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CAN BIOSHIELD EFFECTIVELY PROCURE MEDICAL COUNTERMEASURES THAT SAFEGUARD THE NATION?

HEARING

BEFORE THE

SUBCOMMITTEE ON EMERGING THREATS, CYBERSECURITY AND SCIENCE AND TECHNOLOGY

OF THE

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CAN BIOSHIELD EFFECTIVELY PROCURE MEDICAL COUNTERMEASURES THAT SAFEGUARD THE NATION?

Wednesday, April 18, 2007

U.S. HOUSE OF REPRESENTATIVES,
COMMITTEE ON HOMELAND SECURITY,
SUBCOMMITTEE ON EMERGING THREATS, CYBERSECURITY,
AND SCIENCE AND TECHNOLOGY,
Washington, DC.

The subcommittee met, pursuant to call, at 1:18 p.m., in Room 1539, Longworth House Office Building, Hon. James Langevin [chairman of the subcommittee] presiding.

Present: Representatives Langevin, Thompson, Lofgren, Jackson Lee, Christensen, Etheridge, Green, McCaul, and Lungren.

Mr. LANGEVIN. [Presiding.] Good afternoon.

Today the subcommittee will receive testimony regarding the BioShield program, focusing specifically on some recent difficulties within the program.

Biological threats, both manmade and naturally occurring, present a real danger to the security of the United States. We must, therefore, do everything in our power to create and maintain robust tools to protect against these threats.

Project BioShield can and should be an important component of our nation's defenses against such threats. This critical program is far too important to fail.

Unfortunately, since its creation, BioShield has enjoyed varying levels of success, and, in recent months, there have been some fairly significant setbacks this committee is particularly concerned with.

The cancellation of the $877 million anthrax vaccine contract, the largest under BioShield, after VaxGen invested $175 million of its own funds, does not bode well for the future of the program. Problems must be identified and fixed, and we must learn from any mistakes that have been made.

Also of concern was the decision in March to close the request for proposals for a medical countermeasure to treat acute radiation syndrome.

As this subcommittee is responsible for preparation and response for both nuclear and biological attacks, we are especially concerned about these two cancellations. However, our witnesses on both panels should not assume that this subcommittee has pre-judged these matters.

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The BioShield process is a complicated one, and we are here today to hear from our witnesses about their experiences navigating the process.

Our private-sector witnesses have had different experiences working with the program, and this subcommittee asked them to be here for precisely that reason. Our witnesses from the Departments of Homeland Security and Health and Human Services hold additional pieces of the BioShield puzzle.

Dr. Runge from DHS and Dr. Parker from HHS represent the lead offices for BioShield activities in the two departments.

Although not officially part of the BioShield program, the NIH and the FDA have played important roles in the process, including the VaxGen contract cancellation, and we have to better understand and define their roles if we want the program to succeed in the future.

The new Biodefense Advance Research and Development Authority, BARDA, may also have a role to play by supporting transitional research and development and bridging the so-called "valley of death" between early basic research supported by NIH and final development and production.

However, that will not happen by itself. I believe we need to provide a more definite roadmap on how all these moving pieces fit together. That is the proper role of oversight, and that is our responsibility on this subcommittee.

I am hopeful that today's hearing will shed light on some of the difficulties of implementing Project BioShield. I am also hopeful that after hearing from our two panels, we will gain insight on how best to move forward and fix some of these problems.

We must work together to ensure that Project BioShield remains an effective line of defense. I believe that today's hearing is a good first step towards that goal, but I also understand that the solutions will not be simple—they will take time, cooperation and diligence on all of our parts.

I want to thank both of our panels, witnesses, for taking time to appear before our subcommittee today and I look forward to their testimony.

The chair now recognizes the ranking member of the subcommittee, the gentleman from Texas, Mr. McCaul, for the purposes of an opening statement.

Mr. MCCAUL. Thank you, Mr. Chairman.

In my judgment, the greatest threat we face today is a chemical, biological or nuclear attack on the United States. Such an attack could kill hundreds of thousands, possibly millions of our citizens.

I remember reading the book "The Hot Zone," which described the threat of the Marburg virus and whether that could actually—we could develop an airborne strain that could kill thousands, if not millions of people in a very short period of time.

I also toured several level four facilities and you see up close and personal the threats of these biological agents, what they call "the demon on the jar." We all know the Soviet Union has weaponized many of these agents and after September the 11th, we had a scare and a threat from the anthrax strain that we have still not to this day, in my judgment, adequately addressed.

Project BioShield plays a key role in addressing this threat. It remains unclear how well it is in achieving its goals. The basic premise of BioShield is to increase the strategic national stockpile with medicines to treat those who would be affected by an attack and to encourage private industry to develop new countermeasures.

Obviously, BioShield has had a rough start and it is up to us in the Congress to help solve some of the problems that this program has faced.

There have been problems regarding the rate by which DHS completes material threat determinations. HHS has made what I consider to be missteps. There have also been issues with the transparency and the overall management of the BioShield program.

To be fair, though, without BioShield, we would not be stockpiling the countermeasures we have today, including an antidote to the botchulinum toxin anthrax vaccine and two types of anthrax treatments and two kinds of countermeasures against radiological and nuclear agents.

Without BioShield, no companies would be working on these countermeasures at all. So I have also seen encouraging chances to see how BioShield does business.

DHS used to take about 4 months to complete a material threat assessment on just one agent. They changed their process and have significantly reduced that period of time.

The Pandemic and All Hazardous Preparedness Act, introduced by my Republican colleague, Senator Burr, and passed last year establishes the Biomedical Advanced Research and Development Authority.

And at this time, Mr. Chairman, I would like to ask unanimous consent that that report be entered into the record.

PREPARED OPENING STATEMENT OF HON. MICHAEL T. MCCAUL, RANKING MEMBER, SUBCOMMITTEE ON EMERGING THREATS, CYBERSECURITY AND SCIENCE AND TECHNOLOGY

Thank you Chairman. I' like to preface my remarks by saying if it were not for Project BioShield and the government's grant funding in this arena, we would not be here today. There would be nothing to discuss. While we wouldn't have the failed acquisitions that we'll be hearing about, we also wouldn' be stockpiling the countermeasures that we are currently—including an antidote to botulinum toxin, anthrax vaccine, two types of anthrax treatments, and two kinds of countermeasures against radiological or nuclear agents. No companies would be working on biodefense vaccine and therapeutic targets at all. So while the process may have had a rough beginning, let's bear in mind Congress tasked the Department of Homeland Security (DHS) and the Department of Health and Human Services (HHS) and its agencies with an enormous challenge, building the BioShield initiative from the ground up. The magnitude of the public-private partnership necessary for BioShield to protect the nation from CBRN threats is unprecedented in the area of biopharmaceutical development.

Drug development is an inherently expensive, slow and risky business. It can cost more than $1 billion to launch a technically successful drug and take 12.5 years. And only 8% of the products entering trials actually make it to the market. Perhaps only the movie industry tolerates such enormous costs and failure rates in the search for blockbusters, but they can go from concept to commercial success in a few years, whereas the average for pharmaceutical development is more than a decade. While we sitting here aren't in the movie business, nor can we do much to minimize the failure of programs due to scientific or technical problems, we can confront this risk and ensure the BioShield process has mechanisms in place to address this risk. We must also ensure BioShield is managed with the sense of urgency under which it was conceived. With the terrorist threat growing every day, we don?t nearly have enough medical countermeasures we will need to respond and save lives.

Without a model to provide a blueprint of how best to implement BioShield, one common feature of a successful startup is adaptability, not being afraid to make decisions and change direction. While "adaptability" and "Federal Government" appear to be at odds most of the time, I have already seen positive indications that DHS and HHS are learning from their experiences and evolving their strategy based on both their failures and successes to-date.

During a past hearing, DHS testified that it typically took them four months to complete a material threat assessment on just one agent. At that rate, it would take on the order of 9 years to make it through all the agents on the CDC bioterrorism list, and this only accounts for the biological agents, not the chemical or radiological ones! Fortunately, DHS has found a way to fulfill their responsibilities expeditiously and have now completed threat determinations and associated assessments for *all* the biological agents and is working on the list of chemical agents.

HHS. Well, HHS has the toughest job of managing risk—risk to the government in awarding only one contract for a product that has a large chance of failing scientifically or technically during one of the lengthy stages of development and testing, or risk to the private sector, especially less-established companies, that may not have the necessary financial resources necessary to support advanced product development prior to receipt of payment upon delivery of their product to the stockpile. We owe my Republican colleague, Senator Burr, credit for ushering through legislation last Congress that will provide HHS with the tools it needs to help manage these risks. The Pandemic and All Hazards Preparedness Act establishes the Biomedical Advanced Research and Development Authority (BARDA) to provide much needed late-stage research and development funding and allow for incremental payments that will shift some of the risk away from BioShield acquisition programs. In theory, funding this part of the development process, the so-called 'Valley of Death', could allow countermeasures to mature further through the development process before competing for a Project BioShield contract, and it could allow multiple products to be supported in parallel in case one should fail during development. This will reduce the risk that a countermeasure will fail while under a Project BioShield contract.

What I believe to be most promising is the formation of the interagency Public Health and Emergency Medical Countermeasure Enterprise in 2006 in an effort to streamline the BioShield process. Just using the term 'T3Enterprise demonstrates that HHS and DHS grasp the enormous challenges and understand the limitations within which it has to work to enable BioShield's success.

- First, an enterprise is a readiness and willingness to undertake new, often risky and complicated, ventures and initiatives. What?s more risky and complicated than drug and vaccine development?
- Second, an enterprise represents a business organization. Businesses need to work in partnership, engage in dialogue and coordination, to develop clear and predictable requirements. Businesses can only be successful in developing products with a clear understanding of the end goal. Businesses develop objectives within a framework that addresses the complexities of their industry, in this case the biopharmaceutical industry, and contains the appropriate level of specifications and delivery terms.
- And finally, an enterprise is diligent and systematic in its activities. A comprehensive strategy is needed that addresses the various threats, current and future, for which we must prepare. BioShield is one part of this strategy, BARDA is another, and the basic research funded by NIH is yet another. The objectives of each must be aligned and as products move through the different phases of development, investments must be reevaluated to avoid potentially life-saving products falling into the "Valley of Death".

Only an Enterprise can take on BioShield. With DHS, HHS, and the private sector working together in this Enterprise, to harness modern scientific tools and industry expertise and taking smarter approaches to drug development and acquisition, we can improve BioShield's prospects, making it more efficient—yes faster—with less chance of failed contracts, so that new medicines can get to the Nation's stockpile and ultimately be available to the patients who may need them.

I thank our witnesses for coming today and I look forward to hearing their testimony and hope that this hearing spurs further progress in realizing the true potential of BioShield.

Mr. LANGEVIN. Without objection.

Mr. MCCAUL. Thank you.

In my view, this legislation will provide much needed late stage research and development funding and should reduce the risk that

a countermeasure will fail while under a Project BioShield contract.

And at this time, Mr. Chairman, I would also like to say we are seeing changes to how the interagency process works, including the implementation of Homeland Security Presidential Directive 18 and the formation of the Public Health Emergency Countermeasure Enterprise.

We all know that drug development is an inherently expensive, slow and risky business. It can cost more than $1 billion to launch a technically successful drug and take approximately 12.5 years. And we also know that only eight percent of the products entering trials actually make it to the market.

While we can't do much to minimize the failure of programs due to scientific or technical problems, we can confront this risk and ensure the BioShield process has the appropriate mechanisms in place.

The important thing to remember is that the terrorist threat is growing every day, and we don't have enough medical countermeasures that we need to respond to a weapon of mass destruction attack.

Time is of the essence, and the time to act is now.

I thank the chairman, and I yield back the balance of my time.

Mr. LANGEVIN. I thank the ranking member.

The chair now recognizes the chairman of the full committee, the gentleman from Mississippi, Mr. Thompson, for the purposes of an opening statement.

Mr. THOMPSON. Thank you very much, Mr. Chairman, and I would like to thank you for holding this important hearing and thank our witnesses for being here today.

As Chairman Langevin noted in his opening remarks, BioShield is a new program. That said, new doesn't necessarily equate with a license to make mistakes. Yet, mistakes have been made with regard to the development and implementation of the program.

I would like to believe that those were honest mistakes and that by doing proper oversight, we can figure out what problems exist and address them. We need to get the program to a state where it is procuring enough medicine and vaccine to protect the American people.

To date, Project BioShield has only awarded contracts for immunizing against or treating anthrax, botchulinum toxin and radiological sicknesses, even though the CDC has listed over 30 select agents of concern.

After the VaxGen contract cancellation, BioShield currently has contracts for 10 million doses of the old anthrax vaccine currently used by the military, as well as two much smaller contracts for new anthrax treatment, one of which is held by a witness from Human Genome Sciences.

Now, the largest contract under BioShield is a $363 million contract for 200,000 doses of botchulinum antitoxin. The remaining contracts are for protection from radioactive materials.

These contracts account for nearly $1 billion of the $5.6 billion 10-year BioShield fund and deal with only three agents and not comprehensively, by any measures. In contrast to this fund, Pfizer,

for example, spends over $7 billion annually on research and development.

Does this program make sense at all, Mr. Chairman? Can it succeed if we identify the right problems? That is what I hope we will get to today in the answers from our witnesses.

I look forward to the testimony, Mr. Chairman, and I yield back the balance of my time.

Mr. LANGEVIN. Thank the chairman for his statement.

Other members of the subcommittee are reminded that under the committee rules, opening statements may be submitted for the record.

I want to now welcome our first panel of witnesses. Let me begin by saying, as you may know, VaxGen was originally supposed to be part of today's discussion and I think a very important part of today's discussion.

However, because HHS and VaxGen were unable to reach an agreement concerning the testimony, they will, unfortunately, not come before our subcommittee today, although their testimony, I believe, is critical, a critical element of this discussion and I look forward to a time in the near future when they may testify before this subcommittee.

And for the record, I had the opportunity to speak with representatives of VaxGen, who very much wanted to testify today, and they are here, but for the fact that HHS would not sign off and allow them to testify without repercussion on a recent settlement between HHS and VaxGen after the cancellation of the recent contract to develop the next generation anthrax vaccine.

I am both disappointed and upset that HHS would not grant that sign-off, but we will have further discussions as we go forward and I hope to have VaxGen before us at the earliest possible opportunity.

Our first witnesses are Richard B. Hollis, founded Hollis–Eden in August 1994 and currently serves as chairman, president and CEO. Mr. Hollis has over 29 years experience in the healthcare industry, has a proven track record of launching and marketing important new medical products, and a distinguished career of managing the growth and operations of companies in a variety of senior management positions.

Our second witness is James Davis, executive vice president and general counsel and secretary of Human Genome Sciences, where he has served since 1997. From 1995 to 1997, Dr. Davis was of counsel to the Washington, D.C., law firm of Finnegan, Henderson, Farabow, Garrett and Dunner, LLP.

Prior to this time, Dr. Davis served in a number of capacities with the agricultural biotechnology company, Crop Genetics International. Prior to joining Crop Genetics, Dr. Davis was a partner in the Washington, D.C., office of Weil, Gotshal and Manges.

Without objection, the witnesses' full statement will be inserted into the record and I now ask each witness to summarize their statements for 5 minutes, beginning with Mr. Hollis.

Again, I want to thank you both, again, for being here. We look forward to your testimony.

STATEMENT OF RICHARD HOLLIS, CHIEF EXECUTIVE OFFICER, HOLLIS-EDEN PHARMACEUTICALS, INC.

Mr. HOLLIS. Mr. Chairman, members of the committee, thank you for very much for this opportunity.

Shortly after 9/11, we were contacted by the Department of Defense and asked to develop our investigational drug, Neumune, to protect American citizens from a nuclear terrorist event. Since that time, we have committed over $85 million in developing Neumune and, to our knowledge, Neumune remains the leading drug candidate for the treatment of acute radiation syndrome, otherwise known as ARS, by the Department of Defense's Armed Forces Radiobiology Research Institute.

To date, Hollis-Eden has been recognized as the world leader in developing a drug for this indication because of the following—we have the first and only open IND at the FDA for a drug candidate specifically for the treatment of acute radiation syndrome.

Neumune is the only compound in peer-reviewed published papers to demonstrate a statistically significant survival benefit in non-human primates exposed to lethal doses of radiation without any other clinical support.

Over 120 humans have been involved in the clinical trials with Neumune and the safety profile is similar to placebo. Neumune is further along in the development than any other medical countermeasure for acute radiation syndrome.

With this background, I would encourage you to take a very critical look at the government's words and actions in our case.

Let me focus on the law. The purpose of BioShield legislation was to incentivize the private sector by setting guaranteed markets where none currently exists for promising countermeasures to weapons of mass destruction and to award advance purchase contracts before a drug is fully approved or licensed by the FDA.

This is a creative and market-driven idea to spur investment capital and industry participation. However, that is not how HHS is implementing the BioShield bill today. The legislation clearly states that a BioShield countermeasure must have a sufficient and satisfactory experience or research data to support a reasonable conclusion that the drug candidate will qualify for licensing with the FDA within 8 years.

Instead, the agency now requires countermeasures to be BioShield eligible, a term that appears nowhere in the law, is subjective and can arbitrarily require a drug candidate to be significantly further along in development than the law requires.

This undermines the criteria under BioShield legislation for advancing purchase contracts for promising medical countermeasures well before FDA approval.

Mr. Chairman, considering the facts, I am totally at a loss to explain how the agency could determine our proposal did not meet the requirement of BioShield legislation.

To help us all understand this, allow me to respectfully suggest a few questions I would like you to ask the agency.

If a promising development stage drug like Neumune does not meet the requirements for a BioShield advance purchase contract, what drug does?

Why were we told that our company's proposal was in the competitive range for this award for 9 months before being told, with no warning, that our proposal was technically unacceptable?

The law requires the agency to procure the best possible countermeasures in development today. Was the agency waiting for something better to be developed?

Why didn't the agency comply with the legislation and award the advance purchase contract to allow our company to continue to develop the drug?

Why did the acute radiation syndrome drug evaluation from RFI to RFP take over 2.5 years? And why were there four delays in the final 9 months of negotiations from June 2006 to March 2007?

Does the final decision to cancel this RFP have anything to do with the BARDA legislation that was passed in December of 2006?

Is there a conflict of interest between investor-funded companies and NIH taxpayer-funded entities when the NIAID, which awards research grants to develop biodefense countermeasures, is the same agency that advises HHS on which drugs to award contracts to?

These last questions underscore how HHS's own actions have created the valley of death, which the agency claims has undermined the program.

I want to be perfectly and absolutely clear about this—there is no valley of death in the private-sector markets for known attractive commercial products and market opportunities.

By changing the criteria for awarding the advance purchase contracts and thereby not setting the markets early for these important medical countermeasures, the agency has eliminated the investment community from funding BioShield research and development.

So in other words, the legislation, the way it is being implemented, has created the valley of death.

Mr. LANGEVIN. If you could just—

Mr. HOLLIS. I am almost done here.

When government officials tell you that the pharmaceutical sector has responded to BioShield and so their agencies need more authority, power and money, realize that these actions are the same, come from the same officials that have driven companies and investors away from the program.

So the failing of BioShield, from my perspective, will have serious consequences for our national security and because HHS has failed to act according to the law, we have suspended the development of Neumune.

And in conclusion, as we and other companies have learned in this process trying to do business with the government under Project BioShield, as implemented by HHS, appears to be more about politics than protecting the American citizens and following the law that Congress approved.

Mr. Chairman, thank you very much, and I welcome the opportunity to answer any questions.

[The statement of Mr. Hollis follows:]

PREPARED STATEMENT OF RICHARD HOLLIS

Chairman Thompson, Chairman Langevin, Ranking Members King and McCaul, Members of the Committee, thank you for the opportunity to appear before you to

discuss the state of Project BioShield and the experience of Hollis-Eden Pharmaceuticals.

I have previously testified four times on these issues before various Congressional committees during the last Congress. Unfortunately, not much has changed to fix the BioShield Program. As I have testified before, HHS is not implementing the BioShield legislation as Congress intended. Additionally, Project BioShield will continue to fail unless it can attract private sector participation—and that is the result of the lack of transparency, missed timelines, poor communication and the inexperience of agency representatives. Mr. Chairman, it is my strongest hope that this hearing signals that things will be different going forward. Absent such a sea change, the BioShield program will remain fundamentally broken. Novel next generation medical countermeasures to protect American's from future terrorist attacks involving a weapon of mass destruction may never materialize. I hope this Committee and the other relevant Congressional Committees will do whatever is necessary to remedy this situation.

Allow me to begin with a brief history of our attempt to answer the call by our nation to develop the first practical treatment to the life threatening effects of radiation exposure, a condition known as acute radiation syndrome or ARS.

- Shortly after 9/11 we were contacted by the Department of Defense and asked to develop our investigational compound NEUMUNE® to protect Americans from ARS in the event of a terrorist attack with a nuclear or radiological weapon in one or more of our cities.
- Since that time we have committed $85 million in developing NEUMUNE.
- To our knowledge, NEUMUNE remains the leading drug candidate of DoD?s Armed Forces Radiobiology Research Institute, or AFRRI.
- To date, Hollis-Eden has been recognized as the world leader in developing a drug for this indication because of the following:
    - We have the only open IND with a drug candidate specifically for the treatment of ARS.
    - NEUMUNE is the only compound, in peer reviewed published reports, to demonstrate a statistically significant survival benefit in non-human primates exposed to lethal doses of radiation without any other clinical support.
    - We have shown statistically significant benefits in tests involving more than 300 nonhuman primates
    - Over 120 humans have been involved in clinical trials with NEUMUNE, and the safety profile is similar to placebo.
    - NEUMUNE is further along in development than any other medical countermeasure for ARS.

With our history in mind as you consider the remainder of my testimony I encourage you to take a very critical look at the government?s words and actions here?far more critical than has been the practice to date.

The expertise in these matters lies with the private sector, not with the government. BioShield is intended to incentivize the private sector to develop medical countermeasures to better prepare and protect this nation from a terrorist attack using WMD. With all due respect, in dealing with HHS we were surprised and disappointed with the reasons the agency gave for decisions made during the procurement process. Although HHS may have good intentions, the expertise required to successfully develop a practical medical countermeasure for a nuclear mass casualty scenario resides in the private sector.

Allow me to illustrate this point. In late 2005, the news show "60 Minutes" did a segment on HHS? failure to protect the American people from a nuclear attack by deciding the government needed to stockpile only 100,000 treatment courses of a medical countermeasure for ARS that could save lives in the immediate aftermath. During the due diligence process for the episode, 60 Minutes discovered that HHS? rationale for ordering such a small number of treatment courses was because they were planning to treat the potentially hundreds of thousands of ARS victims in hospitals. Unfortunately, experts who have studied nuclear scenarios have concluded this will be very challenging if not impossible. This is precisely why a safe and effective practical medical countermeasure that could be self administered without any other medical support should be embraced by the agency as the only viable option for the majority of victims.

To highlight the lack of understanding of the appropriate medical treatment for ARS altogether, when HHS was asked by members of Congress as to why the major requirement detailed in the final RFP for the ARS drug focused on treating neutropenia (infection) when the major issue behind mortality for ARS victims is both neutropenia and thrombocytopenia (bleeding), HHS told then-Government Reform Committee Chairman Davis in writing that every hospital in America had

drugs to treat neutropenia as well as a supply of "flash frozen platelets" that could be utilized in the event of a nuclear or radiological event. HHS also suggested to others that there were two Navy ships "off the coast" with similar stockpiles of frozen platelets.

When challenged by 60 Minutes, HHS had to admit that there was no such thing as "flash frozen platelets" and there were no such Navy ships, let alone the hospital beds to treat the hundreds of thousands of victims who may suffer from acute radiation syndrome in a mass casualty scenario. This was not a one-time misstatement; it was the agency?s rationale as to why there was no rush to procure too much of a practical next generation medical countermeasure that may alleviate the need for hospitalization and blood products. The government's response was not to fix the problem; rather it sought to find like-minded experts to support their position and lack of urgency in providing the country with a practical medical countermeasure and adequate nuclear emergency response plan.

As this Committee examines the BioShield program, I would respectfully suggest that the starting point must be the BioShield law that Congress passed and the President signed. As stated in my previous testimonies, the BioShield legislation was written in such a way that it would incentivize the private sector pharmaceutical and biotech industries by setting guaranteed markets for companies having promising technology that might be developed over time and used to protect the American people from WMD terrorism. The concept of awarding advance purchase contracts that would define the market (identify how many doses or treatment courses the government was going to buy and what the government would pay upon successful delivery) up to eight years before FDA approval was a brilliant market-driven idea. However, unfortunately for the American people, that is not how BioShield is being implemented today.

The law clearly states that a qualified BioShield countermeasure "is a countermeasure for which the Secretary determines that sufficient and satisfactory clinical experience or research data (including data, if available, from pre-clinical and clinical trials) to support a reasonable conclusion that the countermeasure will qualify for approval or licensing within eight years." The law further provides that in issuing a call for the development of such countermeasure the Secretary shall state: "(i) estimated quantity of purchase (in the form of number of doses or number of effective courses of treatments *regardless of dosage form*); (ii) necessary measures of minimum safety and effectiveness; (iii) estimated price for each dose or effective course of treatment regardless of dosage form; and (iv) other information that may be necessary to encourage and facilitate research, development, and manufacture of the countermeasure or to provide specifications for the countermeasure." (emphasis added) This is how the law says the program shall work. Implementing the program in accordance with these parameters is a nondiscretionary duty of the agency.

Unfortunately HHS has chosen to implement the law in a manner that conflicts with these provisions and the Congress' statutory intent. They have taken it upon themselves to change the definition of the provision "support a reasonable conclusion that the countermeasure will qualify for approval or licensing within eight years." HHS has stated that countermeasures must be "BioShield eligible," a term that appears nowhere in the law, before they can award an advance purchase contract. And the bar as to what constitutes "BioShield eligible" has been applied in an arbitrary manner that is significantly higher than what the law provides. HHS' BioShield eligibility requirements, as they have been applied to us, are essentially just shy of what we would be required to show to obtain full FDA approval. In other words, to be "BioShield eligible" according to HHS, a countermeasure must be significantly further along in development than was contemplated under the specific language of the BioShield law. This new, arbitrary requirement undermines the BioShield Program and Congress' intent for awarding *advance* purchase contracts for promising medical countermeasures years before they would be FDA approved.

When HHS rejected our RFP proposal, after telling us on multiple occasions that our proposal was in the competitive range, they did so precisely by so changing the criteria for an award. Numerous peer reviewed studies have been published demonstrating the efficacy of NEUMUNE in animal models of radiation exposure. We have shown that NEUMUNE can significantly increase survival rates if administered post exposure. This survival benefit derives from the fact NEUMUNE mitigates both the neutropenia and thrombocytopenia conditions of ARS without the need for other medical support. Over 100 healthy volunteers have been involved in NEUMUNE safety trials, without any significant adverse health effects. In fact, NEUMUNE?s impact on humans isn?t just safe; it is beneficial—increased levels of neutrophils and platelets—such that we have been cleared by the FDA to conduct Phase I/II clinical trials using NEUMUNE to potentially help patients ward off hospital-acquired infections.

Obviously NEUMUNE still needs to be proven safe and effective in large pivotal trials that were planned to take place once an advance purchase contract was awarded. That is how BioShield is supposed to operate under the law. Further, under the specific terms of the RFP, these pivotal studies required pre-approval by HHS *after* contract award. In other words, the reasons HHS gave for rejecting our proposal conflicted not only with the statute, but also with the very terms of the RFP.

Mr. Chairman, I am honestly at a loss to explain how HHS decided to cancel outright the ARS RFP. We clearly met the requirements of the BioShield statutute—we estimate that our drug could have been stockpiled for emergency use in 2008 and approved by the FDA shortly thereafter, far less than the eight-year requirement provided in the law. HHS, even after the RFP was cancelled, admitted we met the mandatory requirements of the RFP. The agency repeatedly stated over the last nine months we were in the competitive range for a contract award, and only on the day of the RFP cancellation were we told otherwise. In fact, the agency has confirmed to third-parties we were the only company that remained in the competitive range. Peer-reviewed, published studies show NEUMUNE has a significant survival benefit against acute radiation syndrome, without significant adverse effects. We had no reason to suspect that HHS would fail to follow the BioShield legislation and not award an advance purchase contract to us, thereby preventing Hollis-Eden from being able to continue developing the drug to protect the nation.

As a result, in order to get to the real reasons for HHS' actions here, the Committee will need to fully investigate this process. Allow me to respectfully suggest a series of questions HHS should be asked to answer as part of that investigatory process:

1. If a promising drug candidate like NEUMUNE does not lead HHS to reasonably conclude "that the countermeasure will qualify for approval or licensing within eight years," then what product does? The agency itself told us that we met the RFP's mandatory requirements even after they cancelled the RFP. The Department of Defense?s experts, AFRRI, to this day continue to identify this drug as their lead ARS countermeasure and are still asking us to develop it. We have shown statistically significant benefits in tests involving more than 300 non-human primates, and to date demonstrated a good safety profile when NEUMUNE was tested in human clinical trials. We have achieved all these milestones at a cost of more than $85 million of shareholder dollars. If NEUMUNE doesn't qualify for an *advanced* purchase contract, what will?

2. Why were we told that our company was in the competitive range for this award for nine months before being told with no warning or discussion that we were "technically unacceptable"? Throughout the entire RFP process, we were repeatedly informed that we were in the competitive range—meaning that our drug met the mandatory requirements of the RFP, or in other words was "technically acceptable.". As is typical in these types of procurements, in June 2006 HHS requested each company in the competitive range to respond to specific technical issues raised by the Technical Evaluation Panel regarding such company's drug candidate.

We submitted complete responses to each issue in July 2006. Then, after reviewing our responses, and after a successful government audit of our costs and accounting system at our facilities, HHS informed us in October 2006 that we remained in the competitive range and that HHS wanted to conduct face-to-face meetings with us in Washington. At that meeting, the agency indicated they expected an award some time in January 2007. On January 31, 2007, HHS informed us that the new expected date of award would be March 7, 2007. For at least the last four and a half months of the RFP process we understand that we were the only company remaining in the competitive range. During this time, and in fact during the nearly eight months since our detailed response to the technical issues raised by HHS, none of the technical issues brought up in June were ever again addressed, not even during the face-to-face meeting with HHS. In fact, the only new information provided to HHS after we were confirmed in the competitive range and were the only company remaining was information that strengthened the case for NEUMUNE.

We answered all of HHS' questions. We provided them copies of a newly published preclinical study demonstrating NEUMUNE provided a survival benefit against lethal doses of radiation when given to monkeys after exposure. We confirmed and demonstrated for HHS that we were not on clinical hold, nor had we experienced any significant safety issues. The record will show we acted in good faith and met every request—for over a year. Given this record, on what basis could HHS determine that a drug candidate that was in the competitive range for months, then somehow, without any new negative information, suddenly was no longer acceptable? And even if there were any issues remaining, if HHS was truly interested in procuring a medical countermeasure for ARS to protect the American people, why

didn?t the agency engage in a good faith dialogue with us to resolve any such issues?

3. The BioShield law makes it patently clear that the agency is to procure **now** the best possible drugs to address the most significant threats this nation faces. Congress specifically created this requirement to ensure that the agency had a sense of urgency that reflected the race against time that we are in against the terrorists and others who want to do us great harm. Congress feared the agency would waste valuable time looking for the perfect drug at the expense of good drugs that could protect people now. Congress also understood that science is not linear. Just because one wants a perfect drug or cure doesn't mean that one will find it now, or perhaps ever. In medicine we constantly rely upon the good now in the absence of the perfect later.

For example, between 1981 and now, NIH, and in particular Dr. Fauci's NIAID, has spent billions in taxpayer dollars on HIV/AIDS research aimed at a cure, yet NIH still has not found one. In fact, the WHO now reports that by 2030 HIV/AIDS is expected to be the third most deadly global disease.

NEUMUNE was judged by HHS? own evaluators to be the only drug in the competitive range. After decades of research and testing thousands of potential drugs, the experts at DoD's AFRRI have identified this as their lead drug candidate. The President and Vice President have both repeatedly said the nuclear threat is the greatest threat we face. Each day we learn of new nuclear threats. NEUMUNE is the most advanced drug for ARS in development today and has an attractive safety profile—under BioShield that is all that should have mattered. Why didn't the agency comply with the legislation and award the advance purchase contract enabling the continued development of this important countermeasure?

4. If the Co-Chairman of the 9/11 commission believes 10 million treatment courses of an ARS drug would be required to protect the American people, and HHS had entered into contracts for anthrax and smallpox seeking tens of millions of doses, why was HHS only interested in procuring 100,000 treatment courses for ARS? DHS? own National Planning Scenario estimate for a single terrorist-size nuclear attack against one US city documents that a mere 100,000 treatment courses is inadequate under even the most favorable conditions.

5. Isn't there a conflict of interest when the NIAID, which awards research grants to develop biodefense countermeasures, then advises HHS on which products are ?BioShield eligible? for an advance purchase contract?

6. How does the determination of technical acceptability relate to the actual ability of a counter-measure to save lives? Bioshield has spent over $21 million to buy two chelating agents that the well-respected NEW ENGLAND JOURNAL OF MEDICINE has stated are useless in the event of either a nuclear or radiological attack. None of these drugs have ever been proven to have a survival benefit against lethal doses of radiation. According to their FDA-approved inserts, these compounds need to be given as quickly as possible after exposure. And the chelating agents must be given by medical personnel, which will be in extremely short supply after a nuclear attack. In contrast, our drug has been shown in DoD-administered, peer-reviewed studies to increase survival from lethal doses of radiation exposure if given up to four hours post exposure. It is self-administrable, requires no special handling, and needs no supportive medical care. How can a compound that has a survival benefit and fits the scenario be determined to be less technically acceptable than ones that do not? If such a paradox is possible under the program, this is a major flaw in its design.

7. Why did the evaluation for a drug to treat ARS, from RFI to RFP, take over 2 1/2 years—from October of 2004 until March of 2007? Why was the award decision delayed four times? In particular, how can the agency justify these delays when we were the only company focused on developing a drug specifically for this indication and now know that ours was the only proposal in the competitive range for much of this process? In late October of last year we had a very positive meeting with HHS officials where none of the technical issues deemed to make our proposal "technically unacceptable" were brought up, leading us to believe we were headed to a contract award. Did this delay, and the final decision to cancel this RFP, have anything to do with the lengthy anticipation and ultimate passage of the BARDA legislation in December? If BARDA didn't pass, HHS would have to stimulate the private sector by implementing BioShield the way Congress intended.

This last question also underscores how HHS' own actions?the agency's history of delays, failure to implement the program in accordance with the law, and failure to create markets?has in fact created the "Valley of Death" that the agency claims has undermined the program. Ironically, this is the same Valley of Death that provided the rationale and impetus for the recently enacted BARDA legislation.

Let me be absolutely clear, there is no Valley of Death in the private sector. If a technology is promising, there is a market for it and the path to approval is clearly defined, companies have no difficulty in obtaining investor capital—even though development of the typical drug costs hundreds of millions of dollars, takes over a decade, and numerous promising compounds never get approved. Pharmaceutical and biotech investors understand risk and reward. By raising the bar—changing the definition of the criteria required by companies to be awarded an advance purchase contract (including identifying the market size)—HHS has pushed the investment community away from BioShield. They have created their own Valley of Death.

When you hear government officials telling you that the pharmaceutical sector has not responded to BioShield—and therefore their agencies need to take the lead in researching and developing new drugs for WMD, and be given a bigger budget—realize that these same officials and their actions are the precise reason why companies and investors are running away from, not towards, this BioShield program. They are like the proverbial arsonist who sets the fire so they can rush in afterward to save the day.

With all due respect to the Members who worked hard to pass the BARDA bill, it is my opinion that the BARDA legislation, though well intended, will only make things worse. BARDA actually shifts biodefense efforts away from market-driven development of deployable countermeasures, to government research grants. BARDA also shifts the risks from the private sector to the taxpayer—with no guarantee of results.

Under the BioShield law, if a BioShield company doesn't produce a drug, it doesn't get paid; if a BARDA company fails to develop a drug it still gets paid. Let me be clear, if a company fails to deliver on a BioShield contract, the government isn't out a penny; if a BARDA-funded drug fails, the taxpayers foot the bill. And, given that there are hundreds of failures for every approved drug, and that each failure can cost a significant amount of money, the cost to the taxpayer will quickly add up.

Finally, given the high-risk, highly technical nature of drug development, there is absolutely no reason to believe that government agencies with very limited expertise in drug development will have nearly the success rate of private industry, which has been doing this for decades.

All that said, perhaps the best way to judge the BioShield program is to look at its record of results—or lack thereof:

- Three years into the program and the agency has issued only nine RFP's against just four of the numerous CBRN threats we face—and roughly a third of those RFP's and/or contracts have been cancelled. This despite the fact that the Centers for Disease Control have maintained a priority list of CBRN threats for years.
- Three years into the program and BioShield has yet to produce a newcountermeasure that was not already in existence before the program began.
- The market cap and share values of nearly every company in this sector have fallen sharply since the program was implemented?despite the fact that Congress intended BioShield to drive the development of a vibrant biodefense industry.
- In just the last two months, no less than three of the leading BioShield companies have all stated that they are quitting their program-related drug development efforts and will never again seek to work with the government—my company, Hollis-Eden, is included in that number.

These failures stand to have real consequences for our national security. For example, had HHS awarded this contract, the government may have begun • protecting the American people from the life threatening effects of ARS in 2008. Instead, because HHS has failed to act, we have suspended the development of NEUMUNE indefinitely. Fortunately for Hollis-Eden our research was not limited to NEUMUNE. We have made great progress over the last few years as we are bringing forward several promising drug candidates addressing well-defined mainstream global medical markets.

Unfortunately, as we and other companies have learned in this process, trying to do business with the government under Project BioShield, as implemented by HHS, appears to be more about factors other than sound science. By the actions outlined in this testimony of how HHS is handling companies like Hollis-Eden, the government is sending the wrong message and is discouraging innovative companies from participating in Project Bioshield. Ultimately, the U.S. citizens future security won't have the benefit of the "best and the brightest" technologies and expertise that industry has to offer, as originally envisioned in the Project BioShield legislation.

Only after the horror of 9/11, have we taken steps to improve airline security. Only after the levies broke during Hurricane Katrina, have we focused on the adequacy of FEMA. Will Americans have to wait until terrorists use a nuclear device in one or more of our cities before our government addresses our lack of preparedness? If we do not act, the weight of those lives lost because we failed to adequately prepare for a nuclear attack will fall squarely upon the people who knew and did nothing to rectify this situation before it was too late.

I fear only then things may change.

Mr. Chairman, thank you for the opportunity to appear before you today.

Mr. LANGEVIN. Mr. Hollis, thank you for your testimony.

Dr. Davis, the floor is yours.

STATEMENT OF JAMES H. DAVIS, PH.D., J.D., SENIOR VICE PRESIDENT AND GENERAL COUNSEL, HUMAN GENOME SCIENCES

Mr. DAVIS. Mr. Chairman, members of the subcommittee, thank you for the invitation to appear today. I am Jim Davis, executive vice president and general counsel of Human Genome Sciences.

In this capacity, I have been extensively involved with all the issues related to the development and anticipated sale of ABthrax, HGS therapeutic treatment for victims of anthrax exposure.

As you know, ABthrax is one of several products that have been procured by HHS under Project BioShield. Our initial contract was awarded in September 2005 and in June 2006, the HHS exercised first of several options for delivery of 20,000 doses of ABthrax to the strategic national stockpile.

We are on track to deliver that product in 2008, subject to FDA approval. We are confident we have the processes and capability to manufacture the product for the national stockpile and to do so on schedule.

By way of background, HGS is a biopharmaceutical company located in Rockville, Maryland that discovers, develops and manufactures drugs to treat and cure disease. The primary focus of HGS has not been nor will it be the development of drugs to protect against the attack by biological and chemical weapons.

The principal focus of our company is the pursuit of innovative biopharmaceutical products for the commercial market.

But for this very reason, HGS also represents one of the successes of Project BioShield. While there is no doubt the program faces numerous challenges, the fact that HHS was able to attract the participation of a company whose focus has not been the biodefense market demonstrates the potential of Project BioShield.

Nearly 6 years ago, we realized that our company had the technology and capability to develop an effective near-term countermeasure against one of the nation's most immediate and serious bioterrorism threats.

As a company headquartered just outside Washington, D.C., we witnessed firsthand the potentially devastating effects of the use of anthrax as a terrorist weapon in late 2001.

Thus, using our own funds, without any assistance whatsoever from the U.S. government, we developed a fully human monoclonal antibody drug called ABthrax that can prevent or treat the lethal effects of anthrax infection.

In contrast to the vaccine, a single dose of ABthrax confers protection immediately. In contrast to antibiotics, ABthrax is effective

against the lethal toxins released by the bacteria and can be used to prevent and treat infections by antibiotic-resistant strains of anthrax.

In a therapeutic setting, we believe that ABthrax could significantly reduce anthrax toxicity and increase the survival of exposed patients. We have initiated the final efficacy and safety studies necessary for FDA approval.

As the first BioShield procurement for a product developed after 9/11, the ABthrax contract allows for the acquisition of a therapeutic product to treat U.S. civilians who have inhalation anthrax disease.

HHS has currently agreed to purchase 20,000 doses of ABthrax. While it has not yet committed to exercise all the options contained in the contract, the contract includes options and pricing for quantities ranging from 10,000 to 100,000 doses.

As is the nature of biological production, the cost per dose of 100,000 doses is significantly less than the cost per dose of 10,000 doses.

Given the limited quantities of vaccine, we believe it may be prudent for HHS to consider purchasing additional quantities of ABthrax.

While HGS appreciates its positive experience with Project BioShield and HHS, Congress and HHS can take several steps to increase industry participation. The BARDA legislation is a significant step by Congress to provide HHS with additional tools to ensure success.

We applaud the bipartisan leadership of Senators Burr and Kennedy, as well as Representatives Rogers and Eshoo in making BARDA a reality. It is now incumbent upon Congress to fund fully BARDA.

HGS strongly supports the industry recommendations to fund BARDA with at least $500 million in fiscal year 2008. We also urge the agency to hire an individual with private-sector development experience to lead BARDA.

HHS should also enact regulations to take into account the regulatory flexibility included in both Project BioShield and BARDA. The agency should make clear that the statute does not require contractors to comply with burdensome government procurement requirements.

Finally, while HGS has found FDA to be extremely responsive in working with us on both the pre-clinical and clinical studies required for approval, there remains a need for greater clarity about the regulatory requirements for an emergency use authorization permit and the decision-making process necessary for final approval to stockpile the product.

I applaud the subcommittee for its continued oversight of this critical biodefense program. In the case of ABthrax, we are working in partnership with HHS as intended by Project BioShield to deliver an effective anthrax therapeutic to the strategic national stockpile.

We look forward to delivering on our commitment to HHS and the American people in 2008 and would appreciate every effort to ensure that additional quantities of ABthrax are made available to the stockpile.

Thank you again for the opportunity to testify, and I look forward to answering your questions.

[The statement of Mr. Davis follows:]

PREPARED STATEMENT OF JAMES H. DAVIS, PH.D

Mr. Chairman, members of the Subcommittee, thank you for the invitation to appear before you today on behalf of Human Genome Sciences. I am Dr. Jim Davis, Executive Vice President and General Counsel of Human Genome Sciences (HGS). In this capacity, I have been extensively involved with the business development, regulatory approval process, and federal procurement issues related to the anticipated sale of HGS' innovative therapeutic treatment, ABthrax™, for victims of anthrax exposure. I have been involved with this project since we undertook to develop this product on our own initiative and at our own expense immediately following the anthrax attacks of 2001.

As you know, ABthrax is one of several products that have been procured by the Department of Health and Human Service (HHS) under the Project BioShield Act of 2004. Our initial contract was awarded in September 2005 for purchase of a test quantity of our novel anthrax therapeutic. In June 2006, HHS exercised the first of several options under the contract for delivery of 20,000 doses of ABthrax to the Strategic National Stockpile (SNS), valued at$168 million. We are on track to deliver the product in 2008, subject to approval of the Food and Drug Administration ("FDA"). We have already initiated both human and animal studies and have manufactured the product at scale for those studies. We are confident we have the processes and capability to manufacture the product for the SNS, on schedule. Of course, if HHS elects to exercise the remaining options for delivery of up to 100,000 doses of ABthrax to the SNS, we stand ready, willing, and able to meet that obligation also.

By way of background, HGS is a biopharmaceutical company located in Rockville, Maryland, that discovers, develops and manufactures gene-based drugs to treat and cure disease. Currently, we have six drugs in clinical development, including five monoclonal antibodies, and a broad pipeline of preclinical compounds. These include novel human protein and antibody drugs discovered through our genomics-based research, as well as new, improved, long-acting versions of existing proteins created using our albumin fusion technology.

Let me be clear. The primary focus of HGS has not been - nor will it be - the development of drugs to protect against attack by biological and chemical weapons. The principal focus of our company has been, and remains, pursuit of innovative biopharma products for the commercial market. We are not a "bio-defense" company as that term has come to be known in the post-9/11 environment. Our business plan, our executives, and our investors do not see the primary focus of HGS, now or in the future, to be the federal marketplace.

For this reason alone, HGS represents, at least in this aspect, the success of Project BioShield. While there is no doubt the program has faced challenges, the fact that HHS was able to attract the participation of a company whose focus has not been—and will not be—the biodefense market demonstrates that the initial objectives of Project Bioshield can be achieved. The background of HGS and ABthrax demonstrates that Project BioShield can succeed, and thus, the procurement of this product must be examined as the program moves forward to address the challenges BioShield has faced, and the potential it holds for the future.

History of ABthrax™

Nearly six years ago, we realized that our company had the technology and capability to develop an effective, near-term countermeasure against one of the nation's most immediate and serious bioterrorism threats—anthrax. As a company headquartered just outside Washington D.C., we witnessed first-hand the potentially devastating effects of the use of anthrax as a terrorist weapon in late 2001. Thus, using our own funds—without any assistance whatsoever from the United States Government—HGS developed a fully human monoclonal antibody drug called ABthrax that specifically binds to a key anthrax toxin, thereby preventing or treating the lethal effects of anthrax infection. The drug can be given prior to or after exposure; and it could be used alone or in conjunction with the current vaccine and antibiotics.

As you know, anthrax infection is caused by a spore-forming bacterium, *Bacillus anthracis,* which multiplies in the body and produces lethal toxins. Most anthrax fatalities are caused by the irreversible and destructive effects of the anthrax toxins; as we saw in the fall of 2001, survival rates for patients who contracted inhalation anthrax were only 50%. Research has shown that protective antigen is the key

facilitator in the progression of anthrax infection at the cellular level. After protective antigen and the other anthrax toxins are produced by the bacteria, protective antigen binds to the anthrax toxin receptor on cell surfaces and forms a protein-receptor complex that makes it possible for the anthrax toxins to enter the cells. HGS' ABthrax antibody blocks the binding of protective antigen to cell surfaces and prevents the anthrax toxins from entering and killing the cells.

Currently, there are only two licensed options available for the prevention and treatment of anthrax infections—the AVA vaccine and antibiotics. Both are essential in dealing with anthrax, but both have limitations for individuals who are suffering from the effects of inhalation anthrax. The only available, licensed anthrax vaccine, BioThrax, coupled with antibiotics, is recommended—but not licensed—for use in a post-exposure setting *prior* to manifestation of symptoms of inhalation anthrax. Antibiotics alone, without the vaccine, are effective in killing anthrax bacteria from spores that have germinated, but are not effective against the anthrax toxins once those toxins have been released into the blood, nor will they kill ungerminated anthrax spores that linger in the bloodstream. Currently available antibiotics, such as Ciprofloxacin, also may not be effective against antibiotic-resistant strains of anthrax. And neither the vaccine nor antibiotics have proven to be effective once symptoms of inhalation anthrax set in.

In ABthrax, HGS has discovered a third critical defense against anthrax infections, including following the manifestation of symptoms. In contrast to the anthrax vaccine, a single dose of ABthrax confers protection immediately following the rapid achievement of appropriate blood levels of the antibody. In contrast to antibiotics, ABthrax is effective against the lethal toxins released by anthrax bacteria. It may also prevent and treat infections by antibiotic-resistant strains of anthrax. ABthrax has the potential to be used both therapeutically and prophylactically.

In a therapeutic setting and based on initial preclinical studies, we believe that ABthrax could significantly lessen the natural progression of anthrax toxicity when given after inhalation exposure to anthrax and increase the survival of exposed patients. Results from preclinical studies previously conducted demonstrated that a single dose of ABthrax administered therapeutically, after an animal begins to exhibit symptoms of anthrax poisoning, increases survival significantly in rabbits exposed to many times the lethal dose of inhaled anthrax spores.

HGS now has initiated the final pivotal rabbit studies necessary for the approval by FDA under an Experimental Use Authorization and under a Biological License Application. HGS is also conducting key characterization studies in non-human primates and will be conducting additional confirmatory efficacy studies in these animals; HGS has previously shown that administration of ABthrax immediately after exposure to anthrax significantly increases survival in non-human primates. HGS will be conducting additional studies in a therapeutic setting. HGS has already conducted a Phase 1 clinical trial in humans to evaluate the safety, tolerability and pharmacology of ABthrax in healthy adults and has initiated the additional human studies that will be required for EUA and BLA approval.

Our preclinical data also show that ABthrax administered prophylactically (before exposure to anthrax) or immediately afterwards increases survival rates significantly and thus ABthrax could be used to protect rescuers entering a contaminated building or soldiers in an infected environment.

Procurement of ABthrax under Project Bioshield

Many companies have the capability and are willing to develop new products to protect against attack by biological and chemical weapons or other dangerous pathogens. However, very few companies, such as HGS, have already done so. In fact, HGS is among the largest, best funded, and most qualified companies to participate in Project Bioshield to date.

The fact that HGS was successful in negotiating a viable business relationship with the federal government to purchase ABthrax should have sent an extremely powerful, positive signal to similarly qualified companies considering whether to enter this market. The primary challenge of bio-pharma companies such as HGS is the absence of a commercial market for such drugs. In most cases, the only viable market is the federal government and, potentially, our foreign allies. Project Bioshield, which aims to harness public and private resources in an innovative effort to develop defenses against bioterrorism, is specifically intended to create such a market. With the consummation of the contract for ABthrax, the promise of Project BioShield's ability to create a market for anthrax therapeutics was realized.

As the first Bioshield procurement for a product developed after 9/11, the ABthrax contract allows for the acquisition and maintenance within the SNS of therapeutic products to treat US civilians who have inhalational anthrax disease. The remaining development and manufacturing will be completed at HGS' Rockville, Maryland

facilities by 2008, pending FDA approval. HHS has currently agreed to purchase 20,000 doses of ABthrax for the SNS. While HHS has not yet committed to exercise all of the options for production quantities for ABthrax contained in the contract, the contract does include options, and pricing, for a broad range of quantities ranging from 10,000 doses to 100,000 doses. As is the nature of biologics production, the cost per dose of 100,000 doses is significantly less than the cost per dose of 10,000 doses. Given the limited quantities of anthrax vaccine currently in the SNS, it may be prudent for HHS to consider purchasing additional quantities of ABthrax to be available in the event of another anthrax attack. The sooner HHS makes the decision, given the lead time required for manufacturing, the sooner we will be able to deliver additional quantities beyond our initial commitment.

Proposed Implementation Improvements

While HGS very much appreciates its positive experience with Project BioShield and its work with HHS in performing under the ABthrax contract, Congress and HHS can take several steps to increase industry participation in Project Bioshield.

To begin, the recently enacted Biopharmaceutical Advanced Research and Development Authority (BARDA) legislation is a significant step by Congress to provide HHS with additional tools to ensure success of BioShield. We applaud the bi-partisan leadership of Senator Richard Burr (R–NC) and Senator Edward Kennedy (D–MA), as well as Representative Mike Rogers (R–MI) and Representative Anna Eshoo (D–CA) in making BARDA a reality. It is now incumbent upon Congress to fund fully BARDA to realize the benefits of these powerful tools. HGS strongly supports the industry's recent recommendations to fund BARDA with at least $500 million in appropriations in Fiscal Year 2008. We also urge HHS to hire an individual with private sector drug development experience to lead BARDA, as was the clear intent of Congress.

In addition to fully implementing—and funding—BARDA as soon as possible, HHS should enact regulations required under the Act that take into account the regulatory flexibility included in both Project BioShield and BARDA in order to realize fully the legislative intent of Project Bioshield. First and foremost, HHS should make clear that the statute does not require contractors to comply with burdensome government procurement requirements, including the requirement for certified cost and pricing data, in order to stimulate the maximum interest possible by commercial companies. Similarly, HHS should avoid the use of cost-type contracts or contract line items (thus, eliminating the need for a proposed contractor to adopt non–GAAP accounting practices) wherever possible.

HHS should also consider structuring Bioshield contracts to avoid a "staged" procurement approach such as what occurred with the Anthrax therapeutic contract, wherever possible. While we recognize the need for staged procurements under certain circumstances, using this method where HHS has conducted proper market research will avoid unnecessary delays and unpredictable results, thereby stimulating far greater private sector interest. Of course, the advance development authority—and eventual funding—available under BARDA should provide the necessary tools to HHS to avoid this result in the future.

Finally, while HGS has found the Food and Drug Administration to be extremely responsive in working with us on the preclinical and clinical studies that will be needed for EUA and BLA approval of ABthrax, there remains a need for greater clarity about the regulatory requirements for an EUA and the decision making process necessary for final approval to stockpile an as yet unlicensed biological product.

All agencies responsible for administering Project Bioshield should take a proactive approach to identifying, evaluating and procuring effective countermeasures. I applaud the Subcommittee for its continued oversight of this critical bio-defense program. In the case of ABthrax, HGS is working in true partnership with HHS, as intended by Project BioShield, to bring ABthrax into production, and eventually, into the Strategic National Stockpile. We look forward to delivering on our commitment to HHS, and the American people, in 2008 and appreciate every effort to ensure that additional quantities of ABthrax are purchased for the stockpile, as appropriate.

Thank you again for this opportunity to testify and I look forward to answering your questions.

Mr. LANGEVIN. Thank you, Mr. Davis, for your testimony.

Just for the record, there is a vote on right now. It is my intent to go until there are 5 minutes left on the vote. We will recess and then reconvene so that members can continue to ask questions.

Let me begin with Mr. Hollis.

I guess let me ask, briefly, both witnesses, your experience, if you had to summarize, given your experience with BioShield, A being the best and F being the worst, what was your experience with dealing with BioShield? Just briefly on that.

Mr. HOLLIS. You said from A to what?

Mr. LANGEVIN. A being the best, obviously, good experience going through the process, and F being the worst, what would you give your experience with BioShield? What grade would you give them?

Mr. HOLLIS. It hasn't been a pleasant experience for us. I would have to grade them an F.

Mr. DAVIS. I would have to say it is probably a solid B. It took us a long time to get the contract, but in working with HHS since we have gotten the contract, it has been a very good experience.

Mr. LANGEVIN. Mr. Hollis, when the contract was canceled for your company, you said it was without warning.

Was there any appeal process that was afforded before it was just done or the contract was just canceled and no further action?

Mr. HOLLIS. There was no appeal process.

Mr. LANGEVIN. Mr. Hollis, you have testified before this committee before and I have heard that your company announced that it would no longer pursue biodefense work and your stock has quadrupled in price, from what I hear.

Is it solely your company's experience with the BioShield process that led to this decision and was it solely your decision to no longer pursue biodefense work that was the sole reason for the increase in stock price?

Mr. HOLLIS. Our stock price actually decreased by 60 percent and, therefore, we can no longer justify from a fiduciary responsibility to invest in this program.

Mr. LANGEVIN. It was solely the experience with BioShield that led to this decision.

Mr. HOLLIS. Yes. We were in an RFI/RFP procurement process for 2.5 years. It is really unexplainable. And as a publicly traded company, to explain to shareholders continued delays over 2.5 years.

Our stock basically has lost $700 million in market capitalization because there has been no transparency in the procurement process and we could not communicate with Wall Street in regards to the transparency and guidance that we were receiving from the agency during this whole procurement process.

Mr. LANGEVIN. Thank you.

Dr. Davis, your company, as you mentioned, is currently on track to deliver another anthrax countermeasure. Before entering into the contract, you also had some concern and confusion about the emergency use designation and initially were not going to sign the contract.

Is that correct? And how was the situation resolved?

Mr. DAVIS. I think there was some initial contract discussions over how you would define what was the criteria for product to go into the national stockpile.

And there was a series of discussions. We did, in fact, end up filing a protest, but we very quickly came to agreement with HHS over how to define that definition and the definition was one that we were quite satisfied with.

Mr. LANGEVIN. So you clarified that before you actually signed the contract.

Mr. DAVIS. Absolutely, yes.

Mr. LANGEVIN. Very good. Well, in the interest of time, I am going to yield to the ranking member for 5 minutes for questions.

Thank you, gentlemen.

Mr. MCCAUL. Thank you, Mr. Chairman.

Mr. Hollis, you talked about the goal of BioShield being to incentivize private markets, and I agree with you. I think this is a high-risk business. The government needs to incentivize. You make profits. And I will touch on BARDA in a minute, but you mentioned the word BioShield eligible.

Could you expand on that in terms of what is your understanding of BioShield eligible?

Mr. HOLLIS. Well, that is a very good question, because I really don't know the answer to it. It is what we heard several times when we were here in Washington trying to get guidance in developing our drug and participating in Project BioShield and it is a term that we heard quite often.

And when we tried to get clarification from it, we really never got clarification and I think that has a lot to do with the lack of transparency and leadership and guidance that the agency has not provided the industry.

Mr. MCCAUL. And as I understand, the RFP was withdrawn in your case.

Mr. HOLLIS. Yes.

Mr. MCCAUL. After about, what, 2 years?

Mr. HOLLIS. Two and a half years.

Mr. MCCAUL. Did they tell you why it was withdrawn?

Mr. HOLLIS. Yes. We had a debriefing here in Washington and basically they said that it was technically unacceptable and it was compared to the standards basically of an FDA approved drug.

They wanted a more robust dataset of safety and efficacy and that can only come through a late stage pivotal trial, of which the company had spent 5 years developing the drug and had incurred tens of millions of dollars.

And before a company would actually conduct a pivotal trial, it would need an advance purchase contract to justify spending that kind of investor money on the project.

So without setting the markets, without advance purchase contracts, you cannot incentivize companies and the capital markets and if you don't incentivize the capital markets, then this will be a taxpayer-funded program and is exactly—I should rectify one of the comments that you made.

Only eight percent of the drugs actually succeed. It can take 10 to 12 years and $1 billion to get a drug approved. With all that risk and failure, do we want to spend all the BARDA money on that risk and failure and or do you want participation by the capital markets and industry?

I do not think that has really been rectified with this legislation.

Mr. MCCAUL. Is it your testimony that your drug would have been FDA approved at what level, again?

Mr. HOLLIS. Excuse me?

Mr. MCCAUL. Was it your testimony that your drug would have been FDA approved or could be?

Mr. HOLLIS. Well, we could have conducted a pivotal trial and our expectations were never to receive any award from the government until we delivered an FDA approved product and that is how the initial legislation was written.

They would guarantee you a market, give you advance purchase contracts and they would pay you upon delivery of an FDA approved product.

So we were never looking for grants or government funding. We were going according to the BioShield legislation that was approved by Congress.

Mr. MCCAUL. And you were not provided any financial incentives.

Mr. HOLLIS. No.

Mr. MCCAUL. With the new legislation, the Biomedical Advance Research and Development Authority, BARDA, do you believe that that would be helpful?

Mr. HOLLIS. No. I think that exacerbates the condition, because what happens is you have a single agency that is becoming the gatekeeper for all technology.

What this country needs is the best in innovation and ingenuity of the industry and that means all-comers and they should open it up to competition for anybody.

And when you have an agency that is controlling what products get grants and what don't, then it is basically prejudiced to begin with. If the legislation was to be implemented the way that Congress passed, the risk would be on industry, not on the taxpayer.

Mr. MCCAUL. Let me—my time is running out—go to Mr. Davis.

You had a totally different experience. Why did you have a different experience from Mr. Hollis's company? And in your view, this new legislation we passed in the last week of the last Congress, will that be helpful in terms of BioShield? And maybe expand on what Mr. Hollis was talking about. What would need to be done to improve that?

Mr. DAVIS. Sure. I can't explain why we have had different experiences. I can only really talk to my own experience.

We had an RFP that was very clear as to what sort of product the agency wanted, what the criteria had to be met. We entered into the contracting process and we were successful in getting a contract.

We had lots of discussions along the way. It is never an easy process to come to a meeting of the minds on exactly what a product is going to deliver, but we were able to do that and we were very successful in getting the contract awarded and now we are proceeding very deliberately along that pathway.

In terms of the BARDA legislation, I think the BARDA legislation is a definite right step in the right direction. I think you need many different avenues to develop these products.

BARDA provides a way for companies who are not willing to fund the initial research themselves to get funding to do the development. It helps in those companies who do face the valley of death.

We did not. We developed this product fully on our own and we will get paid when we deliver it to the stockpile. That is what we signed up for, that is what we were willing to do.

We are a biopharmaceutical company. That is the normal way pharmaceutical companies develop products. You develop a lot of products. You take them through clinical trials. Not every one makes it and you don't get any reward until the end.

So we are willing to take that risk and that is clearly a risk that you want to encourage companies to take. But there are clearly many other companies, smaller companies that can do it with BARDA funding and that can help very much, I think, the biodefense industry and the U.S. government and the people.

Mr. MCCAUL. Thank you. I see my time has expired and we have to vote.

Mr. LANGEVIN. Good, yes. We are going to recess right now. There is about a minute left on the vote. So we are going to have to go quick.

But we will return, and we ask your indulgence. The committee stands in recess.

[Recess.]

Mr. LANGEVIN. I want to thank the witnesses again for their indulgence.

Before I go to other members, I just had one question, if I could, for Dr. Davis.

I understand a while ago that—and this is going back to your testimony in terms of your grading and your experience with BioShield.

A while ago you had said that you would never pursue another BioShield contract, is what I had been told, and, again, during your testimony today, you gave your assessment and gave the BioShield process, in your experience, a B.

Did I hear that correctly in terms of—

Mr. DAVIS. No, you did not hear that. I mean, you did hear correctly about the B, but not correctly about we would never pursue another BioShield.

What I was saying is it is not our primary focus. If we are in a position where we have the right technology and the government has the right need, we certainly want to respond to that need and seek a BioShield contract. It is not our primary business, though.

Mr. LANGEVIN. I see. And your primary business is?

Mr. DAVIS. Is biopharmaceutical products for the general public. We are working on drugs for lupus, rheumatoid arthritis, cancer, hepatitis C. So we are really a pharmaceutical company, but we had the technology, we had the capability to develop an antibody for anthrax.

We saw the need for anthrax. We talked to various people in the government when we first started to develop it. We realized that there was going to be a need. The Bioterrorism Act was passed which allowed for animal testing to prove efficacy and with the passage of BioShield, then there was the opportunity to get a contract.

And so that is why we entered this area. We are certainly interested in continuing to provide more anthrax therapeutic to the gov-

ernment and we would certainly be optimistic as other opportunities arise.

Mr. LANGEVIN. I appreciate you clarifying that for the record.

The chair will now recognize other members for questions they may wish to ask of the witnesses.

In accordance with our committee rules and practice, I will recognize those members who were present at the start of the hearing based on seniority in the subcommittee, alternating between the majority and the minority, and those members who are coming in later will be recognized in the order of their arrival.

The chair now recognizes for 5 minutes the gentlewoman from the Virgin Islands for 5 minutes.

Mrs. CHRISTENSEN. Thank you, Mr. Chairman and Ranking Member, for holding this hearing. The BioShield is something that I have been interested in and never quite satisfied with. So I am glad that we are taking a look at it again.

I guess I would begin by asking, Mr. Davis, you said that, in response to another question, the phrase "BioShield eligible" had been adequately defined for you. Could you tell us in what way it was defined? How did they define it?

Mr. DAVIS. Actually, the term "BioShield eligible" was never used, and I am not familiar with that term.

What I can say is that the RFP made clear what type of products they were looking for, what stage of products and what the criteria was. And then, doing the contract negotiation process, we further clarified the characteristics that would be needed in order to have the product stockpiled and then eventually we will obviously be getting BLA licensure.

So that particular term I am not familiar with, at least in our contract discussions.

Mrs. CHRISTENSEN. Okay. And these two contracts were occurring around the same time.

Mr. DAVIS. I am not sure exactly the timing of the Hollis-Eden one. Ours was originally awarded in 2005.

Mrs. CHRISTENSEN. And your RCA process started in what year?

Mr. DAVIS. I believe 2004.

Mrs. CHRISTENSEN. And yours, Mr. Hollis?

Mr. HOLLIS. October 2004.

Mrs. CHRISTENSEN. So you heard the term "BioShield eligible."

Mr. HOLLIS. We spent a lot of time here trying to get clarification in regards to what was going to be necessary to get an advance purchase contract and initially—

Mrs. CHRISTENSEN. Well, before you answer, because Mr. Davis said he was clear on his product, what was required, the criteria and so forth, that that was clear. Was that clear to you?

Mr. HOLLIS. There was a request for proposal that finally came out and it had requirements on there and we met all the mandatory requirements.

Mrs. CHRISTENSEN. So you were clear what was required in your RFP and what product was to be delivered, just as Human Genome Sciences was. You were clear in your RFP what the product was, what was required, what criteria.

Mr. HOLLIS. It wasn't spelled out thoroughly. It was more broad and general.

Mrs. CHRISTENSEN. I think you have answered the question about BARDA for me.

In other testimony and I believe, also, in the GAO report, the statement is made that not enough the private medical industry is participating in BioShield.

I am asking the question to both of you and I think maybe in the chief medical officer's testimony, it says it encourages more companies to participate.

Well, I would like to hear from you why each of you think that this is the case, that not enough companies are participating in BioShield.

Mr. HOLLIS. I will tackle that first.

When the president first announced BioShield in his State of the Union in 2003, I was also at a conference in New York where the president also gave a follow-up speech to that and he was calling for the industry to participate in Project BioShield.

And subsequent to that, at the time, Dr. Mark McClellan, who was the commissioner at the FDA at the time, also gave a presentation to try to stimulate the industry to respond to Project BioShield.

The cornerstones are guaranteed markets, advance purchase contracts, pay on delivery. This was going to be a new way to finance medical countermeasures.

At first, industry was very interested and so was banking. As a matter of fact, many bankers were looking at a whole new biodefense sector and a way to finance companies that were going to develop these products.

If you were to look at this today, most investment bankers have dropped out almost completely. The investment banker we have no longer funds companies in BioShield.

Industry can't participate because it really doesn't know what the markets are. What are the threats? How many doses do they plan on purchasing? How can you make an economic decision whether you want to develop a product or not when you don't know what the market is?

And there is no transparency and guidance in regards to the procurement process. Is this a government-run program or is this a program to drive incentives for the industry?

Now, if it is one or the other, that is perfectly fine. It just needs to be stated.

Mrs. CHRISTENSEN. Mr. Davis?

Mr. DAVIS. I think what would help the most is if we had a clearer idea of exactly what the market is. We know a number of the threats that HHS is interested in, but it would be much better, as Mr. Hollis said, if we knew exactly what threats, what type of products they want and the number of doses they wanted to buy, because then you can make the market judgment of whether you want to invest in that and I think that is the one thing that is lacking and I am hoping that is what comes out of the BARDA implementation plans is a clearer indication of what those markets are.

Mrs. CHRISTENSEN. Thank you. My time is up. I just wanted to say for the record that I have asked on a number of occasions what was the status of Neumune, had it ever been accepted for Bio-

Shield, but I could never really get a straight answer and this is in hearings that either the committee or subcommittee has had.

So I understand why I couldn't get an answer now.

Mr. HOLLIS. Thank you very much, appreciate that.

Mr. LANGEVIN. I thank the gentlelady for her questions.

I want to thank the witnesses for your testimony and as I said earlier, I look forward to the opportunity to have VaxGen back before the subcommittee to offer testimony about their experiences with Project BioShield.

Your testimony today was valuable and I appreciate you sharing your experiences with us.

BioShield is too important to fail and we need to do what we can to further dot the I's and cross the T's to make sure that BioShield is working at maximum effort and as it was intended.

I am glad to hear, Dr. Davis, that you had a relatively positive experience.

I am disappointed, of course, Mr. Hollis, that you and, it is my understanding, VaxGen, two major contracts, did not have a good experience. But we hope to get to the bottom of this and work to fix the problems.

Again, I just want to thank the witnesses for their valuable testimony and the members for their questions.

The members of the subcommittee may have additional questions for the witnesses and we would ask that you respond expeditiously in writing to those questions.

And, again, I thank you for your testimony. At this time, the first panel of witnesses is dismissed and the chair calls up the next panel.

Thank you.

I want to thank the panel for being here today.

The first witness today is Dr. Jeffrey Runge, the acting assistant secretary for health affairs and chief medical officer, Department of Homeland Security. Dr. Runge's service to the department began on September 5, 2005 as the department's first chief medical officer position, he still holds.

The DHS chief medical officer serves as the principal advisor to the secretary for public health and medical issues across the department. Dr. Runge is responsible for coordination with other federal departments and agencies and the Homeland Security Council on issues of biodefense and medical preparedness.

The next witness is Dr. Gerry Parker. Dr. Parker serves as the principal deputy to the assistant secretary, office of the assistant secretary for preparedness and response at the Department of Health and Human Services.

The office coordinates HHS-wide efforts with respect to preparedness for and responses to public health and medical emergencies and serves as the focal point for coordination with other federal departments, agencies, offices and state and local officials responsible for emergency medical preparedness, and the protection of the civilian population from acts of terrorism and other public health emergencies.

Next we have Dr. Anthony Fauci, director of National Institutes of Allergy and Infectious Disease, a position he has held since 1984. He has had the opportunity to testify, I know, on a number of occa-

sions before the subcommittee in its prior life on prevention of nuclear and biological attacks.

And I have always appreciated your testimony in the past, Dr. Fauci, and look forward to hearing from you today.

In 1968, Dr. Fauci came to the National Institutes of Health as a clinical associate in the laboratory of clinical investigation at the National Institutes of Allergy and Infectious Disease. In 1974, he became head of the clinical psychology section, LCI, and, in 1980, was appointed chief of the laboratory of immunoregulation, a position he still holds.

Finally, we welcome Dr. Jesse Goodman, the director of FDA's Center for Biologics Evaluation and Research, which oversees a broad range of medical, public health and policy activities concerning the development and assessment of vaccines, blood products, tissues and related devices and novel therapeutics, including cellular and gene therapies.

He first came to FDA in late 1998 from the University of Minnesota, where he had joined the faculty in 1985 and most recently served as professor of medicine and director of the division of infectious disease.

Before I turn it over to the panel of witnesses, starting with Dr. Runge, I wanted to mention two things.

First of all, the committee rules require that testimony is submitted no later than 48 hours before the subcommittee. We received the testimony from HHS only at 9:30 last night. Dr. Runge's and Dr. Fauci's testimony was in on time.

And just for the record, I understand that you all have other people that need to sign off before you can actually submit the testimony, but we can't do business this way, in not having the testimony in in a timely manner. And I would hope that in the future it would be in in the 48-hour requirement.

Second, I wanted to say how deeply disappointed I am that HHS would not give a sign-off to VaxGen to testify before the subcommittee. As I said earlier on, prior to the start of the hearing, that VaxGen very much wanted to testify.

We need to have VaxGen's testimony so we fully understand their experience with BioShield if we had to exercise proper oversight and work together to try to fix the problem.

So I would expect that at the earliest opportunity, that the sign-off would be given from HHS and that, in fact, VaxGen will be allowed to testify before the subcommittee.

I can promise you that there will be a follow-up hearing on the BioShield issue, at which time I expect that VaxGen will be allowed to testify.

Without objection, the witnesses' full statements will be inserted into the record. And I now ask each witness to summarize their statement for 5 minutes, beginning with Dr. Runge.

Dr. Runge, thank you again for being before us once again, and the floor is yours.

STATEMENT OF JEFFREY RUNGE, M.D., ASSISTANT SECRETARY OF HEALTH AFFAIRS (ACTING) AND CHIEF MECICAL OFFICE, OFFICE OF HEALTH AFFAIRS, DHS

Dr. RUNGE. Thank you, Mr. Chairman, Ranking Member McCaul and members of the subcommittee. I appreciate the opportunity to be here today.

I also appreciate the attention that you and your subcommittee have given to the subject of bioterrorism countermeasures in the past since my arrival 18 months ago as chief medical officer.

We believe Project BioShield to be an essential component of the overall strategy to combat the effects of bioterrorism and this subcommittee has played a very important role in DHS's responsibilities under the Act.

We have shared with the committee on numerous occasions the results of our assessments of biologic agents as they present a threat to national security and you have been supportive of our maturing relationship with HHS and its various components concerning our roles and responsibilities for the program.

We have deepened our partnership with HHS to become part of its public health emergency medical countermeasure enterprise, along with members of the executive office of the president, as well as the Department of Defense.

HHS possesses most of the moving parts of this enterprise, including the basic sciences of NIH, the advanced research authority of the new BARDA, the safety and regulatory capacity of the FDA and the strategic national stockpile, the CDC.

For our part, we have delivered a comprehensive assessment of the 28 agents of concern and we have delivered to the White House and to this subcommittee a stratified list of agents that present a material threat to national security and population threat assessments on 13 of those agents, as well as an additional assessment for nerve agents.

We have completed a tool that will allow us to conduct detailed modeling of vulnerabilities and consequences as changes occur for various possible scenarios of a terrorist attack.

This model was informed by inputs from the intelligence community, law enforcement, the science community and public health. We will continue periodic assessments to update this list and to restratify it as conditions change and we will keep our partners abreast of these updates to ensure that all of our efforts remain synchronized.

Once DHS determines which agents are material threats, HHS then performs consequence modeling to support the procurement of the appropriate countermeasure. When a countermeasure is identified that meets the eligibility requirements to warrant use of the special reserve fund, both secretaries, HHS and DHS, jointly request that OMB release funds to HHS from the special reserve fund in order that HHS may acquire the countermeasure.

We have greatly improved the processes over the last several months to realize many efficiencies in what started out as a very difficult bureaucratic process.

While DHS completes its responsibility, as I previously described, HHS is ultimately responsible for managing the countermeasure procurement process, including the negotiation of terms, entering

into contracts for research, development, acquisition, procurement, storage and distribution of those countermeasures.

DHS is completely supportive of the new enterprise, of the BARDA law and the transparency to which Secretary Leavitt is committed and we look forward to continued improvements in this process.

Mr. Chairman, from my perspective, what is still missing from the enterprise is a commitment, a partnership from the nation's medical industry as a whole to invest in our biodefense.

If this public-private partnership is going to work, our nation needs investment from both sides. We cannot rely simply on the smaller biotech companies to carry the burden of new countermeasure development.

I believe it would be a worthy investment in time, talent and treasure for companies, large and small, to come to the table, even without the promise of large returns on their monetary investments.

Of course, we can't expect these companies to invest blindly in countermeasure research and development without some economic incentive, but we really need to recognize that success benefits everyone and the lack of success in this area carries a potential for harm to our citizens and to our economy, including companies, large and small, inside the biotech industry and outside.

So we need the ingenuity and creativity of the entire American enterprise to reach a condition of security from bioterrorism.

Mr. Chairman, you have my more detailed remarks for the record. I appreciate it. I will just stop here, if that is okay with you.

[The statement of Dr. Runge follows:]

PREPARED STATEMENT OF JEFFREY W. RUNGE, MD

APRIL 18, 2007 (REVISED)

INTRODUCTION

Good afternoon, Mr. Chairman, Ranking Member McCaul and distinguished members of the Subcommittee. Thank you for the opportunity to describe the role of the Department of Homeland Security (DHS) under Project BioShield.

PROJECT BIOSHIELD OVERVIEW

The Project BioShield Act of 2004 (PL 108–276) amended the Public Health Service Act to provide protections and countermeasures against biological, chemical, radiological, or nuclear agents that may be used in a terrorist attack against the United States by giving the National Institutes of Health contracting flexibility, infrastructure improvements, expediting the scientific peer review process, and expanding the Food and Drug Administration authority to allow the use of unapproved medical countermeasures in a declared emergency.

Today, Project BioShield is a $5.6 billion program designed to stimulate the development of medical countermeasures for natural or chemical, biological, radiological, and nuclear threats for which there are no existing commercial markets. Both DHS and the Department of Health and Human Services (HHS) have major responsibilities under the Project BioShield Act.

DHS RESPONSIBILITIES UNDER PROJECT BIOSHIELD

In accordance with section 319F–2(c)(2) of the Project BioShield Act of 2004, it is the DHS' responsibility, in consultation with HHS and other agencies, to assess current and emerging threats of natural or chemical, biological, radiological, and nuclear agents, and to determine which agents present a significant material threat to the U.S. population.

To fulfill this responsibility, DHS conducted detailed modeling of threats, vulnerabilities, and consequences for various plausible scenarios of a terrorist attack. As a result of this work, DHS identified 12 biological threats, plus radiological and nuclear devices, meeting the statutory requirement to merit a Material Threat

Determination (MTD). As of September 20, 2006, DHS completed the MTD list based on detailed assessments of the agents with inputs from the intelligence, law-enforcement, scientific, and public-health communities. This MTD list will be updated, as needed, based on the outcomes of biennial Chemical, Biological, Radiological and Nuclear (CBRN) risk assessments.

Accompanying each MTD is a Population Threat Assessment (PTA). The PTA estimates the size of the population exposed by the agents identified in the MTDs to gauge the impact on the population and national infrastructure if that particular agent was released for a given high consequence plausible scenario. As of December 2006, DHS completed the PTAs of all MTDs. Moreover, DHS remains engaged in ongoing threat assessments and communicates regularly with our Federal partners to ensure we have accurate, up-to-date material threat information.

THE TRANSITION OF RESPONSIBILITY TO HHS

Once the MTDs are issued and PTAs are completed for any given threat, the results are shared with HHS for consequence modeling to support the procurement of appropriate countermeasures. HHS created the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE), under the direction of the HHS Assistant Secretary for Preparedness and Response, to identify, develop and acquire medical countermeasures that will improve public health emergency preparedness, including preventing and mitigating the adverse health consequences associated with the priority CBRN threats identified by DHS. On the PHEMCE Executive Governance Board (EGB), whose members are the Assistant Secretary for Preparedness and Response, the Centers for Disease Control and Prevention, the National Institutes of Health, and the Food and Drug Administration. DHS serves as an ex officio member along with the Department of Defense, the Homeland Security Council, the Office of Science and Technology Policy, the Office of Management and Budget (OMB), and the Office of the Vice President.

Upon identification of countermeasures that meet the eligibility requirements to warrant use of the Special Reserve Fund (SRF) the Secretary of DHS and the Secretary of HHS jointly request that OMB release funds to HHS from the SRF, to acquire the countermeasures. DHS has worked with HHS to expedite the implementation of BioShield by clarifying roles and responsibilities and by establishing mechanisms to improve efficiencies in this process.

Under section 319F–2(c) (7) (C) of the Public Health Service Act, as amended, HHS is ultimately responsible for managing the countermeasure procurement process including the negotiation of terms and entering into contracts for research, development, acquisition, procurement, storage and distribution of countermeasures.

THE FUTURE OF THE BIOSHIELD ENTERPRISE

DHS is confident that the Secretary of HHS' plan for the future of BioShield will result in addressing the appropriate needs of the Nation in terms of preparedness. In order to address the above, improvement in transparency to the program?s stakeholders was in evidence at the meeting held in September of 2006. The Pandemic and All-Hazards Preparedness Act of 2006 (PL 109–417) provided a missing piece to HHS' ability to stimulate the development of needed countermeasures with the authorization of the Biomedical Advanced Research & Development Authority to help companies through the advanced development process, if funded appropriately. The formation of the Public Health Emergency Medical Countermeasures Enterprise will provide the HHS Secretary with expert advice to make his decisions in collaboration with the interagency and its respective stakeholders. The PHEMCE strategic plan is a key step in defining, in a transparent way, how BioShield will carry out its business moving forward.

What is still missing from the enterprise is a commitment from the Nation's medical industry as a whole to invest in our biodefense. We must find ways to involve the private sector more broadly in this priority for our Nation. The ability of our private sector to thrive depends on their safety and security. It would be a worthy investment in time, talent and treasure for companies large and small to come to the table, even without the promise of large returns on their monetary investments. We thank the Congress for giving us a wide range of innovative acquisition and other authorities to pave the way for increased private investment. We will need to rely on the ingenuity and creativity of the American enterprise to reach a condition of security from bioterrorism.

CONCLUSION

Thank you, Mr. Chairman, for the opportunity to speak to you today on the role of DHS under the Project BioShield Act. I am happy to answer any questions the Subcommittee may have.

Mr. LANGEVIN. Dr. Runge, thank you for your testimony.

Dr. Parker?

STATEMENT OF GERRY PARKER, PH.D., DVM, PRINCIPAL DEPUTY ASSISTANT SECRETARY, OFFICE OF THE ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE, DHS

Mr. PARKER. Mr. Chairman and members of the subcommittee, I am honored to be here today to discuss the development and acquisition of medical countermeasures for chemical, biological, radiological and nuclear threats under Project BioShield, and the new authorities by the Pandemic and All Hazards Preparedness Act.

I am especially pleased to be here with my colleagues, Dr. Fauci from NIH, Dr. Goodman from the FDA, and Dr. Runge from the Department of Homeland Security, with whom we coordinate on a regular basis.

Project BioShield, enacted in 2004, authorized the $5.6 billion special reserve fund for the acquisition of security countermeasures. It was designated to incentivize industry to pursue the development of next generation products, to improve preparedness, and as an important complement to the NIH research program and the CDC's strategic national stockpile.

HHS has already achieved a significant level of preparedness against a number of threats. For example, we have stockpiled antibiotics that provide a substantial level of preparedness for bacterial threat agents, including anthrax and tularemia.

During the 2.5 years of implementation, Project BioShield launched eight acquisition programs for the four material threats defined by the Department of Homeland Security in 2004. These include programs for current and next generation anthrax vaccines, anthrax antitoxins, a next generation smallpox vaccine, botchulism antitoxins, and three medical countermeasures for radiological and nuclear threats, potassium iodine, DTPA, and acute radiation syndrome therapeutics.

Two programs, next generation anthrax vaccines and ARS therapeutics exemplify the challenges encountered in implementation of Project BioShield.

Because of these setbacks for the second generation anthrax vaccine and RPA and ARS are multifactoral, I will take this opportunity to convey, within limitations imposed by the Trade Secret Act and Procurement Integrity Act, HHS perspectives on lessons learned and intentions with regard to the path forward.

In December 2006, HHS terminated the acquisition contract with VaxGen for RPA when VaxGen failed to meet critical contract milestones. This followed a previous contract modification that provided VaxGen with substantial time to develop and deliver their product.

HHS developed a comprehensive strategy for advanced development and acquisition of current and next generation anthrax vaccines. As part of that strategy, the NIH continues to support the development of another second generation anthrax vaccine candidate and we remain committed to procure RPA.

HHS will also pursue the acquisition of an additional 10 million doses of ABA for near-term preparedness, the current license anthrax vaccine.

Last month HHS withdrew a request for proposals for acute radiation syndrome therapeutics because no competing product was sufficiently mature to warrant a BioShield acquisition at this time.

HHS will continue to pursue research, development and acquisition of these medical countermeasures and will take advantage of new authorities and scientific advances in development of potential candidates.

We have observed the following lessons in implementing Project BioShield. First, for the most part, experienced and well resourced companies have not responded to BioShield and the contract terms dictated by BioShield were challenging, particularly for less resourced companies.

Second, it is critical that developers establish effective relationships with the FDA early to gain a clear understanding of the regulatory requirements with respect to their product for the stockpile and for emergency use prior to licensure.

Finally, absence of a robust advanced development program has placed too much risk on BioShield acquisition programs.

We are pleased that the Pandemic and All Hazards Preparedness Act provides HHS with biomedical advanced research and development authority, BARDA, which includes important new tools.

We will use new authorities, such as advanced and milestone-based payments, in future contracts. We will facilitate discussions with the FDA and work to improve clarity on regulatory requirements to stockpile a product for emergency use prior to licensure. But we will also continue to insist on and verify demonstrated understanding of those products by developers for their products.

The importance of advanced development is exemplified by our pandemic influenza advanced development program and we are successfully pursuing a portfolio of countermeasure candidates with industry partners to mitigate acquisition risk in that program.

I cannot overstate the importance of advanced development and the fiscal year 2008 request for advanced development funding is critical to BARDA implementation.

Finally, last July, HHS established a public health emergency medical countermeasures enterprise to coordinate all levels of public health preparedness against terrorist and naturally occurring threats.

We today have submitted to the Federal Register, and hopefully it will be released today, we submitted it yesterday, but hopefully it will be released today, the enterprise implementation plan, which identifies the top priority medical countermeasure development and acquisition thrust.

The implementation plan reaffirms and further identifies our commitments to acquisition of anthrax vaccines, anthrax antitoxins and therapeutics for radiological and nuclear threats. It also identifies the need for continued development and acquisition of broad spectrum antibiotics, antivirals and diagnostics.

The department is committed to fulfilling its role both as a steward of the public's trust and as a reliable and predictable partner for industry.

The release of the enterprise strategy and implementation plan signals our commitment to greater transparency in partnership with our stakeholders. We will build on past successes, lessons

learned, and new authorities under the Pandemic and All Hazards Preparedness Act to continue to improve the implementation of Project BioShield.

Mr. Chairman, this concludes my testimony, and I will be happy to answer any questions. Thank you.

Mr. LANGEVIN. Thank you, Dr. Parker.

Dr. Fauci, the floor is yours.

STATEMENT OF ANTHONY FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTES OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, HHS

Dr. FAUCI. Mr. Chairman, members of the committee, thank you for giving me the opportunity today to discuss with you the NIH's role in the research endeavor associated with the development of countermeasures for emerging public health threats, both naturally occurring, as well as deliberately propagated.

I have some visuals here. On this first chart, I just want to emphasize the traditional role of the NIH whose activities are all based on fundamental matrix of basic research.

In addition, in our approach to emerging public health threats, we have built both physical and intellectual infrastructure in the form of training individuals in this subspecialty, not only of infectious diseases, but also, most recently, in RAD, NUKE and CHEM.

Importantly, we conduct and have considerable experience in clinical trials leading to the ultimate development and use of countermeasures. A typical example of that was the pandemic H5N1 influenza vaccine that was just approved yesterday by the FDA, was done through the NIAID clinical trials network.

All of our activities are ultimately aimed for the development not by us, since we do the research of it, but the ultimate development of countermeasures in the form of diagnostics, therapeutics and vaccines.

This slide, Mr. Chairman, I have shown to you before. It is a map of the world in which we have listed, over the last 25 to 30 years, emerging and reemerging threats, ranging, for example, from a brand new threat like HIV and SARS to a reemerging threat like West Nile and recurrent drug-resistant tuberculosis, malaria, staphylococcus, enterococcus, et cetera, and, finally and unfortunately, deliberately propagated microbes.

We play a role in this endeavor because we have decades of experience in the arena particularly of microbiology and infectious diseases, of dealing with naturally occurring infectious disease threats.

This holds us in good stead to be able to extrapolate the knowledge, the fundamental basic research, as well as the clinical applicability when we are looking at bioterror threats.

And in response to the post–September the 11th anthrax attack, we revved up considerably our research component of the broader HHS effort. On this slide shown here are the original strategic plan and research agendas for the various category A, B and C agents together with the progress reports, the most recent of which was this past summer.

In addition, we have published our radiological and nuclear strategic plan and research agenda and soon to be published, the CHEM component of that.

With regard to the expansion of our research capacity, we have made great strides in the last 5 years. With regard to physical capacity, we have two additional extramural, namely, in the university, BSL–4, the highest level of containment. We have several BSL–313. We have regional centers of excellence and note the name, the regional centers of excellence for biodefense and emerging infectious diseases, because even if we never get and we hope we never will get another bioterror threat, the work that is done at the research level will have important extrapolation to the things that we know will happen and that is naturally occurring and reoccurring threats.

With regard to some of the accomplishments in biodefense research, let me just mention very briefly a few. First, the threat-specific. In regard to vaccines, when we started off post-September 11, there were 18 million doses of smallpox vaccine available for this country.

Based on the clinical trials, using dilutional techniques and the newer generation, we now have a vaccine dose of smallpox vaccine to every person in this country. We have developed a first hemorrhagic fever vaccine, Ebola, which will soon combine with Marburg and Lassa.

In addition, we have done work with anthrax. You have heard about the RPA research that we have done, but also we have shown that when the standard original first generation anthrax vaccine is given with antibiotics, you can decrease the time on antibiotics and allow for greater clearance of those spores.

In therapeutics, we have had some interesting successes. We now have the first what we believe to be effective anti-smallpox antiviral, the SD–246. Parenthetically, that was used, we believe, successfully on the child of the armed forces personnel who had a complication of their smallpox vaccine when the child developed a vaccinia complication, because the child had eczema.

We also have molecular approaches to Ebola and antitoxins against anthrax. In diagnostics, we now have molecular capability, Mchip, to distinguish between influenza A that is pandemic and that is seasonal. And, finally, you may have read in the newspapers just a few days ago, we have the ability now, by looking at gene expression in animals that have been irradiated, as to what the dose of irradiation that they have received, which will allow us to prepare how we might treat that individual.

And then we have these cross-cutting things, such as genomic sequencing, therapeutic screening and understanding what we call host pathogen interaction, namely, how the body responds to threats of microbes.

This is of great importance, because, again, even if we never get another bioterror threat, it will have important spin-offs in other diseases.

And, finally, on this last slide, I thought I would schematically diagram the place that the NIH plays in the schematic between fundamental basic research up through and including the purchase and acquisition by BioShield.

And as you see, classically, our activities are in the area of research that is basic and applied and the early part of product development. BioShield does the acquisitions and what you were talking about in your introductory statement about BARDA and the hopeful role that BARDA will play in bridging that gap between the research endeavor and the acquisitions through BioShield.

Thank you very much, Mr. Chairman. I would be happy to answer questions for you.

[The statement of Dr. Fauci follows:]

PREPARED STATEMENT OF ANTHONY S. FAUCI, M.D.

INTRODUCTION

Mr. Chairman and Members of the Committee, thank you for the opportunity to speak with you today about the role of the National Institutes of Health (NIH) in preparing the Nation to respond effectively to emerging public health threats. In my testimony today, I will describe NIH research that is leading to new and effective countermeasures against these threats. I also will discuss the NIH role in the implementation of the Project BioShield Act of 2004 and the Biomedical Advanced Research and Development Authority (BARDA), established by the Pandemic and All–Hazards Preparedness Act of 2006.

As a Nation, we must be prepared to respond quickly and effectively to any threat to public health. The threats we face include new microbes that might emerge naturally, such as the virus that caused Severe Acute Respiratory Syndrome (SARS), and familiar pathogens that re-emerge with enhanced properties or in unusual settings, such as bacteria that cause extensively drug-resistant tuberculosis (XDR–TB) and influenza viruses with pandemic potential. As was made clear by the terrorist attacks of 2001—including the anthrax attacks in the eastern United States—we must also be prepared for the deliberate release of pathogenic organisms, biological toxins, chemical poisons, or radioactive substances. The primary role of the NIH in confronting these diverse threats is to carry out basic and applied scientific research and early-stage development of potential products, upon which late-stage advanced product development and ultimately approval of vaccines, therapeutics and other medical countermeasures can be based.

NIH RESEARCH ON EMERGING PUBLIC HEALTH THREATS

Research to mitigate emerging threats to public health is a key focus of the NIH. The National Institute of Allergy and Infectious Diseases (NIAID) is the component of the NIH assigned primary responsibility for research on emerging and re-emerging infectious diseases, including the deliberate use of infectious biological agents and toxins that directly affect human health. The NIAID also coordinates NIH research into medical countermeasures against chemical, radiological and nuclear agents; this research is supported by several NIH institutes, including the NIAID, the National Cancer Institute, and the National Institute for Neurological Disorders and Stroke.

Strategic planning to guide the broad NIH biodefense and emerging infections research effort has been extensive, and has involved substantial consultation with outside experts in academia, private industry, civilian government agencies, and the military. The overall strategy encompasses three components of NIH biodefense and emerging infections research: the infrastructure needed to safely conduct research on dangerous pathogens; basic research on microbes and host immune defenses that serves as the foundation for applied research; and targeted, milestone-driven, early-phase development of medical countermeasures to create the vaccines, therapeutics and diagnostics that will be needed in the event of a public health crisis. These efforts enhance the Nation?s preparedness for both potential bioterrorism attacks and naturally occurring infectious disease outbreaks.

The NIH is substantially expanding the Nation?s biodefense research infrastructure, which will greatly enhance our ability to safely and efficiently conduct research on infectious agents. Facilities currently or soon to be under construction will be capable of safely housing research on the most deadly pathogens, as well as microbes that are more familiar and less virulent, but nonetheless deleterious to human health. These facilities include two National Biocontainment Laboratories (BSL–4 - the highest level of containment) and thirteen Regional Biocontainment Laboratories (BSL–3 ? one level down from highest level of containment). In addition, three intramural biocontainment labs?on the NIH campus in Bethesda, Maryland (BSL–3), on the National Interagency Biodefense Campus at Fort Detrick in

Fredrick, Maryland (BSL–4), and at the NIAID Rocky Mountain Laboratories in Hamilton, Montana (BSL–4)?are operational or nearing completion.

In addition to building new facilities, the NIH has strengthened the Nation's intellectual infrastructure by establishing a network of ten Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research. These Centers conduct research and development activities and provide training for future biodefense researchers. Most recently, the NIH announced awards to create six Centers of Excellence for Influenza Research and Surveillance; these centers will bolster influenza research in key areas, including understanding how animal viruses can adapt to cause human disease and how the human immune system responds to infection with the virus.

The NIH role in biodefense research is similar to its role in biomedical research in general; namely, to support basic scientific discovery, applied research and early-stage development activities that start new vaccines and drugs down the pathway toward approval. Early-stage development activities that the NIH often supports include preclinical testing, animal model development, and establishment of pilot lot-scale manufacturing processes. Late-stage advanced product development, such as commercial-scale process development and validation, is usually left to industry. On rare occasions, however, the NIH has supported late-stage medical countermeasure development activities. For example, in 2003, the NIH awarded milestone-driven contracts to two companies, Avecia and VaxGen, Inc., for late-stage advanced development of second-generation anthrax vaccines. These contracts predated the Project BioShield Act of 2004.

The vaccines are based on a purified, recombinant (r) anthrax protein called Protective Antigen (PA), against which the body generates a strong antibody response; studies conducted in the 1990s showed that rPA vaccines could protect animals exposed experimentally to airborne anthrax spores from developing anthrax disease. The Avecia and VaxGen contracts supported activities such as advanced manufacturing process development, Phase II clinical trials, and advanced assay development. As noted above, NIH funding of late-stage advanced development for biodefense countermeasures is the exception rather than the rule.

RESEARCH PROGRESS

NIH research has yielded substantial scientific advances in the effort to counter emerging public health threats. For example, new or improved candidate vaccines and therapies against smallpox and Ebola virus have shown great promise. Among these is ST–246, a promising smallpox drug candidate that has protected nonhuman primates from what would otherwise be a lethal exposure to live smallpox virus, and that is now in human clinical trials. Basic research also has proceeded rapidly. NIH-supported researchers recently determined the structure of botulinum toxin—a Category A bioterror threat agent and the cause of botulism—as it binds to its receptor protein on nerve cells; these findings may lead to the development of new drugs to treat botulism. Further, an NIH program that screens both approved drugs and new drug candidates has identified several promising anti-influenza drug candidates, including FluDase (which binds host cell receptors to prevent viral entry), T–705 (which inhibits replication of viral RNA) and Peramavir (which inhibits an influenza enzyme called neuraminidase). All three of these influenza drug candidates are undergoing further development in partnership with industry sponsors.

With regard to the development of medical countermeasures against radiological, nuclear, and chemical threats, the NIH has established eight Centers for Medical Countermeasures against Radiation, and four Centers for Countermeasures against Chemical Threats. Basic and applied research conducted in these centers and elsewhere is moving forward rapidly. For example, researchers supported by one of these Centers recently characterized changes in gene activity in mice exposed to different doses of ionizing radiation and in cancer patients undergoing radiation therapy; these results may lead eventually to a diagnostic test to distinguish people who have suffered serious radiation exposure from those who have not prior to the onset of clinical illness. That capability would allow treatments to be efficiently directed early on to those who need them most following a radiological incident.

NIH ROLE IN BIOSHIELD AND BARDA

Two landmark pieces of legislation designed to speed the development, approval, and acquisition of biodefense and emerging infections countermeasures have been enacted in recent years: the Project BioShield Act (Public Law 108–276), which became law in July 2004, and the Pandemic and All–Hazards Preparedness Act (Public Law 109–417), which became law in December 2006.

The BioShield legislation provided HHS and its constituent agencies with several new authorities regarding medical countermeasures against a terrorist attack with a biological, chemical, nuclear, or radiological agent or device. Three of these au-

thorities were of particular relevance to the NIH. First, BioShield provided the NIH additional flexibility in awarding contracts, cooperative agreements, and grants for research and development of critical medical countermeasures. Second, BioShield gave the NIH streamlined personnel authority that has allowed expedited hiring to fill key biodefense positions. Third, BioShield provided the NIH with additional authority for the construction of research facilities. The NIH has used all three of these authorities in carrying out its biodefense and emerging infections research and development responsibilities.

Perhaps the most important provision of BioShield was the establishment of a secure funding source at HHS for the purchase of critical medical countermeasures. Many pharmaceutical and biotechnology companies have been willing to help in the development of biodefense countermeasures, but they needed reasonable assurances that a market for these products would, in fact, exist should they invest the resources necessary to fully develop them. To provide these incentives, BioShield established a Special Reserve Fund for the purchase of biodefense countermeasures to be placed in the Strategic National Stockpile for use in an emergency.

Procurement contracts under BioShield are developed and awarded by the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR). As is the case with other scientists within the Federal government and particularly within HHS, NIH personnel often serve as subject matter experts, consultants, and members of committees and boards that participate in the planning and execution of the HHS preparedness activities, including the development of contracts for BioShield acquisitions. Ultimately, however, the decisions regarding acquisitions are made by the Office of the ASPR.

Title IV of the Pandemic and All-Hazards Preparedness Act established BARDA within HHS. When BARDA is fully implemented, the Office of the ASPR will administer the Biodefense Medical Countermeasure Development Fund to support late-stage advanced product development. Because the NIH is likely to have played a role in earlier phases of development of some of the products that BARDA might support, the NIH will coordinate with BARDA staff. However, all decisions concerning products to be supported by BARDA will be made in the Office of the ASPR.

CONCLUSION

Emerging and re-emerging public health threats pose a perpetual challenge. At one time, some in public health thought it might be possible eventually to ?close the book? on the study of infectious diseases because of advances in therapies and vaccines. However, it is now clear that naturally emerging and re-emerging infections will challenge us for the foreseeable future, as will threats from deliberately disseminated infectious diseases, chemical, or radiological terrorist attacks. The task for the NIH is to continue building a strong foundation of basic and applied research and development that is needed to counter these threats, and also to be nimble enough to respond with speed and precision to new threats as they arise. NIH efforts to address these challenges complement those of our colleagues in ASPR, CDC, FDA and other agencies in the Federal government to protect the health and safety of our Nation.

Thank you for the opportunity to appear before you today. I am happy to answer any questions you may have.

Mr. LANGEVIN. Thank you, Dr. Fauci.

Dr. Goodman?

STATEMENT OF JESSE GOODMAN, M.D., MPH, DIRECTOR, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, HHS

Dr. GOODMAN. Good afternoon, Mr. Chairman and members. I am Jesse Goodman, director of the Center for Biologics at FDA, or CBER. I appreciate both your interest in this very important subject and the opportunity to be here to tell you about our role in regulation and development of vaccines, including those intended for response to a threat to our national security.

At CBER, enhancing the nation's preparedness is one of our highest priorities, including the development of vaccines and other products needed to face natural or potential deliberate threats, and I would like to second Tony's comment that really we see this kind of preparedness as dual use for the threats that occur naturally,

building the infrastructure and capabilities will also prepare us for threats that occur not naturally.

So when we think about pandemic, we are also thinking about bioterrorism.

It is essential to do everything we can to assure that such products, though, which really we need to understand could be received by millions of people in an emergency, that those products are safe and that they perform as expected, that they work.

Therefore, while we work very closely with many partners, including those at this table, to achieve our nation's and indeed our global preparedness goals, our responsibility and one that only FDA has is to provide an objective scientific assessment of the safety and efficacy of these products.

To help provide some perspective, I am going to briefly discuss some relevant issues in vaccine development that illustrate some of the challenges there. I won't be discussing any particular product in detail, because my understanding is that under applicable laws and regulations, FDA cannot normally publicly provide information concerning a specific investigational product prior to its licensure.

Vaccines are really different from most drugs in a number of respects and achieving the highest quality in manufacturing can be especially complex, challenging and critical. It is very important to get this, that the vaccine—medical products, in general, are not always predictable and vaccines represent a particular challenge.

The manufacturing includes many steps and requires careful in-process monitoring to assure that the product is safe, pure and potent, and even undetected or poorly understood or not understood changes in process or materials can significantly affect the product and even its safety and effectiveness.

Thus, the process must produce a consistent and well characterized product. In addition, unlike drug products that are often used to treat an existing disease or condition, vaccines, as you well know, are given typically to large numbers of healthy people.

So, therefore, any concerns about averse events, for example, are very special concerns.

In developing a vaccine, there are four major stages that are worth your while to think through.

There is the pre-clinical stage, which is predominantly the testing that occurs before a product can even be used in people, animal testing, toxicology testing, et cetera.

There is the investigational new drug stage, in which, based on that information, FDA may allow a sponsor to then do studies in humans to help establish a dose, safety, effectiveness.

These studies, it is very important, because this is relevant to some of your concerns, have to be done in a well monitored situation and very well understood conditions.

And then there is the license application stage, where the manufacturer submits all of this information together to support our review of the manufacturing process and the safety and effectiveness of the vaccine.

And as many of you know, our responsibilities extend even after the licensure to look at safety, the quality and ongoing inspection and quality assurance of manufacturing.

So again, while all medical product development is challenging, new vaccine development is especially complex and we actually expect that challenging issues will arise.

Such issues can also raise safety concerns or study design concerns that result in FDA placing an IND or a study proposed by a sponsor on what we call a clinical hold and, as you know, that is one of the issues in VaxGen.

A clinical hold is an order by FDA not to initiate or continue human studies until the issues of concern have been satisfactorily addressed. Most of these kinds of issues are eventually resolved, allowing product development to proceed.

What are the typical reasons we might place a study on hold? One would be if companies are—if patients are exposed to an unreasonable risk, for example, a safety risk.

Another would be if the study plan or the protocol is deficient in design to meet its objectives.

So clinical hold is an important human subject protection safeguard and would also help prevent studies in investigational products which might be unlikely to provide useful information.

So a study that isn't going to provide useful information would be an unethical study, because you would ask people to take an investigational product without adequate assurance that you were going to get useful information from that study.

Now, on top of these responsibilities, we strive to develop processes that can facilitate the development of these products that meet public health needs. An example is the animal rule, which provides a mechanism to evaluate the effectiveness of a new product based on data from animals when those studies can't be done in humans, because, for example, the disease doesn't occur or challenge studies would be unethical.

Such approvals still require demonstration of effectiveness in humans. An additional tool made available, in part, under BioShield is for FDA to allow the use of unapproved products or uses of products in a declared emergency.

This is under the emergency use authorization, or EUA. To authorize such emergency use, FDA needs to find that the known and potential benefits of the product's use for that specific emergency situation or scenario outweigh the known and potential risks of the product and that there is no adequate approved and available alternative.

And our approach has been to try to get as much and as high quality of information ahead of time so if we ever face an emergency where we have to make these decisions for the American public, we can make the best decisions.

Now, we work very hard with partners to develop and define these kinds of innovative pathways and tools. Perhaps most importantly, we do provide intensive interactive consultation and technical assistance to facilitate development and availability of products. This can be hundreds or thousands of hours in product development of high priority products like we are talking about here today.

As noted, though, we always come back to our most critical core role, which is to protect the human subjects and provide an independent scientific assessment of the product both during its devel-

opment, in reviewing an application for approval, and particularly in reviewing a request that might come for an emergency use authorization.

Now, I think it is very important to say—I am almost done—that to protect and preserve our scientific integrity, our independence and judgment and that of our review staff, our professional review staff, we do not involve ourselves in specific HHS decisions to award or terminate contracts.

In fact, if myself or staff are present when such issues arise, we will actually leave the room. This was our process at the time of HHS's VaxGen acquisition and it remains so today.

We do provide the technical and scientific assistance that I mentioned. We may provide technical comments to try to help form requests for proposals, et cetera.

At FDA, we base our important decisions on the available scientific information and a careful independent evaluation of risks and benefits to patients. That is what you expect.

We are fully committed, though, and fully engaged in continuing to work with our federal partners and also with product developers and industry to achieve our nation's highest priority public health preparedness goals.

So I really appreciate the opportunity to come and discuss this with you, and I will welcome our discussion and your questions.

Thank you very much.

[The statement of Dr. Goodman follows:]

PREPARED STATEMENT OF JESSE L. GOODMAN, M.D., M.P.H.

Good afternoon Mr. Chairman and members of the Committee, I am Jesse L. Goodman, M.D., M.P.H., Director of the Center for Biologics Evaluation and Research (CBER) at the United States Food and Drug Administration (FDA). I am also a practicing infectious diseases physician and a microbiologist. CBER is the Center within FDA that is responsible for the regulation of most biological products, including vaccines, blood and blood products, and cellular, tissue and gene therapies. Thank you for the opportunity to discuss FDA?s role in the regulation of vaccines including those intended for use in response to a threat to our national security.

At CBER, enhancing the nation?s preparedness is one of our highest priorities, whether it is protecting the safety of our blood supply from emerging threats like West Nile Virus or facilitating the development of vaccines needed to face natural threats or potential deliberate threats, from pandemic flu to smallpox to anthrax. It is essential to do all we can to assure that such products be safe, and that they work. Therefore, while working closely with many partners to achieve our nation?s and our global preparedness goals, our most critical and unique responsibility is to also do all that is possible to provide an objective, scientific assessment of the safety and efficacy of these and other biologic products. To help provide perspective, I am going to discuss relevant issues in vaccine development that illustrate the opportunities and challenges faced in developing these important products. As you know, under applicable laws and regulations, information provided to FDA concerning a specific investigational product is not available for public disclosure prior to licensure of the product.

Vaccines are different from most drugs in several respects and achieving the highest quality in manufacturing can be especially challenging and critical. Vaccines production frequently utilizes living cells and organisms, as well as complex growth conditions and materials often derived from living sources. The manufacturing process for vaccines usually includes many steps and requires frequent in-process monitoring of the product and components to assure that the product is safe, pure, and potent.

The production of most vaccines requires the growth of the immunizing agent (i.e. bacteria, virus, etc.) or the genetically engineered expression, in living cells, of recombinant immunizing proteins derived from that agent. The conditions for accomplishing this are complex and subtle, and even undetected or poorly understood changes in process or materials can significantly affect the composition of the vac-

cine and its safety, efficacy, or both. Thus, the process must be well controlled and monitored, and produce a consistent and well characterized product prior to its licensure. Even after licensure, manufacturers conduct a series of tests on the bulk, intermediate and final vaccine products and typically are required both to meet all product and process specifications and to submit the results of key tests, along with samples of the product to CBER for evaluation prior to CBER?s approval of lot release and administration of vaccine. The tests performed on the final product may include those for sterility, identity, purity, and potency to assess immunogenicity and/or antigen content and, depending on the nature of the vaccine and its manufacturing process, additional tests as required by CBER to assure vaccine safety and quality.

Unlike drug products that are most often used to treat an existing illness or condition, vaccines are generally administered to large numbers of healthy individuals in order to prevent infectious diseases. Therefore, the potential adverse effects of vaccines, even if the events are rare, present unique risk-benefit considerations and may give rise to heightened concerns in the public health context.

From a regulatory perspective, there are four major stages in vaccine development. These stages include:

- The preclinical stage which consists of the development and testing of the product prior to the product being tested in humans. Early in the product development process, sponsors test candidate vaccines *in-vitro* (e.g., in laboratory assays, studies in cell lines, etc) and in animals. These early nonclinical studies give an indication of whether studies would be reasonably safe to proceed in humans and may also provide information regarding the potential effectiveness of the product.
- The Investigational New Drug (IND) stage consisting of multiple phases where the investigational product is studied in human subjects under well-defined conditions and with careful monitoring. In certain cases where studies to demonstrate efficacy in humans are not ethical or feasible, sponsors may conduct studies to demonstrate efficacy of the product in appropriate animal models.
- The license application stage is when manufacturers submit data and information regarding the results of the clinical and nonclinical studies, as well as complete information regarding the product and its manufacturing process to FDA for a complete review of product manufacturing, safety and effectiveness in support of licensure.
- Finally, for products that are approved, FDA continues its oversight during the post licensure stage to include review of post-marketing safety information from adverse event reports, periodic reports, post-marketing studies, review of lot release information and testing, and inspections of manufacturing facilities.

FDA often provides guidance to sponsors, even prior to submission of an IND, in regard to both the types of preclinical studies needed and the design of the clinical trials needed to assess the intended use(s) of the product. FDA?s guidance is intended both to help protect human subjects and to assure that the studies performed are designed in such a manner that the study results are likely to provide sufficient information to allow a determination of the product's safety and efficacy.

While all medical product development is challenging, vaccine development is especially complex, and we expect that new challenging issues will arise during the development process. The issues may arise in any number of areas, and may affect product potency, quality, and safety. Such issues can raise safety or study design concerns that may result in FDA placing an IND on clinical hold. A clinical hold is an order by FDA not to initiate or continue clinical studies until the issues of concern have been satisfactorily addressed. It is important to note that most clinical hold issues are eventually resolved, allowing product development to proceed. I'd like to describe some of the more typical reasons for FDA to place a trial on hold. FDA may determine that study participants would be exposed to an unreasonable and significant risk of illness or injury. Or, the IND application may not have sufficient information for FDA to adequately assess the risk. For later phase studies, FDA may place an IND on hold if the study plan or protocol is deficient in design to meet its stated objectives. Clinical hold is an important human subject protection safeguard and also helps prevent the conduct of studies of investigational products that are unlikely to provide information that is useful in evaluating the product. FDA staff spends a considerable amount of time interacting with sponsors to resolve clinical hold issues.

FDA strives to develop processes that facilitate product development to meet emerging public health needs, such as protection from terrorist agents and prevention of pandemic influenza and other emerging threats. The regulation known as the "Animal Rule" provides a mechanism for FDA to approve medical treatments based

on effectiveness data from animal studies when human efficacy studies are unethical and/or not feasible. Under the "Animal Rule," effectiveness would be evaluated in adequate and well-controlled animal studies that establish that the product is reasonably likely to produce clinical benefit in humans. Such approvals also require the demonstration of safety in humans. These safety studies may be conducted concurrently with the animal studies.

An additional tool available to speed product availability is the ability for FDA to allow the use of unapproved products and unapproved uses (so-called "off-label" uses) of approved products, in a declared emergency, under the Emergency Use Authorization (EUA) provision of the Food, Drug, and Cosmetic Act. This authority was expanded under the Project BioShield Act. To authorize such emergency use, FDA would need to find that the agent can cause a serious or life-threatening disease or condition; that based on the available information it is reasonable to believe that the product may be effective against the disease or condition; that the known and potential benefits of the product's use outweigh the known and potential risks; and that there is no adequate, approved and available alternative.

FDA works very hard to develop and define innovative and needed pathways and evaluation tools, and to provide technical assistance to facilitate development and availability of needed products that are safe and effective. One of our most critical and core roles is to protect human subjects and to provide an independent scientific assessment of the product, both during the development process, and in reviewing product applications and requests for EUA.

To protect and preserve our scientific independence and judgment, FDA does not involve itself in specific HHS contracting decisions to award or terminate contracts. FDA's longstanding practice is to recuse ourselves from HHS decision making in specific contracting decisions. This was our process at the time of HHS's VaxGen acquisition contract and it remains so today. FDA does provide scientific and technical expertise on various HHS-led interagency counterterrorism working groups, which among other things are involved in defining the needs for medical countermeasures being pursued by HHS for the Strategic National Stockpile. In addition, FDA may provide technical comments to HHS upon request on draft Requests for Proposals for such countermeasures.

At FDA, providing the American public with safe and effective medical products is our core mission. We base important decisions, such as to allow specific human studies of an investigational product, or to approve a vaccine or allow its emergency use, on the available scientific information and a careful evaluation of risks and benefits to patients. We also are fully committed and engaged in continuing to work with our federal partners and with product developers to provide an efficient product development pathway to achieve our nation's high priority public health preparedness goals.

Thank you again for this opportunity to discuss vaccine development with the Committee. I welcome your comments and questions.

Mr. LANGEVIN. Thank you, Dr. Goodman.

I want to thank all witnesses again for their testimony.

Let me begin with Dr. Parker, if I could.

Doctor, VaxGen's original contract from November 2004 stipulated that the company begin delivering its vaccine to the strategic national stockpile once it met the standard for contingency use.

In May 2006, HHS unilaterally modified VaxGen's contract to require the company to conduct an additional clinical trial so that the vaccine would meet the higher standard of emergency use before it could be delivered.

What was the rationale for imposing this additional requirement?

Mr. PARKER. Mr. Chairman, thank you for the question.

First, there was no additional requirement. It was clear that VaxGen was not going to be able to make their delivery time by the original contract.

It was necessary to modify the contract to basically reset the clock and give the contractor the ability to continue the development and hopefully be able to deliver product that would be suffi-

cient to meet the requirements for acceptance into the strategic national stockpile.

We actually even used proposed timelines and the most conservative timelines that VaxGen had provided to us in resetting that clock for an imposed additional interim milestone so we could better track progress of this development effort.

So the bar was not changed. The standards remained the same. We had to modify the contract to allow them additional time to hopefully be successful.

Mr. LANGEVIN. Now, when I had discussions with VaxGen, I asked the question in such a way that I said that it is my understanding that some thresholds were missed and we have spoken about that, but that the goalpost, so to speak, was moved further down the field. So that there were alterations that were made and so which is true, and the answer was basically both.

You are saying that the goalpost was not moved.

Mr. PARKER. The goalpost was not moved. We modified the contract because it was clear they were not going to meet the original deadline to deliver product to the SNS. We modified the contract to allow additional development time using their timelines, most conservative timelines for delivery.

The standards for meeting that requirement did not change and that was—in the contract, there was, in fact, spelled out very clearly, as an advanced understanding of what is required in regards to the clinical, non-clinical data, the need to have a validated manufacturing process in three consistency lots, and that they needed to—ultimately, these were going to be requirements that would be agreed upon by the FDA and also in consultation with us.

It was also incumbent on the contractor, who worked very closely with the FDA, to very clearly understand what those ultimate requirement were.

Now, VaxGen perceives and they have an opinion that there was a difference in what is defined as contingency use IND and emergency use authorization. But VaxGen was informed that the requirements, to satisfy requirements for either the use of a contingency use IND terminology or emergency use were the same thing. And so the requirement didn't change.

Mr. LANGEVIN. But didn't modification require additional tests for phase two?

Mr. PARKER. If it did, it was far into the future, but it still was the original terms of the contract did not change.

Mr. LANGEVIN. But additional tests are moving the goalposts down the field. Wouldn't you agree?

Mr. PARKER. No, no.

Mr. LANGEVIN. Doctors Fauci and Goodman, to what extent, if I could ask you, did NIH and CBER participate with HHS in review and evaluation of the RFP responses, in particular, VaxGen's proposed scope of the work and project plan?

If they weren't involved with a program of this importance and viability, why weren't they? And if they were involved, why did CBER claim in December 2005, a year after the contract was issued, that they could not provide regulatory guidance specific to the SNS program because they were unaware of how HHS intended to use the vaccine in the stockpile?

Dr. FAUCI. Mr. Chairman, from the standpoint of the NIH, we were not involved in the evaluation of the contract. We did provide logistical assistance in the actual drawing up of the contract. In other words, people with contracting expertise were able to do that.

We did not get substantively involved at all in the actual evaluation of that, but we did, on an ad hoc basis, the way any of a number of the agencies within HHS and outside of HHS were involved on an ad hoc basis with subject matter expertise, but not in the actual evaluation and scoring of the contract.

Mr. LANGEVIN. Dr. Goodman?

Dr. GOODMAN. Mr. Chairman, we were not involved in reviewing contract applications for any applicant whatsoever and, as I have said, we have really tried to draw a bright line to be very clear and independent then in our evaluations of these projects.

We have, as I have also mentioned, provided—to try to help the process and make things more likely to succeed, we have tried to provide technical input, scientific input to our colleagues at HHS as they develop the RFPs, et cetera.

Now, with respect to your question about, I guess, VaxGen's statement that we, in December, when they asked for details about requirements, information, wanted to consider an emergency use authorization, I can make a couple of points.

One is that that request was received very close in time, is my understanding from the review staff, before a meeting. So that in terms of time to review and do some of the fact-finding needed, that was an issue.

What we needed to do at that point was there had been a number of changes that occurred over several months, including the addition of the licensed anthrax vaccine to the national stockpile, and we wanted to check with our colleagues in HHS and CDC to understand, in a possible emergency use authorization, what was their vision of how this product might be used, because part of our assessment are things like what kind of patients would get it, for what indication, how many patients might get it, how would it be used relative to the licensed vaccine.

Actually, this was an attempt to get the best information in order to be able to provide VaxGen with the most up-to-date advice, which we then provided them very shortly thereafter. And I would say that that advice, also, from talking to my review staff, who had very intensive interactions with this company over many, many months, that that advice was entirely consistent with previous advice that they have received.

Mr. LANGEVIN. Thank you, gentlemen.

The chair now recognizes the ranking member of the subcommittee, the gentleman from Texas, Mr. McCaul.

Mr. MCCAUL. I thank the chairman.

Mr. Parker, on May 9th of 2006, you appeared before a House Government Reform Subcommittee and you were asked by Congressman Shays about what you perceived as the number-one threat to this country and your response was, as you will recall, "Anthrax, anthrax, anthrax."

I think you were correct then and I think it is still correct today. Yet, on November the 4th, 2004, a contract that was awarded to VaxGen, a company that really had no history of any production

success, had no history of a successful vaccine being produced, a company which since then has defaulted on its contract, the contract has been canceled and now they have appealed and have apparently settled with the United States government.

I question that contract award, particularly when you had companies like Emergent Biosolutions, particularly that company, which had an FDA approved vaccine.

Now, I understand the contract was for a second generation vaccine, but I would like to know, and this is more for the panel, why was this contract awarded to VaxGen, again, a company with really no track record of success, over a company which did have a track record, actually had stockpiled doses of anthrax, was actually on contract with the Department of Defense?

This is the number-one priority in terms of bioterrorism and I don't understand why that award was made the way it was.

And I will say that I just received word, though, that HHS has announced that they will be buying 10 million doses of the anthrax vaccine, an additional four million that DOD will be purchasing.

To date, I am only aware of one manufacturer that could possibly comply with that.

And I don't know—and that has happened, Mr. Chairman, during the course of this hearing, which, if that is in any way attributed to this hearing, a policy success in a bipartisan fashion.

Having said that, as a former federal prosecutor, I question the integrity has been compromised in the bidding process when you have a copy such as VaxGen getting this type of award.

So I would like to just go ahead and throw that out to the panel for your comment.

Mr. PARKER. There is a lot in your question, but let me first just take the original award to the VaxGen contract and why it was important to pursue a second generation anthrax vaccine.

And I will just summarize very quickly, but that was originally a recommendation out of the Institute of Medicine at about the same time when formerly BioPort, now Emergent was still undergoing their renovation and really coming out of a tough period in their corporate history.

But there was a strong recommendation out from the Institute of Medicine to pursue a newer generation vaccine that would have some manufacturing advantages, particularly when it comes to consistency and characterization of the product.

And so there was a decision at the time to vet it in the interagency and a decision that went to the deputies committee to pursue the second generation anthrax vaccine.

Now, that was a procurement that was an open, competitive procurement. There was a technical evaluation panel that included government and non-government experts that reviewed the submissions against that proposal and VaxGen received the highest technical score and cost and was the one that was recommended for approval.

The I.G. has subsequently looked back at that acquisition, has rendered an opinion and if you haven't seen it, we will make sure that you get a copy of that.

We are actually going back into doing an acquisition analysis, a well, as part of our quality assurance and lessons learned in the department to take a real hard look at that, as well.

But it was a straight-up, under the FAR, competitive acquisition and was selected. Now, in regard to—

Mr. MCCAUL. If I can say it, it is either a competence issue or something worse as to why a company with absolutely no success gets awarded a contract over one that has an FDA approved vaccine.

It just raises some serious questions—

Mr. PARKER. That particular procurement was only focused on second generation, a recomb protective antigen and anthrax vaccine absorbed wasn't able to submit under that, because it is the current generation's licensed anthrax vaccine.

Now, we do have a comprehensive—I agree, my statement still stands from that former testimony. That is my opinion about the seriousness of the threat and it is extremely important that as we move forward to pursue a very comprehensive strategy for anthrax vaccines, because of—

Mr. MCCAUL. If I could just conclude, because I know my time has expired.

It has been 6 years since we have had the anthrax threat and since 2004—we don't have anymore time to waste on this. It is an urgent matter and I commend the chairman for holding this hearing.

I would hope that when VaxGen returns for their testimony, that we will look into this bidding process, as well, and conduct an investigation into that.

Thank you and I yield back the balance of my time.

Mr. LANGEVIN. I thank the ranking member.

The chair now yields to the gentlelady from the Virgin Islands, Ms. Christensen, for 5 minutes.

Mrs. CHRISTENSEN. Thank you, Mr. Chairman.

Dr. Parker, you were, I think, here when we had the previous panel and there was a question of what did "BioShield eligible" mean, because that is the criteria for eligibility for the contract.

So can you define "BioShield eligible" for me?

Mr. PARKER. BioShield eligibility is not a request for proposal terminology. I think the heart of your question, though, really gets at some of the issues of how we need to move forward with BioShield and some of the shortcomings that were recognized as we began to look at how to better improve BioShield almost a year ago when we began to discuss the merits of BARDA and the need for advanced development.

The BioShield acquisition, they stipulate procurement contracts. We also have, although it sounds like a lot, in the special reserve fund, $5.6 billion. It is fixed and it is limited.

And when we are talking about the development and acquisition of medical countermeasures, when some procurements or development costs may be in the realm of $800 million to $1.5 billion, there are some limitations.

We have to exercise fiscal responsibility. So what BioShield, as in Dr. Fauci's slide, was at that very end of the acquisition procurement and what we didn't have to be able to reduce some of the

risks was the robust advanced development so we could bridge that gap between the basic and applied research, whether it is coming from an NIH-funded, whether it is coming from DOD-funded, whether it is coming from the private sector, without government support, that we could help and bridge that gap and hopefully have more candidates in an advanced development that would be more mature when it is time to do a BioShield procurement.

Mrs. CHRISTENSEN. I have a number of questions. I think I read it in the GAO report and I am assuming that referred to Neumune, that it was canceled because it was not mature, it wasn't at the level of maturity.

So I would like you—

Mr. PARKER. Well, that speaks—

Mrs. CHRISTENSEN. —to tell me that and I would like FDA to tell me if you get involved at that level to decide whether the drug is mature enough to be a part of BioShield, to get a contract.

Mr. PARKER. It is a matter of timing and risk and we actually discussed this in the barriers report to Congress, which we will make sure you have a copy.

It is an issue of timing and risk when you move a product into a BioShield type program.

Mrs. CHRISTENSEN. They have 8 years to develop the project. So how much further does it have to be is what I am trying to figure out.

Mr. PARKER. In any countermeasure, there has to be sufficient and convincing data, whether that is clinical, non-clinical, safety, efficacy data, not just proof of concept, but very convincing data.

There has to be a very strong manufacturing plan and there has to be assurance and confirmation that their whole developmental plan includes all of the necessary studies that is going to allow a product to move in and be eligible for, one, licensure, but also eligible to move into the strategic national stockpile prior to licensure so they can begin to receive payment.

Mrs. CHRISTENSEN. Within 8 years.

Mr. PARKER. The law stipulates that there has to be convincing data that would support licensure within 8 years.

Mrs. CHRISTENSEN. Does FDA get into the decision of level of maturity at that point?

Mr. PARKER. No, not normally, although, again, if our colleagues ask us, we might provide scientific input. We wouldn't evaluate a specific product necessarily.

Mrs. CHRISTENSEN. I have a question that comes out of the GAO report, actually it is two, that was prepared for us this month and you mentioned the limits, the appropriation limits. The funding is available during certain time limits.

To what extent is that limiting factor explaining the contracts lagging behind the MTDs and to what extent is another factor that was raised in the GAO report, which is problems in interagency coordination and communication, a part?

I would ask Dr. Runge to answer, also, both of you.

Mr. PARKER. I will talk about the—the special reserve fund is $5.6 billion over 10 years, $3.2 billion can only be obligated through the fiscal year 2008 and the remainder of fiscal year 2009 to 2013.

And what we have done is moved out with the original four material threat determinations to establish acquisition programs against those original material threat determinations and now we have a larger list of material threat determinations in our implementation plan that is just now going to be coming out, actually establish our development and acquisition thrust targeted against the new material and older material threats, the complete list of material threat determinations to signal what are going to be the priority medical countermeasures, also using the principles that we establish in our strategy and the national strategy, HSB–18, I think, that was mentioned earlier, to make a prioritized list of the highest priority medical countermeasures against the highest priority threats against those material threat determinations.

Again, the advanced development is going to be critical to help us improve in not only implementing BARDA, but to improve the implementation of BioShield which is component of this.

Now, as far as interagency coordination, we have actually done a great deal of work and Dr. Runge and I, with both of our leadership, we have been able to work very, very well over the last year to really streamline and improve any issues that may have been there in the past as far as interagency coordination.

And so I thank Dr. Runge in his help in doing that.

Dr. RUNGE. Dr. Christensen, thanks for the question. Just very briefly, your direct question, does the limitation of BioShield funding affect lag time and MTD development or response to the MTDs, and I don't believe so.

Those funds are strictly for the acquisition. The funding for the material threat determination process and the population threat assessment process is, of course, separate funding that is given to DHS to do that.

Dr. Parker is correct and I do think that the original four were more common sense based on intelligence and history and what we knew at the time. They were not based on the same tool that we use now to stratify the material threats or determine which are material threats and which are not.

I do think that HHS moved out smartly in the beginning on those and DHS was a bit slow in delivering the rest of the list and it was dependent upon the development of a very complex tool that was delivered to the White House on February 1st of 2006.

Since that time, we have completed the look at all 28 agents and have come up with the list of 12 biologicals, as you are well aware, I think.

Mr. LANGEVIN. The gentlelady's time has expired.

The gentleman from California, Mr. Lungren, is recognized for 5 minutes.

Mr. LUNGREN. Thank you very much, Mr. Chairman.

I have probably not delved into this as much as some of the other members of the panel, so my questions might be a little more basic.

But, Dr. Fauci, you mentioned that one of the great accomplishments is that we have gone from smallpox capacity from 18 million to you say now we have it for everyone in the country and I suppose that is so that if we were exposed to a smallpox epidemic either because of natural causes or a terrorist threat, we would want to be able to cover all the potential victims.

Then, Dr. Parker, you said that if you were to line up the most important threats, it would be anthrax, anthrax, anthrax and you said you still look at it that way, correct?

Mr. PARKER. Of the bio threats.

Mr. LUNGREN. Of the bio threats, yes. And we just talked about material threat determination and population threat assessment and I guess if we did all that with respect to anthrax, it would be pretty much up towards the top.

So my question is this—is there something structurally wrong with the legislation that we have given you under which you operate, that as we are attempting to pursue the second generation anthrax medical fix, that we don't do enough to deal with the anthrax medical fix that is currently available to us, as Dr. Fauci said.

You have proven that with the first generation plus antibiotics, we have got a pretty good answer to those who are exposed, if I understand you correctly.

If that is the case and we have an obligation for a strategic stockpile, my question is you have made the determination here, Dr. Parker, or at least it was announced to us that you made the decision to buy 10 million more units, why now? Why not before?

Are you constricted by funding? Is it because we have given you a thrust that you ought to be looking at that which is more perfect in the future than that which is available now?

This is a very practical question. If we had an anthrax attack—excuse me—if we had another anthrax attack, only this one was based on weaponized and it affected a large population base and at least there have been some scenarios to suggest that that could be true in my state of California and Washington or New York, I take it we don't have the capacity to respond right now the way we would want to if we had that, even though we know through the work that has been done that Dr. Fauci talked about we have a fix for it.

And if we had that attack, we had a large number of people severely injured and died and part of the problem was we didn't have enough of the medical response to it, number one, how could I look myself in the mirror, but, number two, how could I respond to constituents to say that we were looking for the second generation that would have really solved the problem, but we didn't put enough money to the first generation?

Is that our fault? Is that Congress, such that we have structured it that you don't have the funds to do that? That is what I am trying to get at.

Can you help me?

Mr. PARKER. Well, first, I just want to say that antibiotics are the first line of defense and we do have a very significant stockpile of antibiotics and that is the first line of defense. Anthrax—

Mr. LUNGREN. But haven't we learned that antibiotics—

Mr. PARKER. Anthrax vaccines—

Mr. LUNGREN. —and the other actually really works?

Mr. PARKER. Pardon me?

Mr. LUNGREN. Didn't Dr. Fauci say it is antibiotics and the combination of the vaccine that really works?

Dr. FAUCI. But that was an experiment to answer a question that was somewhat vaguely answered several years ago that if you chal-

lenge an animal and you know that you would have to give them 60 days of, for example, ciprofloxacin and still not be 100 percent certain that you have eliminated every single anthrax spore, if you give antibiotics with the vaccine versus antibiotics without the vaccine, the time element is less.

That doesn't take away from the fact that the best approach towards anthrax is antimicrobial therapy.

Mr. LUNGREN. So I guess my question is if it were your child or your family member, would you give them both the vaccine and the antibiotic?

Dr. FAUCI. Based on the data in the animal study, based on the data in the animal study, it suggests that you would get an extra kick out of doing both. However, I would point out that following the anthrax attack here in the Congressional area, that the people who took just antibiotics in prophylaxis, there was zero subsequent cases.

Mr. LUNGREN. So what am I get out of that, that we shouldn't worry about having any of the vaccine, we can just satisfy ourselves with the—

Dr. FAUCI. No, I don't think so, because there are other uses for the vaccine besides complementing the antibiotic therapy. When you have people who might be first responders that would have to go in and, for example, decontaminate a building or if there are repeated attacks and you have to have the first responders go in and expose themselves, you would like to have them vaccinated as opposed to keeping them on perpetual antibiotics.

Mr. LUNGREN. But I guess I would ask what the Capitol physician would tell me if I were exposed to anthrax here. Do you think the Capitol physician would tell me to just take the antibiotics or do you think he would tell me to take both the vaccine and the antibiotic?

What I am trying to get at is do we have sufficient already existing first generation vaccine in the stockpile? That is question one.

Mr. PARKER. No, we don't. No. We need—

Mr. LUNGREN. Question two is we are how many years past the anthrax threat and should we in Congress be directing us to do that or would we be wasting money because we want to go for another attempt at the second generation?

Mr. PARKER. Yes, we need a balanced approach to anthrax vaccines. It is critical that we have anthrax vaccines and, you are right, we need to aggressively continue to move forward and we need to have not reliance on one technology, because this is an evolving field, but our strategy needs to—yes, we need to make sure that we can sustain and have the current generation anthrax vaccine, but we need to continue to develop and procure a second generation vaccine.

But we also need to look forward to that third generation that has better characteristics that make it more deployable in an emergency, in a disaster situation.

So we need that balanced approach for anthrax vaccines.

Mr. LANGEVIN. The gentleman's time has expired.

Mr. Etheridge is recognized for 5 minutes, the gentleman from North Carolina.

Mr. ETHERIDGE. Thank you, Mr. Chairman.

Mr. LANGEVIN. Before I do that, Ms. Jackson Lee has joined the committee and I would just ask unanimous consent for her to sit in. I don't know that there will be time to ask questions, but if there is, she would be invited to ask questions last. Without objection.

Mr. ETHERIDGE. Thank you, Mr. Chairman. Thank you.

I am going to try to follow that line of questions for just a minute, too, if I may, because we are now almost 5 years past the anthrax scare here on Capitol Hill.

Ultimately, in the process of all that, a number of people lost their lives. We have yet to find out who was behind it or who was involved in it.

And the VaxGen contract indicates that HHS sees the need for the next generation, as you talked about. So let me ask my question all three in one.

Dr. Parker, you first, and then the rest of you may comment on it, so we can expedite this.

What is the current state of the strategic national stockpile supplies of licensed anthrax vaccine and therapeutics? And, of course, that includes antibiotics, as well as the treatment for post-exposure treatment to anthrax.

Secondly, what is the current state of public health systems readiness for another attack, including specifically the status of vaccines for emergency responders, critical workers at the federal, state and local levels, and should we be stockpiling existing licensed medical countermeasures while new technologies are being developed?

And, finally, has the failure of VaxGen caused significant damage to our state preparedness and what are HHS's plans to meet the required 75 million doses of anthrax vaccine for the strategic national stockpile?

Mr. PARKER. I really think I would maybe answer the last question as we are going to be moving forward in a multi-pronged approach on satisfying enough vaccine in the stockpile to be able to provide protection to post-exposure prophylaxis for 25 million people.

We have already procured 10 million doses of ABA. We are going to and we plan to procure an additional 10 million doses of ABA. We continue the development of the second generation anthrax vaccine through the NIH program and we are looking at the right timing to come out with the next request for proposal for the second generation anthrax vaccine, as I have talked about, risk and timing and we have to time that perfectly.

And then I have forgotten now the first question. Let me go back to that.

Mr. ETHERIDGE. Well, the first one dealt with the current state.

Mr. PARKER. And another thing that is very important here, that another part of our armamentarium, in addition to the antibiotics, are the antitoxins, as well, that we need to have antitoxins to be able to treat symptomatic anthrax disease.

And so that is some of the BioShield procurement programs that are underway. You heard about one of the candidate products earlier this afternoon. So it is the vaccines, it is the antitoxins, and it is the antibiotics and currently in the strategic national stock-

pile, we have enough antibiotics to provide post-exposure prophylaxis for up to 40 million people.

And we also have intravenous—

Mr. ETHERIDGE. And that would take care of all of our first responders and emergency personnel.

Mr. PARKER. Antibiotics, that would be in case there is an anthrax attack to provide antibiotics for post-exposure prophylaxis. And there is also intravenous antibiotics for treatment of anthrax disease, as well.

In addition, what we need is the antitoxins and we have a small amount of antitoxins.

Mr. ETHERIDGE. How small amount?

Mr. PARKER. I don't recall that exact number, but it was—

Mr. ETHERIDGE. Could we get that number?

Mr. PARKER. We can get that number for you, sir.

Mr. ETHERIDGE. Thank you.

Mr. PARKER. But another key component of this, though, is for emergency response and it continues to be something we are going to work very hard on.

These medications in these stockpile have got to be—we have got to be able to get them into patients quickly. So mass distribution of medical countermeasures is also a very key problem and we have a few programs, like city readiness initiative, a program called the MedKit.

We are working at novel ways to help our colleagues at the state and local and the community level be able to—where we can more rapidly, once we have a detection that there is an anthrax attack, deploy the stockpile and more rapidly be able to distribute the medications where they need to be, and that is with people that are potentially exposed, are exposed.

Dr. RUNGE. Congressman Etheridge, if I could just elaborate on that one second.

Dr. Parker has outlined a comprehensive plan within the public health response and I don't think I have to tell this committee that that is only one piece of an end-to-end strategy.

DHS is doing planning around everything from biosecurity overseas, the intelligence necessary to prevent people from coming here to do this sort of thing, working with EPA all the way through the "how clean is clean" protocols and environmental cleanup.

The importance of anthrax vaccine, I might add, also, is that because of these protocols of when do you re-inhabit a building, there will also be significant pressure to vaccinate people so that they can re-inhabit a building that may have been exposed to anthrax.

We are also engaged in early detection through our BioWatch program, which I am sure you all are familiar with.

So it is a great continuum here of our overall approach to what we do believe to be the number-one bio threat.

Mr. ETHERIDGE. Thank you.

Mr. LANGEVIN. The gentleman's time has expired.

We have a vote on right now. My plan is I can go to Ms. Jackson Lee for about 3 minutes, if we can be brief, and then we could keep you here for another 24 hours, I suppose, and keep asking these questions.

But we will adjourn the hearing at that point and we will be back for subsequent hearings and look forward to working with you.

The gentlelady from Texas is recognized for brief questions.

Ms. JACKSON LEE. Thank you very much, Mr. Chairman. I will speak with all deliberate speed and I appreciate the chairman's indulgence.

I was here in Congress when the Senate buildings were shut down with anthrax. I was also in my district when everyone with baby powder were suggesting that anthrax was amongst them.

I was in Asia during the avian flu. It created a great deal of hysteria and this is the government and I asked the question. I am listening to all of my colleagues and I wonder whether or not we are moving fast enough.

And I know that you will quickly answer this question—should we not be engaged in what I call reflective hysteria? This is a pending crisis, if it ever happened, and do we have enough urgency, Dr. Runge, Department of Homeland Security and others? If you could answer that quickly.

Has Congress got their focus on it? Do you have your focus on it—I know you have been answering questions—sufficiently?

And thank you, Chairman.

Dr. RUNGE. Thank you, Congresswoman Jackson Lee. I do believe that we do feel a tremendous sense of urgency and I will confess that our office of health affairs that has been tasked with doing planning around this effort is fledgling.

We were created officially on March the 31st, 2007. So we are about 3 weeks ago. We are awaiting a reprogramming to come over here to actually give us some funds to engage in this planning.

In the meantime, our science and technology directorate has been very actively engaged with HHS, as I have as chief medical officer. There is very little I think we can do to speed up this process. It is kind of like we need a baby in a month, but we can't ask for nine women to produce one.

Ms. JACKSON LEE. Do you have enough money?

Dr. RUNGE. The funding that we have right now, as we have outlined it, will be sufficient to do what we have to do, yes. And, again, welcome to the subcommittee and we would be happy to come over and brief you on the timelines for this.

Ms. JACKSON LEE. Quickly, I don't know if you have a quick answer.

Mr. PARKER. Actually, I do, maybe about the threat and, actually, it is a good discussion. We have had this discussion actually about pandemic influenza and that certainly is a very predictable threat.

One thing we do have to caution against and that is complacency and I really think that is your issue. That may be our biggest threat is complacency.

And so we have got to work hard and this is a sense of urgency. Certainly from my staff, our department, our working relationships, you can bet that we have a sense of urgency. But we have to guard against complacency.

Ms. JACKSON LEE. Yes, Dr. Goodman?

Dr. GOODMAN. I really appreciate the opportunity. One thing I frequently say when I go around and talk about what we are doing is we are not conducting business as usual and at CBER and at FDA, we are looking at this not as that we sit there and wait for these products to come in and have a passive process, but that we are very active.

We engage. We are constantly meeting with our colleagues, with manufacturers. We have come up with our colleagues with new science, new pathways to move stuff forward.

So I think we see this as a very high priority, but I agree with the complacency issue. I think our country is interested in the news of the day or the week and we as the government and as leaders in the government have to keep this important threat on the front burner.

The other comment that Tony and I both made is the investments we make in public health and product development in general will help us in general. So the vaccine industry and its recovery and its infrastructure getting stronger will help prepare for all these threats.

So whether it is pandemic flu, anthrax, et cetera, we need to recognize how important these sort of non-economically-driven public health needs are and how we need to strengthen our infrastructure to deal with those.

Ms. JACKSON LEE. Thank you.

Mr. LANGEVIN. I want to thank the panel for their testimony and thank the gentlelady for her questions.

Ms. JACKSON LEE. Thank you.

Mr. LANGEVIN. As I said in my opening statement, the bio threat is very real. I realize we all take that seriously. We need to move with all deliberate speed in developing countermeasures.

We all want BioShield to work as it was intended and we want to make sure that you have resources to make sure that it does.

We look forward to working with you in this continued challenging issue and, again, I thank you for your expertise, your service to the country and look forward to having you back before us once again.

I thank the witnesses again for their valuable testimony, the members for their questions.

The members of the subcommittee may have additional questions for the witnesses and we will ask that you respond expeditiously in writing to those questions.

Hearing no further business, the subcommittee stands adjourned.

[Whereupon, at 3:56 p.m., the subcommittee was adjourned.]

FOR THE RECORD

PREPARED STATEMENT OF THE HONORABLE RICHARD BURR, SENATOR, NORTH CAROLINA

Mr. Chairman, members of the Subcommittee, thank you for the opportunity to make a statement before your committee on the implementation of the *Project BioShield Act of 2004,* and the improvements authorized in the *Pandemic and All-Hazards Preparedness Act,* which was signed into law in December 2006. Although the Department of Homeland Security has a key role to play in successful implementation of Project BioShield—namely, timely completion of material threat determinations—my comments today will focus on the Department of Health and Human Services (HHS).

Being one of the principle sponsors of Project BioShield in the House of Representatives, our intent was for BioShield to provide incentives for manufacturers of vaccines and drugs to swiftly bring new countermeasures to the market that would help protect us from attacks with chemical, biological, radiological, or nuclear (CBRN) agents. We have certainly made progress since its passage three years ago, but we remain unprepared for the possibility of such an attack. We do not have the range of vaccines and drugs necessary to prevent, contain and treat potential deliberate, accidental or natural disease outbreaks or chemical or nuclear attacks. The pharmaceutical and biotechnology industries and academia are still reluctant partners.

I know there will be criticism voiced today about the recent termination of BioShield contracts and cancellation of Requests for Proposals. However, I hope we will be able to look back and see how the new requirements and authorities provided in the *Pandemic and All-Hazards Preparedness Act* will help alleviate some of the concerns. There will undoubtedly be areas that still need improvement, and I look forward to working with my colleagues to address them in the future. At the end of the day, we all want Project BioShield and the new Biomedical Advanced Research and Development Authority (BARDA) to be successful in order to protect the American people from future threats.

Project BioShield

The *Project BioShield Act of 2004* was an important step forward in accelerating the development of medical countermeasures. It established a $5.6 billion "guaranteed market" for biodefense medical countermeasures developed by private industry. It was the right idea, but we needed more. BioShield has ended up being primarily a procurement mechanism and has not been enough to persuade large experienced pharmaceutical companies to redirect their research and development dollars towards biodefense. The organizations doing biodefense countermeasure research are smaller, less experienced biotechnology companies and research institutions.

Drug and vaccine development is a risky and complicated business—most products under development never make it to market. Since the federal government is usually the only viable market for biodefense countermeasures, these companies and research institutions need a government partner that accepts some of the risk. We also need to get products further along the development pipeline before we expect HHS to make billion dollar procurement decisions.

While the National Institutes of Health supports basic research, BioShield was not structured to support the advanced research and development of medical countermeasures. A lack of funding for advanced development at this critical stage stalls many promising drugs and vaccines in the lab. But BioShield was not set up to be a development program; rather, it is a procurement program.

Biomedical Advanced Research and Development Authority

As Chairman of the Senate Subcommittee on Bioterrorism and Public Health Preparedness during the 109th Congress, I had the opportunity to reevaluate Project BioShield. I developed the model for BARDA after a year of public hearings and roundtables to explore the challenges in biodefense medical countermeasure development.

BARDA, established in the *Pandemic and All-Hazards Preparedness Act,* will improve our ability to quickly develop drugs and vaccines to protect against CBRN threats. The intent of BARDA is to bring more and better medical countermeasures to the public faster in case of emergency. BARDA reorganizes and enhances HHS medical countermeasure research, development, and procurement activities—providing three major benefits.

First, BARDA is the single point of authority within the federal government for the advanced research and development of promising new medical countermeasures to meet the government's civilian needs. This makes it clear to industry and academic institutions where they should go to be connected with necessary guidance, technical assistance, and funding. BARDA will be headed by a Director and will have a lean management staff that is experienced in product development and is not risk averse.

Second, BARDA will be an aggressive venture capitalist partnering with universities, research institutions and industry on the advanced research and development of promising drugs and vaccines, through an open, transparent, and unclassified process. BARDA will have real-time access to the results of drug and vaccine trials and will directly invest in the most promising candidates to bridge the "valley of death" where most products fail. Using milestone-based payments, BARDA will become a financial partner with these institutions and companies during later stages of development to share some of the risk and prove the merit of promising drug and vaccine candidates. Modest investment by the government during the critical ad-

vanced research and development stage can attract four to six times that amount in private investment and can ensure that promising products cross the finish line.

BARDA will cast a wide net in search of promising research on possible medical countermeasures being done domestically and abroad, and will enable HHS to bring products further along the development pipeline, before making a decision to buy them through BioShield.

Finally, BARDA will bring innovation to a process that is too slow to combat terrorist activities or Mother Nature. Modeled after the Defense Advanced Research Projects Agency's successes in defense research, BARDA will make HHS more dynamic, nimble and accountable. There is not enough time or funding to develop one medical countermeasure for each identified threat. It still takes up to a decade and costs hundreds of millions of dollars to develop a new drug or vaccine countermeasure. This one-bug, one-drug strategy must change.

BARDA has the flexible authorities and necessary resources to support research and development of platform technologies, research tools, and other devices that have the potential to revolutionize drug and vaccine development. For example, BARDA has flexible hiring authorities to attract the best and the brightest minds to staff it. BARDA has "other transactions" authority to enter into more flexible arrangements with researchers. And HHS has a limited antitrust authority, which enables HHS and BARDA to engage with industry in a new way ? possibly linking smaller biotechnology companies with larger pharmaceutical companies during advanced development to create new synergies of expertise.

Conclusion

If we fail to overcome the fundamental obstacles to rapidly identifying and developing new medicines to counter biological, chemical, radiological or nuclear agents and emerging pandemic infectious diseases we will miss yet another opportunity to improve America's preparedness for all public health threats. BARDA builds on BioShield to do just this.

I am pleased the Senate confirmed Dr. Craig Vanderwagen as the new HHS Assistant Secretary for Preparedness and Response, a position created in the *Pandemic and All-Hazards Preparedness Act.* I am confident he has the experience to do the job well. Now, HHS needs to recruit a BARDA Director who has the necessary skills and experience in private sector drug and vaccine development, and Congress must appropriate sufficient funds to give BARDA every opportunity for success.

In the fiscal year 2007 supplemental appropriations bills, the House and Senate transferred $49 million to get BARDA up and running. In the 2008 budget resolution, the Senate accepted my amendment to increase funding for BARDA by at least $140 million. This would fully fund the President's request of $189 million for advanced research and development of medical countermeasures.

With a strong BARDA Director, and sufficient funding, BARDA has the potential to fill many of the voids identified in BioShield and ensure that more and better medical countermeasures are available to the public faster in case of emergency.