Dual-use Research of Concern
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Jesse Bloom and Andy Lin

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Dual use research of concern (DURC) is defined by the World Health Organization (WHO) as "life sciences research that is intended for benefit, but which might easily be misapplied to do harm."

National Science Advisory Board for Biosecurity (NSABB) is a "federal advisory committee that addresses issues related to biosecurity and dual use research at the request of the government."

A large majority of biological researchers are committed to the improvement of human health. However these investigators and their research can also harm, which was unfortunately shown by the 2001 anthrax attacks, when anthrax containing letters were sent through the U.S. postal system. Recently there has been concern regarding the publication and conduct of certain types of research. However the current system for determining if and what limits should be placed has been very *ad hoc*. Below are two recent cases that highlight questions that arise from the conduct and dissemination of dual-use research of concern work.

Case study 1:
Historically, transmission of influenza strains from non-human hosts to human has caused global pandemics every few decades. These pandemics require avian influenza viruses to evolve the ability to efficiently transmit from person-to-person. Therefore there is a great deal of concern that avian influenza strains such a highly pathogenic H5N1 might eventually gain the ability to transmit human-to-human. To address whether such H5N1 strains could ever transmit in humans, several research groups have adapted H5N1 strains or their derivatives to transmit in ferrets, which are currently considered the best model for human viral transmission (although it remains unknown how ferret transmission equates to human transmission). This resulted in a lengthy and unresolved debate about the pros and cons of performing and publishing this type of research.

The claimed benefits of the research are that it improves understanding of influenza transmission, aids in identifying pandemic risks, and helps in surveillance of identifying mutations that make strains more likely to transmit. It has also been claimed that this research could help in the design of appropriate vaccines by making it easier to pinpoint the strains most likely to cause a pandemic.

The claimed risks of the research are that it creates a virus that could kill 100 of millions of people if it accidently or intentionally escaped the lab. In addition, it has been noted that *de novo* synthesis of the influenza genome is trivial with existing technologies, and so knowledge of how to make strains more transmissible in mammals could in and of itself be dangerous.

This debate continues today, with extensive NIH regulations limiting so-called "Gain of Function" work that confers new properties related to transmissibility and pathogenicity on influenza viruses. There is still not a clear consensus on the right balance between regulating this work and allowing freedom of scientific exploration.

Case study 2:
In 2013, researchers announced the discovery of a strain of *Clostridium botulinum*, the causative agent of botulism, which expressed a new untreatable form of botulinum toxin. Remarkably, when this work was published, the authors made the unprecedented decision to withhold the genetic sequence of the new botulinum toxin over dual-use concerns. The information could be used to create antidotes. Yet, it could also unnecessarily inform malefactors to a new poison with no known antidote. In addition the publication of the sequence would give these malefactors, if properly trained, instructions to synthesize the toxin.

Prior to publishing, the authors reached out to various government agencies to ensure publishing would not be a security concern. None of these agencies objected to the publication of this work or to the publication of the genetic sequence, as shown in 2014 when the FDA published the genetic sequence in a separate manuscript.

In addition, the authors were also wary of proving the strain to other researchers, causing year long delays in follow on research, over fears the strain could fall into the wrong hands. These research delays proved unfortunate because in 2015, two years after the original announcement, a separate team from the CDC and the University of Wisconsin determined the new toxin was curable with available antidotes.

This incident highlights some of the unresolved questions regarding dual-use research of concern. Who should be involved in deciding what information should be published (the public, scientists, editors, and/or government)? If information is withheld, who should be able to access withheld information to ensure scientific progress? What enforcement mechanism, if any, should there be if researchers disregard recommendations for withholding results.

Further reading:

Michael Selgelid, "**Governance of dual-use research: an ethical dilemma"** *Bulletin of the World Health Organization*
http://www.who.int/bulletin/volumes/87/9/08-051383/en/
"In comparison with nuclear weapons, the production of biological weapons is relatively easy and inexpensive; and information about how to produce biological weapons is readily available in published scientific literature."

"Because scientists generally lack training in security studies, they may lack the expertise [and clearance] required for assessment of the security risks of publication . . . Given what they do for a living . . . [scientists] will be biased in favor of science over security."

"A system involving governmental control over publication . . . may promote security; but this would have costs in terms of academic freedom.

James R. Clapper (Director of National Intelligence), **"Worldwide Threat Assessment of the US Intelligence Community"** *Testimony before the Senate Armed Services Committee*
https://www.dni.gov/files/documents/SASC_Unclassified_2016_ATA_SFR_FINAL.pdf
The Director of National Intelligence (James R. Clapper), the highest ranking intelligence advisor to the President has added genome editing to a list of threats considered to weapons of mass destruction.

Arturo Casadevall et al, **"On the need for a national board to assess DURC"** Journal of Virology
http://jvi.asm.org/content/early/2014/03/27/JVI.00875-14.full.pdf
"Journals considering publication of DURC-containing manuscripts cannot refer such manuscripts directly to the NSABB for advice . . . journal editors are the sole arbiters of whether manuscripts describing dual-use research of concern are published"

"In the current environment, the most likely course of action would be full publication of the DURC-related study . . . possibly with an accompanying editorial explaining the basis for the decision to publish"

"The situation today calls for the establishment of a federal advisory board . . . for the assessment of DURC. It could be argued that the need for a national board with access to security information follows as a necessary outcome of the NSABB definition of DURC, which required a threat assessment.**"**

Peter M. Sandman, **"Science versus Spin: How Ron Fouchier and Other Scientists Miscommunicated about the Bioengineered Bird Flu Controversy"**
http://www.psandman.com/articles/Fouchier.htm
"Both sides in the publication debate have communicated in ways that exacerbated the other side's outrage. And both sides have found it difficult to recognize and change how they were communicating because of their own outrage."

"[When] Fouchier appeared to be trying to arouse interest in his study. His messaging was all about how dangerous he considered the H5N1 virus and how terrifying (but incredibly useful) he considered his own soon-to-be-published study. But as the controversy over publication grew, Fouchier became less focused on arousing interest and more focused on allaying concern. And his messaging altered to match his new goal."

Nell Greenfieldboyce, **"Who's Protecting Whom From Deadly Toxin?"** *National Public Radio*
http://n.pr/2aMbUgs
"[I]t's still unclear what kinds of findings should be withheld from the public, who should make those decisions, and how to ensure that legitimate researchers will get access to the information so that science can advance and protect public health."

Arturo Casadevall et al, "DURC Review at American Society for Microbiology Journals" *mBio*
http://mbio.asm.org/content/6/4/e01236-15.full
Describes dual-use research of concern review process at American Society for Microbiology journals.

"The Darker Bioweapons Future" *Central Intelligence Agency* (2003)
https://fas.org/irp/cia/product/bw1103.pdf
"The same science that may cure some of our worst diseases could be used to create the world's most frightening weapons."

"[A panel of life science] experts [convened by the National Academy of Sciences] emphasized that, because the processes, techniques, equipment and know-how needed for advanced bio agent development are dual use, it will be extremely difficult to distinguish between legitimate biological research activities and production of advanced biological weapons agents."