DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Madam Chair, Ranking Member Lucas, and Members of the Committee:

Thank you for the opportunity to discuss the role of the National Institute of Allergy and Infectious Diseases (NIAID) in the research and development of innovative influenza vaccines. NIAID is the lead institute at the National Institutes of Health (NIH) for conducting and supporting research on infectious diseases, including influenza.

NIAID supports a comprehensive portfolio of basic, translational, and clinical research on influenza. This research is focused on better understanding the influenza virus and the disease it causes as well as developing diagnostics, therapeutics, and vaccines to prevent and treat it. The constantly changing nature of seasonal influenza viruses and the threat of the emergence of a pandemic influenza necessitate the development of

UNIQUE CHALLENGES PRESENTED BY INFLUENZA VIRUSES

Influenza viruses, particularly influenza A viruses, are persistent threats to global health as they cause significant illness and death every year in the United States and worldwide. Influenza viruses evolve and evade the immune system response in two major ways: “antigenic drift” and “antigenic shift.” Antigenic drift occurs when small changes steadily accumulate in key proteins on the surface of the influenza virus. The human immune system focuses its response to influenza primarily on two proteins on the surface of the virus, hemagglutinin (HA) and neuraminidase (NA). Over time, minor alterations in the HA and NA proteins, usually resulting from genetic mutations, can impair the immune system’s ability to recognize a specific influenza virus. This antigenic drift characteristic of seasonal influenza often necessitates the modification of the influenza vaccine from season to season. On the other hand, antigenic shifts are characterized by major genetic changes that, when they occur, are often manifested by the “spill over” 0.00000912 0 612 792 re0 0 10.00000912 0 612 792 reWnBT/F3 12 TfETQq0.00000912 0 u82q0.0000 lower than that of many other licensed vaccines for common infectious diseases, such as the combined vaccine for measles, mumps, and rubella viruses, which has an effectiveness rate of 97 percent against measles. Suboptimal seasonal influenza vaccine effectiveness in part may be due to the six-month timeline required to grow the virus (usually in eggs) for production of vaccines. Once the vaccine production process is initiated, it is nearly impossible to begin anew if a different strain emerges. In years when circulating influenza strains drift significantly, mismatches between the vaccine and circulating viruses can occur, and this may result in low vaccine effectiveness.

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particles, vector-based, and self-assembling nanoparticle vaccines. For example, NIAID-supported scientists are investigating an mRNA vaccine candidate that would allow for a more rapid and flexible response to both seasonal and pandemic influenza than do existing vaccine production strategies.

Moving Beyond Strain-specific Influenza Vaccines

In addition to research into how we can improve influenza vaccine manufacturing, NIAID is working to advance from strain-specific vaccines to vaccines that would provide near universal influenza virus strain coverage. This effort aligns with NIH responsibilities outlined in the Executive Order mentioned previously. The HA protein of influenza is made up of a head and a stem, analogous to a mushroom cap and its stem. Strain-specific vaccines primarily generate an immune response to the head region, which mutates easily and differs between influenza virus strains. NIAID scientists and NIAID-supported researchers are working toward designing vaccines that generate an immune response to multiple influenza strains by targeting conserved parts of the virus – those that are less likely to differ among strains. A key target is the stem region of the HA protein, which is more similar from strain to strain than the head region of HA. The NA surface protein has been identified as another potential vaccine target. Recently, NIAID-supported scientists demonstrated in an animal model that monoclonal antibodies targeting NA of one influenza virus strain can also provide protection against several other strains of influenza. NIAID scientists also are working on new ways of displaying conserved parts of the virus to the immune system to induce a stronger and broader immune response.

The process of moving beyond strain-specific influenza vaccines will be iterative and progressive. The initial

Research (DIR) is evaluating multiple universal influenza vaccine candidates. In collaboration with industry partners, NIAID scientists recently completed a Phase 2 clinical trial assessing a novel peptide-based candidate in a human influenza challenge model. DIR investigators also plan to launch two Phase 1 trials of other promising universal influenza vaccine candidates in early 2020. The first candidate comprises a cocktail of inactivated avian influenza viruses and the second candidate targets the NA influenza surface protein.

NIAID also supports diverse efforts by extramural researchers to develop universal influenza vaccine candidates. NIAID continues longstanding support for its Vaccine and Treatment Evaluation Units (VTEUs), which are currently conducting multiple clinical trials evaluating candidate universal influenza vaccines. In 2018, NIAID began a Phase 2 VTEU clinical trial to evaluate the M-001 vaccine candidate made by the company BiondVax that contains several influenza fragments common among multiple influenza virus strains. In addition, NIAID is sponsoring a Phase 1 VTEU clinical trial to evaluate the safety and immunogenicity of a regimen using an investigational live, attenuated intranasal influenza vaccine followed by a boost with a licensed, quadrivalent inactivated seasonal influenza vaccine. NIAID has recently expanded the capacity of the VTEUs to conduct human influenza challenge studies to assess how levels of pre-existing influenza antibodies impact the timing, magnitude, and duration of symptoms following exposure to influenza virus. These challenge studies also will facilitate the future evaluation of novel universal influenza vaccine candidates.

Recently NIAID initiated the Collaborative Influenza Vaccine Innovation Centers (CIVICs) network to foster a coordinated, multidisciplinary effort to develop more broadly protective and longer-lasting influenza vaccines. Network researchers will conduct preclinical