Proliferation Threats from Biotechnology: What is Dual-Use Research?
In Class Discussion

Break into groups of 3, come up with definition dual use and present to class
Biological Dual-Use Research

“Biotechnology represents a ‘dual use’ dilemma in which the same technologies can be used legitimately for human betterment and misused for bioterrorism.”

*Biotechnology Research in an Age of Terrorism*,
National Academy of Sciences, 2004

“…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, agriculture, plants, animals, the environment, or materiel.”

National Science Advisory Board for Biosecurity
Research on the same biotechnologies

Peaceful Use

Public Health

Diagnostics
Drugs
Vaccines
Antivirals

Biodefense

Defends against use of bioweapons

Dual-Use

Weapons Use

Offensive Military

Bioweapons
States
Terrorists

Fermenter used for production of weaponized anthrax.
Peaceful Use Weapons Use

- Public Health
  - Diagnostics
  - Drugs
  - Vaccines
  - Antivirals

Research on the same biotechnologies

- Dual-Use
  - Biodefense
    - Defense of biological weapons
    - Potential for diversion to offensive military use or bioterrorism

- Offensive Military
  - Bioweapons
    - States
    - Terrorists

Fermenter used for production of weaponized anthrax.
Who Does Dual Use Research of Concern?

• Military
• Governments
• Private Sector
• Academia
It’s not all about the microbes
In Class Discussion

What is the difference between biological warfare and bioterrorism?
Biological warfare:
- Specialized type of warfare conducted by government against a target.
- Goal is to degrade enemy war-fighting capability or deny terrain.
- Requires large amounts of highly purified, stable material that can be packaged, stored and delivered.

R-400 bombs filled with *B. anthracis*.

Bioterrorism:
- Use of biological agents in furtherance of political or social objectives.
- Goal is to terrorize.
- A small amount of relatively unrefined material may be sufficient to achieve the desired outcome.
- Delivery systems are less sophisticated.
Sources of Agents

- Most are naturally occurring endemic diseases that can be obtained from a hospital or clinic laboratory.
- Purchased from commercial repository.
- May be traded, stolen, or obtained gratis from other research, clinical, veterinary laboratories or scientists.
# CDC Classification of Select Agents and Toxins

**HHS AND USDA SELECT AGENTS AND TOXINS**

<table>
<thead>
<tr>
<th>HHS SELECT AGENTS AND TOXINS</th>
<th>USDA SELECT AGENTS AND TOXINS</th>
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<tbody>
<tr>
<td>Abcin</td>
<td>Afrikan horse sickness virus</td>
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<tr>
<td>Botulinum neurotoxin*</td>
<td>African swine fever virus</td>
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<tr>
<td>Botulinum neurotoxin producing species of Clostridium*</td>
<td>Avian influenza virus</td>
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<tr>
<td>Conotoxin (Short, paralytic alpha conotoxins containing the following amino acid sequence: X2CXX(CXX)X2CXX(CXX)X2CXX(CXX))</td>
<td>Classical swine fever virus</td>
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<td>Crotalidae neurotoxins</td>
<td>Foot-and-mouth disease virus*</td>
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<td>Crimean-Congo hemorrhagic fever virus</td>
<td>Goat pox virus</td>
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<td>Diarrhoetoxins</td>
<td>Lumpy skin disease virus</td>
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<tr>
<td>Diarrhoentoxins</td>
<td>Mycoplasma capricolum</td>
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<td>Eastern Equine Encephalitis virus*</td>
<td>Mycoplasma mycoides</td>
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<td>Esoli virus*</td>
<td>Nervous disease virus</td>
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<td>Francisella tularensis</td>
<td>Pestes des petits ruminants virus</td>
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<td>Lassa fever virus</td>
<td>Rinderpest virus*</td>
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<tr>
<td>Lujo virus</td>
<td>Sheep pox virus</td>
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<tr>
<td>Marburg virus*</td>
<td>Swine vesicular disease virus</td>
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<tr>
<td>Monkeypox virus</td>
<td>USDA PLANT PROTECTION AND QUARANTINE (PPQ) SELECT AGENTS AND TOXINS</td>
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<tr>
<td>Reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments (Reconstructed 1918 Influenza virus)</td>
<td><strong>Peronosclerospora philpottiana</strong> (Peronosclerospora sacchari)</td>
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<tr>
<td>Ricin</td>
<td>Phoma glycincola (formerly Pyrenochaeta glycinola)</td>
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<td>Reoviridae poxvirus</td>
<td>Raoulinia solanacearum</td>
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<td>SARS-associated coronavirus (SARS-CoV)</td>
<td>Rathayibacter toxigenes</td>
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<tr>
<td>Serratotoxin</td>
<td>Sclerotinia fructigena</td>
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<tr>
<td>South American Hemorrhagic Fever viruses:</td>
<td>S. hygroscopicus</td>
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<tr>
<td>Chapare</td>
<td>Sphaerobacter phaeus</td>
</tr>
<tr>
<td>Guanarito</td>
<td>Sphaerobacter torrefaciens</td>
</tr>
<tr>
<td>Junin</td>
<td><strong>Sphaerotilus natans</strong></td>
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<tr>
<td>Machupo</td>
<td><strong>Spiniferites sp.</strong></td>
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<tr>
<td>Sabia</td>
<td>Synechocystis sp.</td>
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<tr>
<td>Shigelladotoxin A, B, C, D, E subtypes</td>
<td>Xanthomonas campestris</td>
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<tr>
<td>T-2 toxin</td>
<td>Xanthomonas vesicatoria</td>
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<tr>
<td>Tetanolysin</td>
<td>Xanthomonas xanthii</td>
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<tr>
<td>Tick-borne encephalitis complex (flavivirus) viruses:</td>
<td>Yersinia pestis</td>
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<tr>
<td>Far Eastern subtype</td>
<td>*Denotes Tier 1 Agent</td>
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<td>Siberian subtype</td>
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In Class Discussion

What organisms should be added to or deleted from the Select Agent List?

Does a Select Agent list make us more safe or less safe?
Of greatest concern are those experiments that have the potential to produce information, products, or technologies that could:

- Enhance the harmful consequences of a biological agent or toxin;
- Disrupt immunity or the effectiveness of an immunization without a clinical and/or agricultural justification;
- Confer 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;
- Generate a novel pathogenic agent or toxin, or reconstitute an eradicated or extinct biological agent.
Examples of Risk
Potential Weaponization of New Technologies

• 1997: Dr. David Edwards developed a way to deliver aerosolized medicine using large porous carrier particles.
• The method dramatically increased the amount of drug that made it deep into the lungs.
• His research appeared in *Science*, bringing into question whether someone could use the information for weaponizing anthrax and other aerosolized agents.

See: Dual Use Research in Aerosol Drug Delivery
www.fas.org
Examples of Risk

Unintended Consequences of Genetic Engineering

Australian researchers genetically altered mousepox, an infectious virus that affects mice, to induce sterility in the mice.

The researchers inadvertently produced a recombinant virus with greatly increased lethality.

Their paper was published in the *Journal of Virology* in 2001, leading to concern that the same technologies could be used to weaponize smallpox and other pox viruses that affect humans.

Examples of Risk
De Novo Synthesis of Poliovirus

- In the fall of 2001, Dr. Eckard Wimmer announced that his lab had been able to assemble synthetic poliovirus by piecing together the viral genome based on its sequence, publicly available on the internet.

- These experiments established the proof of principle that more dangerous biological agents could in theory be made from scratch.

See: Cello et al, Science 2002 297:1016-18
Examples of Risk
Accidental Exposure of Laboratory Personnel

• 2005: Three Boston University researchers became ill after being exposed to tularemia, a highly lethal pathogen
• The scientists believed they were working with a research strain that would not cause illness, but a highly infectious strain was accidentally mixed with the harmless variety.
• The researchers violated biosafety procedures that required them to work with tularemia inside an enclosed box, called a hood, that sends air through sophisticated filters.

Examples of Risk
Anthrax: Stolen or Diverted

- 2008: A U.S. Army Medical Research Institute scientist, Dr. Bruce Ivins, committed suicide after the FBI suspected him of diverting anthrax spores from his research lab and using them in the 2001 anthrax letter attacks.
- Dr. Ivins had worked on an experimental vaccine to treat anthrax.
- The FBI claimed that a preponderance of circumstantial evidence led to him, and the strain of the anthrax used in the letter attacks matched the anthrax in his laboratory.

Dr. Bruce Ivins

B. anthracis
H5N1 Avian Influenza Virus Manuscripts and Dual Use Research Concerns
H5N1 Manuscripts - Dual Use Research Concerns

• Two US government-funded studies on respiratory transmission of H5N1 were submitted for publication
• The manuscripts raise “dual use research concerns” in that they contain information that could be utilized to create a potentially human-transmissible form of H5N1 that could be intentionally released to threaten public health and security
Summary: Proliferation Risks of Biotechnology

- Creating a bioweapon requires the skills and materials to handle and grow agents, isolate, and disseminate them.
- Any medical advance that improves the ease of engineering, handling, or delivering treatment has the potential to be applied by those wishing to do harm and can be considered ‘dual-use.’
- Each year hundreds of dual-use research articles are published, making them accessible to any member of the research community.
- Thousands of pieces of scientific equipment are purchased on the Internet.
- This openness creates the risk that available information, reagents, or equipment will be used to create more dangerous biological weapons.
In Class Discussion

What steps can we take to ensure that our resources/equipment/knowledge are not used inappropriately?