COMMENT

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Pathogenic H5N1 avian influenza has led to the culling of hundreds of millions of birds. A human-transmissible form could have much worse consequences.

Adaptations of avian flu virus are a cause for concern

Members of the US **National Science Advisory Board for Biosecurity** explain its recommendations on the communication of experimental work on H5N1 influenza.

We are in the midst of a revolutionary period in the life sciences. Technological capabilities have dramatically expanded, we have a much improved understanding of the complex biology of selected microorganisms, and we have a much improved ability to manipulate microbial genomes. With this has come unprecedented potential for better control of infectious diseases and significant societal benefit. However, there is also a growing risk that the same science will be deliberately misused and that the consequences could be catastrophic. Efforts to describe or define life-sciences research of particular concern have focused on the possibility that knowledge or products derived from such research, or new technologies, could be directly misapplied with a sufficiently broad scope to affect national or global security. Research that might greatly enhance the harm caused by microbial pathogens has been of special concern[1–3]. Until now, these efforts have suffered from a lack of specificity and a paucity of concrete examples of 'dual use research of concern'[3]. 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.

Highly pathogenic avian influenza A/H5N1 infection of humans has been a serious public-health concern since its identification in 1997 in Asia. This virus rarely infects humans, but when it does, it causes severe disease with case fatality rates of 59% (ref. 4). To date, the transmission of influenza A/H5N1 virus from human to human has been rare, and no human pandemic has occurred. 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. Historically, epidemics or pandemics with high mortalities have been documented when humans interact with new agents for which they have no immunity, such as with *Yersinia pestis* (plague) in the Middle Ages and the introduction of smallpox and measles into the Americas after the arrival of Europeans.

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. This information is very important because, before these experiments were done, it was uncertain whether avian influenza A/H5N1 could ever acquire the capacity for mammal-to-mammal transmission. Now that this information is known, society can take steps globally to prepare for when nature might generate such a virus spontaneously. At the same time, 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 with mortality exceeding that of the 'Spanish flu' epidemic of 1918? The research teams that performed this work did so in a well-intended effort to discover evolutionary routes by which avian influenza A/H5N1 viruses might adapt to humans. Such knowledge may be valuable for improving the public-health response to a looming natural threat. And, to their credit and that of the peer reviewers selected by the journals *Science* and *Nature*, the journals themselves, as well as the US government, it was recognized before their publication that these experiments had dual use of concern potential.

The US government asked the National Science Advisory Board for Biosecurity (NSABB; go.nature.com/oeryit) to assess the dual-use research implications of two as-yet-unpublished manuscripts on the avian influenza A/H5N1 virus, to consider the risks and benefits of communicating the research results and to provide findings and recommendations regarding the responsible communication of this research. In our deliberations, we first assessed the potential risks and consequences of the misuse of the information to cause harm to the public.

Risk assessment of public harm is challenging because it necessitates consideration of the intent and capability of those who wish to do harm, as well as the vulnerability of the public and the status of public-health preparedness for both deliberate and accidental events. We found the potential risk of public harm to be of unusually high magnitude. In formulating our recommendations to the government, scientific journals and to the broader scientific community, we tried to balance the great risks against the benefits that could come from making the details of this research known. Because the NSABB found that there was significant potential for harm in fully publishing these results and that the harm exceeded the benefits of publication, we therefore recommended that the work not be fully communicated in an open forum. The NSABB was unanimous that communication of the results in the two manuscripts it reviewed should be greatly limited in terms of the experimental details and results.

This is an unprecedented recommendation for work in the life sciences and our analysis was conducted with careful consideration both of the potential benefits of publication and of the potential harm that could occur from such a precedent. 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. We believe that as scientists and as members of the general public, we have a primary responsibility 'to do no harm' as well as to act prudently and with some humility as we consider the immense power of the life sciences to create microbes with novel and unusually consequential properties. At the same time, we acknowledge that there are clear benefits to be realized for the public good in alerting humanity of this potential threat and in pursuing those aspects of this work that will allow greater preparedness and the potential development of novel strategies leading to future disease control. By recommending that the basic result be communicated without methods or details, we believe that the benefits to society are maximized and the risks minimized. Although scientists pride themselves on the creation of scientific literature that defines careful methodology that would allow other scientists to replicate experiments, we do not believe that widespread dissemination of the methodology in this case is a responsible action.

The life sciences have reached a crossroads. The direction we choose and the process by which we arrive at this decision must be undertaken as a community and not relegated to small segments of government, the scientific community or society. Physicists faced a similar situation in the 1940s with nuclear weapons research, and it is inevitable that other scientific disciplines will also do so.

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Along with our recommendation to restrict communication of these particular scientific results, we discussed the need for a rapid and broad international discussion of dual-use research policy concerning influenza A/H5N1 virus with the goal of developing a consensus on the path forward. There is no doubt that this is a complex endeavour that will require diligent and nuanced consideration. There are many important stakeholders whose opinions need to be heard at this juncture. This must be done quickly and with the full participation of multiple societal components.

We are aware that the continuing circulation of the highly pathogenic avian influenza A/H5N1 virus in Eurasia — where it is constantly found to cause disease in animals of particular regions — constitutes a continuing threat to humankind. A pandemic, or the deliberate release of a transmissible highly pathogenic influenza A/H5N1 virus, would be an unimaginable catastrophe for which the world is currently inadequately prepared. It is urgent to establish how best to facilitate the much-needed research as well as minimize potential dual use.

To facilitate and motivate this process, we also discussed the possibility of the scientific community participating in a self-imposed moratorium on the broad communication of the results of experiments that show greatly enhanced virulence or transmissibility of such potentially dangerous microbes as the influenza A/H5N1 virus. This moratorium would run until consensus is reached on the balance that must be struck between academic freedom and protecting the greater good of humankind from potential danger. With proper diligence and rapid achievement of a consensus on a proper path forward, this could have little detrimental effect on scientific progress but significant effect on diminishing risk.

There are many parallels with the situation in the 1970s and recombinant DNA technologies[5–7]. The Asilomar Conference in California in 1975 was a landmark meeting important to the identification, evaluation and mitigation of risks posed by recombinant DNA technologies. In that case, the research community voluntarily imposed a temporary moratorium on the conduct of recombinant DNA research until they could develop guidance for the safe and responsible conduct of such research. We believe that this is another Asilomar-type moment for public-health and infectious-disease research that urgently needs our attention. ■

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