DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

The Role of the National Institute of Allergy and Infectious Diseases in Research Addressing Ebola Virus Disease

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

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April 15, 2015

Mr. Chairman, Ranking Member DeLauro, and Members of the Subcommittee: Thank you for the opportunity to discuss the National Institutes of Health (NIH) response to the global health emergency of Ebola virus disease. I direct the National Institute of Allergy and Infectious Diseases (NIAID), the lead institute of the NIH for conducting and supporting research on infectious diseases, including viral hemorrhagic fevers such as those caused by Ebola. In fiscal year (FY) 2014, NIH funding for Ebola was approximately $77 million. In FY 2015, the President requested and Congress appropriated $238 million to NIAID to prevent, prepare for, and respond to Ebola domestically and internationally.

For more than six decades, NIAID has made important contributions to advancing our understanding of infectious, immunologic, and allergic diseases, from basic research on mechanisms of disease to applied research to develop diagnostics, therapeutics, and vaccines. NIAID has a dual mandate that balances research addressing current biomedical challenges with the capacity to respond quickly to newly emerging and re-emerging infectious diseases, including bioterror threats. Critical to these efforts are NIAID's collaborations with other Federal

entities, particularly the Centers for Disease Control and Prevention (CDC); the Food and Drug Administration (FDA); the Department of Health and Human Services (HHS) Office of the Assistant Secretary for Preparedness and Response, including the Biomedical Advanced Research and Development Authority (BARDA); the HHS Office of Global Affairs; and the Department of Defense (DOD); as well as with academia, industry, and international organizations. NIAID has a longstanding commitment to advancing research to combat Ebola virus disease while ensuring that potential medical countermeasures are rigorously tested for safety and efficacy.

OVERVIEW OF EBOLA VIRUS DISEASE

Ebola virus disease presents typically with fever, vomiting, and severe diarrhea. It can progress to profound fluid loss; weakness; electrolyte loss; impaired kidney, liver, and other organ function; and in some cases internal and external bleeding. The current Ebola outbreak in West Africa is by far the most severe ever recorded and remains an ongoing public health crisis. There is a critical need to develop improved diagnostics, as well as safe and effective treatments and vaccines for Ebola virus disease. In addition, it is becoming increasingly apparent that the consequences of Ebola virus infection on the infected individual do not end when the virus is cleared from the blood. Survivors report a variety of complications, including eye and joint problems. A study is being launched by the Liberia–U.S. Clinical Research Partnership to better characterize these potential long-term complications of Ebola virus infection.

DEVELOPMENT AND TESTING OF EBOLA MEDICAL COUNTERMEASURES

Since the 2001 terrorist attacks on the United States, NIAID has markedly enhanced its biodefense research portfolio and supported the development and testing of candidate products to

prevent or treat viral hemorrhagic fevers, including those caused by Ebola. NIAID was well-positioned to respond rapidly to the crisis in West Africa because of its longstanding investment in biodefense and emerging infections research. NIAID research on Ebola focuses on understanding how Ebola virus causes illness and on developing and testing new diagnostics, vaccines, and therapeutics.

Diagnostics

Symptoms of Ebola can easily be mistaken for other common causes of fever in affected areas, such as malaria. A rapid diagnostic for Ebola is critical so that isolation and treatment strategies can be implemented without delay. With NIAID support, Corgenix Medical Corporation developed the ReEBOV™ Antigen Rapid Test, which detects the presence of an Ebola virus protein in about 15 to 25 minutes. FDA recently authorized the test for emergency use in the presumptive detection of the Ebola Zaire virus in symptomatic individuals in appropriate circumstances; it was the first rapid diagnostic test for the Ebola virus to receive such a designation. The test represents a new tool allowing rapid isolation of Ebola patients to limit spread of the disease. NIAID also is advancing the development of other rapid point-of-care diagnostics that use novel technologies to detect multiple pathogens, including Ebola.

Rapid and accurate Ebola diagnostics are critical to monitor the outbreak, rapidly diagnose patients, and provide appropriate patient care. NIAID scientists, in coordination with CDC and DOD, have established and staffed laboratory sites to identify the presence or absence of Ebola virus in clinical samples in Monrovia, Liberia. In addition, NIAID scientists and grantees are analyzing genomic sequences of Ebola virus isolated from patients in West Africa to better understand the origin and transmission of the virus. NIAID scientists recently reported that the currently circulating Ebola virus has undergone relatively few mutations, none of which

suggest that it is becoming more severe or transmissible. Moreover, the researchers suggest that these genetic changes are unlikely to affect the efficacy of available diagnostics or candidate vaccines and treatments.

Therapeutics

NIAID supports the development of novel therapeutics targeting Ebola viruses as well as clinical trials to test the safety and efficacy of these treatments. NIAID supported Mapp Biopharmaceutical, Inc., to develop the investigational drug ZMapp, a combination of three antibodies against Ebola. NIAID has worked closely with partners at DOD, BARDA, and FDA to advance the development and testing of ZMapp. These efforts have led to the recent launch of a clinical trial to test the safety and efficacy of ZMapp in infected people at sites in Liberia and the United States. This trial, which is currently comparing treatment with ZMapp plus optimized standard of care versus optimized standard of care alone, is designed so that additional treatments also may be evaluated and compared.

The NIH Special Clinical Studies Unit (SCSU) at the NIH Clinical Research Center is designated to provide state-of-the-art intensive care in a research setting to U.S. citizens who become infected with infectious diseases requiring high containment, such as Ebola. Two American healthcare workers infected with Ebola virus during the current outbreak have been treated successfully at the SCSU. The facility serves as one of three U.S. study sites for the treatment trial evaluating ZMapp.

Vaccines

A safe and effective Ebola vaccine would be a critically important tool to help prevent Ebola virus disease and contain future outbreaks. Such a vaccine could be licensed and used in the field to protect healthcare workers and individuals living in affected areas. Since 1999, the

NIAID Vaccine Research Center (VRC) has pursued multiple early-generation Ebola vaccine candidates, culminating in a vaccine candidate currently in large-scale clinical trials. VRC scientists, in collaboration with GlaxoSmithKline, developed an experimental vaccine that uses the chimpanzee adenovirus type 3 (cAd3) as a carrier, or vector, to express an Ebola virus protein designed to stimulate protective immune responses. An NIAID-sponsored Phase II/III clinical trial of cAd3-EBOZ is now underway in Liberia as part of the Partnership for Research on Ebola Vaccines in Liberia (PREVAIL) study. The study also is testing an additional vaccine candidate, rVSV-EBOV, developed with support from DOD and NIAID. Interim findings in more than 600 people enrolled in the PREVAIL study indicate that the two experimental Ebola vaccines appear to be safe. Given these findings, the study should be able to advance to Phase III testing in a larger number of participants. As a result of the successful control of the Ebola outbreak in Liberia, discussions are underway with West African officials about possibly expanding the PREVAIL study to other West African countries.

NIAID also has collaborated with the biopharmaceutical industry, academia, and other Federal agencies to develop additional Ebola vaccine candidates. NIAID is supporting a Phase I clinical trial of an investigational vaccine regimen targeting multiple species of Ebola virus and the related Marburg virus. The trial will examine a prime-boost vaccine strategy composed of an adenovirus-vectored vaccine developed by Johnson & Johnson and a modified vaccinia virus Ankara-vectored vaccine developed by Bavarian Nordic. In addition, NIAID scientists are collaborating with investigators at Thomas Jefferson University to produce a vaccine candidate based on an existing rabies vaccine that could generate immunity to Ebola, Marburg, and rabies viruses. The investigators plan to pursue a version of the vaccine for human and veterinary use, as well as a version for use in African wildlife that could help prevent transmission of Ebola

virus from animals to humans. Clinical testing of the candidate rabies/Ebola vaccine for human use is expected to begin later this year. NIAID also is partnering with the University of Texas Medical Branch at Galveston to advance a human parainfluenza virus-vectored Ebola vaccine developed by NIAID scientists. This vaccine candidate is designed to be delivered intranasally, and Phase I trials are planned to begin by the end of 2015.

CONCLUSION

NIAID is an active participant in the global effort to address the Ebola outbreak in West Africa. NIAID will continue to work with our global partners to gain a better understanding of the pathophysiology of Ebola virus infection as well as to develop safe and effective medical countermeasures to treat and prevent Ebola.