as described in the *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (Policy for Institutional DURC Oversight)* and the *USG Policy for Oversight of Life Sciences Dual Use Research of Concern (March 2012 DURC Policy)*.
- **Part 2** of this section provides a **framework for IREs** to review institutional risk mitigation plans.

The use of the guidance provided in this section is optional.

1. Policy Requirements for Institutional Review of Risk Mitigation Plans

The *Policy for Institutional DURC Oversight* requires the following:[15]

- Institutions have policies and practices in place for **institutional review of all active risk mitigation plans at the institution**, including risk mitigation plans developed under the *March 2012 DURC Policy*.
- **IREs review, at least annually, all active risk mitigation plans** at their institution, including risk mitigation plans developed by USG funding agencies under the *March 2012 DURC Policy*. If the research in question still constitutes DURC, the IRE should modify the plan as needed.
- Institutions **notify the appropriate USG agency**, within 30 calendar days, **of any change in the status of a DURC project at the institution**, including whether the research has been determined by the IRE to no longer meet the definition of DURC. This notification should include details of any changes to an approved risk mitigation plan. Such changes need to be approved by the funding agency.

In addition, under the *March 2012 DURC Policy*, USG departments and agencies may request that institutions regularly monitor emerging findings for their DURC potential and modify their risk mitigation plans, as necessary, to manage any emerging DURC risks. Institutions should notify funding agencies of any additional DURC and proposed modifications to their risk mitigation plans.[16]

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[15] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*, September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx, Section 7.2.

[16] *USG Policy for Oversight of Life Sciences Dual Use Research of Concern*, March 29, 2012, www.phe.gov/s3/dualuse/Documents/us-policy-durc-032812.pdf, Section IV.e.vi.

2. Framework for IRE Review of Risk Mitigation Plans

This section provides IREs with a framework for reviewing risk mitigation plans for DURC taking place at the institution. The purpose of this review is to ensure that a risk mitigation plan continues to adequately manage the risks associated with a DURC project, to make modifications when needed, and to identify instances where the research in question no longer constitutes DURC and, therefore, no longer requires a risk mitigation plan under the USG policies for DURC oversight.

Step 1: Review the research to verify that it still directly involves nonattenuated[7] forms of one or more of the listed agents.

Step 2: Assess whether the research still produces, aims to produce, or can be reasonably anticipated to produce one or more of the listed experimental effects.

Step 3: Determine whether the research still meets the definition of DURC.

Step 4: Review and, as necessary, revise the risk mitigation plan.

In most cases, the review process will be conducted entirely by the IRE. However, situations may arise that require additional consultation with the Federal funding agency. Institutions may consult with the USG department or agency that is funding the research in question for advice on the review of research for DURC potential.[18] Such consultations should involve the institution's ICDUR. The funding agency program officers can provide guidance on DURC issues. Questions regarding non-USG-funded research should be directed to NIH or to the USG agency to which NIH refers the institution based on the nature of the research in question. Such consultations may be appropriate when, for example, the following situations are present:

- The PI does not agree with the finding of the IRE, and the institution would like to request outside advice;
- The research in question represents a particularly complex case or appears to fall outside the scope of the *Policy for Institutional DURC Oversight*, but it still seems to present significant concerns; or
- Guidance is required to ensure a clear understanding of how the USG interprets the definition of DURC and related terms.

Step 1: Review the research to verify that it still directly involves nonattenuated forms of one or more of the listed agents.

The first step of the IRE review of risk mitigation plans is to verify that the research still directly involves nonattenuated forms of one or more of the agents listed in Section 6.2.1 of the *Policy for Institutional DURC Oversight*. The IRE should consider the most up-to-date descriptions of the research and its findings from, for example, grant proposals, project reports, and other materials supplied by the PI before addressing whether the research still directly involves nonattenuated forms of the listed agents. Note that research involving anything in the following list is not currently intended for review under the *Policy for Institutional DURC Oversight* or the *March 2012 DURC Policy*:

- The use of any of the listed agents in attenuated forms;

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[17] The 15 agents and toxins listed in this Policy are subject to the select agent regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121), which set forth the requirements for possession, use, and transfer of select agents and toxins, and have the potential to pose a severe threat to human, animal, or plant health, or to animal or plant products. It is important to note, however, that the Federal Select Agent Program does not oversee the implementation of this Policy or the March 2012 DURC Policy.

[18] USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern, September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx, Section 8.B.

- The use of the genes from any of the listed agents;
- *In silico* experiments (e.g., modeling experiments, approaches involving bioinformatics) having to do with the biology of the listed agents; or
- Research related to the public, animal, or agricultural health impact of any of the listed agents (e.g., modeling the effects of a toxin, developing new methods to deliver a vaccine, developing surveillance mechanisms for a listed agent).

If the IRE answers "*No*" in Step 1, the research is no longer subject to institutional DURC oversight, and the entity does not need to continue with the assessment. The PI should be informed that if, at some future point, his or her research does involve any of the agents listed above, he or she will need to notify the appropriate institutional authorities (e.g., the IRE, the ICDUR) per the policy of the institution. In addition, institutions should **notify the appropriate USG agency**, within 30 calendar days, that the project no longer involves one of the listed agents and is therefore no longer DURC.

If the IRE answers "*Yes*" in Step 1, the research still meets the first criterion outlined in Section 6.2.1 of the *Policy for Institutional DURC Oversight* and Section III.1 of the *March 2012 DURC Policy* and requires further review.

Step 2: Assess whether the research still produces, aims to produce, or can be reasonably anticipated to produce one or more of the listed experimental effects.

In the second step of the process of reviewing the risk mitigation plan, IREs are required to assess whether the research in question still produces, aims to produce, or is reasonably anticipated to produce one or more of the experimental effects listed in Section 6.2.2 of the *Policy for Institutional DURC Oversight* and Section III.2 of the *March 2012 DURC Policy*.

Before addressing the questions below, the IRE should review up-to-date descriptions of the research in question, any revised or new assessments of the applicability of the categories of experiments by the PI, and other relevant information, as warranted. Some examples of materials to consider include the project proposal, any project reports, any outcomes of previous reviews of dual use research, and examples of similar research in the literature. The *Companion Guide*'s **Appendix 1**, "Definitions to Assist in the Consideration of the Categories of Experimental Effects," may also be useful.

If *none* of the listed experimental effects applies in Step 2, the research *no longer* meets the scope of the *Policy for Institutional DURC Oversight* or the *March 2012 DURC Policy*, and the IRE does not need to continue with the review of the risk mitigation plan. However, the PI should be informed that if at any time the reviewed research produces or can be reasonably anticipated to produce one or more of the listed experimental effects, or if the reviewed research may meet the definition of DURC (see Step 3), he or she must refer it again to the IRE for review. In addition, institutions should notify the appropriate USG agency, within 30 calendar days, that the project is no longer DURC.

If *any* of the listed categories of experimental effects applies in Step 2, the research *does* meet the scope of the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy*, and the IRE should continue its review of the risk mitigation plan by determining whether the research in question still meets the definition of DURC.

Step 3: Determine whether the research still meets the definition of DURC.

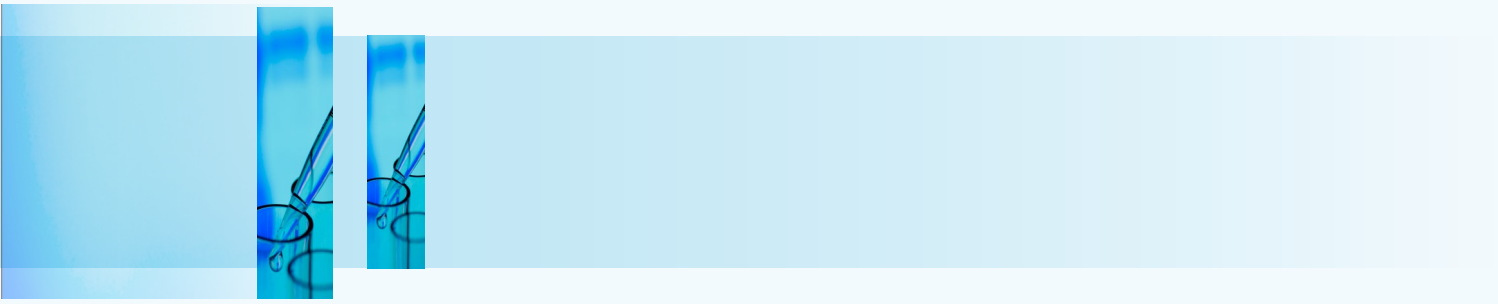
This step of the IRE's review of the risk mitigation plan is to determine whether the research in question still meets the definition of DURC as defined by the *Policy for Institutional DURC Oversight and the March 2012 DURC Policy: "life sciences research that, based on current understanding, can be 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."*

If the IRE determines that the research *does not* meet the definition above, the research is no longer subject to institutional DURC oversight. If significant concerns remain regarding the research in question, the ICDUR should be informed. The ICDUR and the IRE may choose to consult with a representative of the USG department or agency that is funding the research in question. In addition, institutions **should notify the appropriate USG funding agency,** within 30 calendar days, that the IRE no longer considers this project to be DURC.

If the IRE determines that the research *does* meet the definition above, the research is DURC, as defined by the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy*, and is still subject to DURC oversight. The IRE should proceed with the review and, as necessary, revision of the risk mitigation plan.

Step 4: Review and, as necessary, revise the risk mitigation plan.

If the IRE determines that the research in question still constitutes DURC, the next step in the review process is to reconsider the potential risks that the knowledge, information, technology, or products generated by life sciences research could be misused to harm public health, agriculture, or national security. The purpose of this review is to ensure that the risk mitigation plan continues to adequately mitigate the risks associated with the DURC. This step is assisted by the **Framework for IRE Review of Research** included in **Section C** of the *Companion Guide*. If, after reconsidering the risk and benefits of the research, institutions modify or update the DURC's risk mitigation plan, the institution must **notify the appropriate USG funding agency of any changes** within 30 calendar days. Such changes need to be approved by the funding agency.



F. Guidance for Responsible Communication of DURC Findings

F. Guidance for Responsible Communication of DURC Findings

The tools in this section are intended to guide researchers, institutions, institutional review entities (IREs), and journal editors in identifying and assessing the risks and benefits of communicating research information that may be of concern regarding possible dual use. It includes a series of questions that can be considered as well as options for the communication of DURC findings.

- **Part 1** of this section details **points to consider** when assessing the risks and benefits of communicating DURC findings.
- **Part 2** of this section provides details on the criteria for **optional consultation with the U.S. Government**.

The use of the guidance provided in this section is optional.

1. Points to Consider in Assessing the Risks and Benefits of Communicating DURC Findings

Consider the points below when assessing the risks and benefits associated with communicating DURC findings and when formulating a communications plan.

General Overview of the Research Information

a. What information is provided?

b. What are the novel aspects of the communication in terms of the following:

   i. Results

   ii. Methods

   iii. Combining previously communicated information or methods in a novel fashion

   iv. Combining new information with some previously communicated information

c. What is the "scientific context" of this information? For example:

   i. To what extent is similar information already publicly available?

   ii. To what extent has the new information already been communicated (e.g., through presentations and abstracts at scientific meetings, press releases or articles, or on the Internet)?

Risk Analysis

a. Are there reasonably anticipated risks to public health and safety from direct misapplication of the information that would be communicated?

   i. Is novel information provided that could be misused to threaten the public's health and/or safety?

   ii. Does the information point out vulnerability in public health and/or public safety preparedness?

   iii. Does the novel scientific information point out a gap in regulatory oversight (biosecurity or biosafety) or evade existing biosafety measures?

b. How easy would it be for those who intend harm to use the information? For example:

   i. What level of expertise and/or technology is required to reproduce the work described?

   ii. What is the availability of the required expertise, technology, equipment, or reagents?

c. Is it reasonably anticipated that this information could be directly misused to pose a threat to agriculture, plants, animals, the environment, or materiel (i.e., does the information point out vulnerability with respect to agriculture, plants, animals, the environment, materiel, or other aspects of national security)?

d. If a risk has been identified, in what time frame (e.g., immediate, near future, years from now) might this information be used to pose a threat to the public's health and/or safety, agriculture, plants, animals, the environment, materiel, or national security?

e. What is the scope or magnitude of the potential risk(s) identified?

f. If the information were to be broadly communicated "as is" or with specified modification(s), what would the potential be for the following:

   i. Public anxiety (i.e., widespread concern about public health or other safety/security issues)?

   ii. Public misunderstanding, that is, what might be the implications of misunderstandings (e.g., psychological, social, economic, commercial, or decisions on health or diet)?

   iii. Sensationalism (i.e., exaggeration of the potential benefits, risks, impacts) on the part of the authors/presenters or the media?

   iv. Are there other negative consequences that could be anticipated, such as a loss of public trust?

g. If the information were to be communicated in a significantly abridged form, what would be the potential for the following:

   i. Public anxiety (i.e., widespread concern about public health or other safety/security issues)?

   ii. Public misunderstanding, that is, what might be the implications of misunderstandings (e.g., psychological, social, economic, commercial, or decisions on health or diet)?

   iii. Sensationalism (i.e., exaggeration of the potential benefits, risks, impacts) on the part of the authors/presenters or the media?

   iv. Are there other negative consequences that could be anticipated, such as a loss of public trust?

Benefit Analysis

a. Are there potential benefits to the public's health and/or safety from the application or utilization of the communicated information?

b. Are there potential benefits of the information for agriculture, plants, animals, the environment, or materiel (e.g., what potential solution does it offer to an identified problem or vulnerability)?

c. Will this information be useful to the scientific community? If so, how?

d. If a benefit has been identified, in what time frame (e.g., immediate, near future, years from now) might this information be used to benefit science, public health, agriculture, plants, animals, the environment, or materiel?

e. What is the scope or magnitude of the potential benefit(s) identified?

Considerations for Weighing Risks and Benefits of Communicating DURC Findings

Based on the risks and benefits identified above:

a. How are risks and benefits of communicating this information distributed across different stakeholders?

   i. Who stands to benefit (e.g., large vs. small populations, vulnerable or low-resourced populations vs. well-resourced populations)? Is the benefit equally or disproportionately distributed across groups?

   ii. Who bears the risk? Is the burden of risk disproportionate for one or more specific groups?

   iii. Is the distribution of the risks and benefits fair? If the distribution of risks and benefits is not the same, is there a way to extend the benefits more widely or to mitigate disproportionate risks?

b. What is the time frame in which potential benefits or anticipated risks of the communication might be realized?

c. Do the benefits of communicating the information outweigh the risks? If so, how? Alternatively, do the risks outweigh the benefits? If so, how?

   i. Could the information be more readily applied to improvements in surveillance and the development of countermeasures than for harmful purposes? What is this assessment based on?

Formulation of Recommendation(s) Regarding Responsible Communication of DURC Findings

The goal of this analysis is to develop a communication plan in which the information is shared to the fullest extent possible in order to realize the potential benefits while effectively managing the risk of potential misuse of the information. After consideration of the risks and benefits of communicating the findings of DURC, decisions about how to responsibly communicate that information should address the content, timing, and possible extent of distribution of the information. See **Appendix 5** for information on how Export Controls apply to certain research communications.

Possible communication or publication actions (more than one may be applicable)

i. Communicate or publish as is.

ii. Communicate or publish with addition of appropriate contextual information. For example, it may be important to address:

   1) The significance of the research findings for public health and/or public safety, agriculture, the environment, or materiel;

   2) How the new information or technology will be useful to the scientific community;

   3) The biosafety and biosecurity measures in place as the research was conducted; and

   4) The careful consideration that was given to the concerns about dual use in the decision to publish (e.g., a formal biosecurity review).

iii. Communicate or publish openly, but withhold specific information that is of concern. For example, is it possible to "decouple" the material that poses security concerns from some or all of the potentially useful scientific information, or should specific information be removed (e.g., technical details about an enabling technology)?

   1) Delete certain information and then communicate or publish openly.

   2) Communicate information "of concern" through nonpublication/nonpresentation channels. Identify what parties should be given the restricted information and how it should be distributed.

iv. Communicate only to selected parties (not openly communicated).

   1) Communicate to selected parties—need to specify who they are and the mechanisms of communication.

   2) Communicate selected information to selected parties, but the rest of the information is not communicated at all, to anyone.

v. Do not communicate in any way, shape, or form.

Timing of communication, based on considerations set forth above

i. Communicate immediately, to the extent decided above.

ii. Defer communication (to the extent decided above) until a clearly defined and agreed-upon endpoint is reached (e.g., a condition is met such that communication no longer poses the same degree of risk).

Final consideration of the agreed-upon course for going forward

i. Does the proposed course of action mitigate, to an acceptable level, the risks that were identified in the risk-benefit analysis?

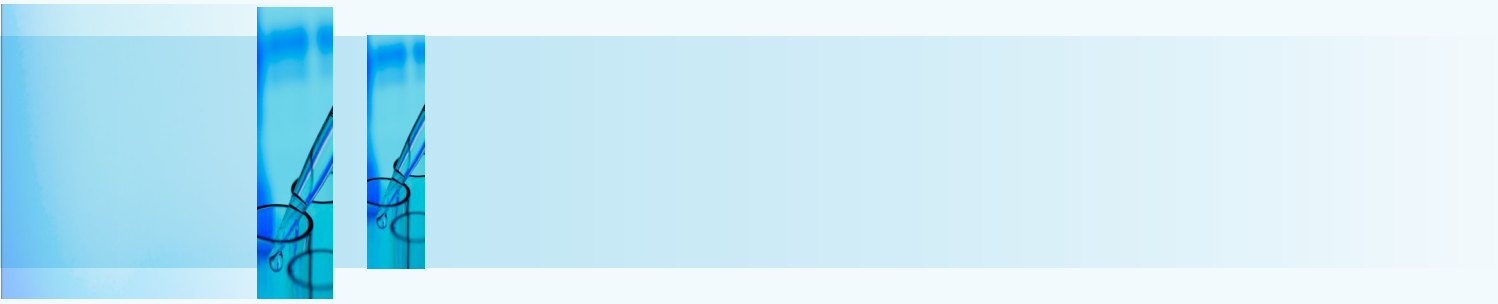
ii. Are new risks introduced as a result of changes/modifications? Are there new concerns or unintended consequences regarding the proposed communication? If so, what are they and can they be mitigated?

iii. Is it likely that the proposed course of action will be challenging to implement or enforce? Is a contingency plan necessary? Would additional resources be required?

2. Criteria for Consulting the U.S. Government (optional)

It is expected that IREs can develop plans for the responsible communication of DURC findings in the majority of cases. However, there may be some rare situations in which consultation with the Federal funding agency may be helpful. The Federal funding agency may be consulted by institutions (not by individual researchers) for cases where:

- Unique expertise (e.g., on national security) is needed to assess the potential risks associated with communicating the research;
- The IRE requires guidance on developing an adequate risk mitigation strategy for communication in cases where the potential risks of communication are perceived as particularly high;
- The IRE considers the only viable risk mitigation strategy to be not conducting the research in question or not communicating its findings;
- The PI whose research has been reviewed does not agree with the IRE's findings, and the institution would like to request outside advice; or
- The research in question represents a particularly complex case or appears to fall outside the definition of DURC but still seems to present significant concerns.



Appendices

Appendix 1: Definitions to Assist in the Consideration of the Categories of Experimental Effects

These definitions[19] were developed by the National Science Advisory Board for Biosecurity (NSABB) to assist in the consideration of the NSABB's categories of experiments that describe information, products, or technologies that, if produced from life sciences research, might define that research as meeting the criterion for being DURC. The definitions have been reproduced below to assist institutions, IREs, and individuals in the consideration of the categories of experimental effects included in the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy*.

Biological agent: As is consistent with 18 U.S.C. § 178, "any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae or protozoa), or infectious substance, or any naturally occurring, bioengineered or synthesized component of any such microorganism or infectious substance, capable of causing - (A) death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism; (B) deterioration of food, water, equipment, supplies, or material of any kind; or (C) deleterious alteration of the environment."

Clinically and/or agriculturally useful prophylactic or therapeutic interventions: Includes first- or second-line prevention and treatment measures or alternative therapeutics used with special populations (e.g., pregnant women and pediatric patients) in the form of vaccines, antibiotics, antivirals, antiparasitics, antibodies, herbicides, fungicides, algaecides, insecticides, etc. "Agriculture" encompasses all methods of production and management of livestock, crops, vegetation, and soil. Therefore, useful prophylaxes and therapeutics would include herbicides, fungicides, algaecides, insecticides, rodenticides, etc.

Dissemination: The process by which infectious diseases or toxins are dispersed. The same routes of entry pertinent to the natural spread of diseases are also relevant when their etiologic agents are delivered intentionally (e.g., inhalation of biological agent disseminated as an aerosol or ingestion of a biological agent disseminated through a water supply).

Eradicated agent: A biological agent that has been exterminated through surveillance and containment resulting in the permanent reduction to zero of the worldwide incidence in the transmission of the agent and the infection/disease it causes; intervention measures are no longer needed. Eradicated agents are thought to no longer exist in circulation in plants, animals, or the environment. Note: Reconstituted eradicated agents of concern are those for which there are no known or widely available prophylactic or therapeutic interventions, those that could evade diagnostics, or those for which there is no known immunity.

Extinct agent: These agents are thought to no longer exist in nature or in the laboratory.

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[19] *Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information,* National Science Advisory Board for Biosecurity, 2007.

Harmful consequences: The ability of a biological agent or toxin to critically alter normal biological functions, inflict damage on public health resources, materiel, and public safety. This would include augmenting properties such as virulence, infectivity, stability, transmissibility, or the ability of the biological agent or toxin to be disseminated.

Host population: A collection of organisms that constitutes a specific group or occurs in a specified habitat. In the context of the DURC definition, this phrase implies that the misapplication of the knowledge, products, or technologies derived from the research has the potential to broadly impact a population of host organisms.

Host range: The number of different species or populations that can become infected by a biological agent, causing disease in the host or allowing the host to become a carrier.

Immunity: Encompasses all aspects of host immunity (e.g., active, adaptive, adoptive, passive, innate, and immune modulators).

Immunization: Refers to the active or passive induction of immunity through inoculation (e.g., natural inoculation or vaccination) with an immunizing agent or with antibodies; this includes antitoxins and toxoids.

Novel agent: An agent that has not existed previously and is considered unique based on its biological or other properties and traits (e.g., genotype and phenotype). Novel agents of concern are those for which there are no known or widely available prophylactic or therapeutic interventions, those that could evade detection, or those for which there is no known immunity.

Small interfering RNA (siRNA): Also known as "short interfering RNA" or "silencing RNA"; a class of RNA molecules that play a variety of roles in biology; most notably, siRNA is involved in the RNA interference (RNAi) pathway where the siRNA interferes with the expression of a specific gene.

Stability: The ability of a biological agent to remain viable when exposed to various environmental factors, including temperature, relative humidity, atmospheric pollution, and sunlight. Stability also includes persistence in a host.

Toxin: As is consistent with 18 U.S.C. § 178, "the toxic material or product of plants, animals, microorganisms (including, but not limited to, bacteria, viruses, fungi, rickettsiae or protozoa), or infectious substances, or a recombinant or synthesized molecule, whatever the origin and method of production, and includes: (A) any poisonous substance or biological product that may be engineered as a result of biotechnology that is produced by a living organism; or (B) any poisonous isomer or biological product, homolog, or derivative of such a substance."

Transmissibility: The ease with which an agent spreads from host to host or from vector to host, e.g., via arthropod vectors.

Tropism: The specificity of a biological agent or toxin for a particular host tissue or cell.

Appendix 2: Template for Notifying the IRE of Research That Requires Institutional Review

Note on this template: This template is designed to assist principal investigators (PIs) in conducting initial reviews and ongoing assessments of research that may be subject to DURC oversight. This template includes information that may be useful for the institutional review entity (IRE), should it be called upon to review the research.

The use of this template by institutions is optional. Institutions may choose to utilize this template as a starting point for developing their own materials or tools based on the specific issues or needs of the institution.

The *Policy for Institutional DURC Oversight* requires PIs at institutions subject to the Policy[20] to notify the IRE as soon as:[21]

A. The PI's research directly involves nonattenuated[22] forms of one or more of the listed agents; or

B. The PI's research with nonattenuated forms of one or more of the listed agents also produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects; or

C. The PI concludes that his or her research with nonattenuated forms of one or more of the listed agents that also produces, aims to produce, or can be reasonably anticipated to produce one or more of the seven listed experimental effects may meet the definition of DURC and should be considered (or reconsidered) by the IRE for its DURC potential.

This notification must include the PI's assessment of the applicability of any of the seven listed experimental effects. More information on the identification and assessment of research that requires institutional review can be found in **Section B** of the *Companion Guide*.

Each institution is responsible for establishing and implementing its own internal policies and practices that provide for the identification and effective oversight of DURC. This includes establishing a mechanism for the PI to immediately refer a project to the IRE, when applicable. The institution may require the use of a specific form and/or additional supporting documentation (e.g., project proposals, progress reports).

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[20] The *Policy for Institutional DURC Oversight* and its oversight requirements apply to the following institutions: (1) USG departments and agencies that fund or conduct life sciences research, (2) institutions within the United States that receive USG funds to conduct or sponsor life sciences research and conduct or sponsor research, regardless of source of funding, that involves 1 or more of the 15 agents or toxins listed in the Policy, and (3) institutions outside the United States that receive USG funds to conduct or sponsor research that involves 1 or more of the 15 agents or toxins listed in the Policy.

[21] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*, September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx, Section 7.1.A.

[22] The 15 agents and toxins listed in this Policy are subject to the select agent regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121), which set forth the requirements for possession, use, and transfer of select agents and toxins, and have the potential to pose a severe threat to human, animal, or plant health, or to animal or plant products. It is important to note, however, that the Federal Select Agent Program does not oversee the implementation of this Policy or the March 2012 DURC Policy.

Template for Notifying the IRE of Research That Requires Institutional Review

1. Contact Information

1.1 Principal Investigator (PI)

Name (Last, First, MI):	
Mailing address:	Phone number:
	Fax:
	Email:
Department (if applicable):	

1.2 Person Preparing This Document (If Not the PI)

Name:	Phone number:
Email:	Fax:

2. Project Information

Please identify any life sciences research you conduct at this institution that directly involves nonattenuated forms of one or more of the agents listed below (please use a separate form for each identified project). If none of the agents are identified, your research is *not* subject to institutional DURC oversight. However, PIs should be aware that, if at any time, research is initiated that involves any of the below listed agents, he or she will need to immediately notify the institutional review entity (IRE) (or appropriate institutional authority), per the policy of this institution.

2.1 Project Title(s)

2.2 Agent or Toxin Involved in Project (Check All That Apply)

- ☐ Avian influenza virus (highly pathogenic)
- ☐ *Bacillus anthracis*
- ☐ Botulinum neurotoxin (any quantity)
- ☐ *Burkholderia mallei*
- ☐ *Burkholderia pseudomallei*
- ☐ Ebola virus
- ☐ Foot-and-mouth disease virus
- ☐ *Francisella tularensis*
- ☐ Marburg virus
- ☐ Reconstructed 1918 influenza virus
- ☐ Rinderpest virus
- ☐ Toxin-producing strains of *Clostridium botulinum*
- ☐ Variola major virus
- ☐ Variola minor virus
- ☐ *Yersinia pestis*

2.3 Type of Funding Source(s) for This Project

- ☐ Department/institutional funds
- ☐ Foundation
- ☐ Federal funds
- ☐ Business /industry
- ☐ Other

If project is supported with Federal funds, name of funding agency and grant or contract number:

3. Training of Laboratory Personnel

The *Policy for Institutional DURC Oversight* requires 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 research with nonattenuated forms of 1 or more of the 15 listed agents have received education and training on DURC. Please indicate below the names of all laboratory personnel involved in this project and include the titles and dates of any DURC training.

Name	Title/Role	Title of DURC Training	Completion Date(s)

(Please insert more rows as necessary.)

4. Assessment by the PI for Experimental Effects

PIs are required to assess whether any research directly involving nonattenuated forms of 1 or more of the 15 listed agents produces, aims to produce, or is reasonably anticipated to produce 1 or more of the experimental effects listed in Section 6.2.2 of the *Policy for Institutional DURC Oversight* (relisted below). Note: the research and this assessment must be submitted to the IRE for review regardless of whether any of the following experimental effects apply.

☐ Enhances the harmful consequences of the agent or toxin.

If checked, please explain below:

☐ Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification.

If checked, please explain below:

☐ Confers to the agent or toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates its ability to evade detection methodologies.

If checked, please explain below:

☐ Alters properties of the agent or toxin in a manner that would enhance its stability, transmissibility, or ability to be disseminated.

If checked, please explain below:

☐ Alters the host range or tropism of the agent or toxin.

If checked, please explain below:

☐ Enhances the susceptibility of a host population to the agent or toxin.

If checked, please explain below:

☐ Generates or reconstitutes an eradicated or extinct agent or toxin listed in Section 2.2 of this form.

If checked, please explain below:

As a reminder, if there is a change in this research with respect to the applicability of any of the seven experimental effects, or if the PI, for any reason, thinks the research needs to be reconsidered by the IRE for DURC potential, the PI should submit this form again to the IRE with his/her revised assessment.

Appendix 3: Template for Assessment by the IRE of Research for DURC Potential

Note on this template: This template is designed to assist the institutional review entity (IRE) in its review and assessment of research for DURC potential. Such a review is initiated after a principal investigator (PI) identifies research directly involving nonattenuated forms of 1 or more of the 15 listed agents. This template guides IREs through the process of verifying that research meets the scope of the *Policy for Institutional DURC Oversight*, determining whether the research is DURC, and considering the risks and benefits of any identified DURC.

The use of this template by institutions or IREs is optional. Institutions may choose to utilize this template as a starting point to develop their own materials or tools based on the specific issues or needs of the institution.

The *Policy for Institutional DURC Oversight* requires that all research identified by a PI as directly involving nonattenuated[23] forms of 1 or more of the 15 listed agents be reviewed by an IRE. The responsibilities of the IRE in completing this step of the review process are as follows:[24]

- Verify that the research identified by the PI directly involves nonattenuated forms of one or more of the listed agents.
- Review the PI's assessment and make a final determination of the applicability of the listed experimental effects.
- If the research is assessed to meet the scope of the *Policy for Institutional DURC Oversight*, conduct a risk assessment and determine whether the research meets the DURC definition; the IRE should then immediately notify the appropriate institutional authority of the review outcomes.
- If the research meets the DURC definition, the IRE must consider both the identified risks and anticipated benefits, and it should then draft a risk mitigation plan (see **Sections C and D** of the *Companion Guide*).

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[23] The 15 agents and toxins listed in this Policy are subject to the select agent regulations (42 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121), which set forth the requirements for possession, use, and transfer of select agents and toxins, and have the potential to pose a severe threat to human, animal, or plant health, or to animal or plant products. It is important to note, however, that the Federal Select Agent Program does not oversee the implementation of this Policy or the March 2012 DURC Policy.

[24] *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*, September 24, 2014, http://www.phe.gov/s3/dualuse/Pages/default.aspx, Section 7.2.B.

Template for Assessment by the IRE of Research for DURC Potential

1. Contact Information

1.1 Institutional Review Entity

Name of entity:	Date(s) of review:
Mailing address:	Phone number:
	Fax:
	Email:
Department (if applicable):	

1.2 Person Preparing This Document

Name:	Phone number:
Email:	Fax:

2. Project Information

2.1 Principal Investigator

Name (First, Last, MI):	
Mailing address:	Phone number:
	Fax:
	Email:
Department (if applicable):	

2.2 Project Title(s)

2.3 Review(s) of Research by PI

Please list prior dates of reviews or assessments by the PI of research for DURC potential. For each date, please include a copy of the review or assessment.

Date

2.4 Agent or Toxin Involved in Project (Check All That Apply).

Please verify that this project directly involves nonattenuated forms of 1 or more of the 15 listed agents.

- ☐ Avian influenza virus (highly pathogenic)
- ☐ *Bacillus anthracis*
- ☐ Botulinum neurotoxin (any quantity)
- ☐ *Burkholderia mallei*
- ☐ *Burkholderia pseudomallei*
- ☐ Ebola virus
- ☐ Foot-and-mouth disease virus
- ☐ *Francisella tularensis*
- ☐ Marburg virus
- ☐ Reconstructed 1918 influenza virus
- ☐ Rinderpest virus
- ☐ Toxin-producing strains of *Clostridium botulinum*
- ☐ Variola major virus
- ☐ Variola minor virus
- ☐ *Yersinia pestis*

3. Assessment by the IRE for Experimental Effects

Please indicate whether the research project identified above produces, aims to produce, or can be reasonably anticipated to produce any of the following experimental effects. The IRE should review descriptions of the research in question, the PI's assessment of the applicability of the categories of experiments, and other relevant information, as warranted. Examples of materials to consider include the project proposal, any project reports, any outcomes of previous reviews for dual use, and examples of similar research in the literature.

☐ Enhances the harmful consequences of the agent or toxin.

If checked, please explain below:

☐ Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification.

If checked, please explain below:

☐ Confers to the agent or toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates its ability to evade detection methodologies.

If checked, please explain below:

☐ Alters properties of the agent or toxin in a manner that would enhance its stability, transmissibility, or ability to be disseminated.

If checked, please explain below:

☐ Alters the host range or tropism of the agent or toxin.

If checked, please explain below:

☐ Enhances the susceptibility of a host population to the agent or toxin.

If checked, please explain below:

☐ Generates or reconstitutes an eradicated or extinct agent or toxin listed in Section 2.4 of this form.

If checked, please explain below:

If *none* of the above experimental effects applies, the research does not meet the scope of the *Policy for Institutional DURC Oversight,* and the IRE does not need to continue with this assessment. The PI should be informed that if at any time the reviewed research produces or can be reasonably anticipated to produce a previously unanticipated experimental effect listed in Section 6.2.2 of the Policy, or if the reviewed research may meet the definition of DURC, he or she will refer it again to the IRE for review.

4. Risk Assessment by the IRE and Determination of DURC

The *Policy for Institutional DURC Oversight* defines DURC as follows:

> *Life sciences research that can be reasonably anticipated, based on current understanding, 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.*

When considering whether the research in question meets the definition above, the IRE should first identify the risks associated with the potential misuse of the information, technologies, or products that may be generated. Although risk assessments may be either quantitative or qualitative, the assessment process outlined below is qualitative in nature and requires the consideration and judgment of the IRE on the following:

- The *ways* in which knowledge, information, technologies, or products from the research could be misused to harm public health and safety, agriculture, plants, animals, the environment, materiel, or national security.
- The *ease with which* the knowledge, information, technologies, or products might be misused and the feasibility of such misuse.
- The *magnitude, nature, and scope* of the potential consequences of misuse.

4.1 Points to Consider in Assessing Research for Its Dual Use Potential

Consider the points below to assess the potential risks associated with conducting the research in question or communicating its results. These points address some of the aspects of potential DURC that could be considered, but they are not exhaustive – IREs should augment these points to fit their needs and the research under consideration. This risk assessment is intended to assist IREs in determining whether the research in question meets the definition of DURC. In cases where the research is determined to be DURC, this assessment will also inform the subsequent process of identifying strategies for mitigating those risks.

1. **The ways in which knowledge, information, technologies, or products from the research could be misused.** Address the following questions and considerations regarding the nature and disposition of the knowledge, information, technology, or products that could be generated by the research under consideration:

   a. What types of knowledge, information, technology, or products are anticipated to be generated through the research?

   b. How will the results or products of the research in question be shared or distributed? *Knowledge, information, technology, or products that are freely available and widely distributed may be more easily accessed by individuals with harmful intent.*

      – Who will have access to the knowledge, information, technology, or final products?

- Will it be shared openly or remain within the laboratory?

c. What is the novelty of the information provided by the research or of the research methods? *Research that adds novel information or consolidates information in novel ways may be of greater concern, whereas information that is already widely available is generally of lower concern.*

- Have the results of the research been previously described or shared?

- If so, at what venues and in what detail?

- How readily available are these results?

d. Are the products of the research under consideration applicable to other more common or less pathogenic organisms or agents? *Knowledge, information, technology, or products generated from research that could be applied to more commonly available organisms to increase their associated risks may be of greater concern.*

e. Does the research highlight vulnerabilities in existing countermeasures or public health or agricultural infrastructure?

- Does the research highlight weaknesses in the ability to prepare for and respond to disease outbreaks that could impact public, agricultural, or environmental health?

- Does the research consolidate existing information in ways that highlight vulnerabilities in public health and/or safety preparedness?

2. **The ease with which the knowledge, information, technologies, or products might be directly misused and the feasibility of such misuse.** IRE members are not expected to have expertise in national security, but IRE members and investigators in general are in a good position to make technical assessments about how readily and in what ways certain knowledge, information, technologies, or products obtained from research might be misused. Address the following questions and considerations regarding factors that impact the likelihood of misuse, including technical feasibility, level of expertise, necessary reagents, or the need for additional scientific advances or technologies.

a. Consider the technical expertise and/or physical resources that would be needed to apply the knowledge, information, technology, or product for malevolent purposes. *The risk of misuse may be lower for knowledge, information, technologies, or products that would be expensive, difficult to procure, or that require a high degree of technical skill to facilitate such misuse.*

   – Would it require a low or high degree of technical skill and sophistication to use the information from dual use research for harmful purposes?

   – Would its misuse require materials, equipment, or reagents that are expensive or difficult to procure?

b. Consider whether the products of the research in question could be directly misused to pose a threat to public health and safety, agriculture, plants, animals, the environment, materiel, or national security. *The risk of misuse may be higher for research information that can be directly misused than for research information that requires significant additional scientific advances to facilitate its misapplication.*

   – Can the products, information, or technologies generated from the research be directly misapplied? If so, how?

   – If not, do these outcomes of the research need to be combined with other knowledge, information, technology, or products in order to pose a threat? If so, is that other information already available?

c. Consider the time frame in which information from the research might be misused. *Information that can be misused in the near term may be of greater concern.*

   – Is there concern about immediate or near-future potential use, or is the concern about misuse in the distant future?

d. Given your responses to the preceding questions, how readily could the knowledge, information, technology, or products from the research be used to threaten public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security?

3. Potential consequences of misuse. When considering the potential consequences of the misuse of scientific knowledge, information, technology, or products obtained from research, think broadly about the potential impacts on public health, agriculture, the environment,

and/or the economy from the intentional misapplication of the results from the research in question. In general, information that could be misused to harm large populations of humans, plants, or animals; cause public panic; or require costly response efforts would be considered a greater risk.

a. Consider the nature of the potential consequences (e.g., harm to the economy, the environment, agriculture, or public health; public terror) that might result from misuse of the research results in question. *Information that could be misused to harm numerous sectors of society or the environment may be of greater concern.*

b. Consider the scope and magnitude of the potential consequences. *Research or research information that could be misused to cause severe harm, disease, or consequences is generally considered to be of greater concern.*

   – Could the impact on people, plants, and/or animals be considered minor, moderate, or major?

c. Consider the available countermeasures. *Adequate countermeasures may help to decrease concern about the consequences of misuse. Countermeasures may include drugs, biological products, public health practices, pesticides, or devices intended for diagnosis, detection, mitigation, prevention, or treatment.*

   – Are there currently any countermeasures to help mitigate the potential consequences?

   – Are they readily available?

4.2 Apply the DURC Definition

The IRE should consider the identified risks in determining whether the research in question meets the definition of dual use research of concern (DURC): *"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."*

If the IRE determines that the research *does not* meet the DURC definition, the research is not subject to additional institutional DURC oversight. However, the institution must still notify the appropriate USG funding agency of the findings of the institutional review. If significant concerns about dual use remain, the ICDUR should be informed. The ICDUR and the IRE may choose to consult with a representative of the USG department or agency that is funding the research in question.

If the IRE determines that the research *does* meet the DURC definition, the research is DURC, as defined in the *Policy for Institutional DURC Oversight* and the *March 2012 DURC Policy*, and is subject to additional DURC oversight. The IRE should inform the PI of its findings and proceed with the review process, which includes the development of a draft risk mitigation plan. The institution must notify the appropriate USG funding agency of the IRE's findings within 30 calendar days of review.

5. Risk-Benefit Assessment of DURC

For research that has been identified as DURC, it is important to assess the research for its anticipated benefits and to weigh those benefits with the risks identified in Step 4. This process will help determine the acceptable level of risk and inform the most appropriate mitigation strategies. The IRE should use the answers to Step 4 and Step 5 in developing a risk mitigation plan for conducting the research and communicating its findings.

5.1 Points to Consider in Assessing the Benefits of the DURC

The benefits inherent to scientific research are many. Such benefits may impact various sectors of society and be realized over different time frames. The points below address *some* of the aspects of the research that could be considered, but they are not exhaustive – IREs should augment these points to fit their needs and the research under consideration.

a. Are there potential benefits to the public's health and/or safety from the research?

b. Are there potential benefits of the research for agriculture, plants, animals, the environment, materiel, or national security?

   – What potential solution does it offer to an identified problem or vulnerability?

c. Will this research be useful to the scientific, public health, or public safety communities? If so, how?

d. Because scientific research can have broad impacts, it is important to consider the scope of the potential benefits.

   – Will the knowledge, information, or technology generated from the research be broadly applicable (e.g., to human health, multiple scientific fields, populations of organisms)?

– What populations of plants or animals might be positively affected?

e. If a benefit has been identified, in what time frame (e.g., immediate, near future, years from now) might this research benefit science, public health, agriculture, plants, animals, the environment, materiel, or national security?

5.2 Points to Consider for Weighing the Risks and Benefits of the DURC

This can be the most challenging step in the risk-benefit assessment; it is often described as a step that entails "weighing" or "balancing" the risks with or against the benefits of DURC. This language, however, suggests that risks and benefits can be quantified and that they are commensurable. This is rarely, if ever, the case.

The process of weighing the risks and benefits of DURC is an exercise in making defensible, rational judgments in the midst of unavoidable uncertainty. Uncertainty can best be managed by ensuring that the process draws on the expertise and perspectives of a group of individuals of diverse backgrounds and experience. Discussion and debate within such a group can help to (a) identify and mitigate the biases that individuals inevitably bring to the challenges of this sort, (b) uncover often implicit assumptions in arguments, (c) scrutinize and test the basis for judgments, and (d) yield conclusions that represent a consensus (literally, "a thinking together") and are optimally defensible.

a. Could the information of concern be more readily applied to improvements in surveillance or to the development of countermeasures than to malevolent applications? What reasons or evidence support the answer to this question?

b. What is the time frame in which potential benefits or anticipated risks might be realized?

c. How might the potential benefits and the anticipated risks be distributed across different populations (humans and animals)?

– Who or what will be the likely beneficiaries of the potential benefits? Will the potential benefits be distributed equally or disproportionately across different populations? (Here, it will be helpful to keep in mind that, for example, human populations may differ in

terms of size: The potential benefits may accrue to a large or, alternatively, to a small number of individuals. Or, human populations may differ along socioeconomic or cultural lines: The potential benefits may accrue to or have little impact on a vulnerable or low-resourced population versus a well-resourced population.)

– Who or what will bear the anticipated risks? Is it likely that one or more specific populations will bear the burden of the anticipated risks?

– Is it likely that the distribution of the anticipated risks and the potential benefits will be fair or just?

d. Considering the anticipated risks in tandem with the potential benefits, are the risks of such a feasibility and magnitude that they warrant proceeding after developing and implementing a risk mitigation plan? Are the potential benefits of significant magnitude to warrant proceeding despite the risks? What is the most responsible way to proceed? For the vast majority of cases of DURC, an appropriate risk mitigation plan can be developed and effectively implemented.

Appendix 4: Template for 30-Day Reporting of Research That Meets the Scope of the *Policy for Institutional DURC Oversight*

Section 7.2 of the *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern* outlines the responsibilities of federally funded research institutions for the oversight of research with DURC potential. This oversight process begins with identification by the principal investigator (PI) of research involving any of the 15 agents listed in the Policy. Any such research must be referred to the institutional review entity (IRE) along with the PI's assessment of whether the research involves any of the seven listed experimental effects. When an IRE determines that research directly involving nonattenuated[25] forms of any of the 15 listed agents also involves 1 or more of the 7 experimental effects, the institution must report this information within 30 calendar days to the appropriate USG funding agency, as described in Section 7.2.B.iv, below. This reporting template is intended for the institutional contact for dual use research (ICDUR) and is designed to assist the institution in meeting the 30-day reporting requirement.

Section 7.2.B.iv:

> *Within 30 calendar days of the institutional review of the research for DURC potential, notification to the USG (US Government) funding agency of any research that involves 1 or more of the 15 listed agents and 1 or more of the 7 listed experimental effects (Section 6.2), including whether it meets or does not meet the definition of DURC. For non-USG-funded research, notification should be made to the National Institutes of Health, which will in turn refer the notification to an appropriate USG funding agency, based upon the nature of the research (per Section 7.E). This initial notification should include: the grant or contract number related to the research (if the research is funded by the USG); the name(s) of PI(s); the name(s) of the agent(s) listed in Section 6.2.1 of the Policy; and a description of why the research is deemed to produce one or more of the experimental effects listed in Section 6.2.2 of the Policy. For research that is determined by the IRE to meet the definition of DURC, the notification should also include: the name of the investigator (if different from the PI) responsible for the performance of the DURC, and a description of the IRE's basis for its determination.*

[25] The only forms of the agents or toxins listed in the USG DURC policies that are considered by the USG to be attenuated and therefore not subject to the requirements of these policies, can be found in the Select Agent and Toxin Exclusions list under "Attenuated Strains of HHS and USDA Select Agents and Toxins" at http://go.usa.gov/8rwQ.

Reports of federally funded research should be submitted directly to the relevant USG funding agency.

Reports of non-USG-funded research should be submitted to the National Institutes of Health via one of the following:

1. U.S. mail, courier service, or facsimile to:
   Attention: Institutional DURC Oversight Policy Reporting
   NIH Program on Biosecurity and Biosafety Policy
   6705 Rockledge Drive, Suite 750
   Bethesda, MD 20892-7985
   (For all non-USPS US Postal Service deliveries use Zip Code 20817)
   Telephone 301-496-9838
   Fax 301-496-9839

2. Email: DURC@od.nih.gov

Template for 30-Day Reporting of Research That Meets the Scope of the *Policy for Institutional DURC Oversight*

Date of Report: _____

1. Contact Information

1.1 Institutional Contact for Dual Use Research (ICDUR)

Name:	Phone number:
Email:	Fax:

1.2 Person Completing This Form (If Different from ICDUR)

Name:	Phone number:
Email:	Fax:

2. Project Information

2.1 Principal Investigator (PI) or Other Scientist Responsible for This Research

Name (Last, First, MI):	
Mailing address:	Phone number:
	Fax:
	Email:
Department (if applicable):	

2.2 Funding Source(s)

U.S. Government agency funding this research *(If more than one source, list all that apply. For non-USG-funded research, please provide the name of the funding entity and point of contact)*:
Grant/contract number *(For non-USG-funded research, please provide a project identifier)*:

2.3 Project Title(s)

2.4 Project Description (Non-USG-Funded Research Only)

If the project is not supported with U.S. Government funds, please provide sufficient detail describing the nature of this research (*e.g., description of agent and how it is to be used, animal models, methods and procedures, biosafety and biosecurity measures*) that will allow for complete and accurate review by the designated USG funding agency. Alternatively, this information may be provided as supplemental material *(see Section 4)*.

3. Institutional Review

3.1 Institutional Review Entity

Name of entity:	Date(s) of review:
Mailing address:	Phone number:
	Fax:
	Email:

3.2 Agent or Toxin Involved in Project (Check All That Apply)

- ☐ Avian influenza virus (highly pathogenic)
- ☐ *Bacillus anthracis*
- ☐ Botulinum neurotoxin (any quantity)
- ☐ *Burkholderia mallei*
- ☐ *Burkholderia pseudomallei*
- ☐ Ebola virus
- ☐ Foot-and-mouth disease virus
- ☐ *Francisella tularensis*
- ☐ Marburg virus
- ☐ Reconstructed 1918 influenza virus
- ☐ Rinderpest virus
- ☐ Toxin-producing strains of *Clostridium botulinum*
- ☐ Variola major virus
- ☐ Variola minor virus
- ☐ *Yersinia pestis*

3.3 Assessment by the IRE for Experimental Effects

Please indicate whether the research produces, aims to produce, or can be reasonably anticipated to produce any of the experimental effects listed below. Check all that apply.

☐ Enhances the harmful consequences of the agent or toxin.

If checked, please explain below:

☐ Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification.

If checked, please explain below:

☐ Confers to the agent or toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates its ability to evade detection methodologies.

If checked, please explain below:

☐ Alters properties of the agent or toxin in a manner that would enhance its stability, transmissibility, or ability to be disseminated.

If checked, please explain below:

☐ Alters the host range or tropism of the agent or toxin.

If checked, please explain below:

☐ Enhances the susceptibility of a host population to the agent or toxin.

If checked, please explain below:

☐ Generates or reconstitutes an eradicated or extinct agent or toxin listed in Section 3.2 of this form.

If checked, please explain below:

3.4 Determination by the IRE of Whether the Research Meets the Definition of DURC

Please provide the IRE's rationale for why the research does or does not meet the definition of DURC. The *USG Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern* defines DURC as "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."

4. Supplemental Materials

Please provide as attachments any additional information relevant to this research that may aid in the USG funding agency's review and assessment of this research, particularly any elements the IRE used during its institutional review process. These may include the following:

- Project proposals
- Progress reports
- Scientific abstracts
- Published manuscripts
- Assessment by the PI for dual use
- IRE meeting minutes
- Institutional biosafety committee meeting minutes
- Risk assessments
- Safety inspections

Appendix 5: Export Controls and DURC – Guidance for Institutions and Principal Investigators

1. What are export controls?

Export controls are a mechanism by which the United States regulates the export of controlled goods and activities to ensure consistency with U.S. foreign policy and national security interests, U.S. law, and its international commitments. This includes prohibiting the export of any goods, technology,[26] or services that would assist anyone in acquiring the capability to develop, produce, stockpile or use weapons of mass destruction (WMD). To implement this prohibition, the United States regulates the transfer of certain technology and materials to foreign parties (including individuals) by requiring export licenses.

2. Which export regulations apply to DURC?

It is expected that most DURC that is subject to export controls would be controlled under the Export Administration Regulations (EAR) administered by the Department of Commerce, Bureau of Industry and Security. There are generally two types of export transactions: (1) transferring controlled material or technology outside the United States; and (2) transferring controlled technology to non-U.S. persons who are within the United States which is considered a "deemed export."

However, under certain circumstances, the International Traffic in Arms Regulations (ITAR) may apply to DURC items (including materials and information). For information on these controls, see Title 22, Code of Federal Regulations, Parts 120 through 130 (ITAR) - including but not limited to: Part 121.1 Category XIV "Toxicological Agents, Including Chemical Agents, Biological Agents and Associated Equipment," and, Part 120.11 "Public Domain." For further assistance, please see www.pmddtc.state.gov. Note that the order of precedence for export controls first requires a determination of whether an item is ITAR-controlled. If it is not ITAR-controlled, DURC may be subject to the EAR. The remainder of this guidance document applies only to the EAR.

Please note that this guide includes discussion on certain aspects of the EAR and may not include all the details associated with the control of an item. For more details on the application of controls and compliance with these controls, please review the applicable regulations, including those listed in Question 8.

3. How do EAR export controls apply to research identified under the USG DURC Oversight policies?

The fifteen agents listed in the USG DURC Oversight policies are all included on the EAR control list (For the complete list, see Part 774 of the EAR available under the "Regulations" tab on the Bureau of Industry and Security homepage at www.bis.doc.gov.) This means that transfers of these materials and/or information or technology

[26]The EAR define "technology" as specific information necessary for the "development", "production", or "use" of a product (Part 772).

related to their development, production, or manipulation are subject to the EAR and may require an export license or a deemed export license.

To foster scientific advances, certain information and technology are exempted from this export license requirement as described in Question 4 below, including information that is in the public domain, information resulting from fundamental research, and information that is normally published. This information is not subject to the EAR.

Note: Identification of research as DURC has no direct bearing on whether or not an export license is required. However, certain risk mitigation measures (e.g., the imposition or acceptance of restrictions on publication) MAY affect whether the research is subject to the EAR. Institutions and researchers should be aware of this possibility. Assistance is available from the Department of Commerce, Bureau of Industry and Security for determining licensing and other requirements. Please see www.bis.doc.gov.

4. What types of information are not subject to the EAR (15 CFR Parts 734.7-10)?[27]

- Information resulting from fundamental research (see details below).
- Publicly available information: generally accessible to the interested public in any form.
- Printed books.
- Educational information: released by instruction in catalog courses and associated teaching laboratories of academic institutions.
- Information contained in patent applications.
- Technology that is subject to other export regulations (see Question 8).

5. What is considered fundamental research under the EAR (15 CFR Part 734.8)?

Fundamental research is described in the EAR as "basic and applied research in science and engineering, where the resulting information is ordinarily published and shared broadly within the scientific community." The techniques used during the research are normally publicly available or are part of the published information. (Please note: The fundamental research exclusion does not apply to physical objects such as pathogens or equipment.)

> **Example:** Researchers from two universities, one in the U.S. and the other in the United Kingdom (UK), are collaborating on a project that involves vector identification for Marburg virus. There are no restrictions on publication of findings generated from the research. Therefore, the research would be considered fundamental and the information resulting from this research, such as the results and methods, are not subject to the EAR. There would be no "deemed export" required for foreign nationals working at the U.S. university and no export license required for discussing research methods and outcomes between the two universities. However, an export license would be required for the export of the Marburg virus samples to the UK university.

[27]The items listed here are not an exclusive list. For additional information, please see 15 CFR Parts 734.7-10.

6. What types of research are NOT considered fundamental research under the EAR (15 CFR Part 734.8)?

Research is not considered fundamental research when the Laboratory, Company, University or researcher restricts the publication of the outcome of the research or restricts the publication of the methods used during the research. The following are examples of research that is not considered fundamental and information that becomes subject to the EAR:

- Proprietary research.
- Any research methods or outcomes of government-funded research for which a decision has been taken to specifically restrict publication. Only the information that is redacted would become subject to the EAR; the remainder of the research methods and outcomes that have not been subject to restriction would be considered information resulting from fundamental research.
- Any research methods or outcomes of government-funded research that have been communicated in violation of any condition that may exist in the funding instrument that requires prepublication security review of the research communication. (Government funding agencies have the discretion to require future prepublication security review of the methods or outcomes of research without changing the fundamental nature of the research as it is being conducted.)
- Research methods or outcomes that an investigator voluntarily decides should not be communicated widely because of a decision that has been taken to specifically restrict publication. Only the information that is redacted would become subject to the EAR; the remainder of the research methods and outcomes that have not been subject to a decision taken to restrict publication would be considered information resulting from fundamental research.

  Example: Government-funded researchers studying *Bacillus anthracis* accept national security prepublication review of their research. If the group complies with the review requirement and does not communicate this research without the required reviews, their research remains fundamental research. However, any of the information resulting from this research for which a decision is taken to restrict from publication due to DURC concerns will become subject to the EAR. Research methods and outcomes from the same project that are not subject to a decision taken to restrict publication would remain information resulting from fundamental research and not subject to the EAR.

Specific decisions taken to restrict publication, regardless of the source of the decision, would mean that the technology not published is technology subject to the EAR. This decision is not retroactive so it would not impose a license requirement for exports of the information that have already taken place, but may trigger a license requirement for future exports of the information and future deemed export licenses as necessary.

If you have questions about whether or not your research is considered fundamental research, then you or someone designated by your institution should contact Kimberly Orr at the Department of Commerce at Kimberly.orr@bis.doc.gov.

7. Do the Export Administration Regulations restrict my ability to publish the results of my research?

Export Administration Regulations are not export "bans." They do not and should not impede legitimate academic freedom and information exchange that are unrelated to chemical and biological weapons, to include

patent applications or the publication of fundamental research in the public domain. There is no export license required to publish information (see Supplement #1 to Part 734 Section A, Question A:1, available under the "Regulations" tab on the Bureau of Industry and Security homepage at www.bis.doc.gov). You must review contract or grant clauses to ensure you do not violate any national security controls that may be required by the funding agency.

8. In addition to the EAR, are there other classes of exports that are regulated?

In addition to the EAR, other departments and agencies have jurisdiction over certain other classes of exports, including:

- The State Department's ITAR addresses goods, technology, and services that are controlled as 'defense articles' or 'defense services,' including technology that could be a subset of DURC. For additional details regarding the ITAR, please see www.pmddtc.state.gov.
- The Department of the Treasury, Office of Foreign Assets Control (OFAC) administers controls against certain countries (Iran, North Korea, Cuba, Syria, etc.), individuals, and entities that are subject to sanctions affecting exports, imports, and financial dealings. For additional details, please see www.treasury.gov/resource-center/sanctions/.
- The U.S. Nuclear Regulatory Commission, the Department of Energy, and the Patent and Trademark Office also control certain exports. For a summary of these agencies' controls, see Part 734.3 of the EAR, available under the "Regulations" tab on the Bureau of Industry and Security webpage at www.bis.doc.gov.