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DEFENDING AGAINST PUBLIC HEALTH THREATS

HEARING

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS

UNITED STATES SENATE

ONE HUNDRED ELEVENTH CONGRESS

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CONTENTS

DEFENDING AGAINST PUBLIC HEALTH THREATS

WEDNESDAY, SEPTEMBER 29, 2010

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 2:35 p.m., in room SD–124, Dirksen Senate Office Building, Hon. Tom Harkin (chairman) presiding.

Present: Senators Harkin, Pryor, Specter, and Cochran.

OPENING STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. The Appropriations Subcommittee on Labor, Health, Human Services, and Education, and Related Agencies, will come to order.

It's sometimes said that, while the Defense Appropriations Subcommittee defends America, this subcommittee actually defines America. For the most part, that's true. This subcommittee also defends America in one very important area, and that's public health. Funding provided by this subcommittee is what pays for the Nation's medical countermeasures (MCM), including the drugs, medicines, and devices that protect Americans against bioterrorism, pandemic influenza, and other emerging infections. This subcommittee has taken that responsibility very seriously, and we can point to important advances. But, America still remains vulnerable to an epidemic or a bioterrorism attack.

A good example is pandemic flu. Since fiscal year 2006, this subcommittee has provided $15 billion—$15 billion—to improve pandemic preparedness in the United States. Many of these investments paid off during last year's H1N1 outbreak. For example, an improved surveillance system allowed us to detect the new strain very quickly. Second, State and local public health agencies had more capacity than ever to administer vaccines. Third, we stockpiled antivirals, such as Tamiflu, which allowed us to treat patients who'd already gotten sick with the flu.

But, despite all those improvements, a continuing vulnerability is our dependence on egg-based technology to produce influenza vaccines. This contributed to serious delays in the development and manufacture of the H1N1 vaccine. Indeed, the vaccine didn't become widely available until after the flu season had already peaked. Fortunately for us, H1N1 was milder than expected. But, we may not be so lucky the next time.

Another example is anthrax. It's been almost 10 years since letters laced with anthrax were sent through the U.S. mail. Future attacks remain a very real threat. Yet, we are still using the same anthrax vaccine that was developed 40 years ago.

One reason that we've been slow to prepare for such threats is that we need a stronger partnership with biotech companies that could produce countermeasures such as the next-generation anthrax vaccine. There's a problem, and that is this: The Federal Government is the only buyer for these countermeasures. So, we have to work closely with small biotech companies to make sure they have the capacity to do what we're asking of them. Right now, this partnership doesn't seem to be working as well as it should.

This summer, Secretary Sebelius released a plan—a very comprehensive plan—to address these various challenges and to take a comprehensive approach to improving our Nation's countermeasures. For that, Madam Secretary, we are all very grateful for your leadership in this area.

Some of what the Secretary has proposed will require this subcommittee's approval, since it requires transferring or redirecting unobligated balances for pandemic flu and Project BioShield. This hearing, therefore, is an opportunity both to take stock of how prepared we are as a Nation to meet the threats that confront us in this area, and to evaluate the administration's plan for addressing these issues. We will hear from Secretary Sebelius, as well as a panel of experts from outside the Government.

And before we begin, I'll turn to Senator Cochran for an opening statement.

Senator COCHRAN. Mr. Chairman, thank you for convening this hearing to consider our Nation's important obligation of defending against threats to public health.

The Department of Health and Human Services (HHS) monitors and recommends how we go about discharging this important responsibility to defend our country against bioterrorism and other public health threats. We're pleased to welcome the Secretary of HHS, Kathleen Sebelius, to the subcommittee hearing, and we look forward to working with her to help develop and implement plans to enhance this Nation's investment in MCM and public health preparedness.

We have other witnesses, as well, who are coming before the subcommittee today, and we look forward to hearing the testimony of all of our witnesses.

Thank you.

Senator HARKIN. Thank you, Senator Cochran.

Senator Specter wanted to——

Senator SPECTER. Well, thank you, Mr. Chairman. I had asked for an opportunity to say a few words, because, regrettably I cannot stay for the hearing.

But, this is a very important project that will be discussed today, and something that you and I and many have worked on. But, flexible manufacturing has been high on my agenda for a long time, when I used to chair the subcommittee. And a portion of my concern is State-oriented, because UPMC is a major player, and seeks to engage in the competitive bidding. And we're just at the—

really, at the second inning of a very long process here. But, I wanted to express a couple of concerns.

One concern is over the $1.2 billion ceiling for funding over the next 25 years, because the analysis which I have seen indicates that will be insufficient. That goes to about $48 million a year. And some people are talking about $300 million. I think that's probably too high, perhaps way too high. There have been some discussions about $100 million. But, I wanted to raise that issue, and would hope that would be addressed by the Secretary during the hearing today.

The other subject of concern is the thrust of having the recipient of the contract to build a facility cooperate with other research entities to produce more vaccines with greater flexibility as these threats arise, and there's a concern that these entities will be in competition with one another and will not be interested in the high level of cooperation which would best suit the Government, best suit the public interest.

So, I raise these two considerations at the outset.

I thank the Secretary for the attention she has given to this matter. I have talked to her about it on several occasions. I even talked to two people who are higher up on the chain of command than is the Secretary about the matter. They call them the Vice President and the President. And I've talked to many people who are lower on the chain of the command. And I—the principle of equality is important, and very often somebody far down on the chain of command can be as influential as somebody at the top of the chain of command. Some say that the staffs run the Senate. I don't think they run all the Senators, but they are very, very influential.

But, I wanted to call those couple of matters to the attention of the Secretary and the subcommittee. And, while I'll be working with Secretary Sebelius much more, because we have a very lengthy lame duck session—I heard it was going to last until December 15—but, I just want to thank her for what she's done, especially coming to Philadelphia on the first Sunday in August of the year 2009, when the first of the raucous town meetings occurred. And she and I were there that day, speaking to a group of lawyers. The organizer was a Philadelphia lawyer who asked me to speak. They finally got a better speaker, but I was second because the president of the association's from Kansas, and knew the Secretary, and was able to get a high-quality speaker without an honorarium. And since she was coming to town—when I say a "high-quality speaker," Madam Secretary, that's because Senators don't charge honoraria; we're not permitted to. But, since she was coming to town, she decided to hold a town meeting. And since I was in town with her at the same lunch, I was asked to join her. And it was historic, and you were terrific.

Thank you, Mr. Chairman.

Senator HARKIN. I have to get a video of that one, then.

Thank you very much, Senator Specter.

Secretary Kathleen Sebelius became the 21st Secretary of HHS on April 29, 2009. In 2003, she was elected as Governor of Kansas and served in that capacity until her appointment as Secretary. Prior to her election as Governor she served as the Kansas State insurance commissioner. She is a graduate of Trinity Washington

University, just up the street from here, and the University of Kansas.

Madam Secretary, welcome. And your statement will be made a part of the record in its entirety. Please proceed as you so desire.

STATEMENT OF KATHLEEN SEBELIUS, SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Secretary SEBELIUS. Well, thank you so much, Chairman Harkin and Senator Cochran and Senator Pryor. I'm sorry that Senator Specter had to leave. He doesn't advertise it much, but he is also a Kansan. He was born and raised in Russell, Kansas, and was the debate champion of his high school. So, it was great to be with him at the town hall in Philadelphia. And I appreciate the opportunity to be here and talk a bit about our recent review of the MCM Enterprise and some recommendations we have about how we can move forward.

As you all know well, we don't really know where the next public health crisis is going to come from. It could be a dirty bomb in a subway car, it could be a naturally occurring superbug that's resistant to all treatments, it could be a biological weapon that we've never seen before, assembled from the building blocks of life by a terrorist in a lab. And, as we've seen, it could be a naturally occurring novel strain of the influenza virus.

So, I had my introduction to MCM less than an hour after I was sworn in on April 29, when I went and was briefed, by John Brennan in the situation room, on the rapidly expanding H1N1 virus, which was beginning to appear, not only in the United States, but in other nations. And we had a rapid and coordinated response across government, made possible in large part by the efforts of this subcommittee, Mr. Chairman, who had been directing resources and planning and preparedness dollars over a series of years so that we would be ready to respond.

So, with the first pandemic in 40 years, the good news is, we were able to develop and distribute a safe vaccine. The bad news is that our production peaked 3 weeks after the peak of the flu season, so we were still not able to respond in a timely fashion.

So, we knew we needed to do better, and the President encouraged our Department to look at not only what occurred during the H1N1, but to use it as an opportunity to review the entire MCM Enterprise. And so, we launched that study in December 2009.

As you know, countermeasures are vaccines, antivirals, antibiotics, pharmaceuticals, diagnostics, and the medical equipment that are the most direct and effective defense in any public health crisis. So, I asked Dr. Nicky Lurie, who's our ASPR—to lead the review. And we engaged not only all of our departments and entities in HHS, but also reached out to our local and State health departments, who had been great partners in the flu response, to industry groups, to venture capital experts, academics, scientists, and our partners in the Department of Defense (DOD), as well as biotech developers around the country, to help us analyze sort of where we are and where the glitches are in the system.

And we found that the pipeline that we rely on to provide critical countermeasures is, unfortunately, full of leaks and chokepoints and dead-ends. And, in an age of new threats, where delays cost

lives, we aren't developing and manufacturing new countermeasures fast enough. And, Mr. Chairman, you referred to both the flu and the anthrax situation as two examples of that. So, at a moment when the most dangerous threat may be something we've never seen before, we don't have the flexibility to adapt. And our challenge is to get from where we are today to the goal that the review laid out, a Nation with, and I quote, "The nimble, flexible capacity to produce MCM rapidly, in the face of any attack or threat, known or unknown, including a novel, previously unrecognized, naturally occurring, emerging infectious disease." That's where we need to be as a Nation. And our plan, which we have submitted to this subcommittee and to Congress, is a step to getting us there.

We think it's important to focus on five major areas where we begin to act now to make big improvements in public health defenses:

First, upgrade regulatory science at the Food and Drug Administration (FDA), to modernize product development and evaluation. By identifying and solving scientific problems earlier, we can take products across the finish line faster, confident in their safety and effectiveness. And I would say, Mr. Chairman, that we used some of these new techniques in the production of the H1N1 vaccine, brought the companies to the table at a much earlier stage, and I think it's one of the reasons we were able, in record time, to get that vaccine into the production lines.

Second, want to work with highly experienced developers—and this is what Senator Specter referenced—to establish facilities capable of providing core, advanced development and manufacturing services here in the United States. So, on September 15, we released a draft solicitation for new centers of innovation for advanced development and manufacturing facilities. These will be new plants, here in the United States, to develop flexible manufacturing platforms, giving us a dependable source of surge capacity for flu vaccine, as well as the ability to manufacture other MCM, so we don't have to rely on foreign producers, as we did during the H1N1 crisis.

We released the draft for comment, and anticipate producing the final solicitation before the end of the year. And, in fact, next week we have interested parties coming in for 3 days of discussion so we can home in on what are the real strategies for the best possible request for proposal.

The centers also can serve as a resource for small biotech companies with big ideas that can help them get the manufacturing and regulatory support they need to get the products to market. Just this week, we've awarded eight contracts to businesses, with the goal of developing innovative tools and techniques that improve numerous aspects of the MCM pipeline, from increasing the shelf life of the flu vaccine to advanced disease surveillance.

The third area where we think we need to turn our focus is doing more to nurture the discoveries at their earliest stages by taking full advantage of the world-class resources and years of experience at the National Institutes of Health (NIH). We'll aggressively seek out those ideas and discoveries that have the best potential to fuel the product pipeline. And to assure that no breakthroughs sunset

with the publication of a paper in a scientific journal, we want to be more proactive in harnessing the ideas and incubating new products.

Fourth, reducing the time it takes to get flu vaccines to people by producing vaccine seed strains that grow better and by modernizing potency and sterility testing methods.

These are some of the steps recommended in the President's Council of Advisors on Science and Technology report, and they'll ensure we're better prepared for flu seasons to come. The Centers for Disease Control and Prevention (CDC), FDA, Biomedical Advanced Research and Development Authority (BARDA), and NIH are already engaged in a planning framework to address each of these needs.

And, again, Mr. Chairman, I want to recognize your leadership and support in this area. You have been a champion of this for years, and it's something we take very seriously.

And finally, we're exploring the possibility of launching a nonprofit venture capital firm that can support critical financial and business planning to small companies with big ideas that have the potential to improve our public health preparedness. In the coming years, HHS will direct nearly $2 billion in preparedness funds to these five areas, helping us build a MCM enterprise with a solid base of discovery, clear regulatory pathway, and the agile manufacturing that's necessary if we're going to be able to respond to any threat at any time.

We've also submitted an amendment to the fiscal year 2011 President's budget to provide the new authorities where they're needed.

So, coming off this review, we hit the ground running. We just awarded a contract to a California company to create next-generation ventilators for use during a potential health emergency or pandemic. And today we're announcing further investment in our ongoing international cooperative agreement with the World Health Organization to support global pandemic influenza vaccine preparedness, a partnership that improves health safety, both here and abroad.

In the end, if a product fails to make it into our national stockpiles, it should only be based on its failure to meet our stringent standards for safety, efficacy, or quality, and not because we failed to provide the needed business, regulatory, and technical support for success.

Mr. Chairman, there's an old saying in sports, that most victories are actually won on the practice field, when no one is watching. And we feel in the same way how successfully we respond to tomorrow's public health crisis when the spotlight's on actually determined by how hard we work behind the scenes to build a 21st century countermeasures enterprise that can respond quickly and effectively to any threat.

PREPARED STATEMENT

So, we'll continue to look for ways to build, not just a stronger countermeasures enterprise, but a stronger end-to-end public health response, all the way from disease surveillance to administering MCM to people in our cities and towns.

I look forward to working with you, Mr. Chairman, and your subcommittee, and again want to applaud this subcommittee for your focus and attention on this over the last number of years.

[The statement follows:]

PREPARED STATEMENT OF KATHLEEN SEBELIUS

Chairman Harkin, Senator Cochran, and members of the subcommittee, thank you for the opportunity to discuss the Department of Health and Human Services (HHS) recent review and recommended initiatives to improve our medical countermeasures enterprise.[1]

Our greatest responsibility in Government is keeping the American people safe. We have always maintained a powerful military that can guard against conventional threats. But in today's world, the range of threats is ever-widening to include biological, chemical, nuclear, and radiological hazards in addition to the conventional threats. The next public health emergency could be a dirty bomb set off in a subway system. It could be a biological weapon we've never seen before, assembled by a terrorist in a lab. And, as we have seen, it could be naturally occurring novel strain of influenza virus.

2009 H1N1 PANDEMIC INFLUENZA

Right after I was sworn in as Secretary of HHS, I was briefed by John Brennan, the President's Advisor for Homeland Security and Counterterrorism, on 2009 H1N1 influenza, and immediately found myself immersed in the national need to respond to this new threat. Fortunately, HHS was already in the process of rapidly responding to 2009 H1N1, working in close partnership with virtually every part of the Federal Government under a national preparedness and response framework. We characterized the new virus, disseminated the information to researchers and public health officials, and developed and began shipping to States a new test to diagnose cases of the infection. We distributed antiviral drugs to the States from the Strategic National Stockpile. We also completed key steps in the vaccine development process—preparing a virus strain for vaccine production, contracting with manufacturers for vaccine, performing necessary clinical trials, and licensing multiple 2009 H1N1 influenza vaccines. After close collaboration with State and local authorities and healthcare providers, we began the voluntary national vaccination program in October. HHS was in constant communication with State health officers and hospital administrators to monitor stress on the healthcare system and to be prepared in case Federal medical assets were necessary to augment State and local surge capabilities.

We responded as quickly as possible to the H1N1 emergency, and the speed of these efforts was due in large part to the prior investments in pandemic preparedness. I would like to thank this subcommittee for its support in this area over the past 4 years. We did, however, experience challenges with the vaccine manufacturing and availability. No matter how quickly we responded, we were still dependent on vaccine technology from the 1950s, relying on the virus to grow in eggs. We also had to depend, in part, on foreign vaccine manufacturers, which meant there were two instances in which our vaccine deliveries were delayed in order to meet another country's vaccine needs first. HHS had already taken steps to expand domestic vaccine manufacturing with the opening of a new cell-based influenza vaccine manufacturing facility in North Carolina in November 2009. But, further action was needed to provide a more robust and nimble domestic manufacturing surge capacity. We continue the process of that investment today.

MEDICAL COUNTERMEASURES (MCMS)

The success of a response to a public health crisis depends on many factors, including the expertise of our healthcare workforce, the capacity of our Nation's hospitals, the ability of Federal, State, local, tribal, and community partners to coordinate, and the engagement of the public. The success of a response also greatly depends on medical countermeasures. These are the medical treatments, vaccines, diagnostics, personal protective equipment, and nonpharmaceutical aids like ventilators that help reduce the spread of infections, reduce health consequences, and ultimately save lives. In a public health crisis, medical countermeasures are typically our most direct and often our most effective response.

[1]The Public Health Emergency Medical Countermeasure Enterprise Review is available online at: http://www.phe.gov/Preparedness/mcm/enterprisereview/Pages/default.aspx.

Medical countermeasures take years to develop, are very expensive, and must follow the rigorous development and regulatory pathway to demonstrate safety and efficacy. Unlike the drugs destined for everyday or frequent use, the countermeasures needed for biodefense threats in many cases may have greater development risks, due largely to the absence of significant commercial markets and the difficulty in demonstrating efficacy in the absence of human clinical trials.

The Federal Government has invested considerable resources over the past 10 years in expediting the development of these products. However, it was apparent from both the 2009 H1N1 experience and the paucity of medical countermeasure candidates moving from early to advanced development that we needed a better understanding of how the Federal Government and industry are generating new products. We realized that the greatest danger we may face is a microbe that we have never seen before and for which we do not yet have a medical countermeasure. We clearly need the capacity to develop a medical countermeasure quickly.

MCM REVIEW

Recognizing this need, with the encouragement and strong support of President Obama, I called for a comprehensive review of our entire medical countermeasure enterprise in order to transform these efforts into the highly responsive and flexible system we know we need. In order to get the 21st century products essential for our national security, we understood that we must invest in 21st century technical approaches as well as 21st century financial, legal, and regulatory frameworks that nurture a viable commercial sector and create incentives for companies to build these advanced countermeasures. In his 2009 State of the Union address, the President called for a renewal of our national capability to respond to bioterrorism and infectious disease.

The review was led by HHS's Assistant Secretary for Preparedness and Response (ASPR), Dr. Nicole Lurie. She was joined by representatives from across HHS (the Office of the ASPR, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the Office of the Assistant Secretary for Financial Resources, the Office of the Assistant Secretary for Planning and Evaluation, the Office of the Assistant Secretary for Legislation, and the National Vaccine Program Office; Federal interagency partners (the Department of Agriculture, the Department of Defense (DOD), the Department of Homeland Security, and the Department of Veterans Affairs); and the Executive Office of the President to dissect the issues, identify critical gaps, and respond to the challenges that would be uncovered as the review proceeded.

The review was conducted in multiple stages. First, we analyzed a large body of work on medical countermeasure development, financial and market incentives, and procurement of science. We looked at how the needs of the medical providers are considered in the design of MCM products, and which mechanisms are employed to get products to those providers. Second, the successes and failures of the MCM enterprise were examined in order to identify the critical components for success and impediments to realizing our goals. In addition, we interviewed numerous opinion leaders, representatives from the pharmaceutical and biotechnology industry, members of the investment community, and leaders in State and local public health for their views on the role of HHS in MCM development. A series of meetings and workshops were conducted, including: a 2-day workshop hosted by the Institute of Medicine's Forums on Public Health Preparedness and Drug Development, a town hall meeting at the National Association of County and City Health Officials Preparedness Summit, and a meeting with leaders of the President's Council of Advisors on Science and Technology. Finally, the ASPR, on my behalf, asked the National Biodefense Science Board, an HHS Federal Advisory Committee, to convene a workshop to review the overall strategic management, leadership, and accountability structure of the MCM enterprise.

I released the review, The Public Health Emergency Medical Countermeasures Enterprise Review: Transforming the Enterprise to Meet Long-Range National Needs, last month. This review highlights the need for the MCM enterprise to adopt a new strategy that incorporates our ability to rapidly and flexibly respond to a new or unknown threat balanced against our longstanding requirements for producing MCMs to counter identified threats. This new strategy is articulated through the following vision statement: Our Nation must have the nimble, flexible capacity to produce MCMs rapidly in the face of any attack or threat, known or unknown, including a novel, previously unrecognized, naturally occurring emerging infectious disease.

The principle at the heart of this strategy is that our public health response is only as strong as its weakest link. So, using it as a guide, we have worked to up-

grade our entire end-to-end response, from how we assess and identify threats to how we distribute and administer products to counter those threats in cities and towns across the country. That is why we will continue to look for ways to build—not just a stronger countermeasures enterprise with a solid base of discovery, a clear regulatory pathway, and agile manufacturing—but also a stronger public health response all the way from disease surveillance to administering countermeasures to people in our cities and towns.

RECOMMENDATIONS

The MCM review recommends five new infrastructure initiatives as well as other enhancements to the MCM enterprise. The review found that the unique products required by the public health emergency medical countermeasure enterprise are not of general commercial interest to the major pharmaceutical companies, due to the risks and opportunity costs to produce and receive approval for products with very limited commercial market value. The Federal Government often partners with smaller pharmaceutical or biotechnology companies, many of whom would benefit from additional resource or management investments to become successful and reliable entities. We came to realize that we need to provide a variety of supports to ensure the viability of these partners. In the end, if a product fails to make it into our national response capability, it should only be based on its failure to meet our stringent standards for safety, efficacy or quality, and not because we failed to provide the needed business, regulatory, and technical support for success. We also realized that the approach to the threats of the future requires building a "capability-based" system that can quickly adapt to a rapidly emerging or sudden, novel threat.

21st Century Regulatory Science

The first infrastructure investment, which enjoyed nearly universal support, is the strengthening of regulatory science at the FDA.

We heard from stakeholders that one of the greatest risks to successfully developing a product was the uncertainty associated with the complex regulatory process that governs the approval of these particular drugs, vaccines, and diagnostics.

FDA has been testing and producing cutting-edge products using science that's decades-old and it is prudent to invest in providing the FDA with the tools, models, methods, and knowledge necessary to 21st century technologies and assist industry in reviewing and regulating these new products.

As part of this initiative, FDA is launching a new program entitled, Advancing Regulatory Science for Public Health, designed to augment the tools used to assess the safety, efficacy, and quality of medical products, with a particular focus on MCMs. The FDA will create new Action Teams to work with those manufacturers who are developing the high-priority products and platforms. This strategy is based on an approach that worked well several years ago when the United States licensed its vaccine for smallpox, ACAM 2000. The Action Teams, composed of experts from across the FDA, will work with sponsors to identify and help resolve scientific issues as early and efficiently as possible, and to facilitate more rapid evaluation of these high-priority candidate products. Finally, the FDA will launch a collaborative project with other HHS and interdepartmental members of the MCM enterprise to resolve several of the real challenges that have been identified for these types of products. For example, one of these challenges is the difficulty in using the Animal Efficacy Rule. This rule allows appropriate studies in animals in certain cases to provide substantial evidence of effectiveness in humans of new MCMs against biological threats.

These initiatives will both give our world-class FDA scientists the cutting-edge resources they need to analyze promising new discoveries faster as well as help industry navigate the complex regulatory processes to ensure that safe, effective, and high-quality products are ready for our use. The FDA has already begun to identify areas of needed scientific investment via internal discussions with science leaders from among its various centers, as well as the processes and metrics they will use to track return on this investment.

Flexible Manufacturing and Advanced Development Core Services Partnerships

The second initiative we are investing in is the development of flexible manufacturing capable of producing the next generation of medical countermeasures.

As noted previously, the Federal Government often partners with smaller pharmaceutical or biotechnology companies in the development of medical countermeasures. Many of these companies would benefit from technical expertise and guidance in scaling up from small to large production and in the approval of an MCM product. Further, many of these innovators do not have the capital or experience to construct and operate commercial-scale manufacturing facilities.

To fill this need, HHS will establish Centers for Innovation in Advanced Development and Manufacturing. These centers will provide a variety of core services to less-experienced innovator companies with federally supported medical countermeasure candidates through public-private partnerships with fully integrated pharmaceutical partners. HHS will coordinate these core services with regulatory science assistance and other services already provided by the Federal Government, such as clinical studies and animal-challenge model development. In addition, these centers will be expected to fill the remaining gap in domestic pandemic influenza vaccine manufacturing and surge capacity, utilizing new recombinant and molecular platform technologies. Last, the manufacturing output from these centers will be coordinated by HHS with a domestic network of fill-finish manufacturers to ensure that the first and last doses of vaccine or other medical countermeasure become available as soon as possible. These centers are expected ultimately to aid in controlling the costs of developing and procuring medical countermeasures in emergencies and of stockpiling. The centers will provide development and pilot-manufacturing activities for vaccine candidates, allowing their associated costs to be absorbed into the center's operating budget and thereby reducing the total amount of the R&D contract. Similarly, the costs for commercial-scale manufacturing of MCMs destined for stockpiling in the Strategic National Stockpile will be lower than the costs under the current fixed-price contracts.

The centers will be managed by the Biomedical Advanced Research and Development Authority (BARDA) within ASPR in coordination with other HHS agencies and the DOD. BARDA issued a draft solicitation earlier this month to seek public comment and engagement in this envisioned public-private partnership capability. We expect that the final solicitation will be available by the end of the year, and that competitive contracts will be awarded in 2011.

Accelerating Discovery and Translation of Product Concepts

The third initiative we will invest in is nurturing discoveries in their earliest stages.

The Federal Government has invested heavily in a strong, vibrant basic research and discovery program with the ultimate goal of translating important scientific discoveries into licensed medical countermeasures. However, most individual scientific discoveries do not lead directly to an identifiable product. Scientists may make a discovery without realizing that it could be turned into a useful countermeasure, or, if they do see its potential, they may have trouble attracting private investment with an uncertain commercial development path to market. The Conception Acceleration Program at NIH's National Institute of Allergy and Infectious Disease (NIAID) aims to change that dynamic.

A key component of this initiative will be Early Development Teams, that will work closely with partner agencies and programs (NIH, CDC, DOD, ASPR/BARDA, and FDA) and with academic researchers, biotechnology companies, and large pharmaceutical companies. NIH, and especially NIAID, has a broad capability to scout the emerging science that comes from its investments. These teams will be responsible for scouring grant portfolios for discoveries that could have applicability to medical countermeasure development. They will be empowered to leverage both additional funding and access to a wide range of NIH core services to foster these potential solutions into promising medical countermeasure candidates. Where necessary, staff could even play a matchmaking function with other investment organizations, the Centers for Innovation in Advanced Development and Manufacturing, or biotechnology and pharmaceutical firms. Such an approach represents a new and potentially transformational model of advancing our science investments at NIH, and could enable benefits far beyond the realm of MCMs. NIAID is in the process of identifying the number and level of skilled personnel that need to be dedicated to this effort.

Modernizing Pandemic Influenza Vaccine Manufacturing

Fourth, we will invest in our domestic manufacturing surge capacity.

The emergence of a novel pandemic strain of influenza virus is a continuous threat to human health. In addition to the experiences of 2009, we are ever vigilant to the possibility that avian influenza H5N1 or other circulating virus strains may become highly transmissible and virulent in humans. Our experience with 2009 H1N1 taught us that we need to respond even faster to an emerging pandemic. Although we were able to manufacture and distribute a safe vaccine faster than in previous years, domestic manufacturing surge capacity needs to be expanded and accelerated.

The MCM Enterprise review, along with a parallel study conducted by the President's Council of Advisors on Science and Technology to improve influenza vaccine

manufacturing, identified immediate needs and opportunities to shorten vaccine production timelines. We need better methods for potency assays and sterility testing, optimized virus seed strains, additional development of diagnostic devices, and expanded capacity to fill and finish vaccine. The review also recommends that HHS support the development of at least three new influenza vaccine candidates whose manufacture does not depend on virus grown in eggs or cells. This initiative is already underway through collaborative efforts by ASPR/BARDA, NIH, FDA, CDC, and the industrial and academic communities.

Strategic Investor Fund

The fifth initiative we have identified is a strategic investment fund for new medical countermeasure technologies.

Biotechnology companies are often founded with a promising novel technology, but without the resources and business acumen necessary to fully develop and license their idea into a marketable product. As I described above, the large manufacturers in the private sector often choose to not invest the needed capital and management expertise in these entrepreneurial endeavors due to the many risks inherent in medical countermeasure development, especially with firms or technologies whose products have no market outside that currently needed for Federal Government stockpiles. We discovered that this same set of problems led the intelligence community and the Department of the Army to each establish "strategic investor" organizations, In-Q-Tel and On Point, respectively, which help in partnering Federal Government needs with companies that are developing technical approaches that match those needs, and which are also capable of producing commercially viable spinoffs, or multi-use products, based on that technology.

The administration's fiscal year 2011 budget amendment transmitted to Congress in August included authorization for HHS to use an independent strategic investor that would nurture biotechnology companies by providing the needed capital and business expertise to yield a successful product for Government needs. The mission of the envisioned MCM Strategic Investor (MCMSI) would be the development of novel technologies that have the potential for sustainable commercial applications to the commercial market and the MCM public health enterprise. In addition to its own investments, the MCMSI could potentially leverage other private capital, provide expert consultation, and link promising companies with potential partners in the private sector. The MCMSI is envisioned as a private, not-for-profit corporation operating outside the Federal Government, but it would still work closely with NIH, BARDA, DOD, and our other Federal partners.

Management, Administration, and Accountability

The review also found that while some program management components are working quite well, better management and administration would provide more clarity and predictability, as well as less risk to development partners. These include: improving coordination across the agencies involved in the MCM enterprise, speeding up the contracting process or using more flexible transaction authorities, clearly setting and prioritizing broad enterprise goals, and coordinating the process of product development itself, from initial concept development to product use.

IMPLEMENTATION OF THE RECOMMENDATIONS

We have re-allocated $1.9 billion in funding already appropriated for pandemic influenza and the procurement of medical countermeasures under Project BioShield to begin implementing these recommendations. This includes:

—$170 million to promote regulatory innovation and investment in regulatory science at the FDA;

—$678 million to build domestic flexible manufacturing infrastructure and advanced development core services;

—$33 million to support promising efforts and translation of concepts and research at NIH;

—$822 million to address immediate development needs related to pandemic influenza vaccines, antiviral drugs, and diagnostics; and

—$200 million to explore alternative capital market mechanisms.

The administration has submitted an amendment to the fiscal year 2011 President's budget to provide new authorities where needed. Specifically, new authority is required to support the efforts at FDA, the efforts at DOD, and the MCMSI.

HHS has begun developing implementation plans for each of the initiatives and enhancements described above. Some have progressed more than others, based on the complexity and novelty of the new efforts. The HHS senior leaders from CDC, FDA, NIAID and ASPR, working with colleagues at DOD, have conducted strategic reviews of our major product portfolios for smallpox, anthrax and radiological/nu-

clear threats. They have identified priority actions to further enhance the production and eventual distribution of these medical countermeasures, looking as well at economies that can be realized so we may be better stewards of the public funding for this capability. As previously noted, BARDA released a draft solicitation to support Centers of Innovation for Advanced Development and Manufacturing.

BARDA has also awarded new contracts recently for the development of products that could be used as medical countermeasures to known or unknown threats as well as having a possible commercial market. BARDA awarded a contract to develop an antibiotic that could be used against two possible types of bioterrorism (plague and tularemia) as well as common infections that are becoming resistant to antibiotics. BARDA also awarded a contract to continue developing a new way to treat an illness caused by exposure to a nuclear blast; this treatment potentially could be used for other blood disorders and complications of cancer. BARDA is also expected to award a contract for the development of a next-generation ventilator as part of all-hazards preparedness generally, and pandemic influenza specifically.

As we transition to this improved approach to medical countermeasure development, we see opportunities for advances in other areas of public health—new vaccines for neglected diseases, rapid response for emerging naturally occurring infectious diseases, and new approaches to treating drug-resistant bacteria in hospitals or other settings. This strategy aligns with our concepts under the National Health Security Strategy,[2] which was developed to galvanize efforts to minimize the health consequences associated with significant health incidents and achieve a national vision of health security. The advances coming out of the medical countermeasure enterprise may ultimately address day-to-day needs as well as the ever-widening threats of biological, chemical, nuclear, and radiological hazards.

CONCLUSION

I called for a review of the MCM enterprise recognizing that we need to incorporate 21st century technology along with 21st century financial, legal, and regulatory frameworks in order to have the medical countermeasures necessary to defend against the diverse threats we face. The review focused primarily on our ability to take an idea or concept in research and move it quickly to producing an approved medical countermeasure. But, we recognize that our ability to respond begins with the rapid identification of a new event through public health or medical surveillance and the ability to identify the requirements of an MCM—how much we will need, for what part or parts of the population. A medical countermeasure is successful only if it reaches the right population at the right time. We must rely on surveillance capabilities and feedback from end—users incorporated at the beginning of development cycle.

The review identifies a variety of initiatives and opportunities to accomplish these intended goals with the ultimate vision of a nimble, flexible capacity that the nation can rely on to produce medical countermeasures rapidly in the face of any attack. As I mentioned earlier, in the end, if a product fails to make it into our national response capability, it should only be based on its failure to meet our stringent standards for safety, efficacy or quality, and not because we failed to provide the needed business, regulatory and technical support for success. By moving toward a 21st century countermeasures enterprise with a strong base of discovery, a clear regulatory pathway, and agile manufacturing, we will be able to respond faster and more effectively to public health threats.

Thank you for this opportunity to speak with you today on this important subject. I look forward to answering your questions.

STRATEGIC INVESTOR FUND AND DEVELOPMENT AUTHORITY

Senator HARKIN. Thank you, Madam Secretary, for that statement. And thank you for taking the lead in this endeavor.

I think the plan is a good plan, from what I've been able to read about it and to take a look at it. I'll be anxious to follow its development to see what kind of input you get on your request for proposals that you've put out there.

But, I do have some, kind of, concerns about a few elements of this. Help me think about this. We worked very hard to establish

[2] Available online at: http://www.phe.gov/Preparedness/planning/authority/nhss/Pages/default.aspx.

BARDA a few years ago, and this subcommittee has funded it to get it going. But, I don't understand how this fund—the Strategic Investor Fund——

Secretary SEBELIUS. Sure.

Senator HARKIN [continuing]. I'm talking about—how that would work different from BARDA, because BARDA was basically set up to provide funds to small companies, promising companies with good ideas. That was a lot of talk, we had a lot of discussion about that. And so, it sounds like that's the same thing as this Strategic Investor Fund (SRF). So, who—how does it differ? And who runs it? Does BARDA run it, or does NIH run it? I can't quite get a handle on that one.

Secretary SEBELIUS. Well, Mr. Chairman, the way that the strategic investor fund is envisioned is similar to some entities that exist in the national security realm, so the CIA has In-Q-Tel, and NASA has the Red Planet Capital Fund. And they are really to make capital investments at an earlier point in the process.

BARDA will remain as the commitment to industry that there is a purchaser for the products that are going to be developed. I think the missing link—and Congress was wise to identify it and fill it—was that there's very little appetite in the commercial market for making a product unless there's some indication that somebody will buy the product.

So, BARDA was funded and is still essential to demonstrate that the Government is a willing buyer, that there are resources set aside, that this won't be a commercial venture without some ability to actually sell the product. And—what we have found, though, is that some of these small companies actually can't—don't have the capital to get to the marketplace. They can't get the product idea all the way through the pipeline. And some have a great idea, but lack the business planning and strategy.

So, with the capital in the strategic investor, with a kind of public-private partnership, using the assets of our NIH scientists, of FDA, we would be able to actually streamline the process, help move the ideas to the market, where BARDA could become a purchaser. So, I think they actually are complementary, not duplicative.

Senator HARKIN. Okay. I think I get that. BARDA would be the purchaser, but this fund would be the investor——

Secretary SEBELIUS. Or at least help—yes—direct capital, business plans, ideas, marketing strategies.

Senator HARKIN. Hmmm. Hmmm.

Secretary SEBELIUS. And, as I say, In-Q-Tel and a couple of the other national security enterprises have done that very successfully. The national security government officials identify a missing piece of equipment or strategy. In-Q-Tel helps to work with the private market to actually produce what's needed; and then, at the end of the day, you know, the DOD becomes the purchaser.

PANDEMIC INFLUENZA PREPAREDNESS ACTIVITIES

Senator HARKIN. Let me just shift, a little bit, here, to pandemic flu. We don't—obviously, we don't know what some of these new strains of bugs that you mentioned in your testimony—I may have mentioned in mine, too—that might come down, or bioterrorism, or

something. But, we do know flu is here. We have the common strain of flu, that happens every year, but we know there are a lot of other strains of flu out there: the bird flu, H5N1, and H1N1, and a lot of variations thereof. And we know they're floating around out there. So, we're going to have that. I mean, we just know that that's going to hit us. How big, we don't know. As I said, H1N1 wasn't as big as we thought it was going to be, fortunately. But, we don't know how big next—we know it's going to happen, we just don't know how big.

Secretary SEBELIUS. Right.

Senator HARKIN. So, therefore—I'm concerned, because this subcommittee put a lot of money—$15 billion through this subcommittee, since fiscal year 2006—for pandemic preparedness activities. One-point-nine billion was used to develop cell-based or recombinant vaccines. And I can remember visiting with people a few years ago about that, and moving ahead. We put—HHS awarded $487 million to Novartis for a cell-based manufacturing facility in North Carolina. I thought—I heard the plant was open, but now I'm told it won't be ready to operate until 2013. Also, none of the influenza vaccines licensed for use in the United States are cell-based, but they are currently licensed in Europe.

So, why—what's the problem with getting them licensed in the United States if they're licensed in Europe? And, why aren't we further along in the area of cell-based or recombinant-based vaccines, which can be turned around a lot more rapidly, of course, than egg-based vaccines?

Secretary SEBELIUS. Well, Mr. Chairman, again, I think you're absolutely right, that the subcommittee has been focused on a series of investments, starting really in fiscal year 2006. And we do have doses of H5N1 purchased and in the stockpile, knowing that that flu is still killing people, it is circulating. There still isn't human-to-human transfer, luckily, but we are very much aware that that's a very real threat. So, some of the funding is actually preparing, in case that were to be present here.

And, in terms of the cell-based technology that we're moving ahead on currently, you're absolutely right, all of the flu vaccine up to date has been developed with egg-based technology. But, HHS did, with the pandemic funding that was provided, support the construction of the new Novartis cell-based manufacturing facility in North Carolina. The ribbon was cut in November 2009. It is scheduled to be on line to apply for licensure early in 2011, we hope in the first quarter of next year, for cell-based, seasonal vaccine, and the licensed vaccine is expected to be manufactured and marketed for the 2011–2012 flu season.

So, we're actually very much on track. They got to get it up and running, they got to get it licensed. And it will be capable of producing 150 million doses of vaccine within 6 months. So, this seriously ramps up our domestic capacity, and that's also very good.

In terms of recombinant vaccine, we did issue a contract to Protein Sciences in September 2009 for advanced development of their recombinant protein vaccine, and the company is working towards licensure again in 2011. We think that is on track. They are expected to begin to manufacture and market their vaccine again for

the 2011–2012 flu season. Right now they're saying they can produce 50 million doses in about 4 months.

So, both of those entities are up and running. It takes a number of years in the pipeline, but your funding, several years ago, has gotten us to that place. And, as I said, we just issued a draft solicitation, this month, which will also come out of the preparedness funding, to have these new centers of innovation for advanced development and manufacturing that Senator Specter has indicated a great deal of interest in.

What we find is that a flu-only facility is too limited. What we're talking about looking at in the future, in two to three centers, is what they call a "flexible platform." So, it could be used as surge capacity for flu vaccine, should that be needed. It also could, essentially, begin with anthrax vaccine, to H5N1 vaccine, to have another MCM. So, it wouldn't be solely dedicated to the flu, but have the ability, really, to mix and match, give us the ability to respond to something that we don't really know is coming.

So, we plan to award the contracts by the—have the request for proposal out by the end of this year. We want each of those facilities to produce at least 50 million doses of cell-based or recombinant vaccine within 4 months. So, that will be the criteria around which we're looking. So, we're leaping over egg-based to either cell, or ideally recombinant, and one is in—already looking at licensure next year, and the other two or three will be up and running, hopefully, fairly quickly.

Senator HARKIN. Very good. Thank you, Madam Secretary.

Senator Cochran.

MCM SPEND PLAN

Senator COCHRAN. Madam Secretary, I was looking at the funding amounts that this subcommittee has already recommended and have been approved by Congress, and looking then at how the funds have been used. You stated, in your testimony, that there may be unspent funds that you are now attempting to reallocate, or propose to reallocate.

Have you come to some understanding, with the leadership in Congress, as to who goes first, who makes the decision? Do you have to get approval? Or do you have license just to start a program and start—sending this money out to beneficiaries or hospitals or public health officials?

Secretary SEBELIUS. Senator Cochran, the plan that I just outlined is based on reprogramming about $2 billion of the preparedness funding which was dedicated to HHS by Congress and has already been approved for preparedness. And what we're doing, after our analysis of where the countermeasure pipeline glitches exist, is suggesting that we would be better served, rather than continuing to fund the traditional pipeline, to look at areas where there were real gaps. So, more manufacturing capacity in the United States regulatory science in FDA and NIH, the areas where I outlined.

There are a couple of those areas, Senator, that we will need specific congressional approval, because we don't have the authorization; and that's the amendment that we requested as part of the 2011 budget. So, until Congress actually gives us the green light for the strategic investor or some of the new authorities within the

FDA, we will not be able to direct the funds there. But, the rest of this funding is actually approved for preparedness, and we have notified the appropriate committees that that's the intent, and produced a spend plan to go along with that.

H1N1 VACCINE

Senator COCHRAN. I'm curious, also, to know about how much money we spent in defending against an H1N1 virus that may have been over-advertised, in terms of its threat to general public health. Did we waste a lot of money by sending money out to State and local health authorities, or in letting them decide how to use the money? Or was there a national plan, with specifics included in the plan, as to how the funds were to be spent?

Secretary SEBELIUS. Actually, Senator, I think that plan that allowed us to move vaccine to about 85 million people in a very rapid timeframe was based on years of planning that had been done. I—as a former Governor, I was one of the beneficiaries of preparedness funding, which allowed us to gather private industry and our public health officials together, and go through exercises: What if we had a pandemic? Little did I know that I would be sworn in as Secretary when we had the pandemic that I had been previously preparing for.

So, our plan with H1N1 followed, really, the strategies. State and local health departments were major partners. And I would say that the new part of the strategy was how we rapidly enhanced the distribution system. We went from what was a fairly limited number of providers who were used to giving children vaccines in the past, to greatly enhancing that. Because one of the key targets were children.

So, school-based clinics and mobile clinics and some of the open doors, I think, were not ones that had been typically planned for. But, there was definitely—at every point along the way, States, in order to draw down funds, had to provide to our Department very specific planning documents for what they would do with the money, where it was going to go. Providers had to be involved and included. We had weekly calls.

I think the good news is that, in spite of the very alarming early days, where it appeared that, you know, this could mirror a 1918 situation, the virus itself proved to be, thank God, less lethal than it could have been. But, I don't think there's any question that those partnerships, that distribution system, the outreach network, was not only money well spent for H1N1, but really helped to rebuild an infrastructure for a public health system that will serve us well, the next hurricane, flood, fire, or disaster that we're going to have, because those are exactly the same folks who need to respond.

Senator COCHRAN. I wonder, based on your experience so far as Secretary of HHS, and also your experience as Governor, do you have any recommendations to the subcommittee for language that might be included in an appropriations bill that would help improve the way we are using Federal dollars in an effort to defend against influenza outbreaks, or any other public health challenge that we may face?

Secretary SEBELIUS. Well, Senator, I think that some of the strategies, that are outlined in some of the recommendations in the lengthier report that we presented, at least deals with the portion of the MCM response that is scientific discovery to stockpile. What we're continuing to do is really this end-to-end look. Is our surveillance system up to speed? I mean, do we know about outbreaks quickly enough in the United States or around the world? How do we get that information? What is that public health infrastructure? All the way through to how we distribute the products. You know, what's the fastest way to get to people? I think that analysis is still going on.

And we would love to work with you. We will look for that language and get it to you. Because I don't think there's any question that each time we go through one of these experiences—I mean, this was the first pandemic in 40 years—that we need to be informed and make sure that we update all of our systems along the way.

I can tell you, I am concerned, and continue to be concerned, and pleased that there are funds again for the State and local level. In this budget downturn, I don't think there's any question that there's been a real hit on the public health infrastructure around the country. A lot of State health departments have less staff than they did; a lot of emergency planners at the State and local level have been cut back. So, that is of concern. And we are trying to pay close attention to that as we anticipate what could come our way. Because—you know, we can have all the great products and ideas here, but, absent the ability to actually get them into communities across this country in a rapid and efficient fashion, there's still a real problem.

Senator COCHRAN. What was the name of that book? We had the author of the book. Was it Barry who wrote about the influenza 100 years ago, or whatever——

Secretary SEBELIUS. Oh, the 1918? Yes.

Senator COCHRAN. And it was interesting experience, learning from him, through his research and writing that book——

Secretary SEBELIUS. You bet.

Senator COCHRAN [continuing]. And everything, some of the things that had been overlooked, that you would think a civilized society, and advanced as we were, as wealthy as we were, would have learned from that experience better than we did. I wonder if you've had a chance to read that book. It's a few years old now.

Secretary SEBELIUS. I have, and I've actually had a chance to meet a bit with the author. We also talked, at the beginning of the influenza outbreak, with a lot of the officials who were involved in the 1970s with what appeared to be—it was a novel strain of the flu. There was a major vaccination effort, and the disease never spread anywhere.

So, to try and learn, again, how—you know, what they learned, and didn't learn, I think it's wise to make sure that, each time we have these experiences, we're better informed by it, and, you know, update our strategies. And that's what this is about, to use some of the money that had been appropriated and allocated for preparedness, study what went right and what went wrong, and try

to redirect it to what we think are more appropriate and timely opportunities.

Senator COCHRAN. Thank you very much.

Secretary SEBELIUS. Sure.

Senator HARKIN. Well, Madam Secretary, thank you very much.

Like I said, we have—I've gone over this with our staff. On your plan, it—there are a couple of things on which you do need signoff here. I think that we'd be very supportive of the plan, but, I must just tell you, forthrightly, so that you can go back and tell the Office of Management and Budget (OMB), that——

Senator COCHRAN. Nobody can tell OMB.

TRANSFERRING FUNDS FROM HHS TO DOD

Senator HARKIN. Well—you can tell them this. You can tell them that I just—that this proposed transfer to the DOD is one exception, and that—I might as well just be up front with you, I'm not going to sign off on it. That's $200 million. I just—in all my years here, I've never heard of anything like transferring money from HHS to DOD. I've heard it the other way around, maybe, once in a while. But, never that way. And with all of the demands that we have at NIH, at CDC, and all of the other demands that we have here—we're having a hard time with our budgets—I think DOD could come up with the $200 million. I really do, Madam Secretary. I don't expect you to respond to that, but I thought I would be fair and be up front with you so that they would know that they would have to do some further planning on that money.

Secretary SEBELIUS. I will convey your message——

Senator HARKIN. I appreciate that——

Secretary SEBELIUS [continuing]. Mr. Chairman.

Senator HARKIN [continuing]. Very much. Thank you very much, Madam Secretary.

Secretary SEBELIUS. Thank you.

Senator HARKIN. And if you have anything else to add to——

Secretary SEBELIUS. I just look forward to working with you as we move along. We will certainly, as we continue this review, continue to report back to the subcommittee. And again, look forward to working with you on the authorities that we may need for——

Senator HARKIN. Great.

Secretary SEBELIUS [continuing]. Some of these——

Senator HARKIN. Great.

Secretary SEBELIUS [continuing]. Novel ideas.

Senator HARKIN. Thank you very much.

Secretary SEBELIUS. Thank you.

Senator HARKIN. Thank you, Madam Secretary.

Now we'll move to our second panel. Colonel Randall Larsen, U.S. Air Force, Retired. Colonel Larsen is the CEO of the Weapons of Mass Destruction Center—a not-for-profit research organization that he founded, along with former Senators Bob Graham and Jim Talent. He previously served as the executive director of the Congressional Commission on the Prevention of Weapons of Mass Destruction, Proliferation, and Terrorism. Colonel Larsen served for 32 years in both the Army and Air Force; received his bachelor degree from Texas State University and his master degree in national security studies from the Naval Postgraduate School.

We have Dr. Eric Rose, M.D. Dr. Rose is the CEO and chairman of Siga Technologies, which develops antivirals against possible bioterrorism agents. He is also the co-chair of the Alliance for Biosecurity. Dr. Rose received both his undergraduate and medical degrees from Columbia University.

And Dr. Andrew T. Pavia is the Chief of the Division of Pediatric Infectious Diseases at the University of Utah Health Sciences Center. He's also the chair of the Pandemic Influenza Task Force of the Infectious Disease Society of America. Dr. Pavia received his B.A. and M.D. from Brown University.

Welcome. Thank you all for being here. And your testimonies will be made a part of the record in their entirety. I ask if you could sum them up in 5 minutes or so. I would appreciate it. And we'll jut go in the order in which I said, here.

We'll start with Colonel Larsen first. Welcome to the subcommittee. And thank you for all of your service.

Colonel Larsen.

STATEMENT OF COLONEL RANDALL J. LARSEN, USAF (RET.), CHIEF EXECUTIVE OFFICER, WEAPONS OF MASS DESTRUCTION CENTER, WASHINGTON, DC

Colonel LARSEN. Mr. Chairman, vice chairman, you asked me to provide an assessment on the threat of bioterrorism. Let me be clear: Bioterrorism is a serious threat, and it will become even more so if we don't take appropriate actions.

Senators Bob Graham, Jim Talent, and I agree with the assessment in the National Security Council document signed by President Obama in 2009. On page 1 of that document, it stated that bioterrorism could place at risk the lives of hundreds of thousands, and cause $1 trillion in economic disruption, per event. The details of that threat are contained in my prepared statement, so I won't focus on that in my oral testimony. But, my concern is, Mr. Chairman, that there are a lot of senior leaders—not this room—but there's a lot of senior leaders in the legislative and executive branch that do not understand this threat, that you and I know very well.

And I accept part of the responsibility for that. I'm an educator, run a think tank, and that's what we're supposed to be doing, is educating senior leaders, and make sure you have the facts to make these very difficult decisions.

I get a lot of senior leaders asking me, "Why don't we just prevent this bioterrorism?" Well, you and I know we can't do that. That is the proper strategy for nuclear terrorism, but it will not work against bioterrorism. The genie's out of the bottle. We've known that since Dr. Josh Lederberg and George Whiteside put out this report in 2001. This is nothing new. So, we must focus on what Senator Graham calls the response side of this equation. If Senator Graham was here, he'd have a big chart up here like this, with his links about what we need to do. He loves this chart and explains it very well.

What we can do, if we properly fund these programs, and manage them, Mr. Chairman, vice chairman, we can push the decimal point to the left, is how Senator Graham describes it. We won't count casualties in hundreds of thousands, or tens of thousands, or even thousands. We can push it down to a level of what we lose

on highways on 3-day weekends. Still be a tragedy for those families, but it will not be a weapon of mass destruction, and it won't change the course of history. That's a realistic goal that we can achieve.

Now, let me give you two examples, since this is the Appropriations Committee, where Senator Graham, Talent, and I have a few problems with this. One of the things that Senator Graham loves to talk about here is environmental cleanup. Now, the reason that the President's document talked about $1 trillion per event—you know, if they put a pound of dry powdered anthrax in New York City subway, we have no clue how long it'll take to clean it up. We know that the British tested anthrax weapons on the island of Gruinard, off the coast of Scotland, in 1944. Took four decades to clean up that island.

Now, sir, do you know how much we're spending on clean-up research at the Environmental Protection Agency (EPA) to clean up anthrax? Half of what we will spend next year on Marine Corps marching bands. Sir, I think we need to think about priorities. Now sir, I'm a big fan of military bands, probably the reason I spent 32 years in the military is because I saw the Marine Corps Band when I was a young boy in the cornfields of Indiana. But, sir, think about that. Half of what we spend on Marine Corps marching bands is what we're going to spend to figure out how to clean up the New York City subway. I think it's 800 miles of subway up there.

That's one problem. The other one is, the funding of this MCM. Now, we—you know, we gave an—WMD Commission gave an "F" to bioresponse preparedness, in the report card that came out in January. The fact that we were using 60-year-old technologies to make important vaccines like H1N1 was one of the reasons that Senator Graham and Talent and the commissioners gave that "F".

But, I have three questions about this initiative. Because we think the strategy is great, and Senator Graham, Talent, and I, we fully support it. But, three questions for you:

First of all, who's in charge? I believe that was the question you asked the Secretary. I really would like to know. In fact, I have a bigger question. Who's in charge, Mr. Chairman, Mr. Vice Chairman, of the architecture, the enterprise of biodefense for America? To the best of my ability and study, there's about 24 presidentially appointed, Senate-confirmed individuals with some responsibility for biodefense. Not one of them has it for a full-time job, and nobody's in charge.

Now, maybe it's because I spent 32 years in the military. I like that authority, responsibility, and accountability. Kind of easy to define, so you can do the oversight of that. With no one in charge, I just don't know who's going to do that.

My second problem is, we don't have an integrated plan. It's great strategy. And maybe they haven't had enough time, so we'll give them a break on that. We need that integrated plan to work with the private and public sector—there's a great model for how we developed penicillin, just before World War II, that made such a big difference in saving GIs' lives. We need to figure out how to do that better. I'm sure these gentlemen will talk about that.

And third, are we going to properly fund this? Now, Senator Graham and Senator Talent, last year, sent letters to you, sent let-

ters to a lot of congressional leaders, and the White House, saying, "We think BARDA was only funded at 10 percent of what were realistic requirements." Now, there were some people who pushed back, and said, "We know BARDA's doing—not doing a very good job. They're not delivering products." Well, our response to that was, "If you funded the U.S. Air Force at 10 percent of their requirements, they probably wouldn't deliver everything you wanted, either."

Sir, I make these statements, not as a scientist or a physician or as a public health expert—I spent many years, like you did, flying airplanes—but, I have studied national security for four decades. And, sir, the serious threats that we'll face in the coming decade are not going to come from missiles, tanks, or bullets, in my opinion; they're going to come from infectious disease, going to come from Mother Nature. We know that for a fact, and I think there's high probability we're going to see attacks, manmade attacks, that'll cause epidemics in our country.

PREPARED STATEMENT

Preparing for these events means we must develop faster diagnostic capabilities, like the Secretary talked about, better, safer, less expensive, and more rapidly produced vaccines and therapeutics. Mr. Chairman, Mr. Vice Chairman, they're critically important for our children and grandchildren, whether we suffer a biological attack or not, from terrorists. These will be no-regret investments that you make in America.

Thank you.

[The statement follows:]

PREPARED STATEMENT OF COLONEL RANDALL J. LARSEN, USAF (RET.)

Mr. Chairman, I speak today on my own behalf, but based on knowledge I have acquired during the past decade. I previously served as the chairman, Department of Military Strategy and Operations at the National War College, and the founding director of the Institute for Homeland Security. Last year, I served as the executive director of the Congressional Commission on the Prevention of Weapons of Mass Destruction Proliferation and Terrorism, and currently serve as the CEO of The WMD Center, a not—for—profit research and education organization that former Senators Bob Graham (D-FL) and Jim Talent (R-MO) created as a follow-on to continue the work of the WMD Commission—and there is much work to do.

Our first mission at the WMD Center is to ensure that senior leaders in both the public and private sectors understand the threat of 21st century bioterrorism—a subject not well understood by many leaders in both the legislative and executive branches of Government. I have concluded this based upon the actions and inactions of the Federal Government.

In the past year, there have been numerous attempts to raid the BioShield Strategic Reserve Fund for nondefense programs.

Organizations, such as the Food and Drug Administration (FDA) are not seen as critical components on America's national security team. Considering the threats we face, both from both from bioterrorism and newly emerging diseases, FDA needs to be funded with the same vigor as the Pentagon's latest weapons systems. Unfortunately, it's not.

No one is in charge of America's biodefense enterprise. No individual has responsibility, authority, and accountability for a program that is vital to America's long-term national security. To the best of my knowledge, there are more than two dozen presidentially appointed, Senate-confirmed individuals with some responsibility for biodefense. Yet, not one of them has it for a full-time job, they answer to no one in common, and no one is in charge. I do not think that is the organizational structure that will lead to success.

Mr. Chairman, I am convinced that if senior leaders understood the threat we face today, and even more importantly, the threat we will face tomorrow, there

would be someone in charge of America's biodefense enterprise, and a clear policy and sufficient funds would be available to properly defend America.

The threat of bioterrorism we face today is far different than that of the 20th century. During the Cold War, only nation-states were capable of producing sophisticated biological weapons. However, as the biotechnical revolution began to accelerate in the latter days of the 20th century, the Defense Science Board (DSB)recognized the national security implications of these rapid changes in the seminal DSB report, Biological Defense, June 2001. The technology that had once been limited to major powers was rapidly becoming available to small nations and some non-state actors.

". . . major impediments to the development of biological weapons—strain availability, weaponization technology, and delivery technology—have been largely eliminated in the last decade by the rapid global spread of biotechnology. There is no way the United States can control the spread of rapidly advancing biotechonology." (page 18)

What was unknown to the members of this DSB was the fact that while they were preparing their report al Qaeda terrorists in Afghanistan and Malaysia were in the process of developing anthrax weapons for use in the United States. Thankfully, al Qaeda did not complete their weapons development program before 9/11, and shortly after 9/11, U.S. troops discovered and dismantled the laboratories.

Nobel Laureate, Dr. Joshua Lederberg and Dr. George Whitesides, the former chairman of the chemistry department at Harvard University, co-chaired this DSB task force. More than 9 years have passed since they warned us about the national security implications of the rapid changes in biotechnology. Those 9 years represent several generations—a great leap forward in biotechnology. The vast majority of these new capabilities represent good news for our families and Nation in terms of medical care and public health; however, there is also a dark side to this rapid progress.

Mr. Chairman, I am concerned that many leaders in the legislative and executive branches of the Federal Government do not understand the dark side of this progress—the nature of current and future threats of bioterrorism. There are four key issues that are not well understood:

—history of biowarfare, including the former U.S. offensive biowarfare program;
—the current technologies available to non-state actors;
—the interest of terrorist organizations in using biological weapons; and
—and the fact that this is not an intractable problem.

For the past 11 years, I have provided briefings on bioterrorism in a course sponsored by the Joint Staff's Anti-Terrorism and Force Protection directorate (J–34) to more 3,500 senior military officers. More than 70 percent of these officers filled out the critiques at the end of my presentation, and by far, the most common statement on these critiques is: "Why hasn't anyone told me about this?"

Considering the fact that so many senior military officers are not well versed on this threat, it should be of no surprise that individuals outside the field of national security are even less well-informed. To properly understand the threat of 21st century bioterrorism, it is essential to have a basic understanding of the history of the use of bioweapons.

In virtually all cases, biological weapons have been used in a terroristic mode—to attack civilian populations. They are not reliable weapons on the battlefield. They would be of little value if there was a strong wind, bright sunlight, rain, or any combination thereof. However, if one's goal is to attack a city, and there is no specific date and time to do it, then they can become very effective tactical or strategic weapons.

When I discuss 250 years of biological terrorism in my presentations, beginning with British soldiers giving Native Americans blankets contaminated with smallpox, to German agents attempting to infect horses and mules in our ports during World War I, and the Japanese dropping bombs filled with plague-infested fleas on Chinese cities, I say that the theories of these early day bioterrorists were sophisticated, but their technologies were not.

During the early days of the Cold War the United States, the Soviet Union, Great Britain, and other nations reached a point where technology finally caught up with the level of theory. This was demonstrated in numerous tests in the United States, and by the fact that in the 1960s, many of America's war plans included the use of biological weapons.

I find it surprising how few citizens, and even senior military officers, actually know that America had a powerful offensive biological warfare capability until Richard Nixon unilaterally shut down America's offensive of program on November 24, 1969.

When America's offensive biological warfare program began in the 1940s, it was low-tech and not capable of producing weapons of mass destruction. Major investments were made in the 1950s and significant advances were made in technical capabilities. By the late 1960s, America's capabilities for the use of biological warfare was rapidly approaching the equivalence of nuclear weapons (in terms of casualties).

After America's unilateral disarmament in 1969, the United States led the effort to get all nations to sign the Biological Warfare and Toxin Convention. After signing this treaty, the Soviet Union then ramped up their offensive program, eventually re aching a level almost beyond imagination. With more than 50,000 scientists and engineers working across 11 time zones in scores of facilities the Soviets managed to hide most of this capability from Western intelligence agencies. While the U.S. offensive program had produced hundreds of pounds of weapons-grade pathogens, the Soviets were producing hundreds of metric tons.

What is not well understood from this history is the fact that bio warfare is not just theory. Tests conducted in the United States, the Soviet Union and Great Britain confirmed beyond any doubt the capability of pathogens to serve as either tactical or strategic weapons against civilian targets—counter-value targets in Cold War terminology. There is no question that in the 1960s, 1970s, and 1980s this capability was only available to nation-states. What is not well understood, however, is the same capability is now available to virtually any nation, and for many terrorist organizations, both international and domestic.

It was nearly a decade ago that Drs. Lederberg and Whitesides stated that the rapid advances in biotechnology had reached the point where non-State actors were capable of producing these terrible weapons. The briefings given by various Government agencies to the WMD Commission during the past 2 years made it clear that further advances in the biotechnical revolution have made the production of sophisticated biological weapons by non-State actors even less challenging than in 2001. Those who say that it is still too difficult for terrorists to produce and deliver sophisticated biological weapons are either unaware of the extraordinary advances in biotechnology and the recent Government studies that demonstrate these capabilities, or have some other agenda that they wish to champion.

Mr. Chairman, four things must occur for a terrorist organization to develop and deliver a sophisticated biological weapon. First they must acquire a sample of the deadly pathogen such as anthrax or plague. How would a terrorist organization acquire such deadly pathogens? For the past few weeks there has been a naturally occurring outbreak of anthrax in humans and cattle in Bangladesh. This is not terribly uncommon in many developing countries. In fact, it even occurs in the United States. In the summer of 2008, Ted Turner lost 278 buffalo to anthrax on his ranch in Montana. The buffalo died because they ate grass in a pasture that contained anthrax spores in the soil. On Monday, a state of emergency was declared in a village in Southern Russia's Krasnodar Territory over an anthrax outbreak in dairy cattle. If terrorists wanted to find a sample of Yersinia pestis, the bacteria that causes plague, they would not have great difficulty finding it in many locations west of the Mississippi River in the United States. Prairie dogs in West Texas and rats above the 5,000-foot level in the Rocky Mountains often carry this deadly pathogen. Earlier this week, the Chinese reported an outbreak of plague in humans in southwestern Tibet.

Obtaining samples of deadly pathogens is not particularly difficult. In fact, all but two of the 80+ pathogens on the Select Agent List exist in nature. Pathogens that cause anthrax, plague, tularemia, Ebola, Marburg, Venezuelan Equine Encephalitis, Q-Fever, and dozens of others can be obtained and isolated from diseased animals or humans.

The second step in creating a terrorist bioweapon is production. Taking a small sample of one of these pathogens from nature and producing enough material suitable for use as a weapon is a standard process used in various industries including pharmaceutical, agriculture, and pesticide. All of the equipment and supplies required for production are available on various sites on the Internet at very reasonable prices.

The third step, and the part that has always been most challenging in creating a biological weapon, is getting material to the proper particle size for airborne release. The most effective way to disseminate a biological weapon is to spray either a liquid or dry powdered form of a pathogen into the air. When in the proper particle size, the pathogen will enter the human respiratory system and then move directly into the blood stream where it leads to systemic illness.

In the 1960s and 1970s it took superpower technology to create the proper particle size without causing harm to the bacteria or virus being disseminated. Today it is standard off-the-shelf technology used in the pharmaceutical and agriculture communities. Techniques far more sophisticated than what was used in the highly clas-

sified U.S. offensive program are now openly discussed in highly respected scientific publications such as Journal of Aerosol Medicine and Pulmonary Drug Delivery, and openly discussed at major conferences hosted by organizations such as the American Association for Aerosol Research (AAAR). The AAAR conference schedule for October in Portland, Oregon, will include tutorials on Aerosol Mechanics I & II (http://aaar.conference2010.org/content/tutorials).

These scientific publications and organizations are incredibly important to medical research. They are important aspects of the biotechnical revolution that will make the lives of our children and grandchildren healthier and better protected from both chronic and infectious diseases that plagued our parents and grandparents. But we must understand, this same technology can be used to make weapons. We must also remember what Drs. Lederberg and Whitesides told us in 2001: "There is no way the United States can control the spread of rapidly advancing biotechonology." (Nor should we try. It would only succeed in reducing our defensive capabilities, and cause serious, perhaps irreparable damage to our important biotech industries.)

The fourth and final step is delivery. In October 2001, the U.S. Congress witnessed a very low-tech and generally ineffective method of disseminating a biological weapon—the U.S. Postal Service. On the other hand, using spray devices available in most agriculture stores, and also available for sale on the Internet, to disseminate a few pounds of dry-powdered anthrax, most particularly in an indoor environment such as the subway or indoor sports arena, would have the enormous consequences of a weapon of mass destruction.

What are those consequences? They were best stated on page 1 of the November 2009 National Security Council document, National Strategy for Countering Biological Threats.

"The effective dissemination of a lethal biological agent within an unprotected population could place at risk the lives of hundreds of thousands of people. The unmitigated consequences of such an event could overwhelm our public health capabilities, potentially causing an untold number of deaths. The economic cost could exceed one trillion dollars for each such incident. In addition, there could be significant societal and political consequences that would derive from the incident's direct impact on our way of life and the public's trust in Government."

There are some who say terrorists prefer to use bombs, and point to such recent attempts as we witnessed on Christmas Day and in May in Times Square. Without question the vast majority of terrorists will continue to use conventional weapons. Those weapons are certainly capable of producing dramatic results for terrorists, such as what we all watched unfold in Mumbai; however, terrorist use of conventional weapons will not change course of history. An event, such as described in the November 2009 NSC report would change the course of history—not only for us, but for our children and grandchildren.

For those who say terrorists have no interest in biological weapons, I guess they just ignore the Aum Shinrikyo attempts in 1994–1995 to produce biological weapons in Japan and disregard the al Qaeda bioweapons program. For a recent terrorist perspective on bioweapons, I suggest you watch a short video at this Web site: http://www.youtube.com/watch?v=M32M-2B2mz8. It was broadcast repeatedly on Al Jazeera TV in February 2009 and has been viewed on the Internet more than 80,000 times.

Perhaps some of the confusion comes from assessments by the Intelligence Community (IC) on the bioterrorism threat. The IC will tell you they have little or no information of any terrorist group developing biological weapons capability. That should not be surprising.

During 15 years of the Cold War, the IC failed to appropriately identify the massive Soviet biowarfare program that consisted of 50,000 scientists and technicians working in scores of laboratories across 11 time zones. (This was the size of the Soviet's offensive biowarfare program after they signed the Biological Warfare and Toxin Convention.) The IC also missed al Qaeda's anthrax programs in Afghanistan and Malaysia, and they missed the Aum Shinrikyo biowarfare and chemical weapons programs. Thankfully, both of the Aum's weapons programs were plagued with technical errors when they went from small-scale to large-scale production.

Do we really think there is a high probability the IC will find a half-dozen individuals working in a make-shift laboratory (standard bio lab equipment purchased on the Internet in a facility no larger than a two-car garage) in a remote village in the tribal regions of Pakistan or Sana, Yemen, or the suburbs of New York City? That is the size and scale of a facility required to produce bioweapons, according a study (BACUS) done by the Defense Threat Reduction Agency in 1999 that determined there would be no perceptible "intelligence signature" of such an operation.

For the threat of bioterrorism, the IC can provide us with sound strategic intelligence information on intent, but little or no tactical level information: status of a bioweapons program of a specific terrorist organization or the time and location of a planned attack.

I think we all understand that there are people and organizations out there that want to kill large numbers of Americans. The WMD Commission said there are two ways to do that, nuclear and biological, and by far, biological is easier. If the senior leaders in the Congress and administration understood the biological capabilities now available—and even more troubling, what will be available in the next couple of years—to small terrorist groups, there would be no requirement for hearings such as these. Biodefense would be a top priority, and we would be making rapid progress in defending our cities, communities, and families.

I sometimes think the reason some leaders are hesitant to take the recommended actions, is that they believe the problem is intractable-it is so difficult and complex, that "there is nothing we can do". There is no question that biodefense in the 21st century is difficult and complex, but the fact is, there are actions we can take to remove bioterrorism from the category of weapons of mass destruction (WMD).

We cannot realistically prevent bioterrorism, but if we develop robust response capabilities, we will effectively remove bioterrorism from the category of weapons of mass destruction. We will be able "to move the decimal point to left" in that number from the November 2009 NSC report. We will not count casualties in the hundreds of thousands, or tens of thousands, or even in the thousands. We can move the casualty count down to the scale of what we lose on America's highway on a 3-day weekend—most certainly it would still be a tragedy, but not a WMD that would change the course of history.

The threat of bioterrorism will not diminish in the years ahead unless we take the required actions to build a robust and nimble resilience capability that includes:

—near real-time detection and diagnosis of disease outbreaks;
—situational awareness and effective communication of actionable information, rapid development, and production of medical countermeasures;
—timely countermeasure distribution and dispensing;
—surge medical care delivery to treat the sick and protect the well; and
—environmental cleanup and remediation.

If Senators Bob Graham and Jim Talent were here today, they would tell you that sufficient and continued funding in support of these programs will not only lead us to a point where bioterrorism can be removed from the category of WMD, it will also provide a deterrent against attack, and just as importantly, that these are all "no-regret investments." Building a system that provides for rapid diagnosis of disease, whether naturally occurring or manmade; better, faster, and less expensive vaccines and therapeutics; and far greater capacity for surge operations in our hospitals and clinics are the types of investments we should be making for our children and grandchildren. On that, we can all agree.

Last month the President recommended an initiative to improve our system for developing MCMs. It is, perhaps, the single most important factor for removing bioterrorism from the category of WMD, but to make it work we need to understand that organizations responsible for this new initiative—Health and Human Services/BARDA, National Institutes of Health, and the Food and Drug Administration are now critical elements of our national security community—no less important than the Department of Defense, the IC, and the Federal Bureau of Investigation.

Mr. Chairman, the threat of bioterrorism is real and will only increase over time. As Drs. Lederberg and Whitesides wrote back in 2001, there is no way to stop the biotechnical revolution that will place ever-increasing asymmetric power in the hands of terrorists. However, that same revolution in technology can be used by America to remove bioterrorism from the category of WMD. The decision will be yours.

I look forward to your questions.

Senator HARKIN. Colonel Larsen, thank you very much. Very stimulating presentation.

Dr. Rose.

STATEMENT OF ERIC A. ROSE, M.D., CHIEF EXECUTIVE OFFICER AND CHAIRMAN, SIGA TECHNOLOGIES; CO-CHAIR, ALLIANCE FOR BIOSECURITY, WASHINGTON, DC

Dr. ROSE. Mr. Chairman, Mr. Vice Chairman, I'm Eric Rose. I'm the co-chair of the Alliance for Biosecurity and the CEO of Siga

Technologies. It's a pleasure to be with you today to provide you with our impression of the HHS report on the PHEMCE Enterprise review.

The Alliance for Biosecurity is a collaboration among pharmaceutical and biotechnology companies that are focused on biodefense countermeasures. My company, Siga Technologies, is in late-stage development of a smallpox antiviral drug, and therefore, I can give you a firsthand perspective of how well our Federal Government is working with small, private-sector biodefense companies like ours.

I've submitted written testimony for the record. At the outset, I would like to make three simple points:

First, the BARDA Advanced Development Program is bearing fruit. While many have criticized the perceived slow pace of development of needed novel biodefense countermeasure, our experience is that the Federal investment in biodefense is generating important novel countermeasures less than 7 years after BioShield enactment, and also just 4 years after the creation of BARDA. And that, I think, you should take in a context, that typical drug development now takes 10 to 15 years for a new drug or vaccine. So, there is a trickle, but that pipeline is beginning to flow. We, at Siga, are now producing commercial-scale validation batches of our smallpox antiviral drug candidate, which we hope will soon be added to the strategic national stockpile.

Second, the administration's proposed enhancement of FDA regulatory science innovation and capacity, along with additional funding, is very welcome to our community. While the FDA is not within the jurisdiction of this subcommittee, we do want to note that we are particularly pleased with the emphasis placed on the review on enhancing FDA's essential role. Therefore, we strongly support the administration's August 20 budget amendment request to transfer available balances from prior pandemic influenza appropriations to modernize FDA regulatory science.

Third, full funding of the BioShield Strategic Reserve Fund ensures that there is an oasis, and not a mirage, on the other side of the valley of death of advanced development. And this is absolutely critical to the success of small biotech companies who rely on private investment to initiate product development.

While we appreciate the need to find offsets for other new spending in order to reduce the Federal budget deficit, I can tell you that every time there is a proposal to transfer unobligated balances out of the SRF for other purposes, it sends shock waves through the private-sector companies involved in this arena, and it shakes our investors' confidence that we desperately rely upon to nurture these projects through the early phases of development.

BARDA's rapidly growing advanced development pipeline is indicative of the strong interest that small companies have in biodefense. However, our success relies upon a reliable and a committed customer. We share and support the overall goal of the review, and the Alliance is thankful to have been consulted by the ASPR, Dr. Nicky Lurie throughout the process. We are particularly also pleased to see the review include plans for HHS to increase transparency, communication, and predictability within the contracting and procurement processes, and across agencies. Further,

we were encouraged that the review included a commitment to develop a 5-year budget plan for the entire MCM enterprise, expand the advanced development program, and increase staff levels.

There are also some elements of concern to us. We were disappointed that the review did not propose fully funding the advanced development program that Colonel Larsen just referred to—it's still grossly underfunded—nor outline a process for restoring funding to the SRF beyond 2013, or otherwise providing long-term and stable funding for the procurement of MCM.

We support plans for the sustainability enterprise, but caution that investments must be made up front in order to guarantee success over the long term. In addition, to reiterate, the SRF should not be depleted for other uses, including proposals put forth in the review. For this reason we're concerned that the administration's August 20 budget amendment request included the transfer of $200 million to DOD that you referred to, and we're delighted to hear your candid and quick response.

And also, the $200 million transfer from the SRF to establish a new countermeasures strategic investment firm. We're supportive of a technical center of excellence, but, as you've concluded, the transfer from DOD, we think, is just wrong.

We think that an independent strategic investment firm for innovation in MCM may have some merit, although little concrete information has been provided to evaluate the value of this initiative, and I think the whole nature of early stage development of biological products, drugs, and vaccines is very different from information technologies and electronics technologies that are part of In-Q-Tel.

It seems highly misguided, however, to create a strategic investment firm to incentivize entry into this space by de-incentivizing private investment through depletion of the SRF. That combination just does not make sense.

Particularly with the SRF, also, we were very pleased to see the bipartisan effort on the part of 17 Senators, over the summer, who wrote specifically to the Senate leadership about the multiple—essentially to counter the multiple efforts to raid the SRF, and we were very, very grateful for their support.

PREPARED STATEMENT

Finally, we urge the subcommittee to work closely with the administration to clarify, execute, and adequately fund the programs needed to sustain the PHEMCE enterprise, and our Alliance is committed to working with the Congress, the administration, and others, of course, to make the countermeasures enterprise a success.

We're very grateful for your attention and consideration, and appreciate the invitation here.

[The statement follows:]

PREPARED STATEMENT OF ERIC A. ROSE

SUMMARY

The Alliance for Biosecurity respectfully submits testimony to the Senate Labor, Health and Human Services, and Education, and Related Agencies Appropriations Subcommittee regarding the Department of Health and Human Services' (HHS) report—Public Health Emergency Medical Countermeasures Enterprise Review:

Transforming the Enterprise to Meet Long-Range National Needs (Countermeasure Enterprise Review) for the "Defending Against Public Health Threats" hearing on September 29, 2010.

We very much appreciate being invited to appear today before the subcommittee to discuss this important report and thank you for the consideration of our views. The Alliance for Biosecurity is a collaboration among pharmaceutical and biotechnology companies that are working in the public interest to improve prevention and treatment of severe infectious diseases—particularly those diseases that present global security challenges. The Alliance promotes a stronger, more effective partnership between Government, the biopharmaceutical industry, and other stakeholders in order to advance their shared goal of developing critically needed medical countermeasures (MCMs).

Bioterrorism and emerging infectious diseases present an extraordinary and potentially grave threat to public health and national security. One of the most effective ways to improve our national preparedness for these threats is through the development of drugs, vaccines, and diagnostics, called MCMs, that can be distributed in the event of an emergency. The Federal Government has a central role to play in developing these MCMs and the Alliance stands ready to work with the administration, Congress, industry, and other stakeholders in our shared mission to identify, create, and obtain MCMs to protect citizens against bioterrorist attacks and potentially destabilizing emerging infectious diseases.

Positive Elements of the Countermeasure Enterprise Review

We share and support the goal of the Countermeasure Enterprise Review, which is "a modernized countermeasure production process where we have more promising discoveries, more advanced development, more robust manufacturing, better stockpiling, and more advanced distribution practices." We support the intention of the Review and look forward to working with the subcommittee and the administration to further evaluate some of the initiatives included in the report as well as other ideas that will help to sustain and further develop the biodefense enterprise.

The Alliance is thankful to have been consulted by the Assistant Secretary for Preparedness and Response, Dr. Nicole Lurie, throughout the course of this important review. In addition to in-person meetings, we submitted a White Paper on March 2, 2010, that incorporated a number of core recommendations, including the need to (i) improve the procurement and contracting process to more effectively promote development of MCMs; (ii) improve the speed and efficiency of regulatory interactions between private industry and the U.S. Government; and (iii) improve coordination among the Food and Drug Administration (FDA), Centers for Disease Control and Prevention, Biomedical Advanced Research and Development Authority (BARDA), and other relevant agencies around the development and approval of MCMs.

Therefore, the Alliance was particularly pleased to see the Countermeasure Enterprise Review include plans for HHS to increase transparency, communication, and predictability within the contracting and procurement processes and across agencies. We hope that this includes transparency regarding setting requirements and specific information such as a target product profile as early as possible and is publicly disclosing allowable requirement and population threat analyses information.

Further, we were encouraged that the Review included a commitment to develop a 5-year budget plan for the entire MCM enterprise, expand the advanced development program, and increase staff levels. We welcome these enhancements and feel strongly that the MCM enterprise and our Nation's preparedness will benefit from increased communication, development of a 5-year budget, continuity, and transparency. We hope the administration will include such a coordinated long-range budget plan as part of the 2012 President's budget.

The Alliance was also pleased with the emphasis placed on enhancing FDA regulatory innovation, science, and capacity in the Review, as well as the recognition of the importance of optimizing the legal and policy framework for MCM oversight and approval. Therefore, we support the administration's August 20 budget amendment request to make available balances from prior pandemic influenza appropriations to modernize FDA "regulatory science." We believe that this new approach to regulatory science must focus on the agency's "animal rule" in order to make it an effective mechanism for the approval of needed countermeasures in the numerous instances where human testing of drugs and vaccines is unfeasible and/or unethical. This focus requires the addition of substantial manpower to the agency to meet the complex needs of this space, and the training of regulatory personnel to facilitate their understanding of the unique national security and public health issues that chemical, biological, and nuclear threats represent.

Elements of Concern Regarding the Countermeasure Enterprise Review

The Alliance's March White Paper also included a core recommendation to "improve predictability and ensure the availability of consistent, robust funding for the development of MCMs." Indeed, this is essential to ensuring that the MCM enterprise is successful. We were disappointed that the Countermeasure Enterprise Review did not propose fully funding the advanced development program at BARDA, nor outline a process for restoring funding to the Special Reserve Fund (SRF) beyond 2013 or otherwise providing long-term and stable funding for the procurement of MCMs. We support plans for the sustainability of the Enterprise, but caution that investments must be made up front in order to guarantee success over the long term.

As you know, in 2004, Congress—recognizing that the country was relatively unprepared for the aftermath of an attack with CBRN agents—passed the Project BioShield Act (Public Law 108–276), which established the SRF. In the Project BioShield Act, Congress described the purpose of the SRF as procuring products to "treat, identify, or prevent harm from any biological, chemical, radiological, or nuclear agent that may cause a public health emergency affecting national security." Congress appropriated $5.6 billion for this purpose in 2004 to remain available until 2013. Since that time several critical MCMs have been purchased and stored in the Strategic National Stockpile with SRF funds.

Predictability and availability of robust funding for the advanced development and procurement of MCMs is one of the most important signs to industry and to private investors that the Government is serious about moving the MCM initiative forward. Although there are a number of initiatives listed in the Review that may help the MCM enterprise in the long term, there was little mentioned about immediate funding. Since advanced development is the most expensive part of MCM development, it must be funded at a higher level. In addition, the SRF should not be depleted for other uses, including proposals put forth in the Countermeasure Enterprise Review.

Private sector firms cannot invest in product development, which requires 10 to 15 years and hundreds of millions of dollars, unless they are reasonably certain that a market will exist for their product when it is finished. The SRF serves as a concrete demonstration of the Federal Government's commitment to procuring MCMs. Diminishing or eliminating the SRF would call into question the credibility of that commitment, and by doing so make it difficult for the private sector to remain in the countermeasure business. While this would significantly affect these companies and their employees, it would be a much larger setback for the country as a whole.

For this reason, we are concerned that the administration's August 20 budget amendment request included the transfer of (i) $200 million from the SRF to the Department of Defense (DOD) in order to establish a Technical Center of Excellence for Advanced Development and Manufacturing; and (ii) $200 million from the SRF to establish a new MCM strategic investment firm.

Establishment of a "Technical Center of Excellence" for advanced development and manufacturing of MCMs is a laudable goal. However, DOD intends to dedicate significant funding to the development of platform technologies and the advanced development and manufacturing of novel countermeasures. We support this initiative but oppose transferring SRF funds to support it. As previously stated, depleting the SRF now raises a number of concerns. Any flexible manufacturing initiative should be funded apart from the SRF with new resources, which do not compete with funding for advanced development at BARDA. Lastly, it is important to ensure that all existing manufacturing capacity is being effectively and efficiently deployed before investing in the creation of new capacity.

Likewise an independent strategic investment firm for innovation in MCM, "to provide necessary support for small innovators and increase the odds of moving innovation into successful development" may have some merit although little concrete information has been provided to evaluate the value of this initiative. It seems somewhat paradoxical, however, to deplete the SRF—the primary signal of a Government market for MCMs—in order to create a strategic investment firm to promote innovation of MCMs. Such an action would send, at best, a confusing signal to industry and private investors, and could have the impact of discouraging further investment in MCMs under development. Additionally, it is premature to transfer funds to create a new investment firm when the administration has not decided on the model, structure, or objectives of such a firm.

The Alliance urges the subcommittee to work closely with the administration to clarify, execute an adequately fund the programs needed to sustain the PHEMCE enterprise as the initiatives included in the Countermeasure Enterprise Report are further developed and implemented. The Alliance is committed to working with Con-

gress, the administration, and others to make the countermeasure enterprise a success. We thank you for your attention and consideration.

Senator HARKIN. Thank you very much, Dr. Rose.

And now we turn to Dr. Pavia.

Dr. Pavia.

STATEMENT OF ANDREW T. PAVIA, M.D., FAAP, FIDSA, CHIEF, DIVISION OF PEDIATRIC INFECTIOUS DISEASES, UNIVERSITY OF UTAH; CHAIR, INFECTIOUS DISEASES SOCIETY OF AMERICA'S PANDEMIC INFLUENZA TASK FORCE, SALT LAKE CITY, UTAH

Dr. PAVIA. Senator Harkin, Senator Cochran, thank you very much for this opportunity to speak to you on behalf of the 9,000 members of the Infectious Disease Society of America (ISDA).

Unlike Colonel Larsen, I am an infectious disease physician, a scientist, and a pediatrician—not much of a pilot, but—I appreciate this opportunity to comment on the matters before us.

IDSA commends Secretary Sebelius for undertaking the comprehensive review of our MCM Enterprise. As a final report makes abundantly clear, there are many components, organizations, factors, and barriers that are vital to the successful development of countermeasures, their deployment and use. And, although it was intentionally left out of the review because of its scope, investments in the U.S. public health system at the Federal, State, and local level are urgently needed.

The recent H1N1 pandemic demonstrated the importance of being able to rapidly develop countermeasures—and these include vaccines, antimicrobial drugs, and diagnostics—and the importance that we be able to develop our responses to biological threats, whether those be the ones that we anticipate easily, such as pandemic influenza or anthrax, or new and unrecognized threats. And an example that I want to bring to your attention is the emergence of antimicrobial resistance, whether it be influenza that's resistant to Tamiflu, or bacteria that are resistant to all available antibiotics.

There have been a number of recent reviews that have looked at the MCM Enterprise, in addition to that done by the Secretary. All have identified similar barriers and opportunities for improvements. Many of these recommendations mirror policy improvements that IDSA has suggested over the past several years. We've put before you our reports from 2004 on "Bad Bugs, No Drugs" and on "Pandemic Influenza"—"Pandemic and Seasonal Influenza, Principles for Action," from 2007. Many of these recommendations will be critical if they can be accomplished, but the proof is in their actual implementation.

We're pleased that HHS is taking a comprehensive approach. As you pointed out in your opening remarks, an effective countermeasure system is one that doesn't focus on individual agents, but that can flexibly respond to a variety of threats, and do so quickly and efficiently, with good stewardship of our resources.

We've recently experienced an influenza pandemic, which was, thankfully, the mildest of the last 100 years. Part of why it was mild was because of the investments that were made in planning and preparation. We produced a vaccine in record time, let's not forget, and yet, that still was not enough, and it was not soon enough.

This was a mild pandemic, by all measures, but that means that it only killed 9,000 to 18,000 Americans; it put some 300,000 in the hospital; it killed 1,200 children, some of whom died in my hospital in front of my eyes.

So, a mild pandemic is still a major threat. A moderate or severe pandemic is one that we have to be prepared for. And it is indeed inevitable, as people have already mentioned. What we don't know is when it will emerge and how severe it will be. And what we have in our power to do something about is whether or not we will be prepared for it.

The threat of antimicrobial resistance is, in fact, intimately linked to the threat of pandemics and bioterrorism. In influenza pandemics, people die of secondary bacterial infections, not just of influenza virus; and in recent years, Methicillin-resistant Staphylococcus aureus, or MRSA, has been the major killer after influenza. Moreover, the antibiotic resistance genes that are emerging naturally can fairly easily be engineered into bioweapons, such as anthrax. And a moderately competent graduate student can do it with a modicum of funds and a decent laboratory.

Several factors have resulted in the dearth of new MCM in development, and these include the lack of financial incentives; insufficient risk-sharing, because of the high rate of failure of new products; regulatory uncertainty; insufficient federally supported research; and lack of coordination across all components of the MCM measure, as Colonel Larsen has mentioned.

To create sustainable MCM R&D, we have to determine the right combination of financial incentives and risk-balancing and -sharing that will allow industry to invest and to succeed. The strategic investment firm envisioned by the MCM report is one potential tool, and IDSA supports it. But, other mechanisms are also needed. We caution, however, that the initial funding level proposed for the strategic investment firm is unlikely to result in useful countermeasures. Other funding and additional mechanisms need to be integrated.

All reviews identify potential barriers from regulatory uncertainty. FDA must develop clear and achievable regulatory pathways for review and approval of new MCM. This will require investment. While not the purview of this subcommittee, it's critical that Congress fund the desperately needed improvements in regulatory science and capacity for public health measures at FDA.

The investments made over the past several years have limited the impact of pandemic flu, but large gaps remain. IDSA appreciates the generous funding that this subcommittee has provided over recent years, as it did in the supplemental appropriations bill. However, we strongly believe that preparedness for influenza and other public health emergencies requires a consistent and predictable stream of funding. We support at least $1.7 billion in multiyear appropriations for BARDA for fiscal year 2011 to fund the development of new countermeasures.

We also recognize a need for a clinical-trials infrastructure that will allow the further clinical development of these MCM. Successful examples exist for HIV/AIDS and for cancer. We need to learn from these examples that have been successful, and integrate that into the MCM enterprise.

Improved management structure has already been mentioned. It's featured in the Secretary's report. Some of the tools that are laid out, including the early development teams at NIH and the action teams proposed at FDA, are promising approaches, but there does need to be coordinated leadership.

PREPARED STATEMENT

The danger posed to the United States by biological threats, including pandemic influenza, biologic weapons, emerging infections, is really very real and very great. Continued thoughtful, efficient investment in the science, in filling the pipeline, evaluating and licensing countermeasures, and efficient management of the enterprise, will provide Americans with the protection that they expect and deserve.

Thank you, and I'll be happy to answer any questions.

[The statement follows:]

PREPARED STATEMENT OF ANDREW T. PAVIA

The Infectious Diseases Society of America (IDSA) appreciates this opportunity to speak before the Senate Labor, Health and Human Services (HHS), and Education, and Related Agencies Appropriations Subcommittee as you examine our Nation's readiness and ability to deal with public health threats, particularly through the development of countermeasures to address biodefense, pandemic influenza, and emerging infectious diseases. My name is Andrew Pavia, MD, FIDSA, FAAP. I am an infectious diseases specialist and the George and Esther Gross Presidential Professor and Chief of the Division of Pediatric Infectious Diseases at the University of Utah. I am the chair of IDSA's Pandemic Influenza Task Force. I am also a member of the National Biodefense Science Board, which was created under the authority of the Pandemic and All-Hazards Preparedness Act, to provide expert advice and guidance to the HHS Secretary and the HHS Assistant Secretary for Preparedness and Response (ASPR) to prepare for, and respond to, public health emergencies resulting from chemical, biological, nuclear, and radiological events, whether naturally occurring, accidental, or deliberate.

IDSA represents more than 9,000 infectious diseases physicians and scientists devoted to patient care, prevention, public health, research, and education. Our members care for patients of all ages with serious infections, including meningitis, pneumonia, tuberculosis (TB) and HIV/AIDS, emerging infections like the 2009 H1N1 influenza virus, food-borne diseases caused by salmonella, campylobacter, and escherichia coli (E. coli), and diverse infections caused by antimicrobial-resistant bacteria, such as methicillin-resistant staphylococcus aureus (MRSA), enterococcus, E. coli, salmonella, pseudomonas aeruginosa, klebsiella pneumoniae, acinetobacter baumannii, and the newly emerging New Delhi metallo-beta-lactamase (NDM–1). NDM–1 is an enzyme that makes bacteria resistant to a broad range of antibacterial drugs. It was first identified in December 2009 in a patient hospitalized in New Delhi with an infection caused by Klebsiella pneumoniae. It has since rapidly spread to other areas of the world, and three cases recently have been reported in the United States. IDSA's testimony will primarily focus on new medical countermeasures essential to address pandemic influenza and antimicrobial-resistant infections.

HHS' End-to-End Countermeasure Review

IDSA commends HHS Secretary Kathleen Sebelius and the administration for undertaking the comprehensive end-to-end review of our medical countermeasures enterprise. As the final report (The Public Health Emergency Medical Countermeasure Enterprise Review: Transforming the Enterprise to Meet Long Range National Needs), prepared by the ASPR, Nicole Lurie, MD, MSPH and her staff, makes clear, there are many components and organizations which are critical to the development, deployment and use of medical countermeasures, including urgently needed investments in the U.S. public health system. The goal of an efficient and effective medical countermeasure enterprise is to be able to rapidly produce effective responses, not only to known threats or biologic attacks, but to previously unrecognized threats and emerging infectious diseases.

We are pleased that the administration is taking a comprehensive approach to developing a medical countermeasure strategy. Many of the recommendations in HHS' end-to-end review mirror policy improvements IDSA has suggested over the past several years, including in our 2004 report "Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates, a Public Health Crisis Brews", which called attention to the dry antibacterial pipeline and the need for the U.S. Government to financially support and incentivize the development of novel antibacterial drugs. The administration's report also reflects several recommendations found in IDSA's 2007 report, "Pandemic and Seasonal Influenza Principles for U.S. Action." In this report, IDSA recommended that HHS and ASPR move quickly to:

—Strengthen pandemic vaccine efforts by establishing a Multinational Pandemic Influenza Vaccine Master Program;
—Strengthen anti-infective pharmaceutical research and development and stockpiling efforts;
—Improve quality and availability of diagnostic tools for influenza;
—Accelerate development of countermeasures to prevent, treat, and diagnose pandemic influenza through additional legislative action and continue to streamline regulatory approval processes;
—Update plans for countermeasure distribution and prioritization of use;
—Expand vaccine uptake, stabilize vaccine manufacture, and test and evaluate vaccine distribution plans during annual influenza seasons;
—Protect the healthcare workforce during a pandemic;
—Build national, regional, and local healthcare systems capable of responding to mass casualty events;
—Develop and test community mitigation measures;
—Improve and coordinate influenza surveillance;
—Continue to strengthen leadership, international collaboration, and communication; and
—Allocate significant and sustainable funding for long-term planning and action.

The implementation of these policy improvements is essential to reduce the threat Americans and the world community faces from the public health threats of greatest concern. Copies of IDSA's Bad Bugs, No Drugs report and the Pandemic and Seasonal Influenza Principles for U.S. Action document are available through IDSA's Web site at: http://www.idsociety.org/10x20.htm and http://www.idsociety.org/influenza.htm. Additionally, IDSA is hosting a meeting on January 27–28, 2011, "Seasonal and Pandemic Influenza 2011", where the influenza principles will be reviewed and further updated to include lessons learned from the novel H1N1 influenza pandemic, with a focus on specific actions and timelines.

Pandemic Influenza and Antimicrobial Resistance

Infectious diseases and public health experts believe that another influenza pandemic is inevitable. The key questions that remain are when it will occur, which influenza virus will cause the pandemic, how severe it will be, and whether the world will be ready. Experts also are extremely concerned about the growing threat of antimicrobial-resistant infections. The need for novel products (drugs, diagnostics, and vaccines) to address these threats is urgent.

There are three types of influenza viruses, classified as A, B, or C, based on their protein composition. Public health experts are most concerned with type A influenza virus. Pandemic influenza typically is a virulent new strain of human influenza that causes a global outbreak of serious illness. Four influenza pandemics have occurred during the past 100 years: the 1918–1919 "Spanish flu," the 1957–1958 "Asian flu," the 1968–69 pandemic or "Hong Kong flu" and the H1N1 pandemic from 2009–2010. The 2009 H1N1 influenza pandemic proved to be the mildest of these in overall deaths, killing an estimated 9,000 to 18,000 Americans according to CDC estimates. The virus did not develop resistance to oseltamivir (Tamiflu), the only widely available antiviral to treat influenza. Focusing solely on the number of deaths, however, masks the overall impact of the H1N1 pandemic. More than 1,200 children younger than 18 died of H1N1 influenza and between 200,000 and 400,000 Americans were hospitalized.

The 2009 H1N1 influenza pandemic was perhaps a best case scenario. If a pandemic similar in virulence to the 1918 influenza strain were to occur, up to 2 million Americans could die and the number of hospitalizations and need for intensive care unit beds would overwhelm our healthcare system and cripple our infrastructure.

On the issue of antimicrobial-resistant infections, the CDC has described antimicrobial resistance as "one of the world's most pressing health problems", while the World Health Organization (WHO) calls it "one of the three greatest threats to human health." Infectious diseases physicians agree. NDM–1, for example, poses a new threat of great concern and illustrates how antimicrobial-resistant infections

will continue to emerge wherever antimicrobial drugs are used. NDM–1 also illustrates how a drug-resistant organism created in one area of the world can quickly threaten all regions. The costs due to antimicrobial resistance, both in the numbers of lives lost or devastated and in economic terms, are exceedingly high. Drug-resistant bacteria, such as MRSA-resistant E. coli, Acinetobacter baumannii and Clostridium difficile (c. diff.) currently affect many hospitalized patients and a growing number of people in the community, including healthy athletes, parents, working people, and children. CDC reports that nearly 2 million healthcare-associated infections (HAIs) and 90,000 HAI-related deaths occur annually in the United States. Most of these infections and deaths involve antimicrobial-resistant bacteria. The direct and indirect economic costs associated with antimicrobial-resistant infections are also enormous in terms of dollars spent, length of hospital stay, and loss of productivity. A recent study indicated that annually in the U.S. antimicrobial-resistant infections are responsible for more than $20 billion in excess healthcare costs, more than $35 billion in societal costs, and more than 8 million additional hospital days. Antimicrobial resistance is a critical issue in viral diseases as well. In 2008, the dominant circulating seasonal influenza strain had become resistant to oseltamivir (Tamiflu) leaving limited options for treatment. For now, this strain has largely disappeared, but if it re-emerges we have few drugs in the pipeline to deal with the threat.

There also is an alarming connection between influenza and antimicrobial-resistant bacterial infections. In addition to the morbidity and mortality caused by the influenza virus itself, many people with influenza will develop life-threatening secondary bacterial infections, many of which are resistant to antibacterial drugs. In recent years, MRSA has been the most lethal cause of postinfluenza bacterial infections.

Re-engineering the Pandemic Influenza Vaccine Production Enterprise

As we stated in our 2007 Pandemic and Seasonal Influenza Principles for U.S. Action, IDSA believes the widespread use of a pandemic vaccine should be the central strategy for protection of human health during a pandemic event. IDSA supports a coordinated effort led by the Federal Government working with public and private partners and the international community to outline a comprehensive approach that will coordinate, and strengthen vaccine research and development, increase production capacity, accelerate licensure, guarantee equitable global distribution, and monitor vaccine performance and safety.

In August 2010, the President's Council of Advisors on Science and Technology (PCAST) issued a report focused on re-engineering the pandemic influenza vaccine production enterprise. In its report, the PCAST emphasized that existing technology for influenza vaccine will never deliver enough vaccine in time to respond to a pandemic. However, they said that targeted investments in key areas could shorten by weeks the time needed to produce enough doses. They found that the development of new types of influenza vaccines is of critical importance, and no single new technology has a high likelihood of success. To ensure success of one, we must pursue several potential vaccine strategies simultaneously. The PCAST recommendations provide a blueprint to significantly increase our Nation's ability to produce vaccine in a timely manner. The recommendations would speed up not only flu vaccines, but also a number of other medical countermeasures against infectious diseases that could emerge naturally or as the result of a bioterrorism attack.

Although the PCAST did not determine anticipated costs for the projects required to make the improvements necessary to re-engineer the influenza vaccine production enterprise and has not attempted to allocate the share of financial responsibility to be borne by the governmental agencies or the companies, they did state that it is fair to assume an initial $1 billion in Federal funds—and at least similar sums over the subsequent few years—would be required to make the changes that will allow the Nation to mount a vigorous effort that can protect its population as well as possible in the event of another pandemic, an event that could have catastrophic consequences.

On-going strong investment in pandemic vaccine technologies is justified on a cost-benefit basis, in part because large numbers of lives could be saved through relatively inexpensive improvements in current methodologies and in part because Federal investments in influenza pandemic response would speed development of technical platforms and production facilities that would support medical countermeasures against a variety of other dangerous pathogens.

Antimicrobial and Diagnostics Discovery and Development

The development of both antiviral and antibacterial drugs as well as point-of-care diagnostics must be treated as priorities in the U.S. medical countermeasure devel-

opment strategy. In IDSA's view, there is an urgent need to address the factors that have resulted in a dearth of new antimicrobials and other countermeasures in development. These include:

—Lack of financial incentives of sufficient strength to make companies choose to engage;

—Regulatory uncertainty caused by the lack of consistent approval pathways and limited regulatory scientific resources at the Food and Drug Administration (FDA);

—Insufficient federally supported research and development efforts; and

—Lack of a coordinated management structure.

In addition, as pointed out in the end-to-end medical countermeasure review, lack of coordination between Federal agencies and complex contracting regulations add additional barriers.

To create a sustainable, national and global medical countermeasures R&D enterprise, it is necessary to determine the right combination of financial incentives ("push" and "pull" mechanisms) to entice industry to invest and to help companies, big and small, with innovative technology to succeed. Examples of the push incentives are grants, contracts, and tax credits. Examples of the pull incentives are milestone payments, guaranteed markets, liability protection, patent extensions or data exclusivity, and prizes. These incentives are intended to change the "return on investment" or net present value calculation of countermeasures to make them more competitive with other medical products. The strategic investment firm envisioned by the medical countermeasure review report also supports the development of high-priority products by sharing the risk of development with companies. The HHS report highlights the need for the strategic investment firm to first focus on novel antimicrobials to address drug-resistant infections. IDSA wholeheartedly supports this effort. We caution, however, that the proposed initial funding level for the strategic investment firm is $200 million, which is wholly insufficient to increase the likelihood of bringing successful antimicrobial drugs and other medical countermeasures to the marketplace. We also strongly believe that additional "push" and "pull" incentives are needed, particularly to address the withering antibacterial pipeline, and urge Congress to act quickly to pass strong legislation in this area. Risk sharing and incentives that stimulate the development of new rapid diagnostics also should be adopted.

FDA must quickly assure a clear regulatory pathway for the review and approval of new countermeasures. For many years, industry representatives have identified regulatory uncertainty as one of the primary obstacles to new antibacterial development, in particular. IDSA acknowledges the strong commitment expressed by current FDA leaders and staff to address the multi-faceted problem of regulatory uncertainty. Despite good faith meetings, workshops, and advisory committee meetings, the situation today for antibacterial review and approval appears no better than it was at this time last year. In some respects, the level of uncertainty has increased. In its medical countermeasure review report, HHS identified a critical need to upgrade FDA science and regulatory capacity. HHS hopes to make a significant investment to provide FDA scientists with the resources they need to develop faster ways to analyze promising new discoveries and give innovators a clear regulatory pathway to bring their products to market. This year, IDSA, FDA, the National Institute of Allergy and Infectious Diseases (NIAID), and pharmaceutical companies have begun to participate in an important effort being led by the Foundation of the National Institutes of Health (FNIH) to study new endpoints that will more easily demonstrate antibacterial effectiveness. The FNIH effort is promising, but to develop this knowledge and quickly implement changes in the regulatory process requires people and money. This spring, IDSA testified in support of additional funding to allow FDA to hire additional staff to develop much needed clinical trial guidance documents and to fund Critical Path Initiatives specific to antimicrobial drug development. We also requested $13.25 million to support a focus on new antibiotics within FDA's new regulatory science initiative with the National Institutes of Health.

We recognize the strains on the Federal budget due to the economic crisis and the budget deficit, but significantly increased Federal research dollars are urgently needed to advance scientific knowledge about pandemic influenza and antimicrobial resistance, as well as to support countermeasure discovery and development. IDSA has for the past several years supported consistently strong funding for these activities throughout HHS. We appreciate that this subcommittee has provided substantial funding for pandemic influenza response, as it did last year in the supplemental appropriations bill. However, IDSA strongly believes that some pandemic preparedness efforts require funding over multiple years. For example, companies consid-

ering investing in countermeasures development need assurance that the financial commitment will be secure in future years or they will not engage.

We strongly support significantly boosting funding for HHS' Biomedical Advanced Research and Development Authority (BARDA). This year, IDSA testified in support of at least $1.7 billion of multi-year appropriations for BARDA in fiscal year 2011 to fund the development of new therapeutics, diagnostics, vaccines, and other technologies, including antimicrobials. Such funding would significantly enhance BARDA's support of countermeasures through the advanced stages of development, as well as BARDA's flexibility to partner effectively with industry. IDSA also wishes to see BARDA take a much stronger role in advancing the development of new antimicrobials and related diagnostics to detect, identify, and treat pathogens that presently are affecting a significant number of Americans in hospitals annually. With modern molecular biology techniques, the resistance genes found in these highly resistant "superbugs" can be readily introduced into bioweapons such as anthrax or tularemia. Specific to NIAID research funding for antibacterial resistance and antibacterial discovery research, this year IDSA testified in support of a substantial funding increase in these areas for fiscal year 2011 to a total of $500 million. Current NIAID funding levels in these areas are extremely limited in IDSA's view and do not match the threats we face from antibacterial-resistant infections.

Moreover, to further strengthen the countermeasures pipeline, we must invest in appropriate infrastructure for clinical trials. Such clinical trials infrastructure should be flexible and agile, with the ability to rapidly respond to new or re-emerging infections as they arise. Further, it must balance both pediatric and adult unmet infectious diseases needs. We are gratified to see NIAID taking steps to achieve part of this goal, as NIAID is broadening its AIDS Clinical Trials Group (ACTG) to expand its tuberculosis and, likely, its hepatitis C clinical research portfolios. Earlier this year, IDSA urged NIAID to build clinical trials infrastructure in areas beyond HIV/AIDS including to address serious bacterial, viral (particularly influenza), and fungal infections. The creation of an NIAID-funded in-patient clinical trials network in these areas will help to create an environment supportive of high-quality research, incorporating experienced investigators and study sites, robust statistical support, specialized laboratories (e.g., pharmacokinetics, immunology) and organizational structures to support clinical trials. Such additional clinical trials infrastructure could contribute substantially to the critical need for advancements in the diagnosis and treatment of drug-resistant bacterial infections, pandemic and seasonal influenza, and other serious infections. Furthermore, the clinical trial infrastructure we have proposed fits squarely within and is supportive of HHS' medical countermeasure review effort. IDSA believes such additional infrastructure is urgently needed.

The global H1N1 pandemic is a striking reminder of the importance of making sustained investments in research as well as public health infrastructure. Investments made over the past several years in surveillance, vaccine capacity and preparedness clearly limited the impact of the H1N1 pandemic. However, in other areas the pandemic showed our continued vulnerabilities. These include early international detection, and rapid production and distribution of vaccines, and antivirals that are appropriate for critically ill patients. The threat of another pandemic remains. The Nation's public health system must maintain robust disease surveillance, epidemiologic investigation, education and outreach, and communications capacity.

Strengthening Leadership, Coordination, and Management Structure

In 2007, IDSA called for strengthened leadership and collaboration in influenza preparedness. We called for HHS and the Federal Government to clarify lines of authority and key responsibilities, involve technical experts and stakeholders, issue and update national standards for planning, and continue to lead international collaborative efforts related to pandemic preparedness. HHS responded and many improvements were considered and implemented. The PCAST report recommends that the administration further strengthen its management structure by vesting authority with the ASPR at HHS to coordinate and task component agencies at HHS with supporting and implementing the influenza vaccine recommendations. In addition, it recommends that HHS create a small advisory committee comprised of representatives from the biotechnology, pharmaceutical and investment communities, to guide the HHS's engagement with industry. This coincides with the recommendation in HHS's end-to-end medical countermeasure review that changes are needed in how the enterprise is managed to greatly strengthen its decisionmaking. The review suggests that HHS identify a leader who would work with program leaders and managers across the span of medical countermeasure development activities as well as with commercial partners and other key stakeholders. The congruence of these

three recommendations emphasizes the critical role of integrated and coordinated planning between all levels of government in pandemic preparedness and medical countermeasure development.

Having the necessary infrastructure in place to both monitor and respond to current and emerging antimicrobial-resistant infections also will play a crucial role in ensuring that we are protecting the health and safety of our citizens. Congress began to address this need several years ago when it passed legislation that became section 319E, "Combating Antimicrobial Resistance" of the Public Health Service Act. This law directed the Secretary to establish an Antimicrobial Resistance Task Force to coordinate Federal programs relating to antimicrobial resistance. This Task Force developed the Public Health Service Action Plan to Combat Antimicrobial Resistance, published in 2001, which has not been sufficiently funded. Comprehensive legislation introduced in the Senate during the last Congress and in the House of Representatives in each of the last two Congresses, the Strategies to Address Antimicrobial Resistance (STAAR) Act (H.R. 2400 in the 111th Congress), will advance the key elements in the Federal Action Plan and authorize adequate funding for these strategies. The STAAR Act strengthens existing efforts by establishing within HHS an Antimicrobial Resistance Office (ARO). The director of this new office also will serve as the director of the existing interagency task force to facilitate the coordination of activities. The legislation also would establish a Public Health Antimicrobial Advisory Board comprised of infectious diseases and public health experts who will provide much-needed advice to the ARO director and interagency task force.

Finally, the bill, when enacted and sufficiently funded, will strengthen existing surveillance, data collection, and research activities as a means to reduce the inappropriate use of antimicrobials, develop and test new interventions to limit the spread of resistant organisms, and create new tools to detect, prevent, and treat drug-resistant "bad bugs."

Conclusion

It is easy to dismiss hyperbolic news reports because of sensationalism and inaccuracies, but the danger posed to the United States by biological threats, including pandemic influenza, biologic weapons and emerging infections, including antimicrobial-resistant infections, is very real and very great. Continued thoughtful investment in science, filling the pipeline, evaluating and licensing countermeasures and efficient management of the enterprise will provide Americans with the protection they expect and deserve. IDSA stands ready to assist this subcommittee and the Federal Government in any way that we can, and we are grateful for this opportunity to express our views.

Thank you.

Senator HARKIN. Thank you again, Dr. Pavia.

And thank all of you for your testimonies, and for your work in this field, and your leadership in this field.

Colonel Larsen, is anthrax the major threat that we have that we should be worried about with regard to bioterrorism? Is it anthrax, or is it something maybe we don't know about?

Colonel LARSEN. That's a very good question. It's very difficult to answer. I worry about anthrax. It's the only one that's really persistent.

Senator HARKIN. Because what you just told me——

Colonel LARSEN. We're going to have a hard time cleaning it up. We don't know how to——

Senator HARKIN [continuing]. About four decades, then——

Colonel LARSEN. We don't know how to do it.

Senator HARKIN. Yes.

Colonel LARSEN. It's deadly. But, it's not contagious. You know, Eric may tell you smallpox is the worst one, because—I've run exercises that—with Senator Nunn, several years ago, looking at smallpox. The fact that it's contagious, we're a highly mobile society, unvaccinated; that is.

April, I was up in J. Craig Ventner Institute, and they were showing me some of the amazing things they were doing up there

just a month before they announced that—you know, a new organism that had a computer for a parent. I'm not worried about people in caves doing that now. Those are the best scientists in the world at the best laboratory. But, 5 years from now? And the decisions you're going to make, in this next year, are going to tell us what kind of defense we have in 5 years. So, I would feel—I would sleep better tonight if I know we were ready for 1960-style bio-attacks, which is anthrax. Or plague.

Senator HARKIN. You can see that—obviously, the problem that confronts us is, there are a lot of threats out there. And, you know, you can't have 100 percent protection against everything. I mean, you just—it's impossible. So, we have to sort of think about what are the priority areas, knowing full well that we can't guarantee absolute, 100-percent protection against anything. But, we can try to lessen the possibility of a bioterrorist attack. We can lessen that, but we can't completely do away with it. And then we can do what we can to build up our responses to it. That's what you're talking about: how we respond to that.

Colonel LARSEN. I'll go back to what I call my bible, what Dr. Josh Lederberg, Nobel Prize winner, was talking about, "Bug to Drug in 24 Hours." When he wrote that, in 2001, that was science fiction. That does not have to remain science fiction.

You know, when H1N1 was discovered in southern California, within 2 weeks they did genetic mapping and had an antiviral that was better than Tamiflu. In 2 weeks. That's a lot of progress we've made in the last decade.

So, we can't build vaccines for everything that's out there, you're absolutely right. But, we've got to figure out how to respond quickly, and make vaccines and therapeutics a lot faster, which is why—the one little statement I left out here is, when it comes to national security, today the FDA, NIH, and BARDA are just as important as DOD and the intelligence community. And we need to understand that, and fund them appropriately.

Senator HARKIN. Yes. I——

Colonel LARSEN. Because the funding you're going to approve now is what kind of defense my kids and grandkids are going to have 5, 10 years from now, sir.

Senator HARKIN. Well, I agree with that. I—you know, we've tried to get BARDA going, and now we've got this. And I'm still wrestling with who's in charge.

Now—you said that, too, but who do you think should be in charge?

Colonel LARSEN. I'll give you two answers. Because I work very closely with Senator Graham and Talent. They wrote a letter to President Obama, and they said, "This is so important that the Vice President of the United States should be in charge of all WMD activities here."

I mentioned that in a hearing at the Judiciary Committee last month, and Senator Kyl said, "Well, you know, the Vice President's a pretty busy guy."

I said, "I know that, but tell me one thing more important than defending America against weapons of mass destruction."

He's the only person that can look—because there are so many Cabinet Secretaries involved in this enterprise of biodefense—he's

the only person in this town—other than the President, and he is kind of busy—he's the only person that can look at Cabinet Secretaries and say, "Do this," and they say, "Yes, sir." Now, that's going a long way. He'd need more of a staff. That's Senator Graham and Senator Talent's answer, I thought I'd give you that, because they've written that several times.

I would just like to see a special assistant for biodefense in the White House. We had that in the Clinton administration, we had that in the Bush administration. We don't have that today. There is no special assistant to the President for biodefense. That would be a good start. I'd be happy with that. Somebody to coordinate that interagency community.

So, somewhere between Senator Graham and Senator Talent saying the Vice President, and my recommendation is at least a special assistant to the President.

Senator HARKIN. And was it special assistant for bioterrorism?

Colonel LARSEN. For biodefense, yes, sir.

Senator HARKIN. Oh, biodefense.

Colonel LARSEN. Yes, sir. That was Dr. Ken Bernard, back in the Clinton administration; Dr. Bob Kadlec, in the Bush administration. That position doesn't exist today.

Senator HARKIN. Okay.

For all three of you, I have been in this subcommittee personally involved in trying to really promote cell-based and recombinant-based vaccine production. Well, I get frustrated at the slow pace of this, but I think things—they do take time. I'll just ask you. How do you feel—all three of you—feel about the state of our—right now, and where we are, in terms of moving to cell-based and recombinant-based vaccine production? Are we dragging our heels? Are we on track, sort of? Could we be faster? How about this idea that cell-based are licensed in Europe but not in the United States?

So, Dr. Rose, go ahead.

Dr. ROSE. Yes. Sure. I think there's a disconnect between the pace of advancement of the technology, which is rapid, and the regulatory response to that technology, which I think has been relatively slow. And I think that pace is quickening.

I visited a company in Israel, earlier this year, that has portable, disposable bioreactors, using carrot cells and tobacco cells, where they're making biological drugs in these kinds of incubators, at cost that's about one-tenth the production costs of similar agents made in mammalian cells.

The particular advantage, too, is that mammalian viruses, animal viruses, don't contaminate vegetable cells. So, there's a safety advantage to it. But, when the regulators look at this, they still look at it from the perspective of safety issues with regard to animal cells.

And the other issue is just with regard to safety, the necessary clinical trials. Protein Sciences firm was alluded to earlier by Secretary Sebelius. They've developed an insect-cell-based flu vaccine that actually was rejected by a panel when it was presented for use in seasonal flu, on the argument that the several thousand patients in which it had been tested, without a safety problem, was just simply not enough to reach that conclusion. And I think—you know, licensure there, I think, arguably, would have sped up, for

the next flu pandemic, the availability of the insect cell base, because it would have allowed it to establish itself that much earlier, commercially.

Senator HARKIN. Dr. Pavia?

Dr. PAVIA. Yes. So, I would agree with the points that Dr. Rose made about regulatory and clinical trials being a holdup. There's also scientific hurdles that emerge. One recombinant technology or another may sound terrific when it's first demonstrated as a proof of concept. But, attempts to scale up sometimes lead to antigen that doesn't work as well, difficulty with contamination, so that when we go after one candidate, it doesn't always deliver on the promise. Just like in drugs, there's a high failure rate.

The other issues that we haven't really talked about are the economics. Influenza vaccine, while not perfect, and slow for seasonal use, is produced relatively efficiently. It's inexpensive. The capital investment to bring some of these new technologies to market is very large. The cost of a dose of vaccine with the new technologies is going to be higher. And the incentive hasn't always been there to bring out a somewhat improved influenza vaccine that's going to cost more, when the demand isn't clear, much as we need it for more rapid response and for pandemic capacity.

Senator HARKIN. Colonel Larsen.

Colonel LARSEN. Sir, you've heard from two scientists. All I can say is, the chief scientist at the WMD Commission last October was 8 months pregnant, and in the State of Maryland, she could not get an H1N1 vaccine, even though she was in the highest risk group. So, from my perspective, we are not where we need to be, sir.

Senator HARKIN. Why aren't they licensed here? I'm sorry, I should—why—what's the problem with licensure here? Someone——

Dr. PAVIA. One would hear, you know, this perhaps more clearly from the FDA, but when you produce a new vaccine in a new technology, it usually requires a different way to measure its potency. There are unanswered questions about the best way to prove safety. And we just don't know what measures need to be taken to look at the safety of something produced in insect cells. And so, these regulatory hurdles in the United States are set higher, perhaps for good reasons. But, FDA has not been able to respond to these as quickly as they should, and in part, as was pointed out in Secretary Sebelius's review, they lack some of the scientific basis for making these decisions right now.

Senator HARKIN. I'll think about that.

Senator Cochran.

Senator COCHRAN. Mr. Rose, in your testimony you mention that the Alliance for Biosecurity has been recommending to the ASPR to improve predictability and assure availability of funding for the development of MCM. What would be the impact of the successful development of such a—an entity if a stable funding stream is not provided by the Federal Government?

Dr. ROSE. Right now, there's no question that the free market is not enough of an incentive, or a funder, provider of either capital for starting up, or funds for advanced development, for companies to advance products in this space. I think BARDA is a splendid and very effective addition, but getting it started—it's not easy to spend

$400 million a year on advanced development, and do it wisely. But, the—BARDA has a terrific leader, the size of the agency has grown exponentially in just the last few years, and the size of its research portfolio has increased dramatically.

I think you shouldn't underestimate the quality of the work that you've already done to put this in motion. But, the nature of this is such that making a new antiviral drug or a new vaccine is not something that happens on a timeframe of weeks and even years. It's a multiyear process that requires the underlying science to be handled, the creation of new chemical entities—be they proteins, vaccines, small molecules, and the like—that target new targets that are abundant now, that have been identified with basic research at institutes like the NIAID. Then it requires setting up a manufacturing capability and clinical trials to document effectiveness, or not. And in the case of agents against things like smallpox and anthrax, you can't do human efficacy testing, because it's not ethical and it's not practical.

So, it is very, very complicated, complex, long-leadtime work. And you've already, I think, had the good judgment to fund it. I think, repeatedly, we see that people want to pull the plug, thinking there's something wrong with this process because you're not seeing, you know, drugs for Ebola, drugs for some of the hemorrhagic fevers, and some of the newer vaccines, that you want to see. But, they're coming. And they're a lot further along than they were just a couple of years ago, because of this mechanism. And, if anything, I'd say, stay the course in that regard.

Senator COCHRAN. Thank you very much for that analysis.

Dr. Pavia, in your statement you mentioned the use of pandemic vaccine in a widespread way should be the central strategy, as I understood, it for the protection of human health during a pandemic. Do you think the Federal Government needs to be the lead on this, or should we create some other body to be in charge?

Dr. PAVIA. Senator, I think that—it's very clear that, in a severe pandemic, we would need to be able to vaccinate everyone in a rapid fashion, and that would require a very large manufacturing capacity, as well as the platforms, the new techniques that would produce the vaccine quickly enough. I don't think that, at present, market forces will either deliver a manufacturing capacity that would make 300 to 600 million doses available a year, nor is it clear that it—that, all by themselves, they will allow the development of these new technologies. So, I think there's a vital role that the Federal Government has to play in facilitating both the science that will allow new products to be developed, and then nurturing them along.

And, at the other end, I think the Federal Government has a role in providing enough manufacturing capacity on U.S. soil that we're not dependent on foreign manufacturers in the event of an emergency. And you've already made investments in this. And you should realize that the investment in egg-based manufacturing, in Pennsylvania, paid off in a large way. Without that, most of the domestic production that we had during this last pandemic wouldn't have occurred. And two of the foreign manufacturers with whom the Government contracted did not deliver the full amount of vaccine that they contracted for.

Senator COCHRAN. Colonel Larsen, what is your reaction to that question?

Colonel LARSEN. Well, sir, I—you know, I'm pretty conservative on the fiscal side, being a fourth-generation Indiana corn farmer, and—but, I tell you, how many B–2 bombers would we have built if we had relied on the private-sector free-market economy? There are certain things that are so important for national security that that's what we have to do up here. And I think we have to rely on the talent and the brainpower and some of the creativity, but this is a national security issue. We would never have built a single B–2 bomber if we'd a just told those companies, "Well, you can just go out and do it all on your own, and if you get something the FAA approves and the Air Force likes, then we'll give you your first dollar."

So, this—I mean, that's my point—this is a national security issue. That's how I see it.

Senator COCHRAN. Well, thank you.

I think this was a very worthwhile hearing, and your contributions have been very helpful. And I think we'll—I hope—have some influence as we go about making the decisions on priorities for funding and carrying out our duty to help protect the security interests and the health of our American public.

Thank you.

Senator HARKIN. I would also say thank you to the panel, and again for all the work that you do and the leadership you provide.

I was reading your testimonies last night, and then following you today, and then—I just—I can't help but think that it's not streamlined enough, in terms of who's in charge, and who does what, and who reports to whom, and who gets the finances to do this. Kind of a mishmash of things. And, quite frankly, I just—I think we're relying too much on the FDA.

Now, before all the press runs out of here and say, "Harkin wants to diss the FDA"—we're about to pass a new food safety bill. It's got great bipartisan support. It's being held up a little bit, but it's going to pass. It's got industry support and consumer support, and everybody, and it's long overdue. We haven't done—had a food—a change in our inspection systems—it's been over three decades. But, that job goes—a lot of that goes—to FDA. It's not agriculture, it's FDA. So, we're going to ask them to do more.

And we're not going to give them the funds or the personnel to do that. It's—you know, we'll give them a little bit, maybe, but not much. And it just seems to me, FDA's got so much on their plate that they really can't give this the kind of focus that it should.

So, I'm just—I'm just thinking out loud here—is it FDA, or do we need to take something out of the FDA, something, maybe, out of DOD, that would be put under BARDA, and let BARDA be the one, the lead agency? At least that's what I thought the concept was of BARDA, that they would be the lead agency, working with scientists, manufacturers, people like the colonel, and others, that think about all these things. And then they would then have line-item authority, in terms of looking at licensure, which I'm—still don't understand why we can't get over that, why we can't have it faster—and doing some of the things that FDA now is charged with the responsibility of doing. Because FDA just—institutionally, I

don't know that they can do it. It's just—because they've got so much to do, and they have other responsibilities, and mostly they're focused on drugs that we take; you know, drug development for new drugs for illnesses and things like that. This is not the biggest thing on their plate. But, in terms of the country itself, it's probably one of the biggest things we've got confronting us right now.

So, I don't know, I just keep thinking that we need some restructuring here—not for restructuring's sake, but to make it more efficient, to make the line items—make the line authority better, and to speed up some of the things that we have to—we just have to speed these things up faster than what we're doing.

So, I don't mean to just pick on FDA, but just recognizing the reality that FDA simply can't do all the things we're asking them to do. They just can't do it. And that's why, I thought, we set up BARDA.

And so, I will be looking at that, both from the standpoint of this subcommittee, but also the authorizing committee, in the next reauthorization bill that comes up. When is that? Aha, next year.

Senator HARKIN. So, next year we'll look at the reauthorization, because I just—I think now's time to take stock and think, on the reauthorization, do we need to do some realignment here? And I'll take into consideration the Vice President. I never thought about that, the—maybe we don't think about the Vice President that much. I mean, you know—what's that old saw about——

Senator COCHRAN. I don't think I'm going to get into this.

Senator HARKIN [continuing]. Some guy said that—he had two sons—one went off to the South Pacific, and the other became Vice President, and neither was heard from again.

Dr. ROSE. Can I comment on the FDA?

Senator HARKIN. Yes.

Dr. ROSE. Because I think that your comments are thoughtful and important, and where we are now is not working. But, I think that the proposal that HHS is making now is a very substantive and important change that they're proposing, particularly the funding issue.

I mean, what we see, in our interactions with the FDA, is, they're just quite short-handed, and their ability to respond to real-time science is hampered by their lack of manpower. This whole issue of regulatory science, I think, is an important issue, but I think there's also an issue of regulatory culture, because there are some things—particularly if you're using things like the animal rule—the level of proof of efficacy of a drug for a measure that you can't test in humans is just not going to be the same standard of certainty. That doesn't mean you can't make a judgment based on a body of evidence. But, I think there's an enormous reluctance to recognize the limitations and still act. And that culture change, I think, needs to be part of the FDA change, as well.

But, delaying that, I think, would be a big problem.

Senator HARKIN. See, now, you and I are coming at this a little differently. You want to change the culture at FDA. And I've been here long enough to think I'm not certain we can do that. I mean, it's just—it's just very difficult to do that, okay? It's just difficult.

Yes.

Colonel LARSEN. Sir, I think leadership is one way to do that. And I know Dr. Peggy Hamburg has said we've got to stop looking at things in black and white and the various shades of gray, which is some of the things that Eric's talking about. And so, I have great confidence in what she's saying.

I am intrigued about your comments, though, because I went through this, sir, with Goldwater Nichols, which is one of the finest things that ever came out of the U.S. Senate, in terms of national security. And we didn't do away with the Army, Air Force, Navy, and Marines, but we did build a structure where they could work together far better.

Senator HARKIN. That's right.

Colonel LARSEN. And maybe what FDA needs the most is enough money to do the job properly. They're too small today. And you said that yourself, sir.

Senator HARKIN. That's absolutely true. For all that we put on their plate.

Colonel LARSEN. Yes.

Dr. ROSE. I've proposed that the FDA actually create a center for biodefense, like CDER, like CBER, where there's actual leadership——

Senator HARKIN. Okay.

Dr. ROSE [continuing]. At a higher level. Because our experience is that, when you bring these complicated products to the FDA, by and large the review is done—I'm a surgeon by trade—before it's done by the intern, instead of having senior leadership engaged in the actual review early on, looking at the raw data. And I think that having a full-blown center, where there's a leader that is responsible for signing off and guiding this, I think, could be very helpful.

Senator HARKIN. Now, that's a good idea. I like that. You got anything more on paper on that at all, any suggestions? Or are you just——

Dr. ROSE. We'll make sure you get it.

Senator HARKIN. Or are you just thinking about that right now?

Dr. ROSE. No—well, I've proposed at the IOM in February, but—there, it got shot down, but I hear it's getting some traction.

I still think it's a good idea.

Senator HARKIN. I kind of like it. Yes, get me some stuff on that, will you?

Dr. ROSE. Yes.

Senator HARKIN. Get it to my staff?

Dr. ROSE. Sure.

Senator HARKIN. Before our reauthorization comes up.

Dr. ROSE. Sure.

Senator HARKIN. I'd like to start thinking about it now, and looking at it.

Dr. ROSE. Yes.

Senator HARKIN. Yes. Okay. Well, anything else anybody want to add to what we've said?

If not——

Yes.

Dr. PAVIA. No, I'd echo what Eric Rose suggested, in that you can't have the same people evaluating a drug for high blood pres-

sure that are evaluating a crucial drug for biodefense or for an influenza pandemic, and yet, we need professionals to look at the safety and efficacy. I think it can be done within FDA, but not in the current structure. And I think Dr. Hamburg has some very good ideas for redoing this. But, it may require some statutory and legislative changes to let them do that and to apply appropriate standards that match the risk that we're facing.

CONCLUSION OF HEARING

Senator HARKIN. Well, thank you all very much. I thought this was very interesting and intellectually challenging, and you gave us some good ideas and suggestions, and we appreciate it very much.

And I look forward to getting that from you, Dr. Rose, about this new structure.

So, thank you all very much.

Anything else? No.

The subcommittee will stand recessed.

[Whereupon, at 4:03 p.m., Thursday, September 29, the hearing was concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

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