



Practical Experience in Dual Use Review: Duke Institutional Biosafety Committee (IBC)



Richard Frothingham, MD, CBSP, FACP

richard.frothingham@duke.edu

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



Regional Biocontainment Laboratory (RBL)



Duke Institutional Biosafety Committee (IBC) Roles



- Official roles in IBC Policy and Procedures document
 - Ensure that all recombinant DNA (rDNA) research at Duke is compliant with NIH Guidelines
 - Ensure that all Select Agent research at Duke is compliant with federal, state, and local requirements.
- Other services provided
 - Provide advice and expertise, upon request, to support Duke safety office, employee health, animal program, etc.
 - Review all research at Duke using Risk Group 3 microbes.
 - Review research with dual use potential as a part of rDNA review, and upon request.



Duke IBC Policy and Procedures



“The IBC is authorized to inspect research facilities, approve research practices and procedures, and to take actions, such as enforcement of cessation of research activities.”



Duke IBC membership



- Rich Frothingham, MD, CBSP, FACP
- Wayne Thomann, DrPH
- Fred Fuller, PhD*
- Tom Kost, PhD*
- Brian LeTourneau*
- Debra Hunt, DrPH, CBSP
- Tim Clay, PhD
- David Pickup, PhD
- Elizabeth Ramsburg, PhD
- Tia-Ping Sun, PhD
- Scott Alderman, MS, CBSP
- Wiley Schell, MS
- Randall Reynolds, MS, DVM

Expertise in biosafety, infectious diseases, public health, virology, bacteriology, mycology, animals, plants, and human gene therapy. Asterisks identify community members.



History of dual-use review by Duke IBC



- In 2003, NIH funded the Southeast Regional Center of Excellence for Emerging Infections and Biodefense (SERCEB), one of 8 RCEs)
- SERCEB included a Policy, Ethics, and Law Core. The PEL core reviewed all SERCEB projects for dual use potential.
- Megan Davidson from PEL core attended Duke IBC meetings as a guest, and encouraged us to consider dual use review as part of our mission.
- SERCEB is currently located at UNC Chapel Hill, and is independent from Duke IBC.



Dual use review by Duke IBC



- Screening questions added to rDNA registration form in 2005
- IBC members trained in 2006 using the SERCEB training module
- Dual use considered, when appropriate, during review of rDNA protocols
- Other protocols reviewed upon request of investigator
- No specific definition or threshold for review



Dual use questions on Duke IBC form



6. **Will this work create resistance to therapeutically useful antimicrobials or antivirals?** (applies to therapeutic agents used to control disease agents in humans, animals or plants) Yes No
7. **Will this work enhance the virulence of a pathogen or render a non-pathogen virulent?** (applies to human, animal or plant pathogens) Yes No
8. **Will this work increase the transmissibility of a pathogen?** (would include enhancing transmission within or between species, and altering vector competence to enhance disease transmission) Yes No
9. **Will this work alter the host range of a pathogen?** Yes No
10. **Could the results of the project potentially demonstrate how to render a vaccine ineffective?** (applies to both human and animal vaccines) Yes No
11. **Could this work enable the evasion of diagnostic/ detection modalities?** (e.g., microencapsulation to avoid antibody based detection and/or the alteration of gene sequences to avoid detection by established molecular methods) Yes No
12. **Could this work enable the weaponization of a pathogen or toxin (e.g., stabilization, synthesis of a “high-risk” agent)** Yes No



Are PIs ready to self-identify research with dual-use potential?



- In cases reviewed by Duke IBC, no PI has prospectively identified and discussed dual-use potential.
- Dual-use questions have provided some positive responses. Sensitivity and specificity of these questions limited.
- PIs did not understand the concept of dual use when it was raised.



How has the potential for dual use been identified at Duke?



- NIH study section (cytokine expression in ectromelia)
- NIH program officer (dengue in drosophila)
- Dual-use questions on registration form
- Duke IBC members identify dual use potential during the review process



Can an IBC reach consensus during dual-use review?



- The Duke IBC often reached consensus that there was “no significant dual-use potential” or that “risk is typical for biomedical research.”
- Difficult or impossible to reach consensus on the classification of other protocols. Discussion of this point often became tangential to the specific protocol. IBC members raised concern about setting precedent, and introduced other hypothetical research.
- Relatively easy for IBC to reach consensus on an appropriate management (next slide).



Management options for research with dual-use potential



- **Education:** PI and/or lab members complete an online training module.
- **More information:** PI provides additional scientific information to assist in the risk assessment process.
- **Contingency plan:** The PI identifies potential outcomes of the research that could result in dual-use material or knowledge, then identifies a contingency plan.
- **Modification:** PI changes the research plan to reduce the dual-use potential.
- **Proposal rejection by IBC.**



Components of contingency plans developed by PIs



- How to recognize the specific outcome (e.g., a superbug)
- Whom to notify
- How to secure dual-use material
- How to communicate dual-use knowledge

[Strategies typically include a plan to notify the Duke IBC, and manage biosecurity and communication in collaboration with the IBC. Will this work? So far we have no experience.]



Dichotomous approach to dual-use review



- Use a single criterion to identify “dual use research of concern”
- Review and manage this research only

“Research that, based on current understanding, can be reasonably anticipated to provide knowledge, products, or technologies that could be directly misapplied by others to pose a threat to public health and safety, agricultural crops and other plants, animals, the environment, or materiel.”

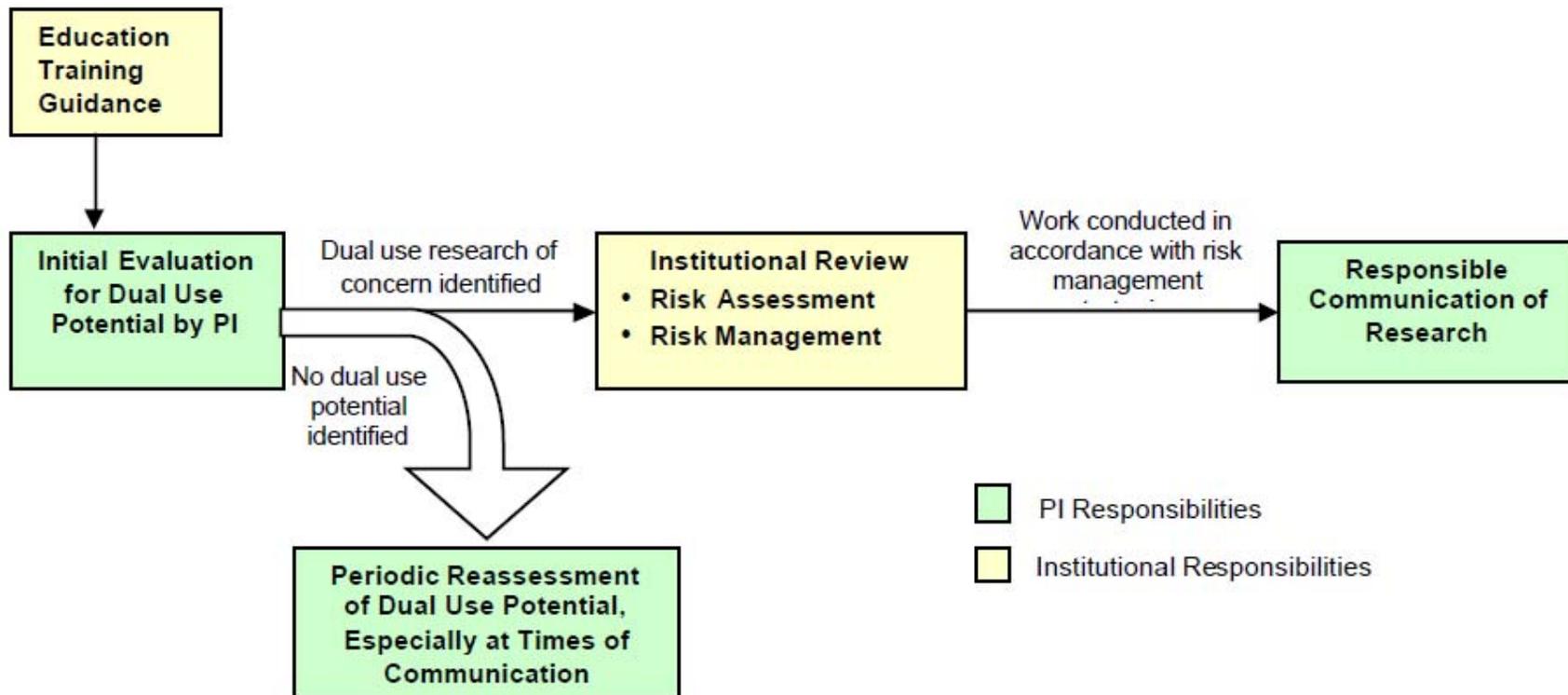
Proposed Framework for the Oversight of Dual Use Life Sciences Research,
National Science Advisory Board for Biosecurity (NSABB), June 2007



Dichotomous approach to dual-use review



Figure 1 : Steps in Local Oversight of Dual Use Research



Proposed Framework for the Oversight of Dual Use Life Sciences Research, National Science Advisory Board for Biosecurity (NSABB), June 2007



Continuum approach to dual-use review



Typical biomedical research

Library expression in a pathogen

Virulence factors in a pathogen

Anthrax spore preparation

Influenza botulinum chimera



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



Continuum approach to dual-use review



- Dual use potential varies across a continuum, from minimal to extreme.
- Dual use potential can be appropriately managed at every point on the continuum. Blue text provides examples of management approaches that **might** be used by the Duke IBC.



March 29, 2009: BAGHDAD — Sixteen people died Thursday when a bomb in a parked car detonated at a market in Baghdad, the fifth big explosion this month in Iraq, Iraqi police said.

- NSABB member Arturo Casadevall has suggested the automobile as an example of a dual-use technology. Automobiles fit the definition of dual use technology: they have many beneficial uses, and have the potential to be misused to harm human populations. Most would place the automobile on the low end of the continuum of dual use potential. Can this risk be managed?



Management of dual-use technology: automobile



- Dual use potential from automobiles is rarely managed by excluding automobiles completely.
- Dual use risk from automobiles is generally managed by vehicle barriers, checkpoints, mirrors.
- This risk could be managed in high risk areas by an open chassis design making it difficult to hide explosives.



Cost of Duke IBC review



- Major effort spent in discussion of the broad topic of dual use
- Modest effort spent in review and management of specific protocols
- Modest effort by PIs in responding to IBC concerns
- Research sometimes delayed by one monthly IBC cycle
- One case reviewed by Duke IBC led to major modification of research, possibly limiting results
- One case NOT reviewed by Duke IBC led to project abandonment



Advantages of IBC review



- Existing entity with institutional resources and authority in place
- Experienced in risk assessment
- One-stop shopping for projects using rDNA
- Management of dual use research



Limitations of IBC review



- Consensus can be reached on management, though not necessarily on classification.
- No mechanism at Duke to capture biological research not using rDNA
- No expertise at Duke to evaluate non-biological research
- Expertise varies substantially among IBCs



Conclusions



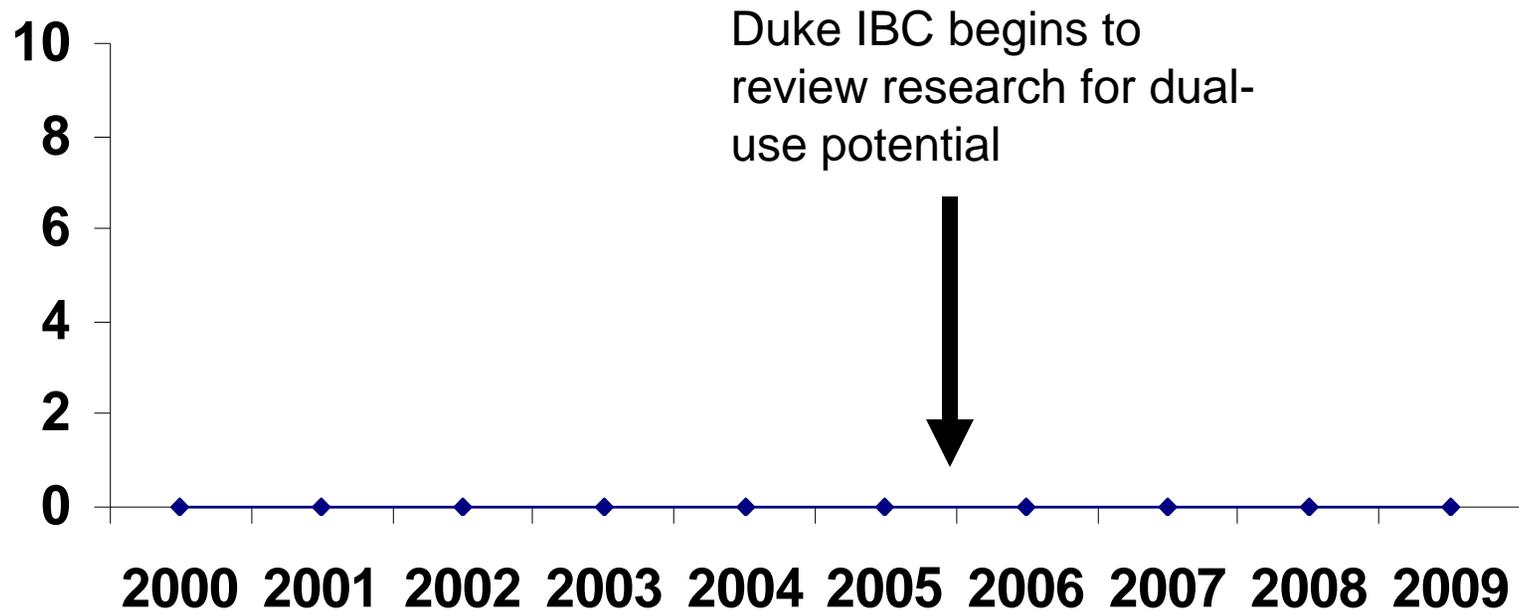
- IBCs can review and manage dual-use potential in the absence of formal regulation or a consensus definition
- Investigators are not currently ready to self-identify or manage dual-use research
- Time and effort required by PI and IBC are modest
- Management strategies are available at every level of dual-use potential
- Benefit of dual-use review is plausible but unproven



Benefit of Duke IBC review



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





More information



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

Schubert C. Bioterror experts split on recommendations for “dual use.” *Nature Medicine* 2008;14:893. News article includes description of Duke IBC dual-use review.

Duke IBC web site (registration form, minutes):

<http://www.safety.duke.edu/BioSafety/ibc.htm>

SERCEB on-line training:

<http://www.serceb.org/dualuse.htm>