DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

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

Testimony before the

Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies

and Senate Health, Education, Labor, and Pensions Committee

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Mr. Chairman and Members of the Committees:

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 virus infection.

For over six decades, NIAID has made important contributions to advancing the 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 partnerships with academia and pharmaceutical companies, and collaborations with other federal entities, particularly the Centers for Disease Control and Prevention, the Food and Drug Administration (FDA), the Biomedical Advanced Research and Development Authority (BARDA), and the Department of Defense.

OVERVIEW OF EBOLA VIRUS DISEASE

Viral hemorrhagic fevers are severe illnesses that can be fatal and are caused by a diverse group of viruses including Marburg virus, Lassa virus, and Ebola virus. Infection with Ebola virus typically causes fever and vomiting, diarrhea, rash, profound weakness, impaired kidney and liver function, and in some cases internal and external bleeding. Since the discovery of Ebola virus in 1976, outbreaks of hemorrhagic fever caused by Ebola virus have had fatality rates

ranging from 25 to 90 percent, depending on the species of virus and the availability of medical facilities to care for infected patients. West Africa is currently experiencing the most severe Ebola virus outbreak ever recorded. As of September 6, 2014, 4,293 cases of Ebola virus disease and 2,296 deaths had been reported in the region, according to the World Health Organization. The ongoing Ebola outbreak in Guinea, Liberia, Sierra Leone, Nigeria, and Senegal has generated more cases and deaths than the 24 previous Ebola outbreaks combined.

The ongoing public health crisis in West Africa demands a major amplification of efforts to identify and isolate infected individuals, perform contact tracing, and provide personal protective equipment for healthcare workers involved in the treatment of infected individuals. This still remains the time-

Diagnostics

Accurate and accessible diagnostics for Ebola virus infection are needed for the rapid identification and treatment of patients in an outbreak because the symptoms of Ebola can be

safe and effective; if so, such treatments can be available for future outbreaks. It is important to note that NIAID-supported candidate therapeutics are in early development and are currently available only in limited quantities.

NIAID has provided support to and collaborated with Mapp Biopharmaceutical, Inc., to develop MB-2003, a “cocktail” of three antibodies that prevents Ebola virus disease in monkeys when administered as late as 48 hours after exposure. An optimized product derived from MB-2003, known as ZMapp, has shown to be substantially more effective in animal models than earlier cocktails and protected monkeys from death due to Ebola virus up to five days after infection. NIAID’s preclinical services are now being used to provide pivotal data to support the use of ZMapp for clinical trials in humans. ZMapp was recently administered to humans for the first time as an experimental treatment to several Ebola-infected patients, including two Americans. NIAID is working closely with partners at the Department of Defense and BARDA to advance development and testing of ZMapp to determine whether it is safe and effective. BARDA has recently announced plans to optimize and accelerate the manufacturing of ZMapp so that clinical safety testing can proceed as soon as possible.

NIAID also has funded BioCryst Pharmaceuticals to develop and test BCX4430, a novel nucleoside analog drug with activity against a broad spectrum of viruses. BCX4430 has protected animals against infection by Ebola virus and the related Marburg virus. A Phase I(0 Tw [(a)TJ -0.004

infection. NIAID scientists also are studying human interferons as Ebola therapies. Other therapeutics being examined by scientists at RML are in early stages of study and if successful, will advance to animal model testing.

Vaccines

A safe and effective Ebola vaccine could be a critically important tool to help prevent Ebola virus disease. The hope is that such a vaccine could be licensed and used in the field to protect frontline healthcare workers and individuals living in areas where Ebola virus exists. Two Ebola vaccine candidates are entering Phase I clinical testing this fall. NIAID will play a critical role in advancing these Ebola vaccine candidates. The results of these Phase I studies will inform essential discussions about whether such vaccines could be of use in the current or future Ebola outbreaks.

The NIAID Vaccine Research Center (VRC) has a robust viral hemorrhagic fever vaccine development program. Since 2003, the VRC has evaluated three early-generation Ebola vaccine candidates and one Marburg vaccine candidate in Phase I clinical trials at the NIH campus. An additional Phase I clinical trial was conducted in Kampala, Uganda, in collaboration with the United States Department of Defense. All of the early-generation vaccine candidates were safe; however, they did not elicit the level of immune response thought to be needed to provide protection against exposure to the virus. The data from those trials have contributed directly to

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response. The vaccine candidate has shown promising results in animal models against two Ebola virus species, including the Zaire Ebola species responsible for the current outbreak in West Africa. A small Phase I study to examine the safety and ability of this candidate to induce an immune response in humans began on September 2, 2014, at the NIH Clinical Center in Bethesda, Maryland. Results from the study are anticipated by the end of this calendar year, and will help inform future development of the vaccine.

Additional Phase I clinical trials of Ebola vaccine candidates are expected to launch before the end of 2014. In October, testing will begin in the United States on a vaccine candidate derived from the ChAd3-vector designed to protect against a single Ebola virus species, the Zaire Ebola virus. NIAID and GSK also will donate doses of this vaccine candidate to enable testing by NIAID partners in the United Kingdom and the West African country of Mali, where existing NIAID research infrastructure will support the vaccine trial. Also this fall, NIH is collaborating with the Department of Defense and NewLink Genetics Corporation on Phase I safety studies of an investigational Ebola vaccine based on vesicular stomatitis virus (VSV). The VSV vaccine will serve as a vector or carrier for an Ebola gene similar to how the Chimp adenovirus served as a vector or carrier as described above for the NIAID/GSK vaccine. This vaccine candidate was developed by and licensed from the Public Health Agency of Canada.

NIAID has supported the biopharmaceutical company Crucell to develop a recombinant adenovirus-vectored Ebola vaccine. This vaccine candidate protected against filovirus infection, including Ebola virus, in animal studies. NIAID and Crucell are now partnering to advance this vaccine candidate into a Phase I clinical trial scheduled to begin in 2015. NIAID has played an instrumental role in the recent announcements by Johnson & Johnson (parent company of Crucell) and Bavarian Nordic that they will collaborate on a prime-boost vaccination regimen that will begin Phase I testing in 2015.

NIAID intramural scientists are collaborating with Thomas Jefferson University investigators to produce a vaccine candidate based on an existing rabies virus vaccine. The researchers aim to generate immunity to Ebola, Marburg, and rabies viruses, important diseases in certain regions in Africa. 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. The wildlife vaccine could help prevent transmission of Ebola virus from animals to humans. The vaccine candidate for use in humans is undergoing preclinical testing and has demonstrated protection against infection by rabies and Ebola viruses in animal models. NIAID is currently partnering with the Department of Defense to produce quantities of the vaccine candidate for clinical testing in early 2015.