Institutional Oversight of DURC

NIH OSP Stakeholder Engagement Workshop

September 25-26, Chicago, Illinois

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THE UNIVERSITY OF CHICAGO | Research, Innovation and National Laboratories
Office of Research Safety

What is the relationship between the structure and functions of the IRE and the IBC at your institution?

Institutional Biosafety Committees

Hyde Park Campus IBC

- Requires registration of ALL rDNA research
- Requires registration of all research involving pathogens (human, animal, plant)
- Requires registration of all research involving biological toxins

Select Agent IBC

- All UCM Select Agent research
- All research conducted at the Howard T. Ricketts Regional Biocontainment Laboratory

Institutional Biosafety Committees and DURC Review
Why Me?

- I have no formal training in biosafety
- I run a small clinical immunology lab that has utilized biohazardous agents (Candida spp. Aspergillus spp., C difficile)
- I came to UCM as Section Chief of Infectious Diseases in 2002
- I joined the IBC in 2002, with the responsibilities as the Infectious Diseases physician member to assess the health and medical recommendations for all agent profiles submitted with IBC protocols
  - Health risk (host factors, mode of transmission, and communicability)
  - Immunizations
  - Surveillance (fever watch, clinical symptoms, and diagnostic work up)
  - Post-exposure prophylaxis
  - Other management of exposures and/or laboratory-acquired infection
    - Treatment
    - Isolation precautions

Institutional Biosafety Committees
Why Me?

- I was asked to chair the new SA-IBC in 2007 when the Select Agent Program was started at UCM and during the planning, construction, and finally commissioning of the Ricketts Biosafety Containment Lab at Argonne
- Again, my individual key responsibilities were
  - Developing fever watch protocols and medical management in the event of illness or known exposure for each select agent, including isolation precautions
  - Involved in a rapid response to any potential exposure
- DURC review policies were established in 2012, 2 years before the US Government Sept 2014 Policy for Institutional Oversight of Life Sciences Dual Use Research Concerns

Briefly describe the composition and operation of your IRE and the procedures in place for initiating project review.

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
Associate Vice-President and Director
University Research Administration

Russ Herron, J.D.
Senior Associate General Counsel
Office of General Counsel

Bill Pugh
Director
Office of Laboratory Regulatory Compliance

Joe Kanabrocki, Ph.D., NRCM(SM)
Professor of Microbiology
Associate Vice-President for Research Safety
Select Agent Responsible Official
Institutional Contact Dual-Use Research

What is the scope of research reviewed by the IRE and what are the parameters used to determine whether research is anticipated to produce one or more of the 7 experimental effects and/or meet the definition of DURC?

DURC Policy

- The DURC policy outlines the agents and toxins as well as category of experiments that would render a protocol dual use
- Although the policy lists the 15 Select Agents and Toxins subject to DURC regulations, our group will also review protocols for any agent that is flagged as DURC at the time of IBC review even though they are not on this list
- Although the PI is responsible for identifying a protocol as DURC, no SA-IBC protocol is approved without a full meeting where the potential for DURC is assessed by the reviewers and the committee members, i.e., we don't only rely on the assessment of the PI

Scope of Research that Requires DURC Oversight
Agents and Toxins

- **Avian influenza virus (highly pathogenic)**
- ***Bacillus anthracis***
- Botulinum neurotoxin
- For the purposes of this Policy, there are no exempt quantities of botulinum neurotoxin. Research involving any quantity of botulinum neurotoxin should be evaluated for DURC potential.
- *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***

9.0 Dual-Use Research of Concern

Dual-Use Research of Concern (DURC) 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, material, or national security. An assessment of the proposed research for DURC potential is an essential element of the responsible and ethical conduct of research.

Assess your research plan for DURC by responding to the following questions concerning the potential experimental outcome:

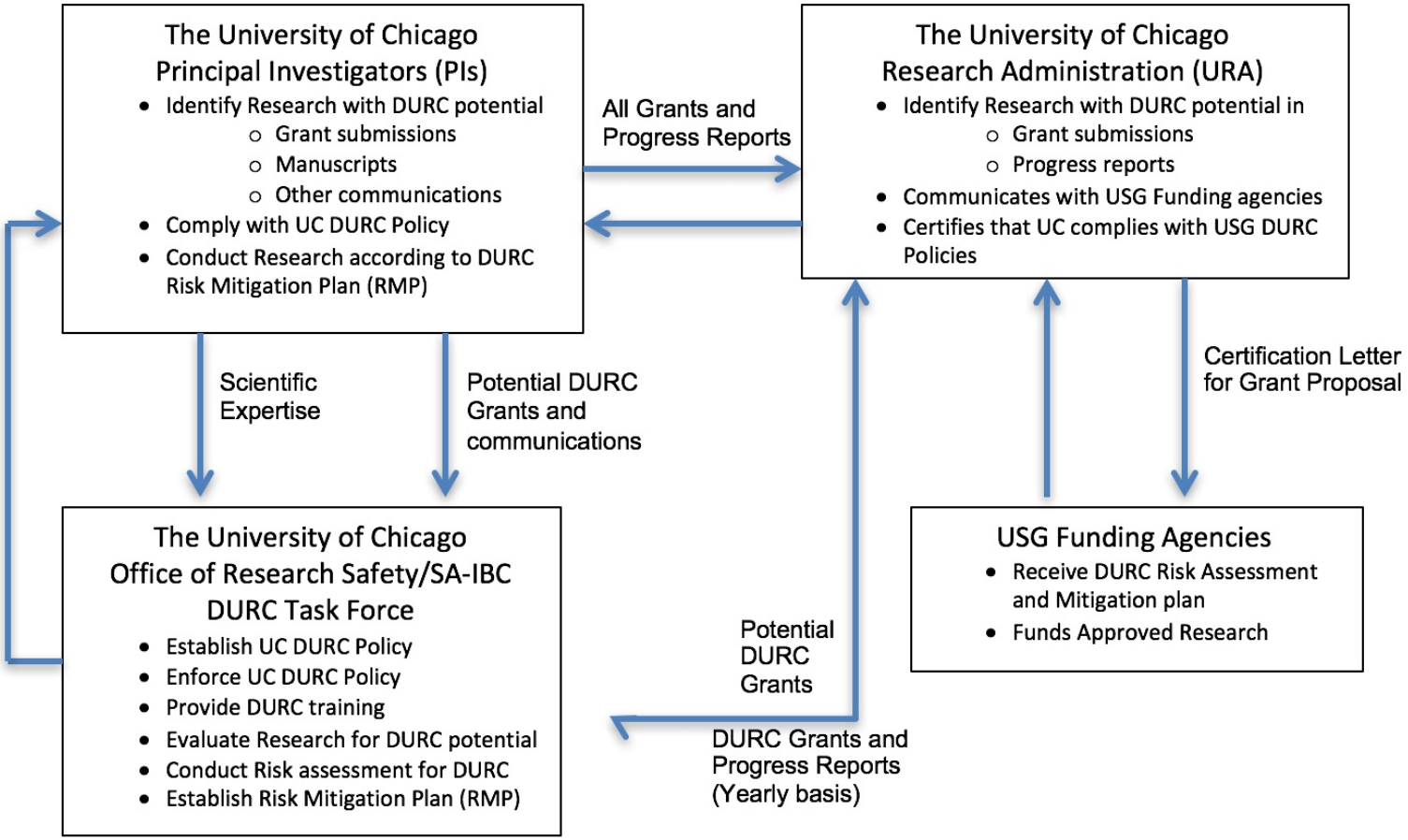
Does the proposed research plan have the potential to alter the public health impact of the pathogen under study in one or more of the following ways:

1.0	* Enhances the harmful consequences of the agent or toxin.	○ Yes	● No Clear
2.0	* Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification.	○ Yes	● No Clear
3.0	* Confers to the agent or toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates their ability to evade detection methodologies.	○ Yes	● No Clear
4.0	* Increases the stability, transmissibility, or the ability to disseminate the agent or toxin.	○ Yes	● No Clear
5.0	* Alters the host range or tropism of the agent or toxin.	○ Yes	● No Clear
6.0	* Enhances the susceptibility of a host population to the agent or toxin.	○ Yes	● No Clear
7.0	* Generates or reconstitutes an eradicated or extinct agent or toxin.	● Yes	○ No Clear
8.0	* Does this potential outcome have an immediate threat to public health and security?	○ Yes	● No Clear

If you answered "Yes" to one or more of the above types of experiments and "Yes" to question #8, you will be contacted by the Office of Biological Safety for assistance in developing a risk mitigation plan.

DURC Governance

University of Chicago



Review Types

1. IBC submission
2. Grant proposal
3. Assessment of funding agency
4. Manuscript preparation or journal review

DURC Policy

- The DURC Task Force meets ad hoc
  - There is no regularly scheduled meeting
- Protocols are flagged during the IBC review process, at the time of grant submission, by URA by request of the funding agency, and at the time of manuscript preparation
  - Review is not only dependent on the PI or funding agency
- If research is deemed DURC by the DTF, a risk mitigation plan is developed by the PI with consensus of the DTF

DURC
Assessment and Communication

DTF 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 Task Force Reviews

- DTF has had formal meetings 10 times since 2012
- 28 communications concerning potential DURC research were made to the DTF by PIs and/or funding agencies for 7 protocols conducted by 5 PIs
- 13 evaluations determined the work to be DURC
- The majority were initiated by the PI, 6 because of a manuscript submission and 21 because of a grant submission, 1 after IBC protocol review, and 1 for a MTA for a BL3 pathogen initiated by the PI
- Two pathogens reviewed were not select agents
  - Staph. aureus , DURC elements identified by IBC review
  - HSV

DURC Task Force Reviews

- We have not needed to formally request annual reviews of mitigation plans due to activity on protocols by the PIs, with each protocol having been subject to review multiple times
  - 1 Anthrax protocol was reviewed for DURC 8 times since 2012
  - 1 Yersinia protocol was reviewed 4 times since 2014
  - Annual updates of all mitigation plans should be formalized

DURC Task Force Reviews

- The DURC Task Force meets to come to a consensus on the best approach to mitigate risk
- There is not a vote, rather a final consensus from the entire group both on the risk evaluation and the mitigation plans
- We have yet to meet an impasse at the meetings or with an investigator

What challenges have you experienced regarding the review and assessment of projects for their DURC potential (or additional IRE actions required under the policy)?

DURC
Assessment and Communication

- Understanding the experiments is difficult, even with an expert group
  - We often need to include the PI in the discussion part of a DURC meeting (they are recused from the consensus decision)
- It may be difficult to determine if a findings could be directly used to pose a threat to human health, animals, plants, or the environment
  - No framework for evaluating risk
  - No best practices
  - Journals do not have clear policies regarding DURC
- The effects of gain of function (GOF) and risk are all theoretical
- The beneficial effects of risk mitigation plans are also somewhat theoretical

DURC
Assessment and Communication

- PIs do not want to limit the scope of their research and want to publish their research findings regardless of risk
  - Restriction on publication is most contentious
- Although reviews are done quickly, it is still regarded as slowing progress
  - Meetings can be difficult to schedule immediately
  - Mitigation plans require some back and forth communication
- Everyone is busy, but the time commitment has been reasonable
- Overall, however, there has been satisfaction on both sides

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