June 2012 COGR Meeting Thursday Afternoon Dual Use Presentation - Mellon

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H5N1
Merry-Go-Round

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THE GRADUATE SCHOOL
University of Wisconsin-Madison
Deliberating Over Danger

The creation of H5N1 bird flu strains that are transmissible between mammals has thrown the scientific community into debate.

The Graduate School
University of Wisconsin-Madison
Timeline of Events, 2006/2011

- Call for proposal (NIAID) and grant submission
- UW-Madison Review [biosafety and dual use]
  - Institutional Biosafety Committee (IBC)
  - Biosecurity Task Force (BTF)
- NIH Funding/Research ongoing
The National Institute of Allergy and Infectious Diseases (NIAID), The Influenza Portfolio

- Report of the Blue Ribbon Panel on Influenza Research 2006 (similar to 2009 WHO Public Health Research Agenda for Influenza)

**Influenza at the Animal-Human Interface**

Scientific understanding of how animal and human influenza viruses interact, including how influenza viruses circulate among various reservoirs and the evolutionary pressures that lead to the emergence and spread of new viral sub-types, could be improved.

- Elucidate patterns of influenza virus diversity and evolution.
- Define patterns of influenza virus transmission in and between human and animal populations.
- Examine interactions of diverse influenza viruses with various hosts.
The National Institute of Allergy and Infectious Diseases (NIAID), The Influenza Portfolio

- BIODEFENSE AND EMERGING INFECTIOUS DISEASE RESEARCH OPPORTUNITIES

- This PA is intended to encourage the submission of investigator-initiated research grant applications in biodefense. The goal is to expedite research leading to the diagnosis, prevention and treatment of diseases caused by potential bioterrorism agents.
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Oversight of Select Agents at UW-Madison

- Responsible Official (RO)
- Biosecurity Task Force: oversight of all aspects of the program including PIs, facilities, biosecurity, and is advisory to the RO
- Institutional Biosafety Committee: Both AROs are consultants for SA proposals, facility issues, biosafety, biosecurity, etc.
Biosecurity Task Force

• Responsible for SA Program Oversight

• Membership:
  - RO (chair)
  - AROs, Director EHS, BSO
  - ADs for Research from 3 schools/colleges
  - State Lab Hygiene (PI)
  - Vet Diagnostic Lab (experienced PI)
  - UW Police
  - Attorney
  - Director, Campus Information Security
  - Director, University Health Services
  - UW Communications
<table>
<thead>
<tr>
<th><strong>BSL-3+</strong></th>
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<tr>
<td>Personal change and shower room</td>
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<td>Lockable doors</td>
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<td>Interlocked Doors</td>
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<td>Bioseals on interlocked double door autoclaves</td>
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<tr>
<td>Independent air supply and exhaust (also redundant *)</td>
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<td>Visible means of displaying pressure differential</td>
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<td>Effluent Decontamination System *</td>
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<td>Duct work prior to HEPA filter is pressure decay tested</td>
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<td>Backup power*</td>
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Courtesy of R. Moritz
<table>
<thead>
<tr>
<th><strong>BSL-3Ag</strong></th>
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<tr>
<td>Facility is primary containment</td>
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<td>Box within a box</td>
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<td>Walls</td>
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<td>Series of entry/exit rooms</td>
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<td>Airlock doors</td>
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<td>Facility and duct work is pressure decay tested</td>
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<td>HEPA supply and double HEPA exhaust</td>
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<tr>
<td>Effluent Decontamination System</td>
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<td>Isolator cages*</td>
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<td>Gas decontamination of facility</td>
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Influenza pandemics of the 20th/21st centuries

- 2009: Spanish Flu Pandemic (H1N1)
- 1918: Spanish Flu (H1N1)
- 1957: Asian Pandemic (H2N2)
- 1968: Asian Pandemic (H3N2)

20-40 million deaths

Courtesy of Y. Kawaoka
THE ‘BIRD FLU’ SCARE

The Bird Flu
The Race To Prevent A Global Epidemic
How to Protect Yourself

How Far the Virus Can Spread?
H5N1 virus infections

Courtesy of Y. Kawaoka
MORTAL DANGER
Since 2003, 584 confirmed cases of H5N1 flu have led to 345 deaths. (Numbers indicate total cases.)
- Non-fatal cases
- Fatal cases

Data from WHO, Graph from Nature
Transmission of H5N1 avian influenza virus to humans
Transmission of H5N1 avian influenza virus to humans

Courtesy of Y. Kawaoka
Transmission of H5N1 avian influenza virus to humans

Courtesy of Y. Kawaoka
What would make bird flu virus transmissible in humans?

Courtesy of Y. Kawaoka
H5N1 virus  A(H1N1)pdm09

H5/pdm09

Courtesy of Y. Kawaoka
Transmission

Courtesy of Y. Kawaoka
Results

No transmission

6/6 - transmission

Courtesy of Y. Kawaoka
Global incidence of the mutation among H5N1 isolates in 2009-2011

- **Japan**: 40/40 (100%)
- **China**: 31/49 (63%)
- **Vietnam**: 33/130 (25%)
- **Other**: 56/137 (41%)
- **Egypt**: 265/352 (75%)
H5N1 viruses in Egypt

- Mutation (-): 30%
- Mutation (+): 70%

Viruses with the mutation are transmitted to humans.

2009-2011 birds

2009-2011 humans
Timeline of Events, Continued 2011/2012

- Aug: Manuscript submitted
- Aug 30: Meeting with the Chancellor, et al.
- Sep 09: The Movie, Contagion
Timeline of Events, Continued 2011/2012

- Sep 12: Fouchier announcement at Malta Conference
- Oct/Nov: NSABB review of manuscripts
- Dec: FBI begins engagement with UW-Madison on “bird flu”
- Dec 20: NSABB statement (surprise and shock)
- Jan 20: Kawaoka, Fouchier and 37 other Flu researchers publish statement and initiate a 60 day pause
- Jan 25: Kawaoka commentary
- Feb 16/17: WHO meeting (the manuscript falls under Export Control!)
Timeline of Events, Continued 2011/2012

- Feb 29: ASM biodefense and emerging disease conference
- March 29/30 – NSABB meets to review “revised” manuscripts
- March 29 – U.S. Policy for Oversight of Life Sciences DURC
- April 23 – Rep F. James Sennsenbrenner (R-Wis) letters to OSTP Director John P. Holdren and NIH Director Francis S. Collins
- April – Increased scrutiny of DURC (refined at UW)
- May 2 – Nature publishes Kawaoka manuscript (enhanced and expanded biosafety/biosecurity methods)
Refining DURC Review at UW-Madison

- Researcher determination
- Researcher discussion with RO and ARO (if SA)
- Researcher discussion with IBC subcommittee
- Discussion of full-IBC and vote
- Discussion of BTF and vote
- UW-Madison acknowledgement/determination communicated to NIH
Stuff Happens!

SPEED BUMP

IT SEEMS THERE IS A DIFFERENCE BETWEEN A "HYPOTHESIS" AND A "GUESSTIMATE."