Limits of Government
Regulation of Science: The
Bird Flu Challenge

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The Studies

- **Erasmus**: Genetically modified avian H5N1 influenza through site-directed mutagenesis and serial passage in ferrets.
  - Produced a version of the virus that was capable of respiratory transmission with only five mutations.
  - Initial reports suggested a high case-fatality rate among the ferrets, but this was later demonstrated not to be the case.

- **Wisconsin**: Reassorted the HA gene segment from H5N1 with the other segments from pH1N1.
  - Produced a virus that could be efficiently transmitted with only four mutations.
  - Produced lung lesions in the ferrets but no severe disease.
The NSABB

- The National Science Advisory Board for Biosecurity is a federal advisory committee for dual use biological research.
- It is composed of members from academia (mostly), advocacy organizations, and industry, as well as non-voting members from a range of Federal agencies.
- It is empowered to make recommendations about dual use biological research, including by reviewing research manuscripts and recommending to HHS whether HHS should ask for voluntary redaction or withholding of manuscripts.
The Controversy (Round 1)

- Last fall, NSABB reviewed both papers after they had gone through review at Science and Nature.

- On its recommendation, HHS requested the journals and authors to voluntarily:
  - Remove some details about the experimental methods
  - Remove details about specifically which mutations allowed for respiratory transmission.
  - Add a statement about the public benefit of the research being conducted.

- This launched a substantial controversy about the role of government in scientific publication and the freedoms and responsibilities of scientists.
What Was at Stake?

- Safety and Security
  - Risk of bioterrorism?
  - Benefits of publication to public health surveillance and response?

- Knowledge
  - Science exists in its methods, not its conclusions.
  - A society committed to scientific knowledge should be uncomfortable making it more difficult to test findings.

- Progress
  - Science, and the technology it produces, operate iteratively.
1. Are the harms of unredacted publication significant?
   - No
   - Yes
     - Are the risks serious in magnitude, if they should occur?
       - No
       - Yes
         - Is the feared harm likely?
           - No
           - Yes
             - Is the information to be redacted already public?
               - No
               - Yes
                 - Is the state of the scientific field such that these methods or conclusions will inevitably become public in the near future?
                   - No
                   - Yes
                     - Does the reduction in risk from redaction significantly reduce the likelihood or magnitude of risks?
                       - No
                       - Yes
                         - Will redaction significantly reduce the benefits from unredacted publication, considering:
                           - A. Will unredacted publication of methods advance the development of an important methodology?
                           - B. Will unredacted publication of methods or results facilitate important public health or welfare objectives or the acquisition of important knowledge?
                           - C. Are the benefits from unredacted publication likely?
                           - D. Can methodological or societal gains be obtained by a release of unredacted information to a limited group of people without entailing the same risks?
                             - No
                             - Yes
                               - Are the likely harms significantly greater than the likely benefits of unredacted publication?
                                 - No
                                 - Yes
                                   - Consider not publishing
                                     - Yes
                                     - No
                                       - Publish with the least redaction necessary.
                                         - No
                                         - Yes
                                           - Publish without redaction.
Unprecedented?

- This wasn’t the first time the federal government had asked a journal not to publish potentially sensitive public health information.

- In 2005, HHS asked *PNAS* note to publish a mathematical model about botulinum toxin in the milk supply.

- NSABB reviewed research to reconstruct the 1918 flu virus in 2005 and recommended that research continue and that it be published (but it recommended added a note about biosafety conditions and public health benefits).
The 1\textsuperscript{st} Amendment

- The 1\textsuperscript{st} Amendment gravely restricts limitations on expression.
- Scientific publications are fully protected by the 1\textsuperscript{st} Amendment.
- Government efforts to restrain publication through legal authority almost always violate the constitution.
The 1st Amend. and This Instance

- By its own terms, HHS’ request for redaction was voluntary and could be rejected by the authors/journals.

- As such, there’s no restraint in the eyes of the law. The government is free to express an opinion that something would be better off not being published.

- The few cases in this area suggest that the extent to which the government “request” is coercive determines whether there might be a 1st Amendment violation.
In 1979, the DOE sought to block an article in The Progressive which would have provided information on how to build a hydrogen bomb.

The article was based on publicly available information, but US law deemed nuclear information to be “born secret.”

A federal trial court ruled that restraining the publication was acceptable as analogous to “the publication of the sailing dates of transports or the number and location of troops” during war.

However, that case dealt with a popular press magazine for whose purposes technical details mattered fairly little.

And most scholars believe the decision would have been overturned on appeal had the issue not been made moot by similar publication elsewhere.
There are very few cases about the extent to which grant agreements can require pre-publication review of papers.

In 1991, Stanford successfully challenged a confidentiality clause in an NIH grant that required approval before publishing preliminary findings about artificial heart research.

The court in Stanford particularly noted that scientific research at universities should be free from restraint.

However, “controlled unclassified information” or “sensitive but unclassified” restrictions on research is fairly common and courts have never squarely addressed them. Stanford suggests CUI/SBU restrictions on publication may be untenable.
The Role of Classification

- Under National Security Decision Directive 189 (from the Reagan Administration), US policy is that basic research is either unrestricted or classified.

- By executive order, US policy disfavors classifying non-applied research in the life sciences, and the mechanisms for classifying extramural life sciences research are unclear.

- Nonetheless, current US policy does make room for classifying dual use biological research.

- While preventing the publication of classified information is still difficult, other penalties can be brought to bear.
The Controversy (Redux)

- In February, WHO convened an international expert group which recommended for full publication.
  - It weighed the public health benefits of the research / publication more strongly than NSABB and the risks less.
  - Its membership was more weighted toward public health and less toward biosecurity than NSABB.
  - It also incorporated international perspectives.

- In March, NSABB reversed its decision and recommended unrestricted publication of both papers.

- Part of that decision was based on evidence that the Erasmus team’s virus became attenuated when it was made more transmissible.
An Ounce of Prevention...

- It is best not to reach the point where research is being evaluated at the time of publication.
- If there are real public risks, they are best addressed before the research, and post hoc assessment is probably most susceptible to entrenched positions.
- Perceptions of censorship or inequity are likely to be felt most strongly when scientists feel the rules changed after they conducted research.
- In March, the Obama administration created policy to require review of dual use research of concern and possible risk mitigation measures, both for ongoing and pre-funded research.
- In rare instances, this could include classification of the research, but it will usually result in voluntary modifications or contract revisions to reduce risk (if necessary).
Institutional Biosecurity Committees

- One of the key proposals of the National Resource Council’s 2004 Fink Report was to apply the institutional biosafety committee approach certain dual use research.

- IBCs are mandatorily used for recombinant DNA research.

- Would apply to research that:
  - Enhances the harmful consequences of the agent/toxin
  - Disrupts immunity or the effectiveness of immunization against the agent/toxin.
  - Confers resistance against treatment or facilitates ability to evade detection.
  - Increases the agent/toxin’s stability, transmissibility, or ability to be disseminated.
  - Alters host range or tropism.
  - Enhances the susceptibility of a host population to the agent/toxin.
  - Generates or reconstitutes an eradicated or extinct select agent.
Strengths of Review + IBC Approach

- Hopefully identifies and mitigates risk before it occurs.
- Primarily leaves control in the scientific community, whether at NIH or at the institution.
- Universities that have voluntarily adopted have reported favorable results, and there is a history of good results with recombinant DNA.
Weaknesses of Review + IBC Approach

- Some institutions will not have relevant expertise.
- Difficulty assessing low-probability risk, especially when infrequently weighed.
- Potentially bureaucratic.
- Does not incorporate international interests.
The Current Situation

- There continues to be a moratorium on research involving making H5N1 influenza viruses more transmissible, while the research community seeks to identify principles to govern the research.

- Both papers have been published.

- There remains no clear consensus on when/whether papers should be redacted.