U.S. House of Representatives
Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

Outbreaks, Attacks and Accidents: Combatting Biological Threats
February 12, 2016

Testimony of Tara O'Toole, MD, MPH; Executive Vice President, In-Q-Tel

Introduction

Chairman Murphy, Ranking Member DeGette, and members of the committee, thank you for the opportunity to address the vital issue of the national security threats posed by biological attacks and natural epidemic disease. I am a physician and public health professional. From 2009-13, I served in the Department of Homeland Security as Under Secretary of Science and Technology, and as Assistant Secretary for Environment, Safety and Health in the Department of Energy from 1993-7. In the decade between government positions, I was a Professor of Public Health at Johns Hopkins University and Professor of Medicine and Public Health at the University of Pittsburgh. In each of these positions I helped found and directed university centers devoted to understanding the threat of bioterrorism and of epidemics of infectious disease, and how such events might be prevented or mitigated.

Currently, I am executive vice president at In-Q-Tel, a non-profit organization created by Congress in 1999 that provides the US Intelligence Community with access to innovative small companies in the private sector. My current project focuses on identifying existing and emerging technologies emerging from the life sciences that could significantly improve the nation's ability to rapidly detect and quench destabilizing epidemics, whether natural or engineered.

I wish to congratulate the members and staff of the Blue Ribbon Study Panel on Biodefense for their important – and hopefully highly influential – report, A *National Blueprint for Biodefense*. I especially endorse and share the Panel's sense of urgency about repairing the country's vulnerability to highly consequential bioevents. We have lately been reminded of the potentially devastating effects of natural epidemics and terrible losses and disruption they impose. As the Blue Ribbon Study Panel wrote,

The biological threat has not abated. At some point, we will be attacked with a biological weapon and will certainly be subjected to deadly naturally occurring infectious diseases and accidental exposures, for which our response will be insufficient. There are two reasons for this: 1) lack of appreciation for the extent, severity and reality of the biological threat; and 2) lack of political will. These conditions have reinforced each other.

-*A National Blueprint for Biodefense,* Bipartisan Blue Ribbon Study Panel on Biodefense, October, 2015, p.3

Today, I will address three points:

1) The coming decades will include more frequent and more disruptive epidemics due to naturally occurring infectious disease as a result of population and commercial pressures.

2) The deliberate use of biological weapons, whether by nation states, terrorist groups or lone wolf actors, represents a strategic threat to US national security. The potential destructive power of bioweapons is equivalent to that of nuclear weapons, and advances in science and technology have removed any technical barriers to building and disseminating highly lethal bioattacks over large areas. Yet, as the Blue Ribbon Panel emphasizes, the U.S. has not moved with determination to reduce our vulnerability to such attacks.

3) The "revolution" in biological science and biotechnologies now underway could – with sufficient foresight, imagination and resources - be used to rapidly detect and quench epidemics – whether from natural causes or bioterror. I will suggest some critical technologies which might help realize the Study Panel's assertions that "dramatic improvements [in biodefense] are within reach".

The Frequency and Impact of Natural Infectious Disease Outbreaks is Increasing

The world is increasingly likely to face an increasing tempo of epidemics of infectious disease in the 21st century, and these epidemics are more likely to spread quickly and be socially and economically disruptive. As a consequence of expanding populations and commercial pressures causing human intrusion into once remote ecosystems, people have come in contact with new microbes such as Ebola and HIV/AIDS. Two thirds of the more than 30 newly emergent diseases of the past 20 years have been zoonoses – diseases which infect both animals and humans - and the majority of zoonoses arise from wildlife.

Many other factors contribute to the increased risk of epidemics, including the rise of "megacities", where tens of millions of people live without clean water, basic sanitation or adequate nutrition and in close contact with animals they raise for food or buy in wet markets. Highly interconnected and rapid global patterns of trade and travel also facilitate the spread of disease. SARS, for example, a virus that originates in bats, "jumped" to humans in 2003. A single person infected with SARS transmitted the virus to four others staying in the same Hong Kong hotel. These individuals then traveled to four continents within 24 hours. The total cost of this relatively small epidemic – only 8000 cases occurred worldwide before public health officials halted the outbreak – was estimated to cost the affected regions

about $60 billion in gross expenditures and business losses over just a single quarter in 2003.

Other infectious disease outbreaks are spread by insects, usually mosquitoes or ticks, as we are witnessing now with the Zika virus outbreak in South America, and as we have seen with mosquito-borne West Nile virus which was discovered in the US in 1999 and is now indigenous across the continent, as well as with Dengue and Chikungunya. Some infectious diseases seem to lie dormant for years, only to "re-emerge". Others are caused by microbes that mutate into new forms to which humans lack immunity or which are resistant to once useful antibiotics or vaccines. Influenza virus, which continuously mutates, necessitating frequent changes the molecular targets of flu vaccine, is the poster child of viral mutation.

Biological Weapons are a Strategic – and Growing – National Security Threat

There is a long and well documented history of biological weapons use, although it was not until the Cold War that technology enabled the creation of bioweapons with a strategic reach. Both the US and the USSR had ambitious offensive bioweapons programs. President Nixon ended the US program in 1969. The USSR created Biopreparat, a secret, sophisticated, large-scale offensive BW program after signing the Biological Toxins and Weapons Convention in 1972. Details of Biopreparat were revealed by defectors in the 90s, and included the production and stockpiling of *tons* of the bacteria that causes anthrax and smallpox virus, and engineering drug-resistant pathogens. The current status of Russian offensive or defensive bioweapons efforts is unknown, though it does retain closed biology labs under military control.

Although the history of the US offensive bioweapons program is not widely remembered, the program was ambitious and highly successful. During the Cold War, both nations considered aerosolized bioweapons to be adjuncts to nuclear weapons attacks. The US field-tested many different bioweapons in realistic conditions, including releases from air, boats, ships and in subways. Now-declassified documents from the US Department of State written in 1975 recognized the strategic potential and possible terrorist use of these weapons:

> *"Certain biological agents appear to pose as great a threat to human life as thermonuclear weapons. They appear to be at least as effective and are available to terrorists."*
>
> -Mass Destruction Terrorism Study, Dept. of State, 9/19/75; E.O. 12958, as amended; Declassified 8/10/2010

In 1993, the Congressional Office of Technology Assessment calculated that 100 kilograms of aerosolized anthrax released in Washington, DC under ideal weather conditions would cause approximately as many deaths as a one megaton hydrogen bomb. Common appreciation of the proven destructive power of bioweapons has been warped by the experience of the 2001 anthrax mailings, which employed gram

amounts of anthrax in a very ineffective delivery device. Although the impact of these attacks included 5 deaths and effectively terrorized the nation, the 2001 attacks are not an accurate reflection of the lethality of what was contained in those envelopes.

This is not the place for a detailed examination of the US Offensive Weapons program, but the 25 year history of this program yielded important scientific understanding of bioweapons and their effects. Many important discoveries are not yet integrated into US biodefense plans. For example, a well-prepared bioweapon - using 1960s technologies – would likely deliver a much higher dose of virus or bacteria than would a natural infection, greatly reducing the "incubation" time between exposure and symptoms, and possibly inciting an overwhelming systemic infection that could not be successfully treated with antibiotics. Very high exposure doses might also thwart protection from vaccines, and could alter the manifestation of illness in ways that make clinical diagnosis difficult.

The US and Soviet Cold War, state-sponsored bioweapons programs were ambitious military efforts (Biopreparat employed 50,000 people at its peak), which required significant innovation and experimentation given the era's limited understanding of biological science and biotechnology. Since then, there has been a veritable revolution in our understanding of and ability to manipulate living organisms. These advances have occurred in pursuit of new ways to treat diseases, including the search for new drugs and new ways to deliver them.

As the Defense Science Board reported in 2001, the technical barriers which confronted bioweapons efforts in the 60s no longer pose barriers to terrorist groups mounting large-scale bioattacks:

…Major impediments to the development of biological weapons – strain availability, weaponization technology and delivery technology – have been largely eliminated in the last decade by the rapid, global spread of biotechnology."

- Defense Science Board, *Biological Defense*, June 2001, p.18

But these dual-use technologies have made successful creation and dissemination of a bioattacks by non-state actors far more feasible than was the case in 2001. Advances in pharmacology, in aerosol biology (essential for the protection of crops and for inhalation delivery of drugs), and in our ability to read, write and edit the genetic code – the "code of life" – have resulted in global spread of biological knowledge and the use of biotechnologies.

The materials and know-how needed to build and disseminate a powerful biological weapon are now cheap and widely available in commercial markets. Advances in biotechnology continue to increase accessibility to this knowledge, making assembly and dissemination of such weapons simpler and more fool-proof. As technologies mature, they become more accessible, easier to use. Biological techniques that once

required great skill and effort are now available in handy kits one can buy on the Internet and are used by scientists, technicians and amateur biologists around the world. Moreover, because bioweapons are self-replicating organisms, adversaries could easily develop multiple weapons, increasing the scale or number of attacks.

It is important to recognize that the knowledge and materials needed to build and disseminate a biological attack have many legitimate uses. This makes the task of collecting intelligence about covert biological weapons programs exceedingly difficult, as the Silberman/Robb *Report on Weapons of Mass Destruction Intelligence Capabilities* made clear. Moreover, assigning attribution for bioattacks will be exceedingly difficult unless we catch the perpetrators in the act.

Finally, the burden of defending against bioattacks or natural epidemics falls on the medical and public health communities. These systems are already highly stressed, fragmented, and under resourced, and largely not under federal control. The US lost over 50,000 state public health officials since 2008 as a result of the financial downturn. As we saw with our 2009 experience with H1N1 influenza, and again with last year's Ebola crisis, even the United States has a very limited capacity to make effective vaccines in time to make a difference.

Towards an Effective Biodefense

It is essential that the country become more effective and efficient at preventing, detecting, mitigating and quenching epidemics, whether natural or man-made. The Blue Ribbon Panel on Biodefense makes dozens of recommendations and advocates a more muscular and centralized leadership of US biodefense programs now scattered across multiple federal agencies.

I would like to offer for Congress' consideration, a few suggestions about how we might build a robust biodefense.

Disease Surveillance Requires a Strategy, Rapid Diagnostic Tests, and Sustained Funding

Needed: Strategic Approach to Biosurveillance

The BRP rightly describes surveillance as a "foundational" capability of public health. But "surveillance" is a broad term used to describe many purposes and approaches. Multiple efforts over decades on the part of many smart and dedicated people, and investments of billions of dollars have brought some progress, but have not dramatically improved the nation's ability to see epidemics coming or to attain useful situational awareness once they arrive.

We need to plan and execute a strategic approach to epidemic surveillance that is practical and sustainable and balanced between the need to detect emerging epidemics and predict their course, and the need to provide actionable situational

awareness once epidemics or bioattacks are underway. We should begin with a rigorous examination of why so many surveillance projects have failed or delivered disappointing results – and what has worked.

Pro-MED – Program for Monitoring Emerging Diseases

One bio-surveillance approach, which spotted and warned of several emerging diseases – including SARS, MERS and Zika – before WHO or governments did so , is ProMED, which is a non-profit effort, now supported by the Infectious Disease Society of America, which receives email reports about disease events around the world and posts these messages on email. ProMED has been a uniquely useful surveillance tool, and has repeatedly shown its worth in spite of its small size and lack of complex analytics. It survives on a very small budget which it strains to meet from private donations and other non-profits. The secret sauce of ProMED has been attributed to its network 70 volunteer professionals - physicians, veterinarians, and plant scientists from around the world – who review and monitor incoming messages, using their own networks to deciding what to post and offering added details or explanation. This "human intelligence" helps make ProMED's reports more trusted - and crucially, *actionable*.

NBIS - the National Biological Integration System

I urge caution before the country invests further in a complex DHS surveillance program called *NBIS – the National Biological Integration System* – that is supported by the Study Panel. NBIS was first conceived over a decade ago, I believe on the basis of erroneous assumptions about the availability and usefulness of digitalized health information, overly optimistic expectations about what data could be collected and analyzed by the federal government and how meaningful such data would be to decision makers. Long experience across the federal government has shown that large, ambitious electronic information systems are difficult to build and often fail. GAO has documented many reasons for these failures, including unclear goals, rapid turnover among inadequately skilled project managers, failure to consult with stakeholders, inadequate funding, etc. I suggest that this program should be part of the strategic review of surveillance programs and should proceed only after we know what, exactly, we are building, how it will work, and who will use it.

OneHealth – Animal and Human Health are Intertwined

As the Study Panel emphasizes, we must do a far better job on surveillance of animals in the wild and in agriculture since the majority of newly emerging diseases originate in animal populations. The likely "hotspots" for spillover of animal diseases into humans are those places where large communities of animals and humans converge: the jungles and forests in tropical zones of Africa, South America and Southeast Asia. Most of our surveillance efforts are, however, focused on temperate zones, and on human disease, so that zoonoses such as SARS, MERS,

Nipah virus, etc. are not recognized until a critical mass of human illness becomes apparent.

Months or even years may pass before animal disease "spills over" into human populations. We should take advantage of this "long fuse" to prepare for oncoming outbreaks – or even better, to stop them. Rapid genomic screening technologies offer new approaches to understanding animal diseases, but field surveillance in general is terribly underfunded, as are established USDA and Dept. of Interior programs for monitoring agricultural and wild animals.

Rapid Diagnostics Tests - Critically Important Tools for Epidemic Control

As we saw with Ebola and are seeing now with Zika, it is very difficult to make sense of what is happening or to control epidemics without rapid diagnostic tests that can distinguish who is truly infected with the pathogen in question - and needs to be isolated or treated - and who is not. Rapid diagnostic tests that can be used in the field or at clinical points of care without requiring elaborate laboratory facilities are an *essential* strategic tool in quenching epidemics.

The lack of such rapid diagnostics greatly increased the toll and duration of the West Africa Ebola epidemic. Our inability to accurately diagnose Zika virus infection is hampering our ability to understand what is happening in South America. We have many innovative technologies for creating new diagnostics, but market forces do not reward investments in this area. The regulatory hurdles for licensing a new diagnostic are sometimes unclear, and as challenging as those for new drug, but diagnostics yield a much smaller return on investment. Plus, current health care billing practices do not value diagnostics. Until the Ebola crisis of last year, BARDA had not invested in diagnostic development. This must change.

I have repeatedly written and testified before Congress on the subject of BioWatch, and would be fairly considered a critic of the program. The governing concept of BioWatch, a collection of environmental sensors located in cities and critical locales across the US and intended to detect specific, aerosolized bioweapons agents, is that detection of airborne agents will enable an earlier "response" to a bioattack and thus save lives. BioWatch was first deployed in 2003, but over the years, questions have been raised as to whether BioWatch detections are reliable and actionable; whether investments in BioWatch sensors are cost-effective or sustainable, and whether BioWatch detections will really speed "response times". A recent GAO report examines in detail some of the technical problems associated with prototypes of the "next generation" BioWatch technology being funded by DHS. The decade-plus experience with BioWatch operations has also revealed a number of practical, operational and strategic problems with the program that also deserve attention before we embark on a new, expensive and technologically complex surveillance program.

Vaccines are Essential to Epidemic Response

The US should strongly consider pursuing an ambitious strategy to take advantage of recent developments in bioscience to rapidly develop, test and manufacture vaccines against emergent infectious diseases. This would require a consolidated approach to vaccine development and testing, and the engagement of both small innovative companies and big Pharma companies. The US should endeavor to determine the best ways to design vaccines against new pathogens, create efficient safety testing protocols under NIH supervision, and seek to improve the speed and lower the risk of large scale manufacturing.

Vaccines have long been recognized as among the most effective interventions in modern medicine. Vaccines are the most cost-effective and efficacious ways to protect against large, lethal epidemics of infectious disease. An effective vaccine was the key to the eradication of smallpox in 1970.

Bioscience has since generated many new and exciting vaccine technologies - we actually have an "embarrassment of riches" in this field according to Dr. Phil Russell, an eminent vaccine specialist and former head of Walter Reed and the US Army Medical Research Institute for Infectious Diseases. But the country currently has no effective strategy for taking advantage of these new technologies. Vaccines take time to develop, in part because human trials of safety and efficacy are needed before they are used in the field. If they have not been fully tested and are sitting in a stockpile – an expensive business – then they must be manufactured by big drug companies who set aside their business plans to make emergency products or by "warm base" manufacturing plants which are built specifically to "stand ready" to go in times of need – also a very costly proposition.

Many small biotech companies are engaged in this field and eager to help – these companies are scientifically cutting-edge and agile enough to quickly design new approaches to fit emerging problems. But innovative small companies need reliable funding streams to produce their products. They cannot wait for months or years while the government contracting and acquisition system grinds away. Several Ebola vaccines were being slowly advanced over years before the West African crisis – both DOD and HHS were funding such vaccines, but funds were limited, and no human safety testing had occurred when the magnitude of the 2015 crisis became apparent.

Manufacturing vaccines at scale requires the skills and facilities of big pharmaceutical companies such as Merck and Glaxo-SmithKline (GSK), and these companies rather heroically leaped into action to produce enough Ebola vaccine for initial trials and use. HHS, NIAID and FDA as well as the involved companies also performed well once the crisis was upon us. But the process itself was complicated and messy and required a lot of negotiation – among multiple US actors and abroad. We need a much smoother and more understandable and predictable decision

process. Vaccine design and production is one area in which a consolidated US government approach would be valuable. The US government must also establish more predictable, transparent and efficient ways of partnering with the private sector.

The January 1, 2016, cover story of *Science* magazine was titled "Unfilled Vials – Scientifically Feasible Vaccines Against Major Diseases are Stalled for Lack of Funds." Science polled 50 experts who ranked the top 10 vaccines in order of R&D priority based on feasibility and need. There is a broad consensus about which vaccines would work and which would address a pressing public health need. What is missing is a methodical process and funding mechanism from moving these vaccines from "the freezer to the field". A collaboration between government and industry to design, test and stockpile vaccines against the ten pathogens most likely to cause large, lethal epidemics is not a crazy idea. It would cost more than the country has traditionally spent on all of biodefense.

Until we come up with a coherent strategy for rapid design and manufacture of effective vaccines, the US defense against lethal epidemics – both naturally occurring and due to bioterror attacks – will rely mostly on nineteenth century public health methods of contact tracing and isolation. The mortality rate among Ebola victims who made it to modern hospitals and received state-of -the -art supportive care was much lower than the death rate in Africa. In a big epidemic, a very small percentage of Americans will be accommodated in intensive care units. In such a situation, vaccines are the world's best bet. Let's get serious about using American ingenuity to create them.

Today, the digital revolution of the 20th century is converging with extraordinary advances in bioscience to create a "biorevolution" that will have immense benefits for humankind. Bioscience and biotechnology is fueling critically important discoveries in medicine, but biology will also be key to solving many of the major problems confronting us – providing safe and sustainable food supply; enhancing pollution free manufacturing; creating new sources of energy; dealing with an increasingly ageing population. As the *Economist* magazine wrote, "Biology will be to the 21st century what physics was to the 20th." It is past time to use one of the United States' greatest strengths – our ability to innovate – and turn it towards building a robust and enduring biodefense.