The Existing Guidance for "Dual-Use" Research

by Gigi Kwik Gronvall

In considering how to weigh the risks and benefits of synthetic biology, Kaebnick, Gusmano, and Murray pose the question of whether there is scientific research that should not be funded or performed or if there are potentially dangerous results that should not be widely disseminated.[1] Such questions, they propose, require a new set of rules and norms for knowledge generation—an "ethics of knowledge."[2] They identify two examples of research that might fall into a nonpermissible category, including "research that is aimed at producing and disseminating knowledge of . . . how to produce more dangerous forms of H5N1 and smallpox." There are already rules and norms to guide the funding and generation of scientific knowledge, however, including research on influenza and smallpox. Even if more rules and guidance were added to the practice of science, potentially problematic, "dual-use" research would still occur, and as a practical matter, it is unlikely that results from those studies can be contained, particularly if the research is of wide interest.

Some lines of scientific research are expressly forbidden. There are regional bans, such as limitations on research with genetically modified organisms in many countries or the recently reversed U.S. ban on stem cell research. Some bans are more widespread, such as restrictions on any experimentation with smallpox virus without World Health Organization approval. But the ban on developing biological weapons, or any straightforwardly malevolent use of scientific research, is universal for science. It is expressed in treaties like the Biological Weapons Convention, U.N. Security Council Resolution 1540, and many nation's laws—including the Patriot Act in the United States. Even if there were no treaties or legal restrictions in place (or if scientists performing the research are not aware of them), there is a widespread norm in the scientific research community that malevolent research is not allowable for science, not scientifically compelling, not publishable, and not fundable. The National Institutes of Health would never fund a researcher who, for example, aims to make *Yersinia pestis*, the causative agent of plague, more contagious for the purposes of harming people.

It becomes more difficult to determine whether some research should or should not be funded, performed, or disseminated, however, when we consider why something potentially problematic—or that will potentially yield problematic results—is being done. It may be forbidden to research the question, how can I make H5N1 into a better killing machine?, but it is perfectly valid, relevant, and broadly interesting to ask, is H5N1 likely to become a pandemic and, if so, by what mechanism? Research aimed at that fundamentally good goal could nonetheless achieve results that caused consternation about publication, as occurred in the H5N1 gain-of-function controversy in 2011 and 2012. This is the dual-use dilemma, that research which is intended for legitimate beneficent purposes could be misused for harm.

Recently developed policies in the United States call for a thoughtful pause before beginning or publishing specific areas of research and to evaluate what may be done to mitigate concerns.[3] Yet questions about the future of H5N1 and other diseases will continue to be asked, potentially yielding dual-use results, because the scientific questions are interesting to a broad group of people, especially considering the funds that are spent on diagnostics, surveillance, culling reservoirs of disease, and medical countermeasures. While some research topics

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How much of a threat to humans does disease X pose? How much would the causative agent of disease Z need to evolve before our medical countermeasures are useless? If such questions are not funded by one agency, they will probably be pursued by another.

may languish in obscurity and never get funded, there will be broad interest in many potentially dual-use questions, such as these: How much of a threat to humans does disease X pose? How does a bacteria become antibiotic resistant, by which mechanism, and how does it spread resistance? Do available vaccines or drugs protect against disease Y? How much would the causative agent of disease Z need to evolve before our medical countermeasures are useless? If such questions are not funded by one agency, they will probably be pursued by another. An agency may decide that some specific approaches to answer the questions—including those involved in the H5N1 gain-of-function studies—may not be safe or relevant or may be deemed inadequate in comparison to newer approaches, and they may thus be restricted, but the fundamental questions are compelling and will likely be addressed by some means.

In the H5N1 controversy, the National Science Advisory Board for Biosecurity stated that the information about what mutations in H5N1 could lead to a mammalian-transmissible strain was scientifically valid and important, but it looked for a mechanism that could handle the information in a wise manner and use it appropriately. The NSABB did not want the information classified by a government or governments, which would bar many public health workers and experts from making legitimate use of the information, but it did not want just anyone to have the information, either. It failed to find such a mechanism. As Kaebnick and colleagues observe, addressing the ethics of knowledge may require "the practical task of developing institutions and systems that would allow for a richer array of possible resolutions."[4]

Certainly, mechanisms exist and can be created to withhold or contain research results within a group. Research performed in a governmental laboratory often requires classification review before becoming widely accessible. Research performed in the private sector may never be publicly disseminated or may be bound by nondisclosure agreements, particularly if there is a competitive advantage to keeping the information closely held. Yet these mechanisms may not successfully dim a broader interest in addressing the question: other interested groups may then decide to pursue the research for themselves. For questions that are addressed using gain-of-function methods, this could lead to safety concerns.[5]

Determining who is in and who is out of a potential information framework will be a challenge: NSABB may have been concerned that H5N1 could be misused and posed a biosecurity risk, but there is no guarantee that either the individuals or governments with legitimate access to the information would use it wisely, either. Another challenge for a framework is the question, who decides? A recent case regarding botulism is instructive: scientists characterized a new botulinum strain to which countermeasures may not be effective, and a scientific journal published the report without the genetic sequence, as is typically required.[6] It was then revealed that neither state nor federal officials had asked for this step, and as of this writing, the researcher will not provide a sample to U.S. government officials for testing.[7] Should an individual (or government) have the ability to decide whether this sequence information is better left unknown? Given the advances and increasing accessibility of synthetic biology and other biological techniques and the ability to make results widely accessible, the answer to that question would seem to depend only on whether, and how many, people care about the scientific issue at hand.

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3. Office of Science and Technology Policy, United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern, *Federal Register* 78 (2013): 12369-72.

4. Kaebnick, Gusmano, and Murray, "The Ethics of Synthetic Biology," S12.

5. M. Lipsitch and B. R. Bloom, "Rethinking Biosafety in Research on Potential Pandemic Pathogens," *mBio* 3, no. 5 (2012), http://www.ncbi.nlm.nih.gov/pubmed/23047752.

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