

PREPARED STATEMENT OF ANTHONY S. FAUCI, M.D.
DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS
DISEASES

Mr. Chairman and Members of the Committee: I am pleased to present the President's Fiscal Year (FY) 2017 budget request for the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH).

NIAID has a dual mandate to not only pursue a robust research portfolio in the areas of microbiology, infectious diseases, immunology, and immune-mediated disorders, but also to quickly launch a research response to newly emerging and re-emerging infectious diseases. This dual mandate has been particularly evident over the past two years as NIAID has accelerated research to address the unprecedented Ebola and Zika virus outbreaks.

INFECTIOUS DISEASES RESEARCH

NIAID continues to advance research to address emerging and re-emerging infectious diseases around the world. In recent years we have faced major threats from diseases that have caused substantial morbidity and mortality, with Ebola virus disease and Zika virus disease being perhaps the most notable; however, other diseases such as dengue and chikungunya also have raised significant concerns. NIAID research supports progress against these and other emerging and established infectious disease threats worldwide. Examples of notable NIAID-supported infectious diseases research are highlighted below.

Zika and other mosquito-borne viruses. The appearance and rapid spread of Zika virus in the Americas has coincided with new and concerning presentations of disease. These include reported increases in the birth defect microcephaly and the immune-mediated neurological disease Guillain-Barré syndrome. NIAID has rapidly mobilized research to address the public health threat of Zika by building upon our prior successes with other flaviviruses, notably West Nile and dengue viruses. Ongoing NIAID efforts include studies of the natural history, viral genetics, and pathogenesis of Zika virus, including how infection may cause the development of microcephaly and other congenital abnormalities in the fetus. In addition, NIAID is expanding efforts to develop countermeasures for Zika virus that could help control current and future outbreaks. NIAID has developed an animal model to test whether therapeutic compounds with activity against other flaviviruses also are effective against Zika virus. NIAID-supported researchers are developing diagnostics that can distinguish Zika virus from other flaviviruses, as well as investigating unique biosignatures that could form the basis of rapid, specific, and sensitive Zika diagnostic tests. The development of safe and effective vaccines against not only Zika but also several other mosquito-borne viruses is a top priority of NIAID. The NIAID Vaccine Research Center (VRC) is developing a DNA-based vaccine for Zika virus that is similar to a West Nile virus vaccine previously developed by NIAID. Phase I clinical testing of the West Nile vaccine candidate showed it was safe and generated a robust immune response, indicating it

could be a promising platform for a Zika vaccine. NIAID scientists also are designing a live-attenuated Zika vaccine. This effort employs an approach similar to that used for an NIAID-developed dengue virus vaccine candidate currently in Phase III clinical trials in Brazil. In addition, NIAID is investigating a Zika virus vaccine candidate that uses the same platform as an Ebola vaccine tested in West Africa and is partnering with BARDA to support a whole-particle inactivated vaccine candidate. We anticipate that one or more of these Zika virus vaccine candidates will begin clinical testing in September 2016. NIAID also has supported the development of additional vaccine candidates for mosquito-borne viruses, notably an NIAID VRC-developed chikungunya vaccine candidate currently undergoing Phase II clinical trials in the Caribbean.

Ebola. Longstanding NIAID investments in biodefense research and collaboration with industry partners enabled the rapid and successful execution of clinical trials of candidate Ebola countermeasures in response to the 2014–2016 Ebola outbreak in West Africa. Recently completed NIAID studies demonstrated that the experimental Ebola vaccines cAd3-EBOZ and rVSV-ZEBOV are safe and immunogenic. A clinical trial evaluating ZMapp, a cocktail of three Ebola virus antibodies, found that treatment with ZMapp likely benefits Ebola virus disease (EBVD) patients. ZMapp remains the leading Ebola therapeutic candidate and has been made available to the recent Ebola cases in Guinea. Finally, ongoing studies in Liberia are enhancing our understanding of the long-term health consequences in survivors of EBVD. NIAID researchers and colleagues recently described initial findings concerning the extent of eye, musculoskeletal, and neurological problems experienced by EBVD survivors, as well as a possible persistent risk of sexual transmission of the virus. These NIAID studies have validated the use of randomized, controlled clinical trials during an infectious disease outbreak. Our efforts continue to evaluate improved vaccine strategies to prevent Ebola virus infection and determine the long-term clinical and public health consequences of EBVD.

HIV/AIDS. Significant progress has been made in combating HIV/AIDS through the implementation of treatment and prevention approaches supported by NIAID research. Despite this progress, continued investment in the development of a safe and effective HIV vaccine and cure is needed to achieve a durable end to the HIV/AIDS pandemic. Research supported by NIAID continues to provide the evidence that informs the development of improved HIV treatment and prevention tools. A recent groundbreaking NIAID study conclusively demonstrated the value of early use of antiretroviral drugs, showing that starting treatment as soon as possible after HIV diagnosis reduces the risk of developing AIDS or other serious illnesses. Growing evidence from clinical trials and real-world implementation supports an approach known as pre-exposure prophylaxis, or use of antiretroviral drugs by high-risk HIV-negative individuals to prevent HIV infection. NIAID also is pursuing research in the development of next-generation interventions, such as broadly neutralizing antibodies; long-lasting injectable therapeutics; multipurpose prevention technologies (including microbicides); and a safe, effective HIV vaccine.

Antimicrobial resistance. NIAID plays an important role in the President's National Strategy for Combating Antibiotic-Resistant Bacteria (CARB) in collaboration with partners across the Federal government. This year, NIAID will maintain and grow a robust antimicrobial resistance research portfolio to understand the mechanisms of resistance and to develop improved countermeasures. Key NIAID efforts include sequencing bacterial strains for the National Database of Resistant Pathogens; developing non-traditional therapeutics; optimizing current treatment strategies to reduce the emergence of drug resistance; and developing diagnostic platforms capable of detecting multiple resistant pathogens.

Influenza. NIAID influenza research aims to address the constant threat of seasonal influenza and the potential for pandemic influenza. In particular, NIAID is pursuing several promising universal influenza vaccine candidates that could protect against multiple influenza strains over multiple influenza seasons. In animal models, NIAID investigators have shown that two different universal influenza vaccine candidates can protect against numerous influenza strains. Both of these vaccine candidates, a nanoparticle vaccine and a virus-like particle vaccine, will be investigated for further development and clinical testing.

Malaria. NIAID research support contributed to the early stages of the development of the RTS,S vaccine, the first vaccine shown to protect against malaria in young children. In a recent study, NIAID-supported scientists used advanced genomic sequencing technology to help explain why the RTS,S vaccine is only partially effective. The researchers found that children infected with malaria parasites harboring genetic variants that did not match the protein targeted by the vaccine were less likely to be protected. These results will inform pilot implementation of the RTS,S vaccine endorsed by the World Health Organization as well as future malaria vaccine development strategies.

Tuberculosis (TB). NIAID is playing a critical role in accelerating basic and applied research to combat multidrug-resistant TB (MDR-TB) as part of the President's National Action Plan for Combating MDR-TB. With MDR-TB cases increasing worldwide, there is a need for new diagnostics to rapidly identify resistance, as well as biomarkers to determine whether a particular TB drug regimen is effective. NIAID scientists have identified two medical imaging technologies that may help predict TB drug treatment outcomes. Positron emission tomography and computed tomography images allow researchers to monitor the burden of bacteria remaining in the lungs after therapy. These technologies potentially could be used in combination to quickly assess effectiveness of drug treatments and shorten the duration of clinical trials. NIAID also supports efforts to develop improved TB vaccines. NIAID research has contributed to more than half of the current clinical pipeline of TB vaccine candidates, and NIAID is working with product developers to transition promising candidates to advanced clinical trials.

Respiratory syncytial virus (RSV). RSV is a serious childhood respiratory infection. Each year in the United States, RSV causes an average of approximately

55,000 hospitalizations among children younger than five years. NIAID-funded researchers have developed a promising pediatric RSV vaccine candidate. Early tests in children and – adults show the vaccine is safe and elicits a stronger immune response than previously developed RSV vaccines. NIAID has launched an RSV human challenge model at the NIH Clinical Center to test the efficacy of this vaccine candidate in adults infected with RSV.

RESEARCH ON IMMUNOLOGY AND IMMUNE-MEDIATED DISORDERS

NIAID remains committed to advancing our understanding of the immune system and immune-mediated diseases. NIAID scientists and colleagues have created an extensive database of genetic information to facilitate research on immune disorders. These researchers used samples from twins to differentiate approximately 80,000 immune traits that are likely to be genetically regulated. NIAID has made this open-access resource available to researchers worldwide who are investigating diverse immune conditions.

NIAID research also has led to significant progress on treatments for immune-mediated diseases. NIAID-supported researchers continue to investigate findings from the groundbreaking Learning Early About Peanut Allergy (LEAP) food allergy study, which demonstrated that consumption of peanut-containing foods beginning in infancy decreased the development of peanut allergy in young children. The recent LEAP-ON trial demonstrated that tolerance to peanut persisted even after stopping peanut consumption for one year. This result suggests that early peanut consumption may be a viable long-term strategy for preventing peanut allergy. NIAID also is supporting research to improve current treatments for asthma. The Preventive Omalizumab or Step-up Therapy for Severe Fall Exacerbation (PROSE) clinical trial demonstrated that treatment with the antibody omalizumab reduced the number of seasonal asthma attacks experienced by inner-city children with a history of asthma attacks. Finally, NIAID continues to investigate treatment options for type 1 diabetes. An NIAID-supported clinical trial of the immune-suppressing drug alefacept in patients newly diagnosed with type 1 diabetes found that the drug helped preserve the function of insulin-producing cells in the pancreas. This effect persisted for more than a year after treatment ended.

CONCLUSION

NIAID continues to confront important historic public health challenges by supporting an established research portfolio in infectious and immune-mediated diseases while also responding rapidly to emerging infectious disease threats. NIAID has assisted international efforts to combat newly emerging and re-emerging pathogens, such as the Zika, Ebola, and dengue viruses. Research supported by NIAID also has advanced progress on persistent infectious and immune-mediated diseases worldwide. NIAID will continue to pursue effective medical countermeasures for these diseases in an effort to improve health globally in collaboration with U.S. and international government partners, academia, and industry.