



Training for Responsible Conduct of Dual Use Research



Richard Frothingham, MD, CBSP
richard.frothingham@duke.edu

“I serve as co-chair of the Duke IBC and IRE. The opinions expressed here are my own, not necessarily those of the IBC or IRE.”



NIAID Regional Biocontainment Laboratory at Duke

Session topic

- Discussion of institutional approaches to educating staff, IRE members, investigators, and laboratory personnel about dual use issues and various roles/ requirements under the policy.

Session topic

- ~~Discussion of institutional approaches to educating staff, IRE members, investigators, and laboratory personnel about dual use issues and various roles/ requirements under the policy.~~
- How can we create a culture of responsible dual use research?
- How do we enable people to comply with USG Policy?

SCIENCE AND SECURITY

Practical Experiences in Dual-Use Review

E. Megan Davidson,¹ Richard Frothingham,² Robert Cook-Deegan^{3*}

The U.S. government is debating how to handle national security risks posed by bioscience research. A research consortium shares lessons learned from their research oversight scheme.



Davidson EM, Frothingham R, Cook-Deegan R. Science and security: Practical experiences in dual-use review. *Science* 2007;316:1432-3.

Selected examples of research evaluated for dual use at Duke

Project	Year
Novel treatment strategy for ectromelia expressing cytokines	2004
Identification of virulence factors in enteropathogenic <i>E. coli</i>	2008
Retroviral expression of tetanus toxin light chain	2007
Adaptation of dengue virus for growth in <i>Drosophila</i>	2007
Evaluation of novel antibiotics against pneumonic plague	2015
Evaluation of novel antibiotics against tularemia	2016
Expression of multiple hemagglutinins in influenza A vaccine	2016
Expression of multiple vaccine antigens by influenza A	2017
Clinical sample processing to inactivate hazardous microbes	2017
Botox for treatment of spastic bladder	2017

Selected examples of research evaluated for dual use at Duke

Project	Listed agent		
Cytokines in ectromelia	n		
Virulence factors in enteropathogenic <i>E. coli</i>	n		
Tetanus toxin light chain in retrovirus	n		
Dengue virus adapted to <i>Drosophila</i>	n		
Antibiotics against pneumonic plague	Y		
Antibiotics against tularemia	Y		
Multiple hemagglutinins in influenza A vaccine	n		
Multiple vaccine antigens by influenza A	n		
Inactivate hazardous microbes in sample	Y		
Botox for treatment of spastic bladder	Y		

Does your institution have a **culture of research safety**?

- Personnel recognize need for research safety.
- Personnel believe that safe practices will make a difference.
- Personnel have knowledge and proficiency in safe practices for their research.
- Personnel will take action if they see unsafe practices in their laboratory.

Does your institution have a **culture of responsible conduct of dual use research**?

- Personnel recognize need for responsible conduct of dual use research.
- Personnel believe that responsible conduct of dual use research will make a difference.
- Personnel have knowledge and proficiency in responsible conduct of dual use research.
- Personnel will take action if have concerns about dual use research in their laboratory.

Why is it hard to create a culture of responsible conduct of dual use research?

- **Dual use is complicated.**

What is the goal of a research safety program?

- Minimize the risk of injury or illness to laboratory workers

How do we achieve research safety?

- Work practices
- Personal protective equipment
- Engineering controls
- Administrative controls
- Training

What is dual use research?

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

Definition of dual use research of concern

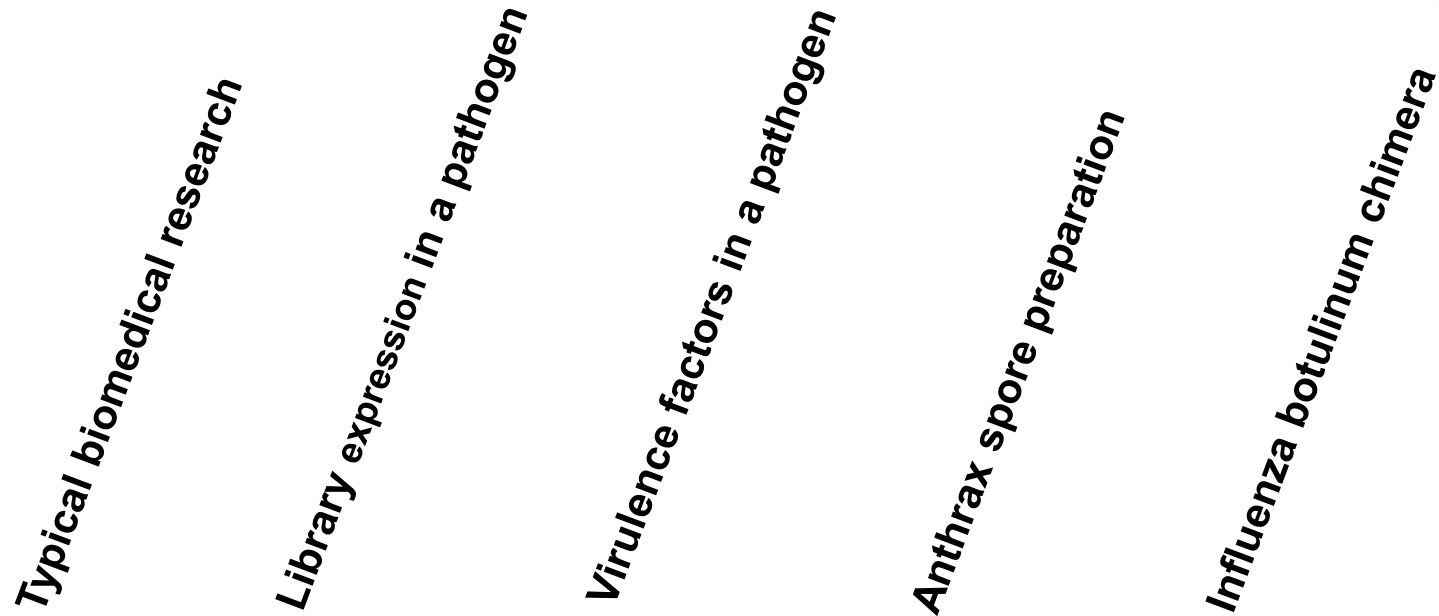
Life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and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

Why is it hard to create a culture of responsible conduct of dual use research?

- Dual use is complicated.
- **Dual use exists on a continuum of risk.**



Continuum approach to dual-use review



- Dual use potential varies across a continuum, from minimal to extreme.



Example of dual-use technology: automobile



- Arturo Casadevall has suggested the automobile as an example of a dual-use technology:
 - Automobiles have many beneficial uses.
 - Automobiles can be misused to harm human populations.

March 29, 2009: BAGHDAD —

Sixteen people died Thursday when a bomb in a parked car detonated at a market in Baghdad.

This was the fifth big explosion this month in Iraq.



Why is it hard to create a culture of responsible conduct of dual use research?

- Dual use is complicated.
- Dual use exists on a continuum of risk.
- **Experts disagree on specific projects.**

Selected examples of research evaluated for dual use at Duke

Project	Listed agent	Listed effect	DURC
Cytokines in ectromelia	n	Y	n
Virulence factors in enteropathogenic <i>E. coli</i>	n	Y	n
Tetanus toxin light chain in retrovirus	n	Y	n
Dengue virus adapted to <i>Drosophila</i>	n	? → N	n
Antibiotics against pneumonic plague	Y	? → N	n
Antibiotics against tularemia	Y	? → N	n
Multiple hemagglutinins in influenza A vaccine	n	? → N	n
Multiple vaccine antigens by influenza A	n	?	?
Inactivate hazardous microbes in sample	Y	n	n
Botox for treatment of spastic bladder	Y	n	n

Selected examples of research evaluated for dual use at Duke

Project	Listed agent	Listed effect	DURC
Cytokines in ectromelia	n	Y	n
Virulence factors in enteropathogenic <i>E. coli</i>	n	Y	n
Tetanus toxin light chain in retrovirus	n	Y	n
Dengue virus adapted to <i>Drosophila</i>	n	? → N	n
Antibiotics against pneumonic plague	Y	? → N	n
Antibiotics against tularemia	Y	? → N	n
Multiple hemagglutinins in influenza A vaccine	n	? → N	n
Multiple vaccine antigens by influenza A	n	?	?
Inactivate hazardous microbes in sample	Y	n	n
Botox for treatment of spastic bladder	Y	n	n

Why is it hard to create a culture of responsible conduct of dual use research?

- Dual use is complicated.
- Dual use exists on a continuum of risk.
- Experts disagree on specific projects.
- **We have good tools for mitigation of dual use material. . .**

Why is it hard to create a culture of responsible conduct of dual use research?

- Dual use is complicated.
- Dual use exists on a continuum of risk.
- Experts disagree on specific projects.
- We have good tools for mitigation of dual use material. . .
 - **Biosafety**
 - **Biocontainment**
 - **Biosecurity**



Management of dual-use technology: automobile



- Dual use potential from automobiles is rarely managed by excluding automobiles completely.
- Dual use risk from automobiles is managed by multiple approaches:

Why is it hard to create a culture of responsible conduct of dual use research?

- Dual use is complicated.
- Dual use exists on a continuum of risk.
- Experts disagree on specific projects.
- We have good tools for mitigation of dual use material **BUT mitigation of dual use knowledge remains problematic.**

Why is it hard to create a culture of responsible conduct of dual use research?

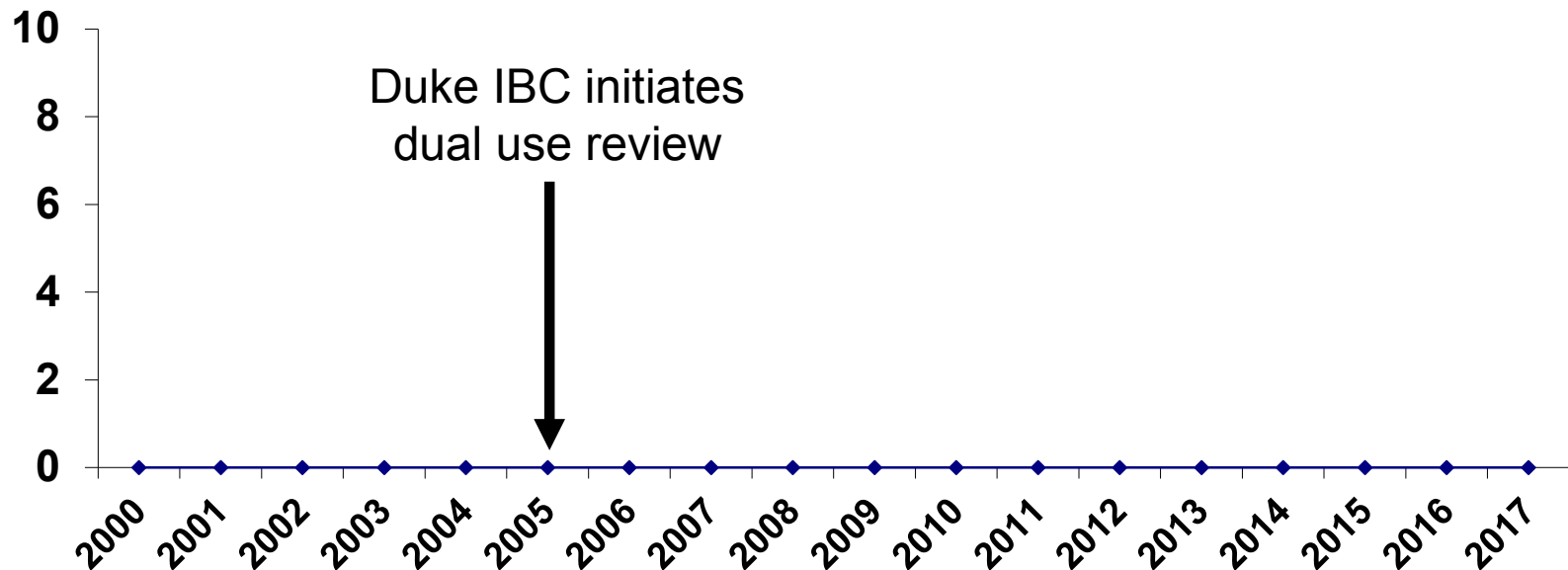
- Dual use is complicated.
- Dual use exists on a continuum of risk.
- Experts disagree on specific projects.
- We have good tools for mitigation of dual use material BUT mitigation of dual use knowledge remains problematic.
- **We don't know how to measure risks from dual use research or success in addressing them.**
- Some of our training is boring or misdirected.



Benefit of Duke review for dual use research



Identified episodes of misuse of Duke research to harm public health, agriculture, plants, animals, environment, or materiel



Why is it hard to create a culture of responsible conduct of dual use research?

- Dual use is complicated.
- Dual use exists on a continuum of risk.
- Experts disagree on specific projects.
- We have good tools for mitigation of dual use material BUT mitigation of dual use knowledge remains problematic.
- We don't know how to measure risks from dual use research or success in addressing them.
- **Some of our training is misdirected or boring.**

Selected examples of research evaluated for dual use at Duke

Project	How was review initiated?
Cytokines in ectromelia	NIH study section
Virulence factors in enteropathogenic <i>E. coli</i>	IBC review (ROSNA)
Tetanus toxin light chain in retrovirus	IBC review (ROSNA)
Dengue virus adapted to <i>Drosophila</i>	NIH program officer
Antibiotics against pneumonic plague	PI (IBC co-chair)
Antibiotics against tularemia	Colleague report (IBC co-chair)
Multiple hemagglutinins in influenza A vaccine	Colleague report (IBC member)
Multiple vaccine antigens by influenza A	IBC review (ROSNA)
Inactivate hazardous microbes in sample	PI
Botox for treatment of spastic bladder	IBC presentation to IRB

Which of the following best describes the types of research with botulinum toxin covered by the USG DURC Policy?

- A. Research is covered when the total amount of botulin toxin exceeds 1 mg.
- B. Laboratory research with any quantity of botulin toxin is covered, but not clinical research.
- C. Laboratory and clinical research with any quantity of botulin toxin is covered, but there is an exemption for FDA-approved drugs such as Botox.
- D. All research with any quantity of botulin toxin is covered.

A clinician has observed severe reactions in people who receive Botox at the same time they receive another FDA-approved drug (Drug A). The clinician is now planning to conduct research to understand more about these reactions. The study will involve administering typical doses of Botox at the same time as Drug A. Which of the following is true?

- A. This research may result in dual-use material.
- B. This research may result in dual-use technology.
- C. This research may result in dual-use knowledge.
- D. This research does not pose dual-use concern since the standard approved dose of Botox is used.



People



Debra Hunt

- Select Agent program Responsible Official (RO)
- Biological Safety Officer (BSO)

Wayne Thomann

- IRE co-chair

Raphael Valdivia

Megan Davidson

Bob Cook-Deegan

IRE members

- Brian Letourneau
- Scott Alderman
- Randall Reynolds
- Pat Condreay
- Arlene Sena
- David Pickup
- Carol Epling
- Peg Hogan
- Tai-Pong Sun