DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Examining the Public Health Response to the Ebola Outbreak

Testimony before the

Mr. Chairman, Ranking Member DeGette, and Members of the Subcommittee:

Thank you for the opportunity to discuss the National Institutes of Health (NIH) response

discovery of Ebola virus in 1976, outbreaks of hemorrhagic fever caused by Ebola virus have had fatality rates ranging from 25 percent to 90 percent, depending on the species of virus and the availability of medical facilities and staff to care for infected patients. West Africa is currently experiencing the most severe Ebola outbreak ever recorded. As of October 12, 2014, there have been 8,997 reported cases, including 4,493 documented deaths according to the WHO. The ongoing Ebola epidemic in Guinea, Liberia, and Sierra Leone

research portfolio in biodefense and naturally emerging and re-emerging infectious diseases. This research targets pathogens that pose high risks to public health and national security. NIAID has designated pathogens with high mortality such as anthrax, plague, smallpox, and Ebola virus as NIAID Category A Priority Pathogens to highlight the need for medical countermeasures against these dangerous microbes.

NIAID's expanded research efforts in biodefense and emerging and re-emerging infectious diseases focus on specific objectives. The first is to advance basic and translational research and facilitate development of effective products to combat deadly diseases such as Ebola. The second is to employ innovative strategies, such as broad spectrum vaccines and therapeutics, to prevent and treat a variety of related infectious diseases. The third is to strengthen our partnerships with biotechnology and pharmaceutical companies to help accelerate the avail(va) shstto ecombatu35 products for affcted and at-risk individuals.

Since 2001, NIAID's biodefense research has supported the development and testing of numerous candidate prodts to prevent or treat viels tral hemorrhagic fevers, including those caused

understand how Ebola virus causes illness in animals and in people, as well as applied research to develop diagnostics, vaccines, and therapeutics.

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 easily mistaken for other common causes of fever in affected areas, such as malaria. NIAID continues to provide resources to investigators attempting to develop Ebola diagnostics. With NIAID support, Corgenix Medical Corporation is developing rapid immunodiagnostics for Ebola viruses using genomic technology to produce recombinant viral proteins. NIAID also is advancing development of other types of diagnostics, including those using novel technologies such as microfluidics, optofluidics and nanophotonics, which are capable of detecting an array of viruses including Ebola. Such innovative approaches can provide information critical to the creation of point-of-care diagnostics that could be distributed and used in areas where Ebola virus outbreaks occur. Intramural scientists from NIAID's Rocky Mountain Laboratories (RML) in Hamilton, Montana, and the Integrated Research Facility in Frederick, Maryland, have responded to the epidemic by providing technical diagnostic support on the ground in Liberia.

Therapeutics

Currently, supportive care, including careful attention to fluid and electrolyte replacement, is the only effective medical intervention for patients with Ebola virus disease; no drugs are available that have been shown safe and effective specifically to treat Ebola virus infection. Experts are now evaluating whether drugs licensed or approved for the treatment of other diseases should be reevaluated for potential treatment of patients with Ebola in the current

epidemic on an emergency basis. In parallel, NIAID is supporting the development of novel therapeutics targeting Ebola virus. These investigational candidate therapeutics could possibly be used in clinical trials in the current epidemic and hopefully will prove to be safe and effective; if so, such treatments could be more widely 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-003, a combination 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-003, known as ZMapp, has shown to be substantially more effective in animal models than earlier combinations and protected monkeys from death due to Ebola virus up to five days after infection, according to Mapp Biopharmaceutical, Inc. NIAID's preclinical services are now being used to provide pivotal safety data to support the use of ZMapp for clinical trials in humans. Mapp Biopharmaceutical, Inc., has announced that ZMapp was recently administered to humans for the first time as an experimental treatment to several Ebola-infected patients, including two Americans. It is not possible at this time to determine whether ZMapp benefited these patients. NIAID is working closely with partners at DOD, BARDA, and FDA 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 drug that interferes with the reproductive process of the virus and has activity against a broad spectrum of viruses. According to BioCryst, BCX4430 has protected animals against infection

with Ebola virus and the related Marburg virus. BioCryst has announced that a Phase 1 clinical trial of this drug is expected to begin in late 2014 or early 2015. NIAID also is evaluating therapeutics licensed or in development for the treatment of other diseases for their potential activity against Ebola virus. One of these investigational agents is brincidofovir, an antiviral originally developed with NIAID support for use against other viruses.

In related work, NIAID intramural scientists at RML are working on therapeutics that might be effective against all hemorrhagic fever viruses, including the filoviruses Ebola and Marburg and the arenavirus Lassa. Ribavirin, a drug currently used to treat hemorrhagic fever viruses such as Lassa virus, is being examined for its potential use in combination with interferon to treat Ebola virus infection. Other therapeutics are in early stages of study by RML 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 and help contain future outbreaks. 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 undergoing Phase 1 clinical testing this fall. NIAID will play a critical role in advancing these Ebola vaccine candidates. The results of these Phase 1 studies will inform essential discussions about whether and how such vaccines could be of use in the current epidemic 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 1 clinical trials at the NIH campus. An additional Phase 1 clinical trial was conducted in Kampala, Uganda, in collaboration with DOD.

None of the early-generation candidates raised safety concerns in these small trials; however, they did not elicit the level of immune response thought to be needed to provide protection against the viruses. The data from those trials have contributed directly to the VRC's current Ebola vaccine collaboration with the pharmaceutical company GlaxoSmithKline (GSK). VRC and GSK have developed an experimental vaccine that uses a chimpanzee virus (similar to the common cold virus), Chimp Adenovirus 3 (CAd3), as a carrier, or vector, to introduce Ebola virus genes into the body; these genes encode Ebola proteins that stimulate an immune response. The vaccine candidate has shown promising results in animal models against two Ebola virus species (bivalent vaccine), including the Zaire Ebola species responsible for the current epidemic in West Africa. A small Phase 1 study to examine the safety and ability of this candidate to in4(sr3)4(c)4(c.624 ot(e)4(c)481.560.humala 0(h)4(Tm[in4(tec)20(Gla)4 otptem0(ht r 2, 2P)-014, teins d)-7(y)

NIAID also is supporting the biotechnology company Profectus BioSciences, Inc., to investigate a second recombinant VSV-vectored vaccine candidate against Ebola and Marburg viruses. Profectus is pursing preclinical testing of the vaccine in preparation for a future Phase 1 clinical trial. Additionally, NIAID is collaborating with the Galveston National Laboratory & Institute for Human Infections and Immunity at the University of Texas Medical Branch at Galveston to further progress made by NIAID intramural scientists on a paramyxovirus-based vaccine against Ebola virus.

Other NIAID-supported efforts include Ebola virus vaccine candidates in early development, such as a DNA vaccine targeting Ebola and Marburg viruses, an adenovirus-5-based intranasal Ebola vaccine, and a combination virus-like particle/DNA vaccine targeting Ebola and Marburg viruses to be delivered by microneedle patch. Knowledge gained through

continue to expedite research while enforcing high safety and efficacy standards, the implementation of the public health measures already known to contain prior Ebola virus outbreaks and the implementation of treatment strategies such as fluid and electrolyte replacement are essential to preventing additional infections, treating those already infected, protecting health care providers, and ultimately bringing this epidemic to an end. We will continue to work with biopharmaceutical companies and public health agencies throughout the world to develop and distribute medical countermeasures for Ebola virus disease as quickly as