The Dual Use Dilemma in Biological Research: Discussion Guide

This guide is intended for life science professionals (faculty members, advisors, biosafety professionals) and other mentors and supervisors whose students, laboratory workers, or colleagues are using the online educational module, The Dual Use Dilemma in Biological Research. Discussion leaders can have a significant impact by encouraging module users to explore and further understand the issues presented in the module. This discussion guide provides bioscience leaders and scholars with additional questions for consideration and case studies to use as follow-up to the online dual use module. The information presented within can be used in leading discussions in small lab group or departmental meetings, RCR workshops, or courses in ethics or the biological sciences.

The discussion leader serves a critical role by encouraging students, colleagues, and other module users to invest time in understanding the rules, policy debates, and ethical issues presented. Thinking through such issues, particularly those as ambiguous and rapidly evolving as are associated with dual use research, in a group encourages consideration of different perspectives and interpretations which can hopefully lead participants to reasoned and well-informed conclusions.

Goals

The overall aim of this module is to help users understand the concept of dual use research of concern and how it relates to legitimate life sciences research. The specific goals are to:

- Describe the dual use dilemma in bioscience research;
- Understand the historical and political background surrounding oversight and regulation of life sciences research;
- Identify and analyze potential ethical, legal, and policy problems which may arise in the course of bioscience research;
- Develop strategies to respond to and resolve dual use scenarios; and
- Develop a sense of responsibility and possibility – Recognize that individual decisions can have important ramifications and the nuances of those decisions are worth contemplating in earnest.

In order to meet these goals, the following guidelines are suggested for approaching the dilemmas presented in the online module and case studies included here:

1. Recognize and identify any dual use concerns or other ethical issues associated with the research protocol(s) presented;
2. Identify and assess the important information and facts available to the parties involved;
3. Determine the regulations, laws, and policy debates which may be applicable to the type(s) of research protocols being proposed or conducted;
4. Identify the public health benefits and security burdens associated with the various courses of action each party might take, the arguments for and against these actions, and their likely consequences;

5. Choose and justify a course of action;

6. Evaluate actions taken and their consequences;

7. Preventive ethics: consider what could have been done to prevent the dual use dilemma from arising.

Considering dual use concerns in bioscience research is part of conducting research responsibly. For more information on research ethics education visit the Responsible Conduct of Research Educational Consortium website.

Case Studies

Case studies have proved an effective vehicle to use in identifying, analyzing, discussing, and resolving ethical issues such as those involved in dual use research. The case studies presented in the online component of the module and in this guide consider laws and regulations governing life sciences research, public policy debates which could impact life sciences research, ethical dilemmas associated with planning and executing a project with dual use concerns, publishing information with dual use potential (Case Study 1); and accessing genomic data with dual use potential (Case Study 2).

Hyperlinks to supporting material are embedded throughout the case studies. It is strongly suggested that a discussion leader reads these primary sources in preparation, encourage discussion participants to do so as well, and utilize them during the group discussion in order to elucidate points made by each case study.

CASE STUDY #1: Ann Lee & Peter Ellison (online module)

Topic: ***Publication of information with dual use potential.*** While the case study presented in the module dealt primarily with Ann's research proposal, it is worth considering the issues that might arise for Ann when she attempts to publish her work.

A. General points to consider and/or raise in group discussion:

- A significant number of broad-reaching laws and policies have been passed since 2001, including some that directly and indirectly impact research in the biological sciences. Life science professionals must be aware of these new laws and rules, and the ethical questions that accompany them. Failure to know about and follow new laws could result in loss of scientific and personal freedoms as well as criminal charges.

- The policy and regulatory landscape for the biological sciences is continuing to evolve and change. By keeping abreast of current science policy debates and proposed regulations, and the ethical issues that accompany them, researchers have the opportunity to help inform how this landscape is shaped.

B. Questions for discussion presented in the module:

The following questions, most of which were raised in the module, have been organized by topic. See hyperlinks to primary and secondary sources and relevant online module slides.

Dual Use Definitions and Criteria

What is dual use research? Dual use research is legitimate scientific research which would be misappropriated for malicious purposes. Most any scientific advancement can be considered dual use, as the manner in which it is used is based upon the intent of the user. It is dual use research that has a high likelihood of being directly misused for harm that is considered "dual use research of concern." This is an important distinction made by entities like the National Research Council and the National Science Advisory Board for Biosecurity (NSABB) which have attempted to set parameters around the types of life sciences experiments which would be most concerning to national and international security.

The 2004 National Academies of Science's National Research Council report *Biotechnology Research in an Age of Terrorism* defines dual use research as that which meets any of seven criteria:

1. Makes a vaccine ineffective;
2. Confers resistance to antibiotics or antivirals;

3. Enhances pathogen virulence or render a nonpathogen virulent;
4. Increases pathogen transmissibility;
5. Alters pathogen host range;
6. Enables evasion of diagnosis of infection; or
7. Enables weaponization of an agent or toxin.

- See Slide III.12

The National Science Advisory Board for Biosecurity (NSABB)'s categories of dual use research of concern are based largely on the 7 experiments enumerated by the National Research Council above. The NSABB's categories include any experiments which:

- Enhance the harmful consequences of a biological agent or toxin;
- Disrupt the immunity or the effectiveness of an immunization without clinical and/or agricultural justification;
- Confer to a biological agent or toxin, resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitate their ability to evade detection methodologies;
- Increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin;
- Alter the host range or tropism of a biological agent or toxin;
- Enhance the susceptibility of a host population; or
- Generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent.

- See Slide III.12

Rules Governing Research

• How have international treaties and agreements impacted bioscience research and the rules that govern it?

- Geneva Protocol, Biological Toxins and Weapons Convention (BWC), and the IAP Statement on Biosecurity

- See Slides II.5, II.6, II.7, and II.9

• What more recent federal laws and regulations have impacted bioscience research in the US, and how?

- USA PATRIOT Act, Bioterrorism Preparedness Act, and Select Agent Rules

- See Slides III.3, III.4, and III.5

- What is the proposed institutional review process for research on biological and select agents?
    - Review of proposals and projects by Institutional Biosafety Committees (IBCs)
    - See Slide III.13

Access to Genomic Data

- Should genomic data for all organisms be freely accessible? If not, is there a logical point at which the line can be drawn on what is and is not publicly available?
    - See Slide V.2
- How would data not available to the public be accessed?
    - Additional resource: See Executive Summary of NRC genome data access report, Seeking Security: Pathogens, Open Access, and Genome Databases
    - See Slide V.7

Security versus Openness

- Scientists want to research infectious diseases in order to better understand and, therefore, better treat them; however, discoveries from this work might also be used to deliberately do harm. How do we best balance the potential benefits of dual use research with the potential harms?
    - Additional resource: Nixdorff and Bender
- The relatively open bioscience research culture is extremely effective and productive. How do we implement guidelines, rules, or regulations to address dual use issues without hampering this culture, and impeding the benefits of its progress? What is the appropriate amount and type of monitoring given the relative potential for harm?

Case Study

The module presents the case of PhD student Ann Lee and her advisor Peter Ellison. Ann's research proposal is flagged by her department chair as having dual use concerns, and after researching the topic, weighing the project's benefits and burdens, and discussing her experiments with the IBC, Ann decides to move forward with her research as proposed. A year-and-a-half later, Ann is ready to publish her results.

- What, if anything should Ann consider doing prior to submitting a manuscript to a journal? Whom should she inform that she is ready to publish?
- Should Ann consult Lori, her department chair, or the IBC? Why or why not?
- What if the editorial board of the journal to which she submits her work raises questions regarding the dual use nature of her work?

- If Ann's paper does get published, what are some potential ramifications for Ann? For Peter and Lori? For their institution? What reactions do you think Ann's and Peter's peers and the broader scientific community will have?

- If the journal initially declines to publish her paper, what options could Ann and Peter pursue?

  - See Slides VI.2, VI.3, and "Research Questions to Consider"

  - Ann and Peter could appeal to the journal's editorial review board to reconsider the decision. What points might Ann and Peter make in their appeal?

  - They could also submit to a different journal. What could they do differently than first submission?

- If one of your colleagues finds him or herself in a similar situation in which his publication gets declined due to dual use concerns, what advice would you give them?

- Should papers like Ann's undergo special review? What should such review entail?

  - See Slide V.8

Next Steps

- Should we have rules or guidelines that address these complex ethical issues surrounding dual use research? If so, who should develop, promulgate, and enforce them?

- If not, in what other ways can we ensure security and the continued success and culture of research in the biological sciences?

- Consider the work that you do. What should your role be in this process?

- What should the scientific community at large be doing?

  - See Slides II.9 and V.6

- Do you agree with recommendations for self-regulation by the scientific community?

• Do you think they will they work? Why or why not?

• What are the responsibilities and obligations of students, life science professionals (post-docs, lab leaders, administrators), members of society, and mentors to the next generation of scientists in the context of dual use research?

- See Slide VII.2

C. Additional points to consider

The organism used in this case, *S. pneumoniae*, is not a select agent. If it had been, consider how the case would have differed for Ann and Peter.

CASE STUDY #2: Chemical Synthesis of Poliovirus

Topic: **Access to genomic information**

A. Background Information

This case study deals with issues of access to data and is based on public, governmental, and scientific community concerns following the publication of papers such as Cello *et al*.'s 2002 piece in *Science*. As explained in this article, the authors synthesized the full-length poliovirus cDNA by mechanically assembling oligonucleotides. They then used RNA polymerase to transcribe the artificial viral cDNA into viral RNA. Placing this viral RNA in a cell-free extract allowed the translation and replication of the virus. Finally, the authors used their virus to infect cells and demonstrated that it had 'biochemical and pathogenic characteristics of poliovirus.' The Cello *et al.* paper attracted significant media attention focusing on the fact that a scientist or bioterrorist could make their own virus from reagents and information available to the public.

The following readings are necessary to understand the context of this case study:

- Cello J, Paul AV, Wimmer E. 2002. Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template. *Science* 297(5583): 1016-1018.

- Committee on Research Standards and Practices to Prevent the Destructive Application of Biotechnology, National Research Council. 2004. Biotechnology Research in an Age of Terrorism: Executive Summary. Washington (DC): National Academies Press. p i-14.

- Committee on Genomics Databases for Bioterrorism Threat Agents, National Research Council. 2004. Seeking Security: Pathogens, Open Access, and Genome Databases: Executive Summary. Washington (DC): National Academies Press. p i-14.

- CDC Select Agent Program Overview

- Excerpt from July 17, 2002 *Washington Post* article "Mail-Order Molecules Brew a Terrorism Debate; Virus Created in Lab Raises Questions of Scrutiny for DNA Suppliers":

> If infectious agents can be made from piecing together pieces of DNA that are individually benign, then government regulators, law enforcement agencies and even DNA synthesis companies may have no way of knowing when someone might be attempting to build a biological bullet.
>
> "The customer gets to design the sequence they want manufactured and there is a limited ability for us to know what people are going to do with it," said Roman Terrill, vice president of legal and regulatory affairs at Integrated DNA Technologies.

> Indeed, Terrill said, with perhaps $10,000 and a few months time, motivated scientists could manufacture the genetic components of a deadly virus. "You could buy your own used DNA synthesizer," he said, "and make whatever you want in the comfort and privacy of your own garage."

• Government response

David Weldon (R-FL) introduced legislation in the House of Representatives of the 107th Congress questioning the publication of the Cello *et al*. paper, labeling it a potential danger to national security, and calling on journal editors to exercise restraint in dual use research publication. The bill also called on the Executive Branch to review government-funded research policies to ensure information that could be used for destructive means by terrorists not be made accessible to terrorists or countries of concern. The bill did not pass.

• Scientists' response

Scientists responded to the Cello *et al.* paper by noting that the basic knowledge that an infectious poliovirus could be created *de novo* from a DNA template was obtained in 1981, when powerful cDNA technology was developed by David Baltimore. Thus, the major findings of the paper had been in the literature for years, and offered no new technological edge to a terrorist or anyone else. In fact, the virus production technique use by Cello *et al*. is technically more difficult and time-consuming than that of Baltimore and colleagues.

- Additional Resource: FAS web-based module on the Cello and Wimmer experiments

B. Proposed action and questions to consider

To balance the risk of terrorist access to dual use information with the need for the continued flow of knowledge and data among researchers, the following proposals have been considered:

• Access to all current public genomic data generated with support from the federal government, be restricted to approved, registered parties only, and that the administration of such a system be analogous to the current select agent system of registration and punishment for violations of policy;

• Institutional Biosafety Committees be responsible for administering and maintaining access systems at their institutions and serve as liaisons for access regulation to the Department of Health and Human Services, CDC, USDA, and other relevant agencies;

• Individuals at approved institutions gain access to genomic data only after successful completion of training in scientific and ethical issues in dual use research, and that requirements of 'approvable individuals' be the same as those for the handling of select agents; and/or

• Scientific publications made available online and in hard copy contain only minimal sequence data and provide accession numbers for those with access (much as is currently the case in most journals) to allow the exploration of relevant sequences more fully.

- What ethical issues are in play in this case?
  - Freedom of information, equal access, security, privacy

- What are the immediate and longer-term ramifications of each of these proposals, for individual researchers and for the scientific community as a whole?

- What are some alternative solutions to balancing the need for security and openness?

- How does the Internet play in to cases such as this? Should anyone who has access to the Internet have access to all genomic sequences? If not, who should not have access and to which sequences should they not have access? Who should monitor this and in what way?

- Significant media reaction followed publication of the Cello *et al.* paper on *de novo* synthesis of an infectious poliovirus. Was this reaction justified? What role should scientists play in such situations and at what points?

- Is unrestricted access to information such as genomic sequences worth the risk of it being used for malevolent purposes?