

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Allergy and Infectious Diseases Research Addressing  
Biodefense and Emerging and Re-emerging Infectious Diseases

Testimony before the  
House Committee on Appropriations  
Subcommittee on Labor, Health and Human Services, Education, and Related Agencies

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Mr. Chairman, Ranking Member DeLauro, and members of the Subcommittee, thank you for the opportunity to discuss the research response of the National Institutes of Health (NIH) to potential attacks with chemical and radiological/nuclear agents as well as biological threats, including emerging and re-emerging infectious diseases. I direct the National Institute of Allergy and Infectious Diseases (NIAID), the lead NIH institute for biodefense research.

The NIH conducts and supports basic and clinical research to better understand the biological effects of, and to develop medical countermeasures (MCMs) for, chemical, biological, and radiological/nuclear threats. Most of this work is conducted by the NIAID at the NIH. NIAID supports basic research on microbiology and immunology as well as applied and clinical research to evaluate candidate MCMs including diagnostics, therapeutics, and vaccines. This strategic effort includes the pursuit of foundational platform approaches that could be used to develop MCMs against multiple threats or pathogens. These platforms include molecular biological technologies for vaccines, targeted antibody therapeutics, and broad-spectrum antibiotics and antivirals.

NIH coordinates its biodefense research with partners in industry, academia, and the Federal Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) to ensure that promising countermeasures for biological, chemical, and radiological public health threats can proceed to advanced development. Since fiscal year 2012, NIH has supported the early development of 20 candidate MCMs for high-priority threats, and ultimately transitioned support for those candidate MCMs to the Biomedical Advanced Research and Development Authority (BARDA) for advanced development, with the goal of Food and Drug Administration (FDA) approval, licensure, clearance, or authorization, and for potential inclusion in the Strategic National Stockpile. NIH funding for emerging infectious disease, including biodefense research, was approximately \$2.6 billion in FY 2017.

### **NIH MEDICAL COUNTERMEASURE DEVELOPMENT**

Innovative technologies and approaches supported by NIH are enabling the development of new medical countermeasures (MCMs) at an unprecedented pace. High-throughput sequencing and platform-based technologies are facilitating the development and manufacture of MCM candidates to expedite their clinical evaluation. For example, during the Zika virus outbreak in the Americas, NIAID scientists used Zika virus genetic sequence information to develop a vaccine candidate that moved from concept to first-in-human trial in less than four months – likely the shortest development period ever for such a vaccine. The vaccine was developed with a readily deployable DNA vaccine platform that is a form of gene-based immunization previously employed by NIAID to develop a candidate vaccine for West Nile virus. These types of genetic platforms could be used to respond similarly to multiple emerging and re-emerging infectious disease threats.

Other broad-spectrum approaches are being used to advance the development of therapeutics that could be used against multiple pathogens. For example, NIAID has supported development of broad-spectrum antiviral agents such as BCX4430 (galidesivir), which has demonstrated activity against Ebola and other RNA viruses, and broad-spectrum antibacterial products, including a compound with activity against the two different bacteria that cause tularemia and plague.

NIAID continues to explore other inventive approaches to treat or prevent bioterrorism threats. Monoclonal antibodies, which precisely bind to a single target, have been used to treat certain cancers, infectious diseases, and autoimmune diseases. Monoclonal antibodies also have the potential to treat emerging and re-emerging infectious diseases, and as a first line intervention to prevent or slow the progress of infectious disease outbreaks as vaccines are being developed. A notable example is ZMapp™, a cocktail of three monoclonal antibodies targeting Ebola virus. ZMapp™ showed promise as a treatment for Ebola virus disease in an NIAID-supported clinical trial during the 2014-2016 outbreak in West Africa. Another innovative approach specific to vaccine development is the use of adjuvants. Adjuvants are valuable tools that can boost immune responses to otherwise modestly effective vaccines, and potentially can expedite development of vaccines for emerging pandemic threats. NIAID supports programs for discovery and development of adjuvants that have led to 50 novel adjuvants and 18 vaccine clinical trials.

NIAID also has invested in critical infrastructure and research resources to encourage the development and testing of biodefense MCMs. NIAID supports research capacity at high-containment laboratories where dangerous pathogens can be studied safely. In addition, NIAID provides qualified scientists with research resources, including microorganisms, research reagents, and preclinical development services that can fill knowledge gaps. These programs lower the financial risk for potential commercial partners, and expedite the development of MCMs.

These NIH-supported activities are advancing a robust pipeline of candidate MCMs needed to ensure the development of safe and effective products to protect the public health. Notable successes are outlined below.

*Ebola.* NIAID partnered with the government of Liberia to establish the Liberia-U.S. clinical research partnership known as PREVAIL. This partnership enabled a series of clinical trials, including studies testing several Ebola virus vaccine and therapeutic candidates, among them ZMapp™ and the NIAID-developed cAd3-EBOZ vaccine. Several candidates have transitioned to BARDA for advanced development.

*Smallpox.* NIAID supported the early-stage development of a novel smallpox vaccine, IMVAMUNE®, and a therapeutic, TPOXX® (tecovirimat), prior to their transition to BARDA for advanced development. IMVAMUNE® was shown to produce a superior immune response compared to the currently licensed smallpox vaccine. TPOXX® currently is under consideration for FDA approval pursuant to the Animal Rule, using pivotal animal model data supported by NIAID.

*Anthrax.* NIAID supported the preclinical and clinical development of the anthrax countermeasure ANTHIM® (obiltoxaximab), prior to its transition to BARDA for advanced development. ANTHIM® was approved by the FDA in 2016 for the treatment and prevention of inhalational anthrax, the deadliest form of the disease. NIAID also has supported the development of AV7909, a third-generation anthrax vaccine with a dry formulation that is easy

to store and has increased shelf life. AV7909 has been transitioned to BARDA for further development.

*Pneumonic Plague.* NIAID supported critical animal model studies of ciprofloxacin and levofloxacin for FDA approval, pursuant to the Animal Rule, as treatments for pneumonic plague. In addition, NIAID scientists conduct foundational research on the bacteria that cause plague, and the fleas that transmit them, to understand plague biology and to aid in the design of new MCMs.

*Pandemic Influenza.* NIAID is partnering with BARDA to support the development of vaccine candidates for influenza strains with the potential to cause a pandemic, including H7N9 avian influenza. NIAID also is working to develop broadly protective, or “universal,” influenza vaccines that could protect against multiple strains of seasonal and pandemic influenza. NIAID recently developed a Strategic Plan to guide research efforts focused on the design and development of universal influenza vaccines.

*Radiological/Nuclear Threats.* NIH investment in radiation/nuclear research revitalized physician training and infrastructure for studying radiation injury and developing effective medical countermeasures. Since 2005, NIAID has transitioned 29 radiation/nuclear countermeasure candidates to BARDA for advanced development. Recent successes include FDA approval of NEUPOGEN<sup>®</sup> (filgrastim) and Neulasta<sup>®</sup> (pegfilgrastim) to treat radiological or nuclear injuries. In addition, NIAID is funding animal studies of Nplate<sup>®</sup> (romiplostim) for acute radiation syndrome for consideration for FDA approval under the Animal Rule.

*Chemical Threats.* NIAID administers a trans-NIH chemical countermeasures program that supports the development of therapeutics for people exposed to dangerous chemicals, including nerve agents, metabolic poisons, and toxic industrial chemicals. NIH recently transitioned several candidate therapeutics to BARDA for advanced development, including those for nerve agent poisoning (midazolam and galantamine), sulfur mustard exposure (tissue plasminogen activator), and inhalation chlorine exposure (R-107 and GSK2798745).

## **CONCLUSION**

NIAID has moved strategically toward a MCM research paradigm that features broader, more flexible platform technologies. This effort is yielding significant scientific advances that help protect against multiple emerging public health threats, whether man-made or naturally occurring. Together with academia, industry, and PHEMCE partners, NIAID remains committed to meeting public health emergency needs by advancing high-priority research toward development of MCMs for radiological/nuclear, chemical, and biological threats, including emerging and re-emerging infectious diseases.