Can BioShield Effectively Procure Medical Countermeasures That Safeguard the Nation?
Testimony of Richard Hollis
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Subcommittee on Emerging Threats, Cybersecurity, and Science and Technology
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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 <u>regardless of dosage form</u>); (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 ½ 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.

Sincerely

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