insights

American Society of International Law

January 19, 2012 Volume 16, Issue 2

Risky Research and Human Health: The Influenza H5N1 Research Controversy and International Law

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Introduction

In the last months of 2011, a controversy emerged involving research on highly pathogenic avian influenza A (H5N1) undertaken in The Netherlands and the United States. The projects produced H5N1 strains more transmissible among mammals. These results alarmed those worried about bioterrorism and accidental release of dangerous pathogens. A U.S. federal advisory body recommended that aspects of the research not be published. The controversy drew attention to governance of research designed to protect health but that creates biological agents, knowledge, and/or scientific methodologies potentially dangerous to national security and public health. This *Insight* describes this controversy and identifies international legal issues it highlights.

Background

H5N1 is a global health concern. It first caused human infections and deaths during a poultry outbreak in Hong Kong in 1997.[1] It re-emerged globally in 2003 and 2004, resulting in more human cases and fatalities. This H5N1 strain is virulent in humans, with a mortality rate of approximately 60%.[2] However, it does not readily transmit between people. The virus' spread through avian populations, and increased human cases caused by contact with infected birds, created global health nightmares by the middle of last decade. Experts feared that this virulent strain might mutate to be more transmissible in humans. Such a mutation could trigger a catastrophic pandemic. The H5N1 virus caused national and international authorities to scale-up pandemic preparedness. Although this virus has not mutated into a human pandemic strain, it continues to cause concern—including that mutations with pandemic potential could emerge.

H5N1 Research Controversy

In September 2011, scientists in The Netherlands and the United States announced that independent experiments produced H5N1 strains with enhanced transmissibility in

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DOCUMENTS OF NOTE

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BWC's Seventh Review Conference in Geneva, December 2011

International Covenant on Civil and Political Rights

International Covenant on Economic, Social and Cultural Rights

International Health Regulations (2005)

United Nations, Disarmament: Confidence-Building Measures

mammals. The projects sought to generate information about the H5N1 virus given concerns about potential mutations. The U.S. National Institutes of Health funded both projects.

However, the research caused national security and public health anxieties and produced controversy about whether the findings should be fully published. The National Science Advisory Board for Biosecurity ("NSABB"), which advises the U.S. Department of Health and Human Services ("DHHS"), recommended in December 2011 that the researchers and journal editors publish "the general conclusions highlighting the novel outcome . . . but not include the methodological and other details that could enable replication of the experiment by those who would seek to do harm."[3] DHHS agreed with these recommendations, but neither the researchers nor the publishers are legally bound to follow them. However, experts raised concerns that such research potentially also threatens public health through accidental release, escape, or theft of the research strains because of inadequate biosecurity and biosafety in laboratories,[4] leading to arguments that these strains should be destroyed.[5]

The scientific journals in question have agreed not to publish the research findings in full, but the matter is far from resolved, especially in terms of what should happen to the H5N1 strains produced by the research and who should have access to the full findings. More generally, the controversy generated questions about the prudence of conducting this kind of research, the standards under which it is undertaken and managed, disclosure of findings and methodologies, and post-research handling of more dangerous strains produced through research. The controversy's international dimensions fostered calls for strengthened cooperation given perceived weaknesses in international governance.[6]

This is not the first time these questions have arisen. Previous research, such as re-creation of the influenza strain responsible for the great pandemic of 1918-1919, stimulated similar issues. Advances in life sciences, such as synthetic biology, continue to provide more ways to manipulate microbial organisms for a range of scientific, medical, and commercial purposes. Concerns about the H5N1 research have again forced scientists and policy makers to think about risks associated with well-intentioned, lawful, and potentially valuable research that might facilitate bioterrorism or result in accidental release or escape. The World Health Organization ("WHO") captured the conundrum when it expressed concern about potentially adverse consequences of the H5N1 research but stressed that research continue "so that critical scientific knowledge needed to reduce the risks posed by the H5N1 virus continues to increase."[7] Balancing costs and benefits requires governance of risky research, and the international scale of such research brings international law into the picture.

International Law and the H5N1 Research Controversy

Biological Weapons Convention

The Biological Weapons Convention ("BWC")[8] prohibits development, production, stockpiling, and transfer of "microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes" (Article I). Other BWC obligations flow from this prohibition, such as the requirement to "take any necessary measures to prohibit and prevent the development, production, stockpiling, acquisition, or retention of the agents, toxins, weapons, equipment and means of delivery specified in article I of the Convention,

WHO, Laboratory Biosafety Manual

WHO, Pandemic Influenza Framework

ORGANIZATIONS OF NOTE

World Health Organization

United Nations Office for Disarmament Affairs

U.N. Security Council

U.S. Department of Health & Human Services

U.S. National Institutes of Health

Centre for Biosecurity of UPMC

within the territory of such State, under its jurisdiction or under its control anywhere" (Article IV). States parties supplemented these obligations with non-binding confidence building measures that encouraged information sharing on biological defense research and research facilities.[9]

No one has argued that the H5N1 research violated the BWC. The BWC does not apply because the H5N1 research has a peaceful purpose related to health protection. This outcome reflects the difficulty of using the BWC to address potentially adverse consequences of research undertaken to benefit health. At most, the BWC prohibits states parties with jurisdiction over potentially dangerous pathogens associated with lawful research from using them for purposes with no legitimate justification.

However, BWC states parties have concerns about dangers scientific developments present to the treaty. At the BWC's Seventh Review Conference in December 2011, states parties agreed to examine developments in science and technology during intersessional meetings from 2012 to 2015.[10] Even so, the BWC's focus on hostile uses of biological agents means that it cannot, as constructed, regulate research that has prophylactic, protective, or other peaceful purposes.

International Law on Bioterrorism

International law specific to bioterrorism does not regulate the kind of research done on the H5N1 virus. A UN treaty criminalizes use of biological agents in terrorist bombings, which is irrelevant in this context.[11] Binding Security Council decisions require UN members to "take and enforce effective measures to establish domestic controls to prevent the proliferation of . . . biological weapons and their means of delivery, including by establishing appropriate controls over related materials."[12] These requirements apply to pathogens (such as more transmissible H5N1 strains used, created, or altered by peaceful research) and underscore the importance of physical biosecurity in research laboratories. The Security Council decisions do not, however, expressly address the processes of vetting lawful research or publishing research results.

International Law on Health Threats

International law on health threats, principally the International Health Regulations (2005) ("IHR") adopted by the WHO,[13] does not regulate the kind of research undertaken in the H5N1 projects. The IHR seeks to strengthen surveillance and response concerning public health emergencies of international concern (Article 2), including those associated with new influenza viruses (Annex 2). However, the IHR does not regulate scientific research.

WHO observed during the H5N1 research controversy that researchers should comply with the Pandemic Influenza Preparedness Framework ("PIP Framework") approved by the WHO in May 2011. The PIP Framework[14] is a non-binding arrangement to facilitate sharing influenza viruses and benefits, such as vaccines, produced by research on shared samples. WHO stressed the PIP Framework's requirement for researchers to collaborate with, and acknowledge, scientists from the country of origin in studying shared viruses.[15] The PIP Framework has not elsewhere formed part of the concerns generated by the H5N1 controversy.

However, WHO's linkage of the research with the PIP Framework raises other questions, such as how the Framework's benefit-sharing components apply to research using shared viruses that produces more dangerous pathogens or methodologies. If concerns exist about

publishing research findings (including scientific methodologies), worries about sharing such information through the PIP Framework might arise. Elsewhere, the PIP Framework incorporates biosecurity and biosafety standards in provisions on sharing viruses, which would apply if countries with jurisdiction over more dangerous strains produced by research shared them under the Framework.

International Law and Scientific Research Generally

More generally, states have used international law to regulate applications of scientific advances but not basic research informing those advances. Treaties (including the BWC) ban or regulate weaponization of certain technologies created through scientific research. The treaty banning human cloning does not regulate the science of cloning as such because it acknowledges "the progress that some cloning techniques themselves may bring to scientific knowledge and its medical application[.]"[16]

International Human Rights Law

Although no government has acted against the researchers and their findings, the H5N1 controversy implicates international human rights law. In terms of research process, international law bans research on humans conducted without informed consent,[17] which is not at issue here. The H5N1 controversy also raised questions about restricting publication of research, which touches on freedom of expression as a human right.[18] Under international law, governments can restrict this right by law when necessary to protect national security or public health[19] —the reasons people worry about the H5N1 research. The controversy provoked thinking about whether governments should restrict or prohibit certain kinds of lawful, well-intended research, which brings the freedom of scientific enquiry into play. [20] This freedom, too, is not absolute because governments can limit it to protect national security or public health.[21]

Summary

This overview reveals few binding international rules applicable to lawful but potentially dangerous scientific research. In terms of permitting such research, international law—beyond the right to freedom of scientific enquiry—contains no specific regime. As the H5N1 controversy demonstrates, state practice prohibiting or seriously restricting potentially dangerous research designed to benefit health does not, at present, exist. Similarly, the H5N1 and earlier research controversies reveal reluctance by governments responsible for, or with jurisdiction over, the research or its publication to exercise coercive powers to prevent dissemination of research findings or methodologies.

States have used international law to obligate governments to ensure that researchers working with dangerous pathogens conduct research under appropriate and adequate biosecurity and biosafety standards. However, as the H5N1 controversy highlighted, these obligations remain general in nature, with specific guidance provided by non-binding documents.[22] As such, these duties do not require countries, for example, to engage in H5N1 research only in laboratories having the highest biosecurity and biosafety requirements (i.e., BSL-4 labs). Nor is national implementation of the general biosecurity obligations subject to international oversight. The H5N1 controversy prompted criticism of the status quo and support for strengthened cooperation.

Models for International Research Governance

The Smallpox Model

One strategy could reflect how states handle the smallpox virus. A WHO-led effort eradicated smallpox—one of history's great microbial killers—at the end of the 1970s, and WHO members have allowed WHO to establish policies for secure handling of the remaining virus samples and to oversee smallpox research.[23] This approach provides for international oversight of smallpox research and assurance that it is undertaken securely and safely. The strategy is not binding under international law because it arises from WHO resolutions, which do not create legal obligations. Governments could adapt this model to legitimate but potentially dangerous research, such as research with influenza strains virulent in humans. However, differences between an eradicated virus held in very limited number of laboratories and pathogens present in nature and laboratories all over the world would create severe challenges for adapting the smallpox approach.

Mandatory International Oversight

Well before the H5N1 research controversy, experts proposed addressing potentially dangerous research on biological agentsthrough binding international regimes. One effort envisioned creating a treaty that "would involve three major innovations over existing oversight mechanisms: it would subject the most consequential areas of research to international jurisdiction; it would apply oversight comprehensively within all jurisdictions; and it would make the oversight process a legal obligation."[24] Achieving a mandatory and comprehensive regime would face many obstacles, even in the aftermath of the H5N1 research controversy.

Next Step: WHO-Led International Talks

In response to the controversy and calls for it to play a leading role, the WHO has agreed to facilitate negotiations to identify the key issues and work towards solutions.[25]These negotiations have to address issues related to the Dutch and American research, including what should be done with the H5N1 research strains and who can get access to the full research findings. Longer-term challenges involve developing rules and processes for better handling the scientific, public health, and national security interests affected by risky research on pathogens. Whether these negotiations produce new international policy, law, and governance mechanisms is too difficult to predict but too important to ignore.

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Endnotes:

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[16] Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings, Preamble, CETS No. 168, Jan. 12, 1998.

[17] International Covenant on Civil and Political Rights art. 7, Dec. 16, 1966, 999 U.N.T.S. 171 (entered into force Mar. 23, 1976)

[18] *Id*. art. 19(2).

[19] *Id*. art. 19(3).

[20] International Covenant on Economic, Social, and Cultural Rights art. 15(3), Dec. 16, 1966, 993 U.N.T.S. 3 (entered into force Jan. 3, 1976).

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