A Role for 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" for creating potential pandemic pathogens (PPPs) in the laboratory. To date, perhaps more than thirty-five laboratories are creating or researching lab-created PPPs.

This research has spawned two parallel intense debates: (1) Should details of this dual use research be published? (2) Could these pathogens escape from the laboratory and seed a deadly human pandemic?

This probably of escape into the community from one of the labs in the research enterprise is uncomfortably high, as a world-wide pandemic with tens-of-millions of deaths could be seeded.

Moreover, the possibility has been raised by authoritative sources that lab-created, mammalian-airborne-transmissible highly pathogenic avian influenza viruses could be used as biological weapons. For these and other lab-created PPPs, any quantity, however small, could seed an outbreak with means of delivery just one or a few infected people.

There is urgent need for international regulations over some of this research. Since there is only a small likelihood of hostile intent based upon academic research creating or researching lab-created PPPs, the BWC is likely not the international treaty to take action. But the Parties to the BWC could be the catalyst to launch discussions for a different international treaty, on oversight and regulation of work on agents that would not make useful tactical weapons but could potentially escape and cause serious harm. Whenever a new case arose, the treaties would need to discuss the possibilities and decide which treaty—or both—is relevant.

Background

Dr. Ron Fouchier published in 2012 the creation of genetically- modified, airborne-transmissible, highly-pathogenic avian influenza (HPAI) viruses. Fouchier's research is an example of lab-created potential pandemic pathogens. PPPs may be defined as pathogens that are potentially highly transmissible among humans and potentially have a significant fatality rate. They now live only in the laboratory, and are not present in the population.

The native unmodified virus starting strain employed by Fouchier was the H5N1 virus responsible for bird flu outbreaks in Asia. The virus kills 60% of poultry workers who become infected through close contact with infected poultry.

The Fouchier research along with that of Yoshihiro Kawaoka marked the beginning of a "research enterprise" for creating PPPs in the laboratory. Subsequently in 2013, letters to the journals Science and Nature, 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 submitted to the National Science Advisory Board for Biosecurity (NSABB) titled "The Potential Pandemic Influenza Research Enterprise," identified at least 35 publications from laboratories, mostly in Asia, where PPPs were created or researched. Now, there is likely more published research, and many unpublished research projects are likely underway.

Research creating PPPs in the laboratory has spawned two parallel intense debates:

(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 these PPPs brings up the serious biosecurity concern of their use for hostile purposes. Should the Parties to the BWC have a role as to whether particular research should be published?

Criteria, laid out in 1982 for making decisions about publication of dual use research, have been applied recently by David Relman to lab-created PPPs. The criteria from Relman's article 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."

In the case of lab-created PPPs, the cat is already out of the bag as details needed for airborne transmission in mammals have already been published.

(2) Could these pathogens escape from the laboratory and seed a deadly human pandemic?

What is the likelihood of release or escape from the laboratory? From the simple equation $E=1-(1-p_1)^{yn}$, the likelihood or probability of escape can be calculated. Here, E = the probability of escape from at least one laboratory from the research enterprise, p_1 is the probability of escape for one lab in one year, n is the number of laboratories in the research enterprise, and y is the number of years PPPs are created or researched. It is calculated that E = 0.086 or 8.6%, using an estimate of p_1 = 0.000256 or 0.0256%, y = 10 years of research, and n = 35 laboratories. The

estimate of p_1 was determined from a calculation in another commentary to the NSABB titled "Toward absolute probabilities for escape from a laboratory."

This probability of escape into the community is uncomfortably high, as a world-wide pandemic with tens-of-millions of deaths could be seeded. There is urgent need for international regulations over some of this research.

Are lab-created potential pandemic pathogens biological weapons?

The possibility has been raised that lab-created HPAI could be used as biological weapons.

For instance, in a 2012 Comment in the science journal Nature, 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 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 forbids the development, production or stockpiling biological weapons.

The BWC 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 PPPs, any quantity, however small, could seed an outbreak with means of delivery just one or a few infected people. From a military point of view, however, lab-created PPPs would not be good biological weapons as they would boomerang back on the attackers since they could be highly transmissible. Nonetheless, a suicidal terrorist group or a desperate State might employ them as a last resort. Or the threat of employing them might serve as a means of extortion.

The closest analogy to lab-created PPPs is smallpox, which has been recognized as a potential biological weapon. By international agreement, smallpox is retained in only two laboratories.

Should the Parties to the BWC have a role in oversight and regulation of this dangerous research?

When Fouchier and Kawaoka carried out their research, it is 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 risk of biological weapons use of their information or agents. If there is little public-health benefit or little defense rationale for the research, the Parties to the BWC could question if the research is biological weapons development and act accordingly. Perhaps, this is one route to partial international control of these dangerous pathogens.

The Parties to the BWC need to focus on new research and technologies that could be violations or lead to violations of the BWC, Recent publications call for the Parties to intensify their focus (for instance, see here, here, and here). Lab-created PPPs, because they are already present in laboratories around the world, are an urgent focus. Hopefully, the BWC Eighth Review Conference will set in motion the process of overseeing relevant new research and technologies. Indeed, 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."

The Implementation Support Unit for the BWC is at present too small and overworked to deal with this issue. The States Parties should supply funding for one additional ISU person and for an advisory committee of international scientists to track new technologies and research projects in a timely manner to inform the yearly Meeting of Experts. An immediate focus should be lab-created potential pandemic pathogens.

Since there is only a small likelihood of hostile intent based upon creation or re-creation of PPPs, the BWC is likely not the international treaty to take action. But the Parties to the BWC could be the catalyst to launch discussions for a different international treaty, on oversight and regulation of work on agents that would not make useful tactical weapons but could potentially escape and cause serious harm. Whenever a new case arose, the treaties would need to discuss the possibilities and decide which treaty—or both—is relevant.