

**United States Senate  
Committee on Homeland Security and Governmental Affairs**

*Biological Security: The Risk of Dual-Use Research.*

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Mr. Chairman, Senator Collins, and members of the Committee, thank you for the opportunity to speak to you today on the issues related to Biological Security and the Risk of Dual Use Research.

My name is Tom Inglesby. I am the Director and CEO of the Center for Biosecurity of UPMC and Associate Professor of Medicine at the University of Pittsburgh. The Center for Biosecurity is an independent nonprofit organization of UPMC. Our mission is to strengthen U.S. national security and resilience by reducing dangers posed by epidemics, biotreats, nuclear disasters, and other destabilizing events. Our staff comprises experts in medicine, public health, national security, law, economics, the biological and social sciences, and global health. Our Center is the biggest and longest serving academic think tank dedicated to biosecurity.

As requested by the Committee, I will first offer my views on the issues surrounding research with mammalian-transmissible strains of H5N1 influenza virus. I will then provide the Committee my views on the new U.S. Government Policy for Oversight of Life Sciences Dual Use Research of Concern.

### **H5N1 Mammalian Transmissibility Research**

Let me start with my professional background to give you sense of my perspectives on the H5N1 issue. I'm an infectious disease physician by training. I've seen many patients with influenza infection in the last 2 decades. I've seen flu spread through families and communities quickly. I've seen many people die from influenza despite medical care from excellent hospitals.

My colleagues at the Center for Biosecurity and I have committed a substantial part of our professional lives to analyzing biological threats and pandemic flu as well as the public health policies and actions that would help us prepare for and respond to those threats. We have published academic papers on many aspects of flu preparedness, including hospital preparedness and medical surge, antiviral and vaccine development, countermeasure distribution and dispensing, legal issues, and non-pharmaceutical public health interventions. We have served on advisory committees to the U.S. CDC, the National Academy of Sciences, and other entities on flu preparedness. We've worked to enlist business sectors in greater flu preparedness efforts, and we've argued for increased funding for flu vaccine and antiviral development.

I am certainly convinced that the H5N1 influenza virus poses a serious threat. I also believe that wherever one stands in this dialogue about H5N1 research and dual use research more generally, we are all seeking to protect the public from life-threatening pandemics.

In my testimony today, I will address 3 topics:

1. The reasons why I am concerned with research on H5N1 avian influenza virus engineered for mammalian transmissibility.
2. The steps I believe we should take now to address these issues.
3. My recommendations for ensuring the success of the new U.S. Government Policy for Oversight of Life Sciences Dual Use Research of Concern

I have been opposed to the publication of the revised Fouchier manuscript now under consideration at *Science*. The reason I am opposed is because this new modified virus, if released through accident or intention, could have an extraordinarily high case fatality rate in humans and a capacity to spread by aerosol transmission which would be very difficult to stop with isolation, quarantine, antivirals, or a vaccine, particularly in countries with limited resources and limited access to medical care. The breakthrough in Dr. Fouchier's experiment was rendering the H5N1 virus transmissible through the air between ferrets—the best mammalian surrogate for transmissibility between humans. The experiment is reported to not have made the virus more virulent, or deadly. However there is no clear evidence yet presented publicly that the engineered virus has a lower virulence than wild-type H5N1 virus which has an approximately 60% case fatality rate in the series of cases in the WHO database.

Some proponents of full publication have stated that the experiment was not as dangerous as the community first thought, since ferrets infected via the respiratory route did not die of the disease until they were directly injected with the virus. I think we can take very little comfort from this, however, since transmission via respiratory route is not a reliable procedure for assessment of actual virulence in ferrets. Furthermore, once these viruses enter new mammalian host populations and transmit via respiratory routes, they will evolve and acquire new virulence properties that we have no way to predict. We will then have lost any control over these viruses.

I agree with experts on both sides of this issue that we need a disciplined evaluation of the risks and benefits of research that attempts to increase the human transmissibility of avian influenza. As for the potential benefits of the H5N1 mammalian transmissibility research, I do not judge that the published results would be immediately helpful for pandemic preparedness, as I will explain below.

That said, I do appreciate the deliberative process that has taken place in the scientific community over the last 6 months. I acknowledge that the majority of NSABB members, the involved U.S. government agencies, and the journal *Science* have decided that the benefits of this work outweigh the risks, and so it appears that the paper will be published with all details. I am concerned about this outcome, but I do recognize that decisions have been made regarding the publication of the paper. Now it is time to look forward and anticipate the future related research by these and other scientists and the attending issues that will come next. Unless there is a change in direction, scientists will continue work on virulent H5N1 strains engineered for mammalian transmissibility.

Therefore, it does not make sense to wait for the next paper that explains how to create yet another novel virulent H5N1 mammalian-transmissible strain to be submitted for publication before we reach agreement on how to consider this line of research. I will offer my thinking about the future of this work by summarizing what I see as the possible concrete benefits of the work, its risks and consequences, and what I recommend.

## Questions and Risks

### **Will engineering novel H5N1 mammalian-transmissible viruses help us improve surveillance for avian flu?**

Everyone in the flu community can agree that we need better tools for surveillance and early detection. In defense of this H5N1 research, it has been argued that if we know the mutations that (experimentally) confer mammalian transmissibility, we could use that knowledge to improve surveillance for H5N1.

This could be a valid argument if the data from the H5N1 studies in question would lead to on-the-ground, practical improvements within our existing avian flu surveillance systems. This is highly unlikely at the present time and for the near future because: (1) genetic mutation data is not now routinely used in our surveillance systems; (2) it would be a mistake to narrow surveillance efforts to only look for mutation data coming from these particular experiments, since a vast number of potential mutations in nature are possible; and (3) even if we did discover that this particular genetic mutation was present in birds, the prescribed response would still be the same—that is, culling of the whole bird flock, regardless of the specific mutation of the virus infecting them.

Specimens from only a tiny fraction of avian influenza (AI) infections are sequenced now. In fact, very few specimens are submitted from countries that experience H5N1 infections. A recent study indicates that half of the Asian and African countries that submitted any specimens for the relevant genetic sequencing, submitted 10 or fewer specimens over the last 8 years. Cambodia submitted 37 specimens over that time.

Out of the millions of H5N1 infections that have occurred in birds, people, and other animals since this strain started circulating, only 2,934 HA sequences have been submitted in the last 8 years to the Influenza Resource databank which compiles data from Genbank, NIAID, and the J Craig Venter Institute. Last year, only 160 partial sequences were submitted to Genbank. Even when countries do submit specimens, the resulting sequence data may not be analyzed or published for months or years.

We should think clearly and concretely about what we would do with the data generated from future transmissibility studies. What surveillance-related actions might be prompted? Right now the standard recommended action is to cull all flocks of poultry known to be infected with H5N1. What would we do differently if we knew these strains had mutations that matched mutations engineered in the lab? If there are other actions (beyond culling) that might be taken on the basis

of finding a match to engineered strains, let's make sure those actions are actually feasible before additional studies of engineered transmissibility are pursued.

Finally, we can't and shouldn't narrow the genetic search to only the mutations we find in a particular set of experiments, because in nature an H5N1 virus that is configured very differently might emerge as the strain that starts a future pandemic.

We all hope that in the future there'll be a much more robust system for collecting and sequencing H5N1 viruses. We do need better surveillance to monitor how viruses are evolving in nature, to ensure that diagnostics can identify emerging strains, and to make sure that medicines and vaccines are effective against new strains as they evolve naturally. Improved surveillance systems will require substantial investments in animal and human health infrastructure in the countries now coping with H5N1. Everyone would like to see that vision realized. But we also have to acknowledge that this vision doesn't reflect current reality. Until we do have in place systems that collect far more sequence information, that do so in timeframes that are meaningful, and that have widely accepted predictive value sufficient to lead to additional actions in the field, the results of this research seem unlikely to have practical surveillance applications.

For these reasons, I suspect, more than a dozen flu scientists contacted by *Nature News* in January said that virus surveillance systems are now ill-equipped to detect such mutations arising in flu viruses, and so this work is unlikely to offer significant, immediate public health benefits.

If we are able to improve surveillance systems, the benefits of identifying mutations through studies of virulent mammalian-transmissible H5N1 strains might increase, but the benefits of this research would still have to be weighed against the risks.

### **Will research on novel mammalian-transmissible H5N1 virus help us improve vaccine development?**

In Europe, the U.S., Japan, China, and elsewhere, big pharmaceutical companies, with funding support from the NIH and BARDA and other sources, have done crucial work on H5N1 vaccine development. In the EU, there are 4 approved pandemic vaccines in a "mock-up" format, with the intent to grant final EMEA approval for a vaccine during a pandemic, after the strain-causing disease is identified.

If a pandemic occurs, the vaccine would be designed to include a close match to the actual pandemic strain and then put on a fast track for approval. H5N1 vaccine development does not depend on knowledge of engineered mutations, and it does not depend on animal testing of an engineered mammalian-transmissible strain of H5N1. In short, vaccine can be created without testing it against the mammalian-transmissible H5N1 strain. An editorial about the H5N1 research published by *Nature* in February 2012 concurs: [Creating vaccine] *faster and in much larger quantities is the most urgent public health priority when it comes to planning for the next pandemic. These studies offer no serious immediate application in vaccine research.*

Although I do not see near-term, concrete benefits of this work for surveillance or vaccine development, I do recognize that there is scientific value to these recent basic research experiments on H5N1, in that they may help us to better understand the potential mechanisms of

transmissibility of H5N1. Given that value, I would be in favor of open publication of this research were it not for the grave consequences if something went wrong.

### **What could go wrong in future work with novel virulent mammalian-transmissible strains of H5N1?**

One of the reasons why scientists publish is so their work can be readily replicated by other scientists and their results validated. After this H5N1 research is published as expected in *Science*, it would be prudent to expect that other scientists will seek to replicate these studies and build on the results. As new H5N1 transmissibility experiments are conducted by additional scientists, in the same lab or in other labs, it would also be prudent to expect that the risk of accidents will increase, along with the risk of misuse.

### **Could an accident occur?**

Biosafety at modern biocontainment labs is generally excellent. Even in the uncommon event of accidental infection of a laboratorian, most pathogens would lead to no further consequence. Most pathogens have little capacity for ongoing spread in society. However, the accidental escape of an engineered mammalian-transmissible H5N1 strain into a population with little or no immunity could result in a catastrophe.

Although it's uncommon, accidents do happen. We saw the results when a mini-pandemic was started in 1977 by H1N1 influenza virus that is believed to have resulted from a lab release. We saw this again 9 years ago, in the year after the SARS outbreak. At a time when this lethal disease was at the very forefront of international public health concern, there were at least 3 incidents in which researchers working in BSL-3 and -4 laboratories in Singapore, Taiwan, and China accidentally infected themselves with SARS. In at least one case, an infected researcher transmitted SARS to a person who then transmitted it to another, who in turn transmitted it to another. In all of these SARS accidents, subsequent investigations identified breaches in laboratory protocol and improper procedures. Clearly, mistakes are made and accidents happen—even at high containment labs during times of extraordinarily heightened awareness and caution.

I am not singling out laboratorians for criticism. Mistakes are made by all types of professionals—doctors, pilots, rocket scientists, anyone—because we are human. That means we have to factor human error, surprise, and accidents into our calculations of the risk of this research, just as we factor those elements into calculations of risk in other fields.

### **Could an individual, or a group, or a state replicate or steal an engineered flu strain with the intention of deliberately releasing it?**

Some people involved in this debate have asserted that it is ridiculous to be afraid of terrorists living in caves doing this work. That is an overly simplistic and dismissive way of viewing the potential for terrorism as we consider the issues at hand.

We can't accurately predict the chances of this work being replicated by a malevolent or deeply disaffected scientist somewhere in the world, a terrorist group, or, a nation-state. We can't accurately judge the capabilities and actions of all those who may seek to cause harm. We can hope that nations, groups, or individual terrorists will not be knowledgeable enough or adequately equipped to re-create mammalian-transmissible H5N1, although it is clear that publishing this work will lower the technical barriers to doing so. We can imagine that all terrorists live in dirty caves, with little or no lab equipment, and insignificant science education. But history is full of examples of our misjudgments of the intentions and/or capabilities of others; it provides many examples of science and technology used in ways for which they were not intended. We would be fooling ourselves if we think we know the full range of competencies and intentions of countries, groups, individual terrorists, or individual researchers at the present, let alone going into the future.

### **What could happen if an engineered strain of mammalian-transmissible H5N1 started to spread widely in the world?**

If a new engineered H5N1 strain has no or minimal capacity for mammalian aerosol transmission, then it is a risk only to those working with it directly. But one of the explicit purposes of this line of work is to engineer strains of avian influenza that are transmissible between mammals, which means we should consider the potential impact of deliberately increasing transmissibility.

If a new engineered H5N1 strain that is as transmissible in humans as seasonal flu were to be released into the population, either intentionally or by accident, it could lead to a new flu pandemic. Seasonal flu infects 10% to 20%, or a billion or more, of the world's population every year. The case fatality rate of wild H5N1 in the WHO database of confirmed cases is nearly 60%. If the case fatality rate of a novel engineered strain of H5N1 approached that level, and if that strain spread as effectively as seasonal flu, then hundreds of millions of people could be killed.

With a case fatality rate 10 times lower than that of wild H5N1, but the ability to spread as effectively as seasonal flu, that engineered virus could kill tens of millions of people. Even with a case fatality rate 100 times lower than that of wild H5N1, a novel engineered strain able to spread as effectively as seasonal flu could threaten the lives of millions of people.

Some have argued that if an engineered mammalian-transmissible H5N1 strain did start spreading in the human population, it would be possible to contain and stop it. I don't agree. If an engineered H5N1 strain as contagious as seasonal flu started spreading in the world, I think it's highly unlikely we could contain and stop it.

Flu is like a wildfire—it ignites and spreads very quickly and widely. The incubation period and generation time of flu is very short. Viral shedding can occur before people have fever. In other words, by the time you know you have flu, you may have already spread it. As we saw with the 2009 H1N1 influenza virus, by the time we recognized it, we were in the middle of a new pandemic. The virus had already been spread around the world, and there was nothing to stop it.

Every year a number of influenza strains circulate in the world despite large supplies of vaccine, large numbers of vaccinated people, and ready availability of antiviral medication. The strains circulate despite advance forecasting, preparation, and prevention measures. Although vaccines and antivirals prevent many people from getting ill, they are not able to stop flu from circulating around the world.

To cope with an H5N1 pandemic, we have enough vaccine only for a small portion of the world's population. We should not push ahead with this research based on the assumption that we would be able to stop an engineered H5N1 pandemic strain from spreading if it were deliberately or accidentally released in the world.

## **What Should We Do Now?**

It already has been decided that the papers in discussion will be published. I don't agree with that decision, but I do agree that we should now focus on how to handle future experiments in this area. The question of how to do that has not yet been sufficiently resolved. I now offer my recommendations for how we should manage studies of novel H5N1 mammalian-transmissible strains going forward.

### **Extend the moratorium on research involving engineered virulent mammalian-transmissible H5N1.**

Research on influenza is extraordinarily important. Understanding transmissibility is valuable. But before proceeding, we have to work through substantial issues of public health, biosafety, and biosecurity in an open and transparent way. We should have confidence in the useful application of this research and in our ability to reap the proposed benefits. We also should strive to reduce the risks of this research to the greatest degree possible by, for instance, examining other possible ways to study transmissibility without engineering live virulent strains that are mammalian-transmissible. In short, we should not rush forward when the stakes are so high—a sentiment echoed in *Nature's* February editorial: *The fact that the risks seem to far outweigh the public-health benefits of the research, at least in the short term, means that there is no need to rush headlong into an expansion of the work.* If this work must and is allowed to continue, then it should be limited to the smallest number of labs possible.

### **Define redlines now.**

If this work with engineered mammalian-transmissible H5N1 virus is allowed to continue, then we should now engage in a focused discussion to identify whether there are any redlines for that research; we should know going into this where the uncrossable lines are. That means asking and answering some important questions well in advance. For instance: Should H5N1 strains be engineered to increase the efficiency of airborne transmission while maintaining full virulence? Should virulence and lethality be enhanced in H5N1 strains that have been engineered for transmissibility so we can understand what would make them even more virulent? Should other highly pathogenic influenza virus strains be engineered for mammalian transmissibility so that we can understand the mechanisms of transmissibility? Should those novel mammalian-

transmissible influenza virus strains be engineered for increased lethality and virulence as well? Should transmissible avian flu strains be engineered further to make them resistant to vaccines or antivirals so we can discern the genetics of vaccine or antiviral resistance? Will we already have stepped over them before we know we need them?

Even as the new U.S. Government Policy on Life Sciences Dual Use Research of Concern (DURC) policy is implemented, it is important that the scientific and policy communities consider these H5N1 redline questions now to avoid trying to reconcile them after new grants have been awarded, research conducted, and papers submitted for publication. I encourage the U.S. government to consider an appropriate process to have this dialogue. The time to wrestle with these issues is now, before the next controversial paper comes to the fore and while we are already thinking about these questions.

**Increase U.S. efforts to prepare for influenza pandemics so we can diminish their consequences should they occur.**

The U.S. should continue its important pandemic planning efforts and continue to place priority on developing the capacity to manufacture large quantities of flu vaccine during crises. Developing a universal flu vaccine should be a top priority of pharmaceutical companies, funding entities, and regulators. The U.S. and its partners also should continue work to develop new antivirals and continue research on the role of statins and other anti-inflammatory agents. The U.S. and its partners should prioritize efforts to improve surveillance and culling of avian flu infected flocks by committing greater and stable funding.

**U.S. Government Policy for Oversight of Dual Use Research of Concern**

The new DURC policy is an important step toward addressing the types of issues raised by the H5N1 controversy. This policy begins the process of systematizing a number of review processes that were proposed in the 2003 National Academy of Sciences Report “Biotechnology Research in the Age of Terrorism” and in several subsequent reports of the National Science Advisory Board on Biosecurity.

The policy puts forth a set of principles as guidance. I believe these principles (or judgments) are correct and critical for the policy’s success. In summary, they state the following:

- Life sciences research is essential to scientific advances in public health and safety, agriculture, environment, and national security.
- Despite this, some research could be misused for harmful purpose.
- Some degree of federal and institutional oversight of dual use research of concern is necessary.
- Mitigating risks associated with this research should be done in a way that minimizes the impact on research and is commensurate with the risks.
- The U.S. government will continue to be committed to the principle of broad sharing of research while taking into account U.S. national security interests.



This new policy is a pragmatic step forward toward reducing the risks of DURC, but its effectiveness will depend on how well it is implemented. I believe there are 5 ingredients for success, which I detail below.

## **1. Implement Effectively at the Local Level**

The policy espouses the right principles. It defines the 7 research questions that should trigger review. The policy offers a number of possible mitigation plans if one is called for in a review process. It directs federal agencies to review their portfolios for DURC. The policy stipulates a logical process that serves the goal of reducing the risk of DURC. To be effective, though, local implementation will have to be successful.

By “local implementation” I mean this: scientists, the institutions they work for, and their Institutional Biosafety Committees (IBCs) will be very important to the success of this policy. Earlier research from some of my Center for Biosecurity colleagues found that scientists often respect the decisions made by their own institutions and peers more than they respect the decisions of federal agencies, regardless of the esteem with which they regard an agency. To engage scientists and to garner their respect for the new policy, it must be implemented effectively at the local, institutional level.

For local implementation to succeed, institutions will have to have training and educational materials, such as those now available through the NIH Office of Biotechnology Assessment. The responsibility for managing these issues at the institutional level will presumably be assigned to institutional IBCs, which are not currently constituted or educated to consider biosecurity issues. IBCs will, therefore, require need new training and possibly additional members or resources.

IBCs will also have to develop clear decision making processes to address DURC issues when they arise. The process for resolving disagreements will have to be practical and accessible. Anecdotally, we have learned that some IBCs have lost members who felt ill-equipped to review select agent research. Training and education have to be provided to prevent loss of IBC members who do not feel prepared to review DURC.

## **2. Learn from Experience**

We need to learn from experiences with this policy as it is implemented, and be able to evolve the policy as we go. My understanding is that the NIH review of its portfolio found only 10 experiments warranting further risk management. It would be valuable for the scientific community to understand more about the 10 cases that were noted in the initial review of the NIH portfolio. Specifically, what caused the concern, and how were risks mitigated? If made available to the scientific community, those 10 cases would be a valuable learning tool. They could be de-identified to avoid public intrusion into the work of the scientists.

Determining the applicability of the DURC policy to particular experiments and deciding what, if any, measures will mitigate the attendant risks will be a challenging and subjective task. Therefore it would be helpful for the federal government to provide hypothetical scenarios that

demonstrate both the types of research that would raise concern under the DURC policy and the possible measures that would effectively mitigate the risks. It would be instructive to know the types of mitigation measures that would be insufficient for addressing various types of DURC risks. While the government could not address every possible situation, the community would benefit greatly from a range of instructive examples that make clear how the DURC policy is meant to work in practice. This would be a key part of the education of the life sciences community that has been called for by the NSABB, and which will be critical to the success of this effort. My sense is that few in this community now would know how to successfully implement the new DURC policy should they identify experiments that pose dual use concerns.

It also would be useful to understand the effect of the DURC policy on the H5N1 research under discussion for the past 6 months. I suspect the review process would have triggered additional risk mitigation. It would be helpful to understand how that process would have played out had this new DURC policy been in place

This new U.S. policy importantly commits to domestic dialogue, international engagement, and input from scientists, national security officials, and global health specialists. While informal exchanges with these communities will be valuable, to the government should consider whether to engage other countries more formally, as well as other national and international scientific bodies, to ascertain their views. For instance, perhaps it is time to solicit input from the inter-academy council of national science academies.

In the 1970s, when the NIH released guidelines for safety oversight of recombinant DNA research, there was concern initially that the guidelines would affect only U.S.-funded research. Over time, the guidelines have been widely adopted internationally. In the same vein, it would be in the best interest of all if the U.S. DURC policy prompted broad international discussion of these issues.

### **3. Attend to Regulatory Burden**

While I do think that the new DURC policy is a step in the right direction, it will add another administrative process to be navigated by a scientific community that is already heavily regulated. As we add the DURC policy into the mix, we should understand the burden imposed on U.S. scientists by existing policies and regulations.

At a recent presentation, Carrie Wolinetz, Associate VP for Federal Relations of the Association of American Universities, provided a useful hypothetical example that illustrates this point: Dr. XX, working in a lab funded by both NIH and Amgen, is searching for a therapy for a serious viral infection. She plans to take a cell from a patient and use it to create pluripotent embryonic stem cells. Then, she plans to introduce those cells into an animal model and use radioisotopes to study physiological changes. Before she can do any of this, her work must be reviewed and approved by her IRB and IBC; it must be in compliance with the select agent regulations and radiation safety regulations; she must comply with the guidelines of the Association for the Accreditation of Human Research Protection Programs; comply with the USDA Animal Welfare Act (AWA); have an assurance on file with the NIH Office of Laboratory Animal Welfare (OLAW); comply with rules of the Association for Assessment and Accreditation of Laboratory

Animal Care (AAALAC); work under the oversight of the Embryonic Stem Cell Research Oversight (ESCRO) Committees and NIH Stem cell guidelines; and comply with Conflict of Interest policy. She must also ensure that all laboratorians have training in animal care and use, biosafety, chemical safety, research ethics, and management of human subjects.

In an effort to increase U.S. lab security in recent years, some new regulations have been imposed that in my view have not improved security appreciably. For example, my colleagues and I initially supported creation of tiers of select agents because we believed doing so would sharpen focus on the select agents of greatest concern, while reducing the regulatory burdens related to lower tiered agents. Implementation, though, has not produced this result. Instead, top tier agents are now more heavily regulated while the rest of the restrictions still apply to agents on lower tiers. This is an unfortunate outcome.

Current select agent regulation also requires periodic inventory of specimens stored in every lab. Counting the number of vials containing select agents provides a false sense of security and raises false alarms of no significance. Word has it that vials of pathogens are being removed from freezers so frequently to be counted that specimen viability is being compromised.

We have to make sure that we don't impose such a heavy regulatory burden on U.S. scientists that they cannot continue their work, or that they come to consider it more trouble than it's worth to conduct research that is of importance to the country. The greater the regulatory burden, the more likely it is that our best scientists will stop working on the pathogens that cause the most dangerous diseases, or that they will leave the U.S. to conduct their research elsewhere. Beyond this, the regulatory burden overall threatens to diminish the U.S. competitive edge in the life sciences.

I recommend engaging the National Academy of Sciences to examine the extent and effects of existing policy and regulatory burdens on U.S. scientists. The NAS could consider as well the benefits and consequences of both the overall regulatory regime and individual policies and regulations, and could make recommendations for change when a burden is greater than any benefit it confers, whether related to security, safety, or other concerns.

#### **4. Reaffirm the Role of NSABB**

The NSABB deserves great deal of credit for its efforts. Over the last few years the group has released a series of valuable documents and guidelines that appear to have informed the new U.S. DURC policy. Under time pressure and with the international community watching, NSABB members expended a great deal of thought, effort, and personal and professional time in addressing the issues surrounding the H5N1 research. Perhaps most importantly, the NSABB members have no personal or professional stake in the outcomes of their deliberations.

The NSABB has expertly assisted the government, including in the preparation of the very useful June 2007 document titled *Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information*. The NSABB has served the government with great professionalism, though often under the radar screen. It is a good moment to reaffirm and recognize the role of this committee going forward.

The charter for the NSABB outlines what I think should continue to be important roles going forward: recommend strategies and guidance for personnel reliability; provide recommendations on the development of programs for outreach, education, and training in dual use research; advise on policies governing publication, communication, and dissemination of dual use research; recommend strategies for international engagement on these issues; advise on codes of conduct; and, advise on the conduct of dual use research and the Select Agent Program.

In some ways, the NSABB is like other safety/security programs and entities that are criticized for adding cost and time to an effort and assigned blame when something goes wrong. The FDA is perhaps the best example of this: the agency is urged to speed up the drug approval process, criticized roundly for slowing the advance of progress, and then castigated if a patient is harmed or, worse, killed by an adverse drug effect. Going forward, if the NSABB has the responsibility of advising the government whether to proceed with or publish high risk research, we should recognize these pressures in the event that it issues recommendations to alter a research proposal or recommend against publication. When the NSABB does support a project or publication, it will, predictably, shoulder blame if something goes wrong.

It is my hope that with effective implementation of the DURC policy, NSABB would rarely be in the position again of entering into the review of research at the tail end, and considering DURC experiments for the first time only after the research has concluded and manuscripts have been submitted for publication.

## **5. Focus Attention Where Risk is Greatest**

Most U.S. labs have good safety records. Even when accidents have occurred, the consequences for the surrounding communities almost always have been insignificant. Nonetheless, an accident or misuse of a very small set of experiments could pose risks—perhaps of great consequence—to surrounding communities and perhaps to the public at large. Research with agents that pose the greatest risk to the public in the event of an accident is, in my view, the kind of research that should prompt the greatest dual use concerns.

Experimental work that, through accident or deliberate misuse, poses the greatest potential direct adverse consequences to society should be the highest priority of the DURC (and biosafety related) policies. As I have explained above, my view is that future experimentation with novel strains of H5N1 influenza engineered for mammalian-transmissibility is research that falls into this category.

One clear potential benefit of the new DURC policy, if properly implemented, is that it will help us to address dual use issues of risk much earlier in the process, so that we avoid a situation when the debate is happening only after the research is funded, concluded, and submitted for publication to scientific journals. I believe that the policy takes us an important step in the right direction.

## **Conclusion**

It is worth underscoring that the scientists who undertake research on influenza and other agents of infectious diseases are doing so to improve our fundamental understanding of biology and to improve the world. The U.S. needs to continue funding the entrepreneurial and talented scientists with the best ideas. The support and publication of their work will help drive serious improvements in our preparedness and response to these diseases.

At the same time, we do need to acknowledge that there are rare situations in which the consequences of an accident or misuse regarding a certain line of research are so serious that special processes are needed to assess and mitigate the risks to the public. This new DURC policy provides a practical framework for moving forward in this process. The details of its implementation will determine its effectiveness going forward.