Is there a Role for the States Parties to the BWC in Oversight of Lab-created Potential Pandemic Pathogens?

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Summary

Research by Ron Fouchier and Yoshihiro Kawaoka marked the beginning of a "Research Enterprise" creating mammalian-airborne-transmissible highly-pathogenic avian-influenza viruses. For the sake of brevity, they will be called matHPAI. At present, likely more than ten laboratories are creating or researching matHPAI live viruses. While most of our concern has focused on matHPAI, the recent *de novo* creation of horsepox virus, an orthopoxvirus related to smallpox virus, is also of highly worrisome.

Both these viruses are examples of lab-created potential pandemic pathogens (PPPs), which bring up questions reflecting our concerns: Should details of this dual use research be published? Could lab-created PPPs be accidentally released from a laboratory and seed a human pandemic? Could they be employed as biological weapons?

The probability of accidental release into the community from one of the laboratories in the matHPAI Research Enterprise is uncomfortably high. For these and other lab-created PPPs, just one or a few laboratory-infected researchers could seed an outbreak or a pandemic. Concern over a pandemic from a Research Enterprise laboratory release should rival our grave concern over a natural pandemic as the likelihood of both are similar. Furthermore, a laboratory worker with hostile intent could introduce a PPP into the community.

This is not a problem for future consideration, it is upon us now. There is urgent need for international oversight and regulation of this research.

The BWC States Parties may not believe it to be within the BWC mandate to oversee academic research whose goal is public health. However, if the Parties decide this is within its mandate under Article XII of the BWC, it could speed up the enactment of guidelines and regulations. At the very least, the BWC Parties could and should be the catalyst to launch discussions for a different international treaty on oversight and regulation of this dangerous research, perhaps even banning some research. In the meantime, since enacting new treaties is an uncertain and long process, the BWC Parties should work to pass legislation in their own nations.

Background and Commentary

In 2012, Fouchier published[1] the creation of mammalian aerosol-transmissible H5N1 avian influenza virus (matH5N1). This virus is responsible for bird flu outbreaks in Asia, and it kills 60% of poultry workers who become infected through close contact with infected poultry.

The Fouchier research along with that of Kawaoka[2] marked the beginning of the "Research Enterprise" for creating matPPPs in the laboratory. Subsequently in 2013, letters to the journals Science and Nature,[3,4] twenty-two virologists notified the research community of their interest in creating airborne-transmissible strains of the also deadly H7N9 Asian influenza virus.

A 2015 commentary[5] submitted to the U. S. National Science Advisory Board for Biosecurity (NSABB) identified at least 35 publications from laboratories, mostly in Asia, where matHPAI and other influenza viruses were created or researched. Now, there is likely more published research, and many unpublished research projects are likely underway.

(1) Should details of this dual use research be published?

The methods to create these airborne-transmissible viruses are straight-forward and could be reproduced by researchers not highly skilled in molecular virology. Furthermore, skilled molecular virologists could re-create these viruses by directly making the genetic modifications in the laboratory. Re-creating matHPAI and other PPPs brings up the serious biosecurity concern of their use for hostile purposes.

Criteria[6], established in 1982, for making decisions about publication of dual use research, have been applied recently by Relman[7] to lab-created PPPs. The criteria as described by Relman are:

> "[Four] criteria to define research for which communication ought to be limited (all of which must be met): (1) research with dual use or military applications, (2) research with a short time to such applications, (3) research when dissemination could give short-term advantage to adversaries, and (4) research when the information was believed not to be already held by adversaries."

For some matHPAIs, the dual use concern is now moot, as details needed for airborne transmission in mammals have already been published.

The recent publication providing the details of the *de novo* creation of horsepox virus is of great concern, as the methods could be used to resurrect the smallpox virus. Smallpox ravaged the world until it was eliminated in 1980. As Koblentz has pointed out[8]: "The synthesis of horsepox virus takes the world one step closer to the reemergence of smallpox as a threat to global health security." The international community must do whatever is possible to prevent the re-emergence of smallpox.

(2) Could a release from the laboratory into the community seed a pandemic?

A calculation[9]of the probability of release from a single lab in the Research Enterprise in a single year was found to be 0.20%. For ten labs in the Research Enterprise carrying out research for ten

years, the probability of release from one of the labs is about 10 x 10 x 0.20% = 20%, an uncomfortably high number.

Lipitch[10] and Merler[11] estimate the probability of a pandemic from a laboratory release ranges from 5% to 50%. Using an intermediate value in that range, 25% or 0.25, the probability of a pandemic in ten years from the Research Enterprise is the probability of release times the probability that a release leads to a pandemic, which is 0.25 x 20% x 0.25 = 5%. The likelihood of a natural pandemic in the next ten years is about 31% [12]. Therefore, concern over a pandemic from a Research Enterprise laboratory release should rival our grave concern over a natural pandemic.

Are lab-created potential pandemic pathogens biological weapons?

The possibility has been raised that matHPAIs could be used as biological weapons.

For instance, in a 2012 Comment in the science journal Nature[13], the NSABB voiced their concern:

> "Dual use is defined as research that could be used for good or bad purposes. We are now confronted by a potent, real-world example…If influenza A/H5N1 virus acquired the capacity for human-to-human spread and retained its current virulence, we could face an epidemic of significant proportions…Recently, several scientific research teams have achieved some success in modifying influenza A/H5N1 viruses such that they are now transmitted efficiently between mammals, in one instance with maintenance of high pathogenicity…these scientific results also represent a grave concern for global biosecurity, biosafety and public health. Could this knowledge, in the hands of malevolent individuals, organizations or governments, allow construction of a genetically altered influenza virus capable of causing a pandemic? ...Our concern is that publishing these experiments in detail would provide information to some person, organization or government that would help them to develop similar mammal-adapted influenza A/H5N1 viruses for harmful purposes."

Another concerned voice is found in a lead editorial in the journal Science[14] by Nobel Laureate Paul Berg:

> "Recent research with a highly pathogenic influenza virus has highlighted the importance of this issue. Reviews of the influenza research concluded that given "the risk of accidental or malicious release," the benefits of such studies must be well justified. Thus, specific guidelines must be enforced to thwart not only intentionally harmful outcomes but accidental releases as well… Earlier this year, the NSABB was embroiled in a high-profile decision regarding the publication of research on enhanced transmissibility of the avian H5N1 influenza virus. The principal concern was that publishing such findings might embolden those with sinister motives to use that information to create a worldwide pandemic."

The phrases "malevolent individuals, organizations or governments," "intentionally harmful outcomes," and "sinister motives" describe employment of these lab-created pathogens as biological weapons.

The Biological Weapons Convention[15] was written with a focus on military tactical biological weapons, where significant quantities would usually be employed. Article I of the convention speaks to this focus:

> "Article I
> Each State Party to this Convention undertakes never in any circumstances to develop, produce, stockpile or otherwise acquire or retain:
> (1) 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;
> (2) Weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict."

For lab-created PPPs, any quantity, however small, could seed an outbreak or pandemic. In this circumstance, development also implies production and stockpiling, since a single vial and one to a few infected individuals is all that is necessary to launch an attack.

From a military tactical point of view, however, lab-created PPPs would not be good biological weapons as they would boomerang back on the attackers, since they are highly transmissible. Nonetheless, a suicidal terrorist group or a desperate State might employ them as a last resort, or threaten to employ them as a means of extortion.

Call for action from the Parties to the BWC

When Fouchier and Kawaoka carried out their research, it was unlikely that biological weapons even crossed their minds. Since that possibility has now been brought up, researchers who are creating PPPs must take into account the biological weapons risk of dual use information and laboratory release of their pathogens. If there is little public-health benefit or little defense rationale for particular research, the Parties to the BWC should question whether it is biological weapons development and act accordingly.

This is a complex issue. The question of what constitutes biological weapons development is complicated. Many biodefense activities of the U.S Department of Homeland Security's proposed and now abandoned National Biodefense Analysis and Countermeasures Center would be considered biological weapons development. As pointed out in a letter[16] in the journal Politics and the Life Sciences: "Taken together, many of the [proposed] activities…— most particularly the ''Store, Stabilize, Package, Disperse'' sequence and the ''Computational modeling of feasibility, methods, and scale of production'' item — may constitute development in the guise of threat assessment, and they certainly will be interpreted that way."

Recent articles directed to the Eighth BWC Review Conference (for instance, see here, here, here, here, and here)[17,18,19, 20,21] call for the Parties to intensify their focus on new science and

technology that could lead to violations of the BWC. Lab-created PPPs, particularly matHPAI, because they are already present in laboratories around the world, are an urgent focus.

Article XII of the BWC calls for

> "review [of] the operation of the Convention…assuring that the purposes of the preamble and the provisions of the Convention…are being realized. Such review shall take into account any new scientific and technological developments relevant to the Convention."

Hopefully, the States Parties to the BWC will set in motion a process for overseeing relevant new research and technologies. If the Parties decide lab-created PPPs are within its mandate under Article XII of the BWC, it could speed up the enactment of guidelines and regulations. At the very least, the Parties should be the catalyst to launch discussions for a different international treaty on oversight and regulation of creation and research on highly dangerous agents. In the meantime, since enacting new treaties is an uncertain and long process, Parties to the BWC should pass legislation in their own nations.

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