

Hearing on “Project BioShield Reauthorization Issues”

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Mr. Chairman, Congressman Dingell, and members of the committee, thank you for the opportunity to address the vital issue of biodefense and the difficult challenges surrounding the US government’s efforts to procure medicines and vaccines against biological agents that could be used in terrorist attacks against US civilians. My name is Tara O’Toole. I am the Director and CEO of the Center for Biosecurity of the University of Pittsburgh Medical Center and a professor of medicine at the University of Pittsburgh Medical School. The Center for Biosecurity is a non-profit, non-partisan, multidisciplinary organization located in Baltimore which includes physicians, public health professionals, and biological and social scientists. The Center is dedicated to understanding the threat of large-scale, lethal epidemics due to bioterrorism and natural causes. My colleagues and I are committed to the development of policies and practices that would help prevent bioterrorist attacks or destabilizing natural epidemics, and, should prevention fail, would mitigate the destructive consequences of such events.

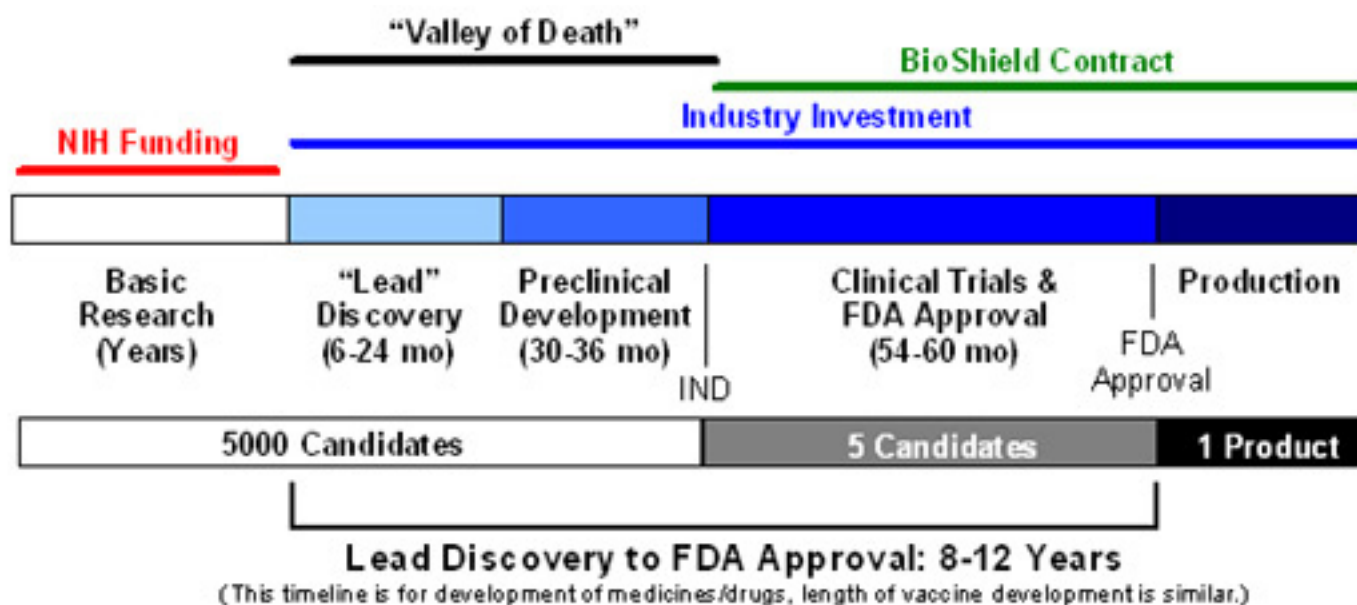
For several years now, the Center for Biosecurity has been working in collaboration with academia, industry, and government to stimulate development and procurement of new medicines and vaccine for biodefense. In March 2005, we initiated the formation of the Alliance for Biosecurity, a collaboration between the Center and leading biotechnology and pharmaceutical companies with the intention of working together in the public interest to promote the creation of a robust and sustainable biomedical research and development infrastructure that we believe is needed to prevent and treat the infectious disease threats that present US and global security challenges in the 21st century. These threats include large-scale epidemics of natural disease as well as bioterrorist attacks using conventional or bioengineered weapons.

Biological weapons have been proven to work, are capable of causing massive lethality, are relatively cheap, and are increasingly easy to design, build and disseminate. We are in the midst of a bioscientific revolution that will make building and using biological weapons even more deadly and increasingly easy. Finally, the materials and technical know-how needed to make a bioweapon that could infect hundreds of thousands of people are already widely distributed around the planet, and the number of people who possess the expertise needed to create bioweapons is rapidly growing as biotechnology and pharmaceutical research and production expand into developing countries.

Preventing either a natural epidemic or a bioterrorist attack is, unfortunately, unlikely. Therefore, the nation’s ability to rapidly and effectively respond in the face of a biosecurity crisis should be a central pillar in our biosecurity strategy. The nation’s response to an outbreak must be designed to prevent potentially destabilizing social, economic, and political consequences, in addition to preventing illness and death on a large scale. Medicines and vaccines that can counter illnesses caused by exposure to bioweapons agents are obviously an essential component of biodefense and would be critical to controlling the spread of contagious disease. A recent report from the Institute of Medicine found that the array of biological agents that pose a significant threat to biosecurity is much larger and more diverse than any of today’s “threat lists”[1] Yet, since 2001, the US has acquired only a single countermeasure—smallpox vaccine. Why is this?

Funding for Biodefense Countermeasures Is Not Comprehensive and Is Not Commensurate with the Threat of Bioattacks

Thus far, the US government has focused efforts to acquire biodefense countermeasures on basic research investments and on Bioshield funding for acquisition of countermeasures that are sufficiently advanced that they are eligible for Investigative New Drug (IND) status. What's missing from the US government's biodefense funding strategy is support during the so-called "valley of death", the crucial middle phase of drug development between basic research and acquisition of final products (see figure).



Drug and vaccine development is an expensive, high risk undertaking. Of 5000 drug "candidates" identified by scientists, only 5 make it to clinical trials and only one of these, on average, will become a licensed product[2]. The lack of support from the US government during the crucial intermediate stages of development results in premature failures of potential countermeasures as biopharma companies struggle to maintain operations through long periods of uncertainty without outside support. The priorities of the private capital markets, instead of the priorities of government, are driving products through the "valley of death." Unfortunately, countermeasure development is unattractive to private investors because there are no markets outside of governments for most of these products, and even in the most profitable scenarios, biodefense countermeasures—as with anti-infectives generally—cannot generate profits comparable to successful medicines for chronic disease that are taken for years by large populations[3]. This is one of the prime reasons that there are only 5 major vaccine manufacturers left in the world. One expert in drug development was quoted in a 2004 study performed by the Center for Biosecurity and the Sarnoff Corporation as saying:

"You make a new antibiotic and if it's really terrific you'll have peak sales of \$300 – 500 million per year. If you make a drug for cancer that extends life by 4 months, you can charge \$40,000 per dose. The difference is so staggering . . ."[4].

Without some form of government support for the "valley of death," perhaps in the form of grants, contracts, or significant milestone payments such as the Department of Defense uses in the acquisition of complex weapons systems, few companies will be able to secure outside financing or invest their own capital in countermeasure development.

Government-funded basic research is an essential part of biodefense strategy, partly because research into infectious diseases has, in recent times, been less well funded by the private-sector than research for cancer and other types of illness (HIV/AIDS is the exception). As noted, the private sector has been systematically abandoning R&D investments in infectious disease generally because other investment opportunities are much more lucrative[5]. As a result of industry's retreat

from infectious disease research, there is less innovation. Since 1998, FDA has approved just 10 new antibiotics—only two of which had a novel mechanism of action[6]. The strong support Congress has accorded basic biodefense research though the NIH should continue. Efforts to facilitate the transition from discoveries in the laboratory to the development of useful products by offering more support to innovators trying to traverse the “valley of death” could result in many more success stories and more “bang for the buck” from basic research investments.

With the passage of the 2004 Bioshield legislation (P.L. 108-276), the nation undertook to pay for the acquisition of countermeasures. The Bioshield Purchase Fund of \$5.6 billion sounds like a lot of money, particularly in the context of public health expenditures. But it is not much money when viewed as a necessary national security investment. A single Nimitz class aircraft carrier costs about \$4 billion; ten such ships have been built for the US Navy. The size of the Bioshield procurement fund must also be examined in light of the actual costs of drug development: it is estimated that the average out-of-pocket cost of developing a new drug is \$400 million; if opportunity costs are included, the cost is \$800 million[7]. A more recent study calculates the costs of drug development could be even higher[8]. Indeed, the first Bioshield contract, for 75 million doses of recombinant anthrax vaccine, amounted to \$877 million. The reality is that \$5.6 billion will not go far, particularly when the entire threat spectrum is considered and the costs of actually acquiring (not just developing) medicines and vaccines are contemplated.

Current HHS Structure and Staffing Levels Need To Be Strengthened

Biodefense is a relatively new and complex mission for the Department of Health and Human Services (HHS). Although many competent people within HHS are working hard to manage countermeasure development and acquisition, too few federal staff, many with little relevant experience, are trying to do too much under ferocious time pressures. It is imperative that HHS be granted the authority to hire about 100 new staff, many of them at the senior level, to manage these important programs. It is especially important that HHS hire people with experience in drug and vaccine development and production.

The current processes associated with threat identification, countermeasure development and acquisition are poorly coordinated, slow moving, confusing and often contrary to routine business practices. This is due in part to the number of different agencies involved (OPHEP, ORD, FDA, NIH, DHS). But it is also the case that HHS lacks experience managing complicated, long-term acquisition projects such as DOD handles routinely. The Federal government has chosen to pursue biodefense countermeasures through partnerships with the biopharma industry. Such an approach is a sensible way to make efficient use of the prodigious know-how and resources of the private sector. But for this approach to work, the Federal government must be a reliable partner. From biopharma’s perspective—and the perspective of investors—it is critical that the government maintain a transparent, predictable process with clear timelines, explicit liability protection and fair compensation rights, and develop predictable rules for the protection of intellectual property rights. Failure to recognize these realities means that few companies will choose to pursue countermeasure development and production, and the country will not have the medicines it needs in times of crisis.

After the terrorist attacks of 2001, HHS was tasked to take on a welter of new missions related to homeland security. The management structure and staffing of HHS has simply not kept pace with these assignments. HHS is larger in dollar terms than the Department of Defense—and yet HHS does not have a single undersecretary. Secretary Leavitt has noted that he has 27 direct reports—a situation he recognizes as “not at all an ideal organizational structure.”

Cabinet Secretaries should have broad discretion in how their agencies are organized, but I believe that Congress should consider authorizing HHS to establish at least one—or better, two or three—Undersecretary positions. This would provide the agency with more senior managers capable of coordinating HHS’s vast programmatic span of control. In the realm of public health preparedness, an Undersecretary for Public Health (which could be combined with the present Assistant Secretary for Health or the position of Surgeon General) could better coordinate the varying HHS programs now spread among the Assistant Secretary for OPHEP, CDC, HRSA, NIH, AHRQ, and ONCHIT. In addition, an Undersecretary would be better able to represent HHS in the interagency process.

Focus on Accelerated Development of Countermeasures

The US does not yet have a coherent biodefense strategy, nor do we have a strategy for countermeasure research, development, and production that takes account of the full spectrum of possible bioweapons agents, including engineered threats. It is clear that a handful of pathogens such as anthrax, smallpox, plague, etc. are at the top of most threat lists because of their availability, lethality, contagiousness, historic development as bioweapons, etc. Developing and stockpiling specific countermeasures against these high-priority threats is a rational and pressing national security need.

However, in the long term, the current approach of developing countermeasures against each potential bioweapon agent will prove futile. Natural outbreaks of novel infectious diseases (e.g. SARS) are commonplace, and there are dozens of naturally occurring pathogens which could serve as bioweapons agents today. Moreover, the ongoing revolution in bioscience will enable the creation of more and more bioweapons agents covering an enlarging spectrum of targets[9]. As the “threat space” expands, it will become increasingly difficult and costly to use a “one-bug-one-drug” strategy to define the appropriate armamentarium of countermeasures that must be developed and stockpiled—and perhaps never used. In addition, the country will have to confront the specter of covert bioattacks using heretofore unanticipated bioengineered agents. Avoiding the destabilizing effects of a large-scale, lethal campaign of such attacks will require the ability to rapidly design, develop and produce new countermeasures from a standing start—in weeks, if not days. The need to anticipate and prepare for such bioengineered weapons is not in the far-off future. We are already living in the age of bioengineering. Scientists estimate that in five years it will be possible to synthesize any virus from non-living components.

A major strategic goal of US biosecurity strategy should be the radical acceleration of drug and vaccine development. The US government should embark on an ambitious program to incrementally reduce drug development and production time across the entire development spectrum. Important reductions in development time might be achieved across the timeline of drug and vaccine development with efforts such as:

- Technology improvements such as in silico modeling, genomics, and synthetic biology;
- Wider sharing of, and access to, improved research tools such as toxicological databases, test-tube and animal models of diseases, chemical libraries of possible medicines, and high throughput screening of potential drug candidates;
- More efficient clinical testing, such as might be accomplished with integrated electronic health records;
- Streamlined regulatory review such as might be achieved by adding staff and leadership in FDA and developing policies that account for the unique aspects of biodefense countermeasures;
- The creation of public-private consortia to facilitate sharing of information between developers, to address predictive safety testing (i.e. to focus on scientific ways to predict toxicity), and to tackle other key countermeasure development challenges.

This is not just about developing new technologies. The US government will need to foster new systems to enable private sector developers—many of whom are direct competitors—to work together with the government and academia so that we can take advantage of the complete storehouse of knowledge and expertise available.

If the US were to undertake an ambitious long-term effort to focus on accelerated countermeasures development, it is likely to be successful. The US currently has the advantage in bioscience expertise and experience—invaluable assets that could be well leveraged in such an effort, although we are also rapidly outsourcing most drug and vaccine development overseas, mostly to India and China.

Success in such a venture would bring many benefits in addition to forming the foundation of a coherent and sustainable biodefense strategy. In biopharma, time is money; the average drug now requires a decade to develop from concept to licensed product. Learning how to accelerate countermeasure development would necessarily mean that the costs of countermeasures would decrease, probably substantially. This effect would have direct implications for the costs of pharmaceuticals generally—even during “peacetime”—thereby reducing health care costs and placing the cost of vital drugs and vaccines within reach of developing countries.

Such a program of accelerated drug development should proceed in partnership with biopharma companies in the private sector, much as the Department of Defense developed partnerships with major military contractors. If such a project was ambitious enough, and properly structured and financed, and if the Federal government made a long-term commitment to such a project, it is likely that the leaders of biopharma would agree to participate.

It would not be easy to achieve radical acceleration of countermeasure production. But incremental progress is almost certain, and would over time have potentially significant impacts. I am convinced that such a project will be undertaken; the remaining question is whether the US will make such a commitment before we experience a large-scale bioevent, such as a terrorist attack or a naturally occurring pandemic, or after.

The Biodefense and Pandemic Vaccine and Drug Development Act (S. 1873) being proposed by Senator Burr as a next step beyond Bioshield is not perfect. It is a modest bill that will not transform countermeasure R&D or dramatically reshape HHS. But it is an extremely useful piece of legislation and should be enacted into law. The bill makes important incremental improvements in the structure of HHS, allowing the agency to acquire competent staff and bring more clarity and transparency to its countermeasure procurement processes. It provides mechanisms for supporting companies in the “valley of death”, in a manner similar to the DOD acquisition process and appropriate to the development of complex products with limited markets. The related bill being proposed by Senator Kennedy (S. 1880) also makes the point that improvements in the current approach to countermeasure development are needed. These bills send the message that the US government is concerned about biodefense and wants to improve countermeasure development. Should the Congress fail to pass meaningful Bioshield legislation this session, there is a real danger that the biopharma industry will read this as a clear message: Congress is not serious about biodefense.

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