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

House Committee on Energy and Commerce

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 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 November 11, 2014, there have been 14,413 reported cases, including 5,177 documented deaths according to the WHO. The ongoing Ebola epidemic in Guinea, Liberia, and Sierra Leone has generated far more cases and deaths than the 24 previous Ebola outbreaks combined. The recent death of a patient diagnosed with Ebola in Dallas, Texas, after traveling from Liberia, and the cases transmitted outside of Africa (to two healthcare workers in Dallas and a nurse in Spain) intensify our concerns about this global health threat.

The ongoing public health crisis in West Africa demands a major amplification of efforts to identify and isolate infected individuals, perfor7dh1 0 075 Tm[7w(publi)-3(c)4.h1)7r7dh1 0 075 1m[Da)6and

HISTORY OF NIAID EBOLA VIRUS RESEARCH: RELATIONSHIP TO BIODEFENSE RESEARCH

The ability to safely and effectively prevent and treat Ebola virus infection is a

Monrovia, Liberia, in coordination with CDC, to identify the presence or absence of Ebola virus in clinical samples. These real-time data are critical to patient care and monitoring of the epidemic. NIAID and CDC researchers also have established collaborations with Malian public health institutes, providing training in laboratory testing for identification of Ebola and other fever-causing viruses.

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

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 addit ah1

vaccine). NIAID and GSK also have donated doses of this vaccine candidate to enable further testing by NIAID partners in the United Kingdom and the West African country of Mali. In October, GSK and WHO partners began an additional, larger clinical study of the monovalent vaccine in Geneva/Lausanne, Switzerland.

Additionally, NIH is collaborating with DOD and NewLink Genetics Corporation on Phase 1 safety studies of an investigational Ebola vaccine based on the vesicular stomatitis virus (VSV). The VSV will serve as a vector or carrier for an Ebola gene similar to how the Chimp adenovirus serves 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.

In addition to these Ebola candidates entering Phase 1 trials in 2014, NIAID supports a broad portfolio of Ebola vaccine research. NIAID has supported the biopharmaceutical company Crucell to develop a recombinant adenovirus-vectored Ebola vaccine. In animal studies, this vaccine candidate protected against filovirus infection, including Ebola virus. NIAID has played an instrumental role in the recently announced collaboration between Johnson & Johnson (parent company of Crucell) and Bavarian Nordic. Crucell will contribute its adenovirus-vectored vaccine and Bavarian Nordic will contribute its modified vaccinia virus Ankara (MVA)-vectored vaccine for a two-dose (prime-boost) vaccination regimen that will begin Phase 1 testing in early 2015.

NIAID intramural scientists are collaborating with Thomas Jefferson University investigators to produce a vaccine candidate based on an existing rabies 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 DOD to produce sufficient quantities of the vaccine candidate to begin clinical testing in 2015. In September, NIH licensed the candidate rabies/

animal models and assays that NIAID has developed over many years. Several of these candidates qualified for further testing and a number are currently in the product development pipeline.

Clinical Trials to Evaluate Efficacy

It is important to balance the urgency to deploy investigational medical countermeasures in an emergency such as the current Ebola outbreak with the need to ensure the maximal safety and to determine the efficacy of candidate drugs and vaccines for Ebola. We will do this with the strictest attention to safety considerations, established scientific principles, and ethical considerations, and compassion for and realization of the immediate needs of the affected populations. The United States Government, working in partnership with industry, has an established mechanism for testing and reviewing the safety and efficacy of potential medical interventions. Randomized controlled clinical trials remain the "gold standard" for the evaluation of candidate drugs and vaccines because they represent the most efficient way to prove efficacy and lack of an unexpected harmful effect. This is particularly important for vaccines since they are administered to healthy individuals.

NIAID is committed to working with our partners to evaluate candidate drugs and vaccines for safety and efficacy. We are working to generate the evidence to show whether potential interventions are safe and effective to reassure affected communities that we are developing the tools needed to prevent and treat this deadly disease. Our partnerships with industry will be critical to move these products expeditiously along the development pipeline into clinical trials. The data from the current Phase 1 trials will help demonstrate whether these candidate Ebola vaccines are safe in humans and are capable of generating an immune response. Candidate Ebola treatments will be similarly evaluated for safety and markers of potential

efficacy. If successful, these candidates will be advanced to efficacy testing in larger numbers of people in West Africa. As we proceed through clinical testing, we will continue to work with our partners in the FDA and BARDA to accelerate development of and speed access to the products, while also protecting the safety and rights of study volunteers.

CONCLUSION

While NIAID is an active participant in the global effort to address the public health emergency occurring in West Africa, it is important to recognize that we are still in the early stages of understanding how infection with the Ebola virus can be treated and prevented. As we continue to expedite research while enforcing high safety and efficacy standards, the