Beyond the 15 Agents
Should your Institution Review Life Sciences Research for Potential DURC?

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Dual Use Research of Concern

"Good science can be put to bad uses"

Dual use research (DUR) is research conducted for legitimate purposes that generate knowledge, information, technologies, and/or products that can be utilized both for benevolent and harmful purposes

USG DURC Policies

March 2012: United States Government Policy for Oversight of Life Science Dual Use Research of Concern

September 2014: United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern

15 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
Marbug virus
Reconstructed 1918 influenza virus
Rinderpest virus
Neurotoxin-producing strains of *Clostridium botulinum*
Variola major virus
Variola minor virus
Yersina pestis

** Except attenuated strains of the agents that are excluded from the Select Agent List and inactive forms of botulinum neurotoxin*

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7 Experimental Effects

1. Enhance the harmful consequences of a biological agent or toxin

2. Disrupt immunity of the effectiveness of an immunization without clinical or agricultural justification

3. Confer to a biological agent or toxin, resistance to clinically and/or agriculturally useful prophylactic of therapeutic interventions against that agent or toxin or facilitate their ability to evade detection methodologies

4. Increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin

5. Alter the host range or tropism of a biological agent or toxin

6. Enhance the susceptibility of a host population

7. Generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent

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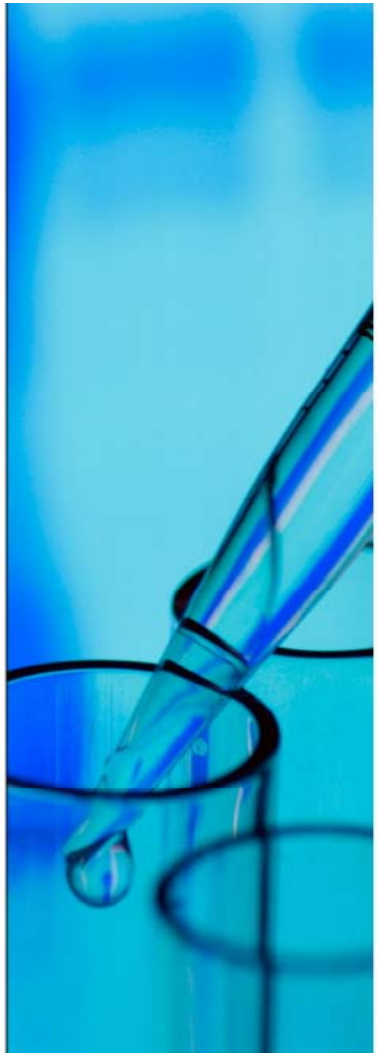

Tools for the Identification, Assessment, Management, and Responsible Communication of

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

http://www.phe.gov/s3/dualuse/Documents/durc-companion-guide.pdf

UW- Madison IRE

Permanent Subcommittee of the IBC

- Chair- ICDUR (Biosafety, biosecurity, and regulatory)
- Bacteriology
- Virology
- Immunology
- Infectious Disease
- Public Health
- Consultants as needed

Additional Review of Potential DURC

- IBC
- Biosecurity Task Force

*Reviews all research meeting one of the seven experimental effects

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CSU IRE

- At CSU the "Institutional Review Entity" is our existing IBC
  - DURC meeting is convened/adjourned prior to IBC
- Institutional Contact for Dual Use Research (ICDUR)
  - VP for Research
- Institutional Review Committee
  - Composed of at least 5 members
- Define procedure for assessment and mitigation
- We ask the PI to determine whether any of the seven experimental effects apply to their research
- In addition: Could you envision a reasonable scenario where your research findings could be directly used by individuals with malicious intent to develop bioweapons?
  - Yes or No
- If you answered Yes to any of the above, please explain in the following textbox:

UW-Madison Research Affected

2.4 % of research portfolio

- 10 PIs
  - 5 select agent
  - 3 select agent exempt quantities of botulinum neurotoxin
  - 2 not working with one of the 15 agents

Material	Not DURC	DUR	DURC	Total
Grants	1	3	8	12
Manuscripts	7	3	12	22
Experiments/Assessment	9	1	2	12
Risk mitigation plans	N/A	N/A	N/A	6

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CSU DURC Reviews: 9/2015 – 9/2017

- Total of 15 PIs approved for select agent research
- Seven PIs are approved for DURC agents/toxins
  - Those seven accounted for the 54 DURC protocols
- We have reviewed a total of 54 protocols, including renewals, since September 9, 2015
  - Average 27 per year/1230 total IBC protocols = 2.2%
- One was thought to meet one of the 7 experimental effects
  - Determined not to meet the definition of DURC
  - Notified NIH OBA
- One that the sponsor "determined" was DURC, drafted the risk mitigation plan, ICDUR signed
  - IRE determined did not meet definition of DURC

Should you review beyond the 15 agents?

AUSTRALIAN MOUSEPOX STUDY

Research: Expression of mouse interleukin-4 by a recombinant ectromelia virus

Goal: Continuation of studies into the development of virally vectored immunocontraceptive vaccines

Assessment of DURC: None of the 15 agents; none of the 7 effects

Results: Recombinant ectromelia virus was lethal for all mice, including susceptible and resistant strains

Risks: Results were not anticipated/predicted; possibility of other similar research leading to lethal recombinants

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SYNTHETIC HORSEPOX VIRUS

Research: Synthesized horsepox virus

Goal: Develop a safer vaccine against smallpox virus

Assessment of risks:

- **Open the door to routine and widespread synthesis of orthopoxviruses for vaccine and anti-cancer therapies**
- **Labs will have the ability to re-create smallpox virus**
- **Potential re-introduction of smallpox**
- **Create modified smallpox viruses that are resistant to countermeasures**

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BOTOX IN MILK PUBLICATION

Research: Mathematical analysis of the possibility of adding enough botulinum toxin to the milk supply in a major city to cause deaths in that city

Goal: Determine the amount of toxin needed to contaminate the milk supply with enough botulinum toxin to cause human deaths

Assessment of DURC: One of the 15 agents (botulinum toxin), one of the 7 effects (4. Increase ability to disseminate a biological toxin)

Risks: Risks to populations; milk and/or other food supplies

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CLINICAL STUDY

Research: Describe the clinical effectiveness, safety, and exposure from patients treated with a drug used against one of the 15 agents

Goal: To understand clinical benefits, safety, and information patient care and treatment choices

Assessment: Not one of the 15 agents or one of the 7 effects

Risks: Depends on the data generated by the study

- Target certain populations or locations
- Modify the agent to make the drug ineffective
- Other way to make treatment ineffective

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Conclusions

Change in thought process

Many aspects of Life Science research could be DURC

DURC potential is not always clear until experiments or studies are completed

What might be or might not be DURC today could or could not be DURC tomorrow

Take Home Message

DURC is NOT bad

DURC does not mean the research should not be done

No "one size fits all" model for reviewing research

Do what is best for your institution and the resources available to you

Ultimately help promote a culture of awareness, safety, and responsible communication

Thank You

Questions and Discussion

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