U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCICENCE, SPACE, AND TECHNOLOGY

HEARING CHARTER

Fighting Flu, Saving Lives: Vaccine Science and Innovation

Wednesday, November 20, 2019
10:00 a.m. – 12:00 p.m.
2318 Rayburn House Office Building

Purpose

On Wednesday, November 20, 2019, the Committee on Science, Space, and Technology will hold a hearing to highlight the effectiveness and safety of vaccines, review the rationale for continuing to invest in vaccine science and innovation, use influenza as a case study to examine the science, innovation, and data challenges to developing an even more effective vaccine and eventually a universal flu vaccine, and consider the common technology and data platforms that could accelerate progress in vaccine development for many diseases. The Committee will also examine the public-private partnerships and state-federal partnerships to advance vaccine innovation and deployment, as well as efforts to communicate vaccine safety and effectiveness to the public.

Witnesses

Panel 1:

- **Dr. Daniel B. Jernigan, MD, MPH**, Director, Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention
- **Dr. Anthony S. Fauci, MD**, Director, National Institute for Allergy and Infectious Disease, National Institutes of Health

Panel 2:

- **Dr. Sharon Watkins**, **PhD**, State Epidemiologist, Director, Bureau of Epidemiology, Pennsylvania Department of Health and President, Council of State and Territorial Epidemiologists
- **Dr. Robin Robinson**, **PhD**, Vice-President for Scientific Affairs, RenovaCare and former Director, Biomedical Advanced Research and Development Authority, U.S. Department of Health and Human Services

Overarching Questions

- How does the flu vaccine work? What makes it safe and effective? How many lives have been saved since the flu vaccine was first developed and used during World War II?
- What research and development is needed for next generation vaccine production methods? What are the additional hurdles to innovation in the annual flu vaccine?
- What research and development is needed for a universal flu vaccine?
- How does the government collect data about the prevalence and severity of flu and other infectious diseases and how do these data inform vaccine development? How can new data science tools be applied to disease surveillance?
- What are the common research, technology, and data platforms that can be applied broadly across diseases and associated vaccine development?
- What is the role of the Federal government in supporting flu vaccine development from basic research through deployment? How does the Federal government partner with state governments, the private sector, and other stakeholders in improving public health through vaccine development?

Background

The development of vaccines was a pivotal public health breakthrough and has played an important role in reducing or eliminating instances of deadly disease. Smallpox is one such example; between 1900-1980 approximately 300 million people died from smallpox.[1] Today, smallpox is the only human disease to have been eradicated by vaccination.[2] Polio is another example. Cases due to wild poliovirus have decreased by over 99 percent since 1988, when there were approximately 350,000 new cases, to just 33 reported cases in 2018.[3]

Influenza is another infectious disease for which vaccines are an important public health intervention. On average, eight percent of the U.S. population gets sick from flu each season.[4] In the 2017-2018 influenza season, the Centers for Disease Control and Prevention (CDC) recorded an estimated 48.8 million illnesses and 79,400 deaths.[5] During that season, CDC estimated that flu vaccination coverage among adults was 37.1 percent.[6] Influenza also has a significant economic impact. The estimated average annual economic burden of influenza, which includes

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[1] Azimi, Tara et al. *Refueling the innovation engine in vaccines.* May 2019. https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/refueling-the-innovation-engine-in-vaccines (Accessed Nov. 2019).
[2] WHO. *Smallpox vaccines*. https://www.who.int/csr/disease/smallpox/vaccines/en/ (Accessed Nov. 2019).
[3] WHO. *Poliomyelitis*. July 22, 2019. https://www.who.int/en/news-room/fact-sheets/detail/poliomyelitis. (Accessed Nov. 2019).
[4] CDC. *Key Facts About Influenza (Flu)*. September 13, 2019. https://www.cdc.gov/flu/about/keyfacts.htm (Accessed Nov. 2019).
[5] CDC. *Estimated Influenza Illnesses, Medical visits, Hospitalizations, and Deaths in the United States — 2017–2018 influenza season*. December 18, 2018. https://www.cdc.gov/flu/about/burden/2017-2018.htm (Accessed Nov. 2019)
[6] CDC. *Estimates of Influenza Vaccination Coverage among Adults—United States, 2017–18 Flu Season*. November 5, 2018. https://www.cdc.gov/flu/fluvaxview/coverage-1718estimates.htm. (Accessed Nov. 2019).

direct medical cost and indirect cost, is $11.2 billion.[7] Influenza viruses have the potential to cause pandemic illness; the best-known example of an influenza pandemic was the 1918 influenza pandemic, commonly known as the Spanish flu pandemic. This pandemic is estimated to have caused at least 50 million deaths worldwide with approximately 675,000 of those in the United States.[8]

Vaccination Rates and Benefits

The current influenza vaccine is designed to be administered annually as every flu season there are different influenza viruses circulating, and an updated annual vaccine provides the best protection against the viruses. Most influenza vaccines in the United States for this season are designed to protect against four different influenza viruses: two influenza A viruses (H1N1 and H3N2) and two influenza B viruses. There are also influenza vaccines that protect against three of the four influenza viruses. Two of these vaccines are designed for use in people aged 65 and older to elicit a stronger immune response.[9]

The CDC currently recommends that everyone 6 months or older receive a flu vaccine except in rare cases.[10] The CDC also identifies populations that are at increased risk of developing serious complications from an influenza infection including: adults aged 65 or older, pregnant women, people with heart disease, people with asthma, and young children.[11]

Influenza vaccination rates in the United States vary year-to-year and are tracked by the CDC. Children are more likely to be vaccinated than adults. For the 2018-2019 influenza season, CDC estimated the vaccination coverage in adults 18 or older at 45.3% and coverage in children aged 6 months to 17 years at 62.6%. The vaccination coverage also varied by state ranging from 33.9% to 56.3% in adults and 46.0% to 81.1% in children.[12]

While the vaccine does not always prevent illness, it is still beneficial even in people who do get sick. The influenza vaccine can reduce the severity of the symptoms of an illness and help prevent hospitalizations due to influenza infection. The vaccine can also help protect people who work or live with someone infected with influenza.[13] Given the potential for complications from influenza, especially in the at-risk populations, reducing the severity of the illness saves lives.

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[7] Putri WCWS et al. *Economic burden of seasonal influenza in the United States*. Vaccine. June 22, 2018; 36(27): 3960-3966. https://www.ncbi.nlm.nih.gov/pubmed/29801998. (Accessed Nov. 2019)

[8] CDC. *1918 Pandemic (H1N1 virus)*. March 20, 2019. https://www.cdc.gov/flu/pandemic-resources/1918-pandemic-h1n1.html (Accessed Nov. 2019).

[9] CDC. *Key Facts About Seasonal Flu Vaccine*. October 21, 2019. https://www.cdc.gov/flu/prevent/keyfacts.htm (Accessed Nov. 2019).

[10] CDC. *Who Needs a Flu Vaccine and When*. October 11, 2019. https://www.cdc.gov/flu/prevent/vaccinations.htm. (Accessed Nov. 2019).

[11] CDC. *People at High Risk for Flu Complications*. August 27, 2018. https://www.cdc.gov/flu/highrisk/index.htm (Accessed Nov. 2019)

[12] CDC. *Flu Vaccination Coverage, United States, 2018–19 Influenza Season*. September 26, 2019. https://www.cdc.gov/flu/fluvaxview/coverage-1819estimates.htm (Accessed Nov. 2019)

[13] CDC. *What are the benefits of flu vaccination?*. Jan 24, 2019. https://www.cdc.gov/flu/prevent/vaccine-benefits.htm (Accessed Nov. 2019).

Flu Vaccine Development and Production

The design and production process for the annual influenza vaccine takes place year-round and begins in February or March. The virus strains are selected based on data on which viruses are circulating and predictions about which viruses are most likely to circulate in the upcoming season. The data is collected from more than 100 countries through the World Health Organization (WHO). The CDC houses one of the five WHO centers for collecting the data. While the WHO recommends which viruses to include in the annual vaccine, each country makes the final decision on which viruses are included in their own vaccines.[14] In the United States, the Food and Drug Administration (FDA) is responsible for the final decision on which influenza viruses will be included in the annual vaccine.[15]

The FDA has approved three production methods for the annual influenza vaccine: egg-based vaccines, cell-based vaccines and recombinant vaccines.[16] The most common production method for influenza vaccines in the United States remains the egg-based method, in which the selected virus strains are grown in chicken eggs. The entire process can take up to six months from the selection of the viruses and the initial laboratory work to the time needed to grow the viruses in eggs and produce the required number of doses each year in time for the start of the influenza season. The cell-based manufacturing process involves growing candidate vaccine viruses in cultured mammalian cells rather than eggs.[17] The recombinant vaccine production method involves isolating a certain protein from a naturally occurring influenza virus, combining these proteins with portions of another virus that is then mixed with insect cells and allowed to grow. An influenza surface protein is then extracted from the insect cells and purified.[18]

The long lead time for vaccine production can lead to a mismatch between the viruses included in the vaccine and the viruses found to be circulating at the start of the flu season, resulting in reduced vaccine effectiveness. The CDC estimates that the vaccine effectiveness for the 2017-2018 influenza season at 38 percent while preliminary estimates for the 2018-2019 influenza season estimate the vaccine effectiveness at 47 percent.[19] The time lag can be disastrous if there is a pandemic. Replacing the egg-based production method, which currently dominates the market, with a more effective and significantly shorter lead time method is a major challenge in current flu vaccine development. For a while, there was hype around the cell-based methods, and they are much faster than the egg-based. However, they have not been demonstrated to be more effective than the egg-based, and the initial capital costs to build new production plants is very high. Another scientific challenge is accurately diagnosing an illness as being caused by

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[14] CDC. *Selecting Viruses for the Seasonal Influenza Vaccine*. September 4, 2018. https://www.cdc.gov/flu/prevent/vaccine-selection.htm (Accessed Nov. 2019).

[15] FDA. *FDA's Critical Role in Ensuring Supply of Influenza Vaccine*. March 1, 2019. https://www.fda.gov/consumers/consumer-updates/fdas-critical-role-ensuring-supply-influenza-vaccine. (Accessed Nov. 2019).

[16] CDC. *How Influenza (Flu) Vaccines Are Made*. September 24, 2018. https://www.cdc.gov/flu/prevent/how-fluvaccine-made.htm. (Accessed Nov. 2019).

[17] NIAID. *Influenza Vaccine Production and Design*. June 5, 2019. https://www.niaid.nih.gov/diseases-conditions/influenza-vaccine-production-and-design. (Accessed Nov. 2019).

[18] *Id.*

[19] CDC. *Past Seasons Vaccine Effectiveness Estimates*. April 5, 2019. https://www.cdc.gov/flu/vaccines-work/past-seasons-estimates.html. (Accessed Nov. 2019).

influenza. Many winter illnesses with flu-like symptoms may not be caused by influenza. Accurately diagnosing which influenza virus is causing an illness will provide more data for scientists to use when deciding which influenza viruses to include in the annual vaccine.

Universal Influenza Vaccine

Work is underway in both federal agencies and the private sector to develop a universal influenza vaccine. The National Institute for Allergy and Infectious Disease (NIAID) states that a universal influenza vaccine should: be at least 75 percent effective, protect against group I and II Influenza A viruses, have protection that lasts at least one year, and be suitable for all age groups.[20] NIAID released its strategic plan for developing a universal influenza vaccine in February 2018. This plan identified three main research areas for NIAID: improve understanding of transmission, natural history, and pathogenesis of influenza virus infection; precisely characterize influenza immunity and correlates of immune protection, and; support rational design of universal influenza vaccines.[21]

Cross-Cutting Vaccine Science and Innovation Challenges

There are a number of challenges to developing and producing any new vaccine. Some of these challenges involve the financial and time costs of developing a new vaccine. The average new vaccine takes over ten years to develop and only has a six percent chance of making it to the market.[22] A potential new vaccine may have an uncertain return on investment, especially if the vaccine is not intended for a large percentage of the population or if there are alternatives to the vaccine. This uncertainty can disincentivize work to develop a new vaccine.

In addition to the financial challenges of developing new vaccines, there are a number of scientific challenges. Some of these scientific challenges are in fundamental human biology, specifically improving our understanding of the human immune system and human immune response, as well as the mechanisms by which vaccines act.[23] Some of the scientific challenges also stem from the nature of the infectious disease in question. The challenge of the influenza virus constantly changing has already been discussed. Malaria, a disease for which there is currently no licensed vaccine, is another infectious disease for which there are a number of scientific challenges to developing a vaccine. The parasite that causes malaria is complex and there is not good understanding of the human immune response to infection. This complexity also means there are a large number of potential antigens that might be used in a vaccine. Finally, infection with malaria parasites only results in partial future immunity, further increasing

[20] NIAID. *Universal Influenza Vaccine Research*. September 5, 2019. https://www.niaid.nih.gov/diseases-conditions/universal-influenza-vaccine-research. (Accessed Nov. 2019).

[21] Emily J Erbelding, Diane J Post, Erik J Stemmy, Paul C Roberts, Alison Deckhut Augustine, Stacy Ferguson, Catharine I Paules, Barney S Graham, Anthony S Fauci, A Universal Influenza Vaccine: The Strategic Plan for the National Institute of Allergy and Infectious Diseases, *The Journal of Infectious Diseases*, Volume 218, Issue 3, 1 August 2018, Pages 347–354, https://doi.org/10.1093/infdis/jiy103

[22] The Sabin-Aspen Vaccine Science and Policy Group. *Accelerating the development of a universal influenza vaccine*. 2019. https://www.influenzer.org/app/uploads/2019/07/sabin-aspen-report-digital.pdf. (Accessed Nov. 2019)

[23] *Encouraging Vaccine Innovation: Promoting the Development of Vaccines that Minimize the Burden of Infectious Disease in the 21st Century* December 2017. https://www.hhs.gov/sites/default/files/encouraging_vaccine_innovation_2018_final_report.pdf. (Accessed Nov. 2019).

the difficulty in producing a vaccine.[24] New biotechnologies such as CRISPR are helping to accelerate the basic microbiology research needed to inform new vaccine development for malaria and other infectious diseases.

Role of Data Science in Vaccine Development

Data science and data collection are integral to developing an effective vaccine and the annual influenza vaccine is an important example of this. As noted earlier, the WHO uses data collected from over 100 countries when making recommendations for which influenza viruses should be included in the annual vaccine. However, data standards and reporting formats may be different, and as noted previously, the data itself can contain incomplete information about which influenza viruses (if any) caused someone's illness. In addition, many of the data systems being used are outdated, including in the U.S.

There is a significant effort underway to fund the modernization of data systems at the CDC, as well as action at the state level to modernize state data systems, led in part by the Council of State and Territorial Epidemiologists. Increases in the effectiveness of data collection, sharing, interconnectivity, and analysis will give scientists better surveillance data to inform vaccine development, especially in the case of the flu since it requires an annual vaccine. Further, advanced data analytics and artificial intelligence systems could benefit data analysis relating to infectious disease due to the strengths of these systems in pattern recognition and classification.

Social Science Research and Applications

Communication with the public about vaccines is another factor in vaccine effectiveness. This includes making people aware of the benefits of vaccines as well as communicating the dangers posed by infectious diseases. Campaigns aimed at increasing the rate of influenza vaccination occur at national, state and local levels, including the CDC's National Influenza Prevention and Vaccination Campaign.[25] Social science research may offer more insight into why people make certain vaccination choices and into effective messages for increasing rates of vaccination, including how to most effectively communicate across different subsets of the population.

Role of Federal Agencies

There are a number of federal agencies that are involved in the development and production of vaccines in the United States. These agencies include the National Institutes of Health (NIH), which conducts basic, applied and translational research on vaccines. NIH also conducts clinical evaluation to identify vaccine targets and advance vaccine candidate. The FDA is responsible for vaccine review and licensing, regulatory science and innovation, international collaboration, and post-licensure manufacturing and safety monitoring. The work conducted by CDC during the process includes disease surveillance, setting immunization schedules, the national immunization

[24] CDC. *Vaccines*. January 25, 2019. https://www.cdc.gov/malaria/malaria_worldwide/reduction/vaccine.html. (Accessed Nov. 2019).

[25] CDC. *Join CDC's Seasonal Flu Prevention Efforts*. November 14, 2016. https://www.cdc.gov/flu/resource-center/partners/general.htm. (Accessed Nov. 2019)

program, and post-marketing vaccine safety and effectiveness evaluation in collaboration with FDA. The Biomedical Advanced Research and Development Authority (BARDA) is responsible for developing and obtaining needed medical countermeasures, including vaccines. BARDA helps support late-stage development of new products and supports advanced R&D alongside a number of other federal agencies. Much of BARDA's work is accomplished through public-private partnerships. The National Vaccine Program Office (NVPO) is responsible for strategic leadership and coordination and coordinating the National Vaccine Advisory Committee (NVAC).[26]

[26] *Encouraging Vaccine Innovation: Promoting the Development of Vaccines that Minimize the Burden of Infectious Disease in the 21st Century* December 2017. https://www.hhs.gov/sites/default/files/encouraging_vaccine_innovation_2018_final_report.pdf. (Accessed Nov. 2019).