

Institutional Oversight of DURC

NIH OSP Stakeholder Engagement Workshop

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Select Agent Responsible Official

Institutional Contact for Dual-Use Research



THE UNIVERSITY OF
CHICAGO

Research, Innovation
and National Laboratories
Office of Research Safety

DURC Risk Mitigation

Describe the process and expertise involved in the development and implementation of risk mitigation plans.

UC DURC Task Force

Membership

Dave Pitrak, M.D.

Professor and Chief, Infectious Diseases

Chair-Select Agent Institutional Biosafety Committee

Nick Dulin, Ph.D.

Associate Professor of Medicine

Chair-Institutional Biosafety Committee

Gopal Thinakaran, Ph.D.

Professor of Neurobiology

Former Chair-Institutional Biosafety Committee

Sean Crosson, Ph.D.

Professor of Biochemistry and Molecular Biology

DURC Principal Investigator

Balaji Manicassamy, Ph.D.

Assistant Professor of Microbiology

DURC Principal Investigator

Mike Ludwig

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Russ Herron, J.D.

Senior Associate General Counsel

Office of General Counsel

Bill Pugh

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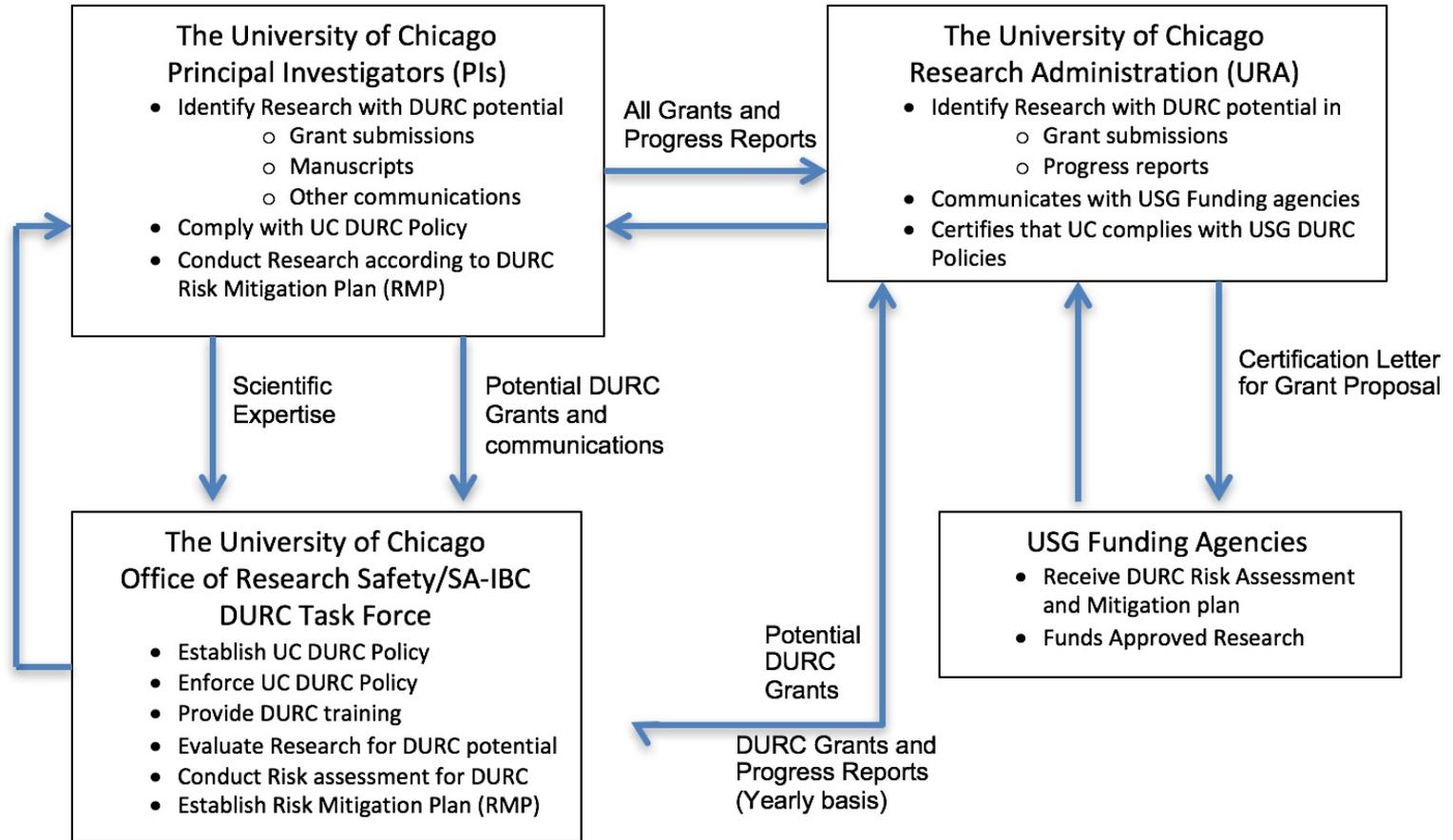
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DURC Governance

University of Chicago



What challenges and/or best practices associated with developing or implementing risk mitigation plans have you encountered?



Framework for IRE Review of Risk Mitigation Plans*

Step 1: Review the research to verify that it still directly involves non-attenuated 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.

*Tools for the Identification, Assessment, Management, and Responsible Communication of Dual Use Research of Concern : A Companion Guide to the USG 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



Possible risk mitigation measures:*

- Consider changing the timing, mode, or venue of communication for the DURC in question.
- Establish a mechanism for prepublication or pre-communication 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.

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UC DURC Management

The UC IBC DURC Task Force provides binding recommendations and supervision on any one of the following:

1. Design or conduct of the investigator's research with DURC;
2. Requirements for enhanced biosafety or biosecurity measures for the investigator's research with DURC;
3. Evaluation of existing evidence of medical countermeasure (MCM) efficacy, or conducting experiments to determine MCM efficacy against agents or toxins resulting from DURC, and where effective MCM exists, including that information in publications;
4. Utilizing the educational tools of NSABB on biosecurity and Dual Use Research of Concern to educate and train the investigator and the scientific team involved in this research.

UC DURC

Assessment and Communication

DFT assessment of DURC

- 1. Could this research yield information that could be intentionally misused to threaten public health and safety or other aspects of national security?**
- 2. What is the nature of the threat that could be posed from intentional misapplication of the information, and what are the potential consequences?**
- 3. Could this research yield information that could potentially benefit the life sciences and/or public health and safety and other aspects of national security?**
- 4. Do the potential risks of publishing these research findings and conducting the proposed experiments outweigh the potential benefits?**

DURC Risk Mitigation

ELEMENTS COMMON TO ALL UC DURC RISK MITIGATION PLANS

- Description of enhanced biosafety and biosecurity measures in place in all formal communications (e.g. manuscript, abstract, poster, etc.);
- Training investigators on DURC;
- Forum for on-going monitoring of DURC projects;
- Installment of an ethical *Code of Conduct* for all research involving Select Agents (SA);
 - Signed annually by all DURC investigators;
 - Discussed during annual interviews with all SA Investigators;
- Discussion of the public health benefits to be derived from DURC research included in all forms of formal communication.

How is the potential for “information risk” considered and addressed?

- Description of enhanced biosafety and biosecurity measures in place in all formal communications (e.g. manuscript, abstract, poster, etc.);
- Discussion of the public health benefits to be derived from DURC research included in all forms of formal communication.
- Language used to describe findings crafted carefully to draw attention to benefits while deflecting focus from nefarious outcome potential



What has been your experience interacting with funding agencies and/or scientific journals, or others entities within your institution, on mitigating risks?



Elements unique to specific DURC risk mitigation plans

Herpes simplex virus (April, 2010):

- Unanticipated generation of a hyper-virulent strain of Herpes simplex virus reported to IBC by PI;
- Work with hyper-virulent HSV moved to BSL3 and soon thereafter placed on permanent hold;
- PI requested that the IBC require any MTA related to this virus only be executed with the following language:

Elements unique to specific DURC risk mitigation plans

Herpes simplex virus (April, 2010):

This Material Transfer Agreement is contingent upon receipt by the University of Chicago Office of Research Administration of a letter from the Institutional Biosafety Committee of the requesting institution that a protocol for the use of this virus in vitro has been approved at BSL3 containment and that a protocol for in vivo use has been approved at ABSL3 (as described in the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories, 5th edition.



Elements unique to specific DURC risk mitigation plans

Bacillus anthracis:

1. Grant flagged by NIH as DURC in 2011; grant aimed at development of *B.a.* vaccines.
2. Manuscript prepared for publication. One study described a virulent *B.a.* strain that could evade immune protection conveyed by licensed vaccine.
3. NSABB reviewed manuscript and determined that the manuscript *“does not rise to the level of concern”*.
4. NSABB made recommendations and suggested revisions concerning manuscript, concluding that *“the manuscript has the potential to be misunderstood by the public and sensationalized as dual use research of concern.”*
5. UC DURC Task Force formed in response to NIH requirements for management of this research.



Elements unique to specific DURC risk mitigation plans

Yersinia pestis:

1. Grant flagged by NIH as DURC in 2011; grant aimed at development of *Y.p.* vaccines.
2. UC DURC Task Force (DTF) formed in response to NIH requirements for management of this research.
3. Manuscript submitted (Feb., 2014) to UC DURC task force describing generation of hyper-virulent *Y.p.* strain.

Elements unique to specific DURC risk mitigation plans

Yersinia pestis:

4. DTF determines findings to represent DURC;
5. NIAID confirms DURC assessment (March, 2014) and provides recommendations:
 - 1) *Include procedures undertaken by your institution to assess DURC;*
 - 2) *Include results of this assessment;*
 - 3) *Describe how the benefits of communication outweigh the risks; and*
 - 4) *Describe the risk mitigation strategies employed.*
 - Biosafety and biosecurity;
 - Antibiotic sensitivity confirmed;
 - *Code of conduct*

Elements unique to specific DURC risk mitigation plans

Staphylococcus aureus:

- **January 2015:** PI requested that the IBC approve a study to examine *Staphylococcus aureus* virulence factors and proposed cloning and expression of genes associated with these factors in opportunistic pathogens *Staphylococcus epidermidis* and *Staphylococcus simulans*.

Elements unique to specific DURC risk mitigation plans

Staphylococcus aureus:

- **June, 2016:** PI requested that the IBC weigh in on the DURC potential of a manuscript reporting findings of this research:

“...does not result in the generation of a pathogen exhibiting the invasiveness of pathogenic Staphylococcus aureus. As such, we agree with your assessment that conferring this invasive phenotype does not result in a pathogen that could be used to threaten public health.”

Elements unique to specific DURC risk mitigation plans

Influenza virus: *Gain-of-Function (GoF)* reviews:

1. Principal Investigator #1: July, 2014:

- Proposed research involved the expression of neuraminidase and hemagglutinin H1 and H5 from Influenza A, the work involves only the epitopes of these gene products and does not involve either H5N1 HPAI nor 1918 H1N1 influenza.
- Work neither GoF nor DURC more broadly.

Elements unique to specific DURC risk mitigation plans

Influenza virus: *Gain-of-Function (GoF)* reviews:

2. Principal Investigator #2: October, 2014:

- PI informed by NIH that one of the Specific Aims of grant was covered under the USG funding pause;
 - This Aim was to investigate how a particular viral protein antagonizes innate immune responses *in vivo*.

Elements unique to specific DURC risk mitigation plans

Influenza virus: *Gain-of-Function (GoF)* reviews:

2. Principal Investigator #2: January, 2015:

- UC DURC Task Force determines that experimental design mitigates risk and that, as proposed, the research did not represent *Gain-of-Function Research of Concern*.
- NIH subsequently disagreed, determining that one specific aim did represent *Gain-of-Function Research of Concern*.

Elements unique to specific DURC risk mitigation plans

Influenza virus: *Gain-of-Function (GoF)* reviews:

2. Principal Investigator #2: April, 2015:

- UC DURC Task Force determines that research plan did represent *Gain-of-Function Research of Concern*, but that proposed experimental design mitigates the risk:
 - a. Conduct experiments in PR8 background (attenuated);
 - b. Employ BSL3 practices for these studies.
 - c. Antiviral sensitivity confirmed.

USG Biosafety Incidents Summer 2014 *GoF* Moratorium

- Centers for Disease Control and Prevention
 - June 6-13, *Bacillus anthracis*
 - March - July 9, Avian influenza H5N1
- Food and Drug Administration
 - July 2 discovery of Variola virus at FDA facility on National Institute of Health campus