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Introduction to Dual Use Research of Concern

Module 12

BIOSECURITY ENGAGEMENT PROGRAM

CBEP

Course Objectives

1. DURC is an issue relevant to all researchers
2. All scientists have a responsibility to conduct research responsibly
3. When a researcher identifies potential DURC, the project must undergo a review process to determine actual concern
4. Reviewing and determining DURC does not necessitate cessation of the project
5. Key to review of potential DURC is documentation and justification of conclusions and decisions

What is DURC to you? Exercise

- Individually, spend 10 minutes writing down in your notebook what types of experiments could be considered potentially DURC.
  - Consider the following question:
    - What about the experiment makes it Dual Use?
    - How could this information be misused?
- Discussion on your answers will follow as a large group.

Dual Use Research Definitions

- What is Dual Use? Traditional Definition -
  - "Goods and technologies are considered to be dual-use when they can be used for both civil and military purposes."
    - » European Commission – Trade Website http://ec.europa.eu/trade/creating-opportunities/trade-topics/dual-use/
  - "'Dual-Use items' shall mean items, including software and technology, which can be used for both civil and military purposes, and shall include all goods which can be used for both non-explosive uses and assisting in any way in the manufacture of nuclear weapons or other nuclear explosive devices"
    - » Council Regulation (EC) No 428/2009

Dual Use Research Definitions

- What is Dual Use? Biology Specific-
  - "Biotechnology represents a 'dual use' dilemma in which the same technologies can be used legitimately for human betterment and misused for bioterrorism."
  - "…the capacity for advanced biological research activities to cause disruption or harm, potentially on a catastrophic scale. Broadly stated, that capacity consists of two elements: (1) the risk that dangerous agents that are the subject of research will be stolen or diverted for malevolent purposes; and (2) the risk that the research results, knowledge, or techniques could facilitate the creation of "novel" pathogens with unique properties or create entirely new classes of threat agents."
    - » National Academies of Science: *Biotechnology Research in an Age of Terrorism* (2004)

Dual Use Research of Concern

- **Criterion for Identifying Dual Use Research of Concern**
  - 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.
    - » NSABB

BREAK

Seven Categories of Experiments

1. Enhance the harmful consequences of a biological agent or toxin.
2. Disrupt immunity or the effectiveness of an immunization without clinical and/or agricultural justification.
3. 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.
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.

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

- Rationale:
  - Enhancing the pathogenic consequences of an agent or toxin could increase the likelihood of disease and compromise the ability to treat the disease(s) they cause if extant therapeutics are no longer effective.

- Examples:
  - Includes rendering a non-pathogenic microbe pathogenic
    - Converting seasonal flu virus to a virus as deadly as the 1918 pandemic strain
  - Routine techniques for restoring the virulence of viral stocks by back-passaging in animal hosts
  - Identification of virulence factors through genome-wide screening or gene knockout techniques

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

- Rationale:
  - Immunity is a key component in a host's defense against pathogens and toxins, thus rendering an immunization ineffective or disrupting immunity could have harmful consequences for public health, agricultural crops and other plants, and animals.

- Examples:
  - This could make a host population vulnerable to the pathogenic consequences of a microbe from which the host population would have otherwise been protected or for which protection such as a vaccine was available.
  - The insertion of an immunosuppressive cytokine into a viral genome to render the antiviral immune response less effective.
  - Information about the immunosuppressive properties of chemotherapeutic drugs for cancer or autoimmune disorders could also fit this category although it is unlikely to be dual use of concern.

3. 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.

- Rationale:
  - Anything that might compromise the ability to detect, treat, or prevent disease or illness (human or agricultural) caused by biological agents or toxins could result in a significant public health and/or economic burden.

- Examples:
  - Conferring doxycycline resistance to *Vibrio vulnificus* or conferring antibiotic resistance to agriculturally relevant microbes, such as rendering *Ralstonia sloanacearum* (a bacterium on the U.S. Department of Agriculture list of high-consequence organisms0resistant to rifampin.
  - Use of standard laboratory selection procedures with antibiotics using host-vector systems that do not present a significant risk to health or the environment – not likely to be dual use of concern.

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

- Rationale:
  - This could facilitate the purposeful malevolent use of a biological agent or toxin and increase the rate or ease by which an agent could spread, impeding attempts to contain disease outbreak.

- Examples:
  - Changing genetic factors to increase transmissibility
  - Altering the route of transmission or vector to increase the ease and effectiveness by which an agent may be transmitted.

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

- Rationale:
  - This could endanger a host population that normally would not be susceptible.
  - Prevention and therapy measures for the newly vulnerable host population may be lacking, possibly allowing for the uncontrolled spread of disease.

- Examples:
  - Converting non-zoonotic agents, altering the tropism of viruses, and expanding the varieties of the same plant that a pathogenic agent could infect.
  - Certain vaccine research and the development of animal models for infectious disease, which may involve alterations of the host range or tropism, are unlikely to constitute dual use research of concern as well as the attenuation of viruses for vaccine development.

6. Enhance the susceptibility of a host population.

- Rationale:
  - This could be used to compromise immune responses and enable the acquisition and spread of disease on an epidemic scale.

- Examples:
  - Creation of a stable recombinant Lactobacillus casei that could effectively block the host's ability to synthesize an important immune signal, such cytokines which may directly facilitate the evasion of normal host defenses.
  - Unlikely to be considered dual use of concern are research on the systemic exposure to immunostimulatory and immunosuppressive DNA and their effect on host susceptibility to local inflammatory challenge, studies to develop immunosuppresive drugs for cancer or transplantation.

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

- Rationale:
  - Host populations may not be immune to novel agents and reconstituted eradicated agents and there may not be existing diagnostics or known or widely available prophylaxes or therapeutics for such agents.

- Examples:
  - De novo construction of a microbial pathogen using wholly unique gene sequences or combinations of sequences that do not exist in nature and reconstitution of a pathogen that no longer exists in nature, such as the 1918 pandemic influenza virus.
  - Not likely to be dual use of concern includes standard experimentation that generates knockouts, mutants, reassortants, complement strains, or infectious molecular clones of viruses that are similar to naturally occurring agents.

BREAK

Examples of Potential DURC

- Reconstruction of the 1918 Influenza Virus
- Publication of Complete 1918 Genome Sequence
- Synthesis of Poliovirus
- Insertion of Interleukin-4 in Mousepox Virus
- Generation of an avian flu variant that can spread (airborne) between mammals

- Any other examples come to mind?

Examples of Potential DURC

Botulism Toxin in the Milk Supply

- Reason for Concern?
  - "Considered a roadmap for terrorists"
  - Gave dosing requirements
  - Gave total deaths upon use of various quantities.
  - Step in processing to undertake the attack.

What To Consider? Activity

- Discuss amongst your group what you would need to consider to determine if your research is DURC.
  - Ask yourself:
    - Do you need to consider just the seven categories?
    - When do you need to make these considerations?
  - Time limit: 10 minutes

Limitation to the Seven Categories

Limiting pool of potential DURC

National Science Advisory Board for Biosecurity (U.S.)

- The Fink Report recommended the creation of a national Science Advisory Board for Biodefense. "We recommend that the Department of Health and Human Services create a National Science Advisory Board for Biodefense (NSABB) to provide advice, guidance, and leadership for the system of review and oversight we are proposing."

- National Science Advisory Board for Biosecurity: *Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information* (2007).

  – Described a subset of dual use **research that has the highest potential** for generating information that could be misused.

What To Do?

- You have determined that you have potential DURC. What do you do about it?
- In your group, construct a timeline covering a research project and determine what constraints need to be undertaken to reduce the concern.
- After 15 minutes, groups will present their findings to the larger group.

Possible Actions

- Change in Performance of Research
  - Decided against conducting a specific research project/experiment
  - Decided against seeking funding for a proposed research project
  - Decided to shift my research away from an area altogether
- Change in Collaboration
  - Decided against collaborating with particular scientists, postdocs, students, etc
- Change in Research Communications
  - Limited conversations about research
  - Decided against presenting research at a conference
  - Modified a conference presentation
  - Decided against submitting a manuscript to a journal
  - Modified a manuscript

Review of Dual Use Research of Concern

Review

To wrap-up, let's discuss what we learned. . .

What did we learn?	What does it mean?	Where do we go from here?

Review

- What is Dual Use Research of Concern?
- Who does it apply to?
- When does it apply for me?
- Who should be involved?

Review

1. DURC is an issue relevant to all researchers

2. All scientists have a responsibility to conduct research responsibly

3. When a researcher identifies potential DURC, the project must undergo a review process to determine actual concern

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Action Plan

By the end of this lesson, I would like to:					
KNOW		FEEL		BE ABLE TO DO	

Your learning doesn't stop with this lesson. Use this space to think about what else you need to do or learn to put the information from this lesson into practice.

What more do I need to know or do?	How will I acquire the knowledge or skills?	How will I know that I've succeeded?	How will I use this new learning in my job?

Use space on back, if needed