June 2012 COGR Meeting Thursday Afternoon Dual Use Presentation - Thomann

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UNDERLYING PREMISE

- Good People Doing Good Things
  
  *Therefore*

- Misuse is Not an Interest or Consideration
  
  *Therefore*

- Awareness should be Increased when Appropriate

  *Most Importantly*

- Balance in Supporting Good Science Must be Maintained
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 protocol review, and upon request.
Duke IBC Became Aware/Involved with Dual Use in 2003
Southeast Regional Center of Excellence for Emerging Infections and Biodefense (SERCEB) Participated in Duke IBC Meeting
Duke has Participated in the National Debate
Duke Began Developing an Awareness Plan/Process in 2005
AWARENESS PLAN

- Plan Focused on:
  - Educating the IBC
    - IBC members trained in 2006 using the SERCEB training module
  - Increasing awareness among investigators
- Did not Limit the Scope to Select Agents
  - Included all rDNA research
  - Included other BSL3 research considered by IBC
AWARENESS PLAN

- Focus is not Restricted to the “Directly Misapplied to Pose a Threat” Definition
  - That is an unlikely status
  - Our plan considers incremental or sequential threat or risk
    - Relates to the evolution of research and discovery
  - Intended to induce a proactive thought process in researchers
Southeast Regional Center of Excellence for Emerging Infections and Biodefense (SERCEB)

- The Dual Use Dilemma in Biological Research
  - [http://www.serceb.org/dualuse.htm](http://www.serceb.org/dualuse.htm)

- Required for IBC and Targeted PIs
Learning Objectives

- Describe the Dual Use Dilemma in Bioscience Research;
- Identify and Analyze Potential Ethical, Legal and Policy Problems which may Arise in the Biosciences; and
- Develop Strategies to Respond to and Resolve Dual Use Scenarios.
AWARENESS STATEMENT ON DUKE’S RECOMBINANT DNA REGISTRATION FORM

In reviewing registrations, the Duke IBC considers "dual use" potential, namely the potential for research projects with a beneficial purpose to provide knowledge, products or technologies that could be directly misapplied to pose a threat to public health and safety, agricultural crops and other plants, animals, the environment, or material. For a full discussion of this topic, consult <NSABB web site>. Consider whether your research is reasonably anticipated to do any of the following based on current understanding:
• Enhance the harmful consequences of a biological agent or toxin.
• Disrupt 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 to the pathogenic consequences of an agent or toxin.
• Generate a novel pathogenic agent or toxin or reconstitute an eradicated or extinct biological agent.
• Provide other knowledge, products or technologies that could be directly misapplied to pose a threat to public health and safety, agricultural crops and other plants, animals, the environment, or material.

Comment on aspects of your research, if any, with potential for dual use:
DUKE CASE 1: VIRULENCE FACTORS IN UROPATHOGENIC *E. coli* (2006)

- **Proposal:** Express potential virulence genes in uropathogenic *E. coli* to determine their effect in an animal model
- **Goal:** Understand host-pathogen relationships. Develop vaccine or therapeutic for urinary tract infections
- **Risk:** Enhance harmful consequences of agent.
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- **rDNA registration addressed biosafety but not dual use**

**Outcome:**
- PI took dual use training
- PI amended registration to discuss how potentially hyper-virulent *E. coli* would be recognized and handled
DUKE CASE 2: TETANUS LIGHT CHAIN (2007)

- Proposal: Use retroviral vector (replication-deficient, three plasmids, VSV-G envelope) to express light chain of tetanus toxin in specific neurons in an animal model.
- Goal: Determine the downstream effects of blocking transmission from these neurons.
- Risk: Increase transmissibility of toxin.
- PI addressed biosafety issues but not dual use.
- Duke IBC raised dual-use concerns as part of its review of the rDNA registration.
- Outcome: PI modified proposal to use a marker gene in place of the light chain of tetanus toxin.
DUKE CASE 3: DENGUE IN DROSOPHILA (2007)

- **Proposal:** Adapt dengue virus to grow in *Drosophila* cell culture
- **Goal:** Study cell/virus interactions using *Drosophila* genetic tools
- **Risk:** Alter host range of agent
- After grant approval, NIAID program officer raised dual use concern and requested review by Duke IBC
- **Duke IBC review:** (1) Serial passage is old technology. (2) Attenuation is expected result. (3) *Drosophila* not a dengue vector.
- **Duke IBC conclusion:** No meaningful dual-use potential
- **Risk management:** PI and lab staff completed on-line training in dual use
- **Outcome:** NIH awarded the funding. Research proceeded without modification.
GOVERNMENT POLICY FOR OVERSIGHT

Institutional Responsibilities

- Collaborate with Federal Agencies to:
  - Assess the risks for “covered” agents or toxins
  - Develop a risk mitigation plan
    - Consider incorporating risk mitigation into the grant for proposed research
    - Consider modifying the grant/contract for currently funded DURC projects
    - Adopt the appropriate risk mitigation measure(s) defined in the Policy
DUKE’S STATUS RELATED TO GOVERNMENT POLICY

- Currently Assessing Risks for Covered Agents and More
- Proactively Addressing Mitigation Planning for *Duke* Identified Research
- However, We are Not Working at the “Proposal/Granting Level”
SCALING-UP?

- Duke has Moved Beyond the Proposed Scope of the Government Policy
  - All rDNA and high-risk BSL3 research

- Synthetic Biology
  - Big challenge/dilemma
  - Expands the scope significantly
    - Identification/capture would be challenging
CONCLUSIONS

- IBCs can Review and Manage Dual Use Potential in the Absence of Formal Regulation or a Consensus Definition
- Investigators are Not Fully Ready to Self-Identify or Manage Dual Use Research
  - However, awareness and training can improve that performance
CONCLUSIONS

- Time and Effort Required by PI and IBC are Modest and Manageable
- Management Strategies are Already Available at Many Levels of Potential Dual Use Review
- Benefit of Dual Use Review is Plausible but Unproven