

Dual Use Research of ConcernHow we do things at St. Jude

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Why does DURC affect St. Jude?

- NIAID Centers of Excellence for Influenza Research and Surveillance; WHO Collaborating Center for Studies on the Ecology of Influenza in Animals
- Influenza-positive samples (of unknown genotype) submitted to St.
 Jude from all around the world
- Highly pathogenic avian influenza (HPAI) virus is one of the organisms regulated by DURC
- Sequencing, biochemical, and in vivo studies are performed on derived virus
- Swapping of viral segments into low risk category virus is frequently undertaken to assess role of identified mutations
- Relatively small group of faculty that work with HPAI
- HPAI is the only agent subject to DURC used at St. Jude



How is DURC research identified at St. Jude

- Pls use an online submission process for IBC protocols and amendments
- One section addresses the NSABB concerns
 - Does the proposed research have the highest potential for yielding knowledge....
 - Will the research enhance the harmful consequences of a biological agent or...
 - Does the research have the potential of disrupting the immunity....
 - Can the proposed research confer to a biological agent resistance to....
- Answering 'Yes' to any of these questions (regardless of pathogen) triggers review by BSO and DURC (IRE) chairman
- Any member of the IBC can suggest DURC review of a protocol
- We (St. Jude) err on the cautious side, i.e., we review all HPAI research to consider the possibility of DURC



How we evaluate potential DURC science

- Ad hoc DURC (IRE) subcommittee with expertise from different disciplines
 - Chair (V. Chair IBC), 2-4 faculty experts, BSO (ICDUR), Director EH&S, Chief Compliance Officer, scientific editing, legal counsel
- PI delivers detailed proposal to committee in advance
- 1-2 hr meeting for PI presentation and Q&A
- Specifically asked to address the DURC issues based upon the 15 + 7 'algorithm'
- In camera discussion with vote
- Chair of DURC subcommittee writes memo to IBC with summary of discussion and result of vote
- PI is required to submit an update if any unexpected events occur and an annual update coincident with IBC reapproval



DURC subcommittee (IRE) – IBC relationship

- DURC (IRE) is a subcommittee of the IBC
- Meetings scheduled separate for IBC meeting (frequently held 'back to back' so that any members of IRE can attend IBC)
- Limits public dissemination of sensitive information
- Overlap of personnel
- IRE Chair (and others) provides overview of science and discussion at IBC meeting



The good and the bad

Good

- Expectations are clear
- Criteria are easy to interpret (except one!)
- PI has to explain proposed studies to non-scientists
- Institution has sufficient expertise to evaluate science without conflicts of interest
- Non-scientist members clearly add value to the DURC committee

Bad

- Wording in DURC policy has led to significant ambiguity of interpretation by PI and committee
- Policy not all encompassing
- Increased workload (mainly for BSO, EH&S)



Problems interpreting the 'algorithm'

- In general, following the DURC policy algorithm works well, however there are two areas where we, as a committee, struggle
 - '5. Alters the host range or tropism of the agent or toxin'
- A decrease in these properties triggers DURC review
- We realize that the criteria will evolve over time, but currently H7N9 virus is not subject to DURC
- We recently reviewed studies that proposed to evaluate the biology of H7N9 virus and concluded that this was durc (not DURC), i.e., that the results may be enabling, but since HPAI was not used (H7N9 is not an HPAI/DURC agent), technically it may not be covered by the guidelines



DURC Algorithm

Step 1 - Does the work involve one of the 15 agents/toxins listed in the policy?

- 1. Avian influenza virus (highly pathogenic)
- 2. Bacillus anthracis
- 3. Botulinum neurotoxin
- 4. Burkholderia mallei
- 5. Burkholderia pseudomallei
- 6. Ebola virus
- 7. Foot-and-mouth disease virus
- 8. Francisella tualrensis
- 9. Marburg virus
- 10. Reconstructed 1918 Influenza virus

YES

- 11. Rinderpest virus
- 12. Toxin-producing strains of Clostridium botulinum
- 13. Variola major virus
- 14. Variola minor virus
- 15. Yersinia pestis

Step 2 - Does the work involve any of the seven effects in the policy?

- 1. Enhances the harmful consequences
- 2. Disrupts immunity
- 3. Confers resistance
- 4. Increases the stability or transmissibility
- 5. Alters the host range or tropism
- 6. Enhances the susceptibility of a host population to the agent
- 7. Generates an eradicated or extinct agent

Step 3 – Does the work meet the definition of DURC in the policy?

"Life sciences research that. based on current understanding, can be reasonably anticipated to provide knowledge. information. products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, or materiel or national security".

YES

Apply Dual Use of Concern Criteria



Requires additional Federal and local oversight and risk mitigation strategies to address dual use concerns

YES

If NO, not Dual Use Research of Concern