The consequences of a lab escape of a potential pandemic pathogen

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In letters to the journals Science and Nature (1, 2), 22 virologists notified the research community of their interest in expanding research to develop strains of the already deadly H7N9 Asian influenza virus that would be transmissible via aerosols among mammals, thus creating potential pandemic pathogens. PPPs are defined as pathogens that are potentially highly contagious, potentially highly deadly, and not currently present in the human population. Mammalian contagious avian flu, the 1918 pandemic flu, and SARS are examples. The letter writers cite their scientific reasons for the need for such research, much the same reasons as given by those working on similar projects for the H5N1 avian flu virus (3, 4). This new proposed research signals wider interest in making dangerous pathogens in the first place? To answer this question, the critical question is: what is the probability that a worker acquires an undetected infection in the lab in the first place? To answer this question, we reproduce here one part of the Klotz (2014) analysis: the probability of an escape when the infected person leaves the lab.

Thus, the probability of escape for a single year, \( p_1 \), can only be calculated as \( 4 \frac{LAIs}{2,044 \text{ lab years}} \). But the denominator in our calculation should be just the number of BSL-3 labs, so the denominator is underestimated since BSL-2 and BSL-4 labs contribute to the denominator. (The denominator used here, 2,004, equals the number of BSL-2 plus number of BSL-3 plus number of BSL-4 labs. But the denominator in our calculation should be just the number of BSL-3 labs, so the denominator is overestimated and the percent escape is then underestimated. Although requested, the CDC has not supplied us with the number of BSL-3 labs for us to do the exact calculation.) This basic probability is consistent with that for SARS escapes in Asia through LAIs (12) and with all known escapes from BSL-4 labs in the Soviet Union from LAIs and Great Britain from a mechanical failure (13).

To illustrate potential risk, the probability of no escape from a single lab in a single year is (1 − \( p_1 \)), so

\[
p_{no} = (1 - p_1)^{N \times Y}
\]

is the probability of no escape from \( N \) labs in \( Y \) years. And
The basic probability of escape, \( p_m \), is significantly higher escape risk, for the planned National Bio- and Agro- of Homeland Security risk assessment overseeing the risk assessment remarked year. The National Research Council (14) leading to a pandemic is 30% in case of a worst-case scenario, it is not improbable. Recent self-reported mistakes at the CDC (15), involving a particularly deadly strain of anthrax removed from BSL-3 containment and H5N1 Asian bird flu released from the CDC laboratories altogether, lend support to our concern that the probability of escape may be much greater than the 0.2% per lab per year from just LAIs. The CDC report spawned a congressional inquiry (16) and led to dozens of newspaper articles with concerns about lack of safety in high-containment laboratories.

Our concern is shared by many virologists and epidemiologists. A recent letter to the President of the European Commission (17) co-signed by 56 scientists from more than a dozen countries warned, “The probabilities of a lab accident that leads to a global spread of an escaped mutated virus are small but finite, while the impact of global spread could be catastrophic.” The European Centre for Disease Prevention and Control (18) weighed-in with its concerns as well, as did the Cambridge Working Group (19). It must be noted that some of the signers of the European Commission letter and the Cambridge Working Group’s consensus statement are the same.

The risk of a man-made pandemic from a lab escape is not hypothetical. Lab escapes of high-consequence pathogens resulting in transmission beyond lab personnel have occurred (20, 21). The historical record reveals lab-originated outbreaks and deaths due to the causative agents of the 1977 pandemic flu, smallpox escapes in Great Britain, Venezuelan equine encephalitis in 1995, SARS outbreaks after the SARS epidemic, and foot and mouth disease in the UK in 2007. Ironically, these labs were working with pathogens to prevent the very outbreaks that they ultimately caused.

Do benefits outweigh risks? Those who support PPP experiments either believe the probability of PPP escape is infinitesimal or the benefits in preventing a pandemic are great enough to justify the risk. In making decisions for what lines of research will lead to new knowledge, experts must rely on intuition honed by years of research in a particular field. In the case of this PPP research, in our opinion it would take extraordinary benefits and significant reduction of risk via extraordinary biosafety measures to correct such a massive overbalance of highly uncertain benefits to too-likely risks (Wain-Hobson, 2013).

Whatever number we are gambling with, it is clearly far too high a risk to human lives. This Asian bird flu virus research to develop strains transmissible via aerosols among mammals, and perhaps some other PPP research as well, should for the present be banned. We must emphasize that we have been considering only a very small subset of pathogen research. Most pathogen research should proceed unimpeded by unnecessary regulations.

Special precautions in BSL-4 laboratories for work with PPPs should be adopted (22). These would include:

- Training a full-time technical staff for work with PPPs. Experiments could be directed by scientists outside the laboratory using modern audio-video technology.
- Requiring the staff to follow up extended work shifts with periods of quarantine before they leave the containment area to assure that no PPP escapes from the containment area through an LAI.
- Restricting these PPP laboratories to remote locations, where an aerosol escape or other containment failure would pose the least risk of infecting an outside community.

We label BSL-4 laboratories with the special precautions, BSL-4+. While PPP experiments would be carried out primarily under BSL-4+ containment, BSL-3 containment with the special precautions might suffice for some work.

Given the global threat, the international community should insist on discussions leading to an international agreement that would require the strictest oversight to conduct this particular research anywhere. To place responsibility with the international community where it belongs and to provide maximum transparency, policy makers should require that international inspectors have access to facilities at any time on short notice.
As it stands, there is no proactive oversight nor regulations for this PPP research, so any and all of the world’s nations can carry out this dangerous work without regard to consequences. But consequences would be shared by all of us. In the meantime, insurance companies who routinely provide insurance for biological research should consider excluding such risky research from coverage.

REFERENCES


Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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