

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 Energy and Commerce  
Subcommittee on Oversight and Investigations

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Mr. Chairman, Ranking Member DeGette, 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 more than 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 Partnership for Research on Ebola Virus in Liberia (PREVAIL). This clinical research partnership enabled a series of clinical trials, including studies testing several Ebola virus therapeutic and vaccine candidates, among them ZMapp™ and the cAd3-EBOZ vaccine developed by the NIAID Vaccine Research Center (VRC) in partnership with industry. Several Ebola countermeasure candidates developed by NIAID have transitioned to BARDA for advanced development, including a novel vaccine approach using two candidate vaccines in a prime-boost regimen. NIAID currently is utilizing its expertise in Ebola research to respond to the ongoing Ebola outbreak in the Democratic Republic of the Congo (DRC). NIAID is providing technical assistance to the DRC-World Health Organization (WHO) effort to plan and implement a research response to the outbreak, including vaccine, therapeutics, and diagnostic research. NIAID also has developed as a therapeutic candidate mAb14, a monoclonal antibody active against Ebola. The antibody, which has shown promise in animal testing, was originally isolated from a survivor of the 1995 Ebola outbreak in Kikwit, DRC, through a research partnership between the NIAID VRC and the DRC's Institut National de Recherche Biomédicale. At the request of the Minister of Health of the DRC, NIAID is providing courses of mAb14 for treatment of Ebola Virus Disease, with specific research protocol design to be determined. NIAID also has deployed a team to the National Public Health Laboratory in nearby Brazzaville,

Republic of the Congo, to establish additional Ebola diagnostic and sequencing capacity in case the epidemic spreads to that country.

*Nipah.* NIAID conducts and supports research on countermeasures for Nipah, a deadly virus with case fatality rates of 40 to 75 percent. NIAID researchers have developed a candidate Nipah vaccine that was shown to protect against infection in a monkey model. NIAID-funded researchers, in collaboration with NIH scientists, discovered a potential monoclonal antibody treatment for Nipah virus. This treatment candidate, m102.4, effectively protected ferrets and non-human primates after exposure to Nipah virus. Based on this research, NIAID is assisting with the research response to the ongoing Nipah virus outbreak in India. At the request of the WHO, NIAID researchers have been working with scientists and clinicians from India to develop a clinical trial protocol to test the experimental monoclonal antibody m102.4 against Nipah virus. NIAID researchers also have evaluated an antiviral treatment for Nipah virus in collaboration with CDC and industry. This candidate, GS-5734, has been shown to protect against Nipah virus disease in monkeys.

*Smallpox.* NIAID supported the early-stage development of a novel smallpox vaccine, IMVAMUNE<sup>®</sup>, and a therapeutic, TPOXX<sup>®</sup> (tecovirimat), prior to their transition to BARDA for advanced development. IMVAMUNE<sup>®</sup> was shown to produce a superior immune response compared to the currently licensed smallpox vaccine. TPOXX<sup>®</sup> 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<sup>®</sup> (obiltoxaximab), prior to its transition to BARDA for advanced development. ANTHIM<sup>®</sup> 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 research and development of therapeutics for people exposed to dangerous chemicals, including nerve agents such as Sarin and VX; metabolic poisons such as cyanide; chemicals affecting the skin, eyes, and mucous membranes such as sulfur mustard; chemicals affecting the respiratory tract such as chlorine; 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.