FIGHTING FLU, SAVING LIVES: VACCINE INNOVATION AND SCIENCE

HEARING

BEFORE THE

COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY HOUSE OF REPRESENTATIVES

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Appendix II: Additional Material for the Record

FIGHTING FLU, SAVING LIVES: VACCINE INNOVATION AND SCIENCE

WEDNESDAY, NOVEMBER 20, 2019

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY,
Washington, D.C.

The Committee met, pursuant to notice, at 10 a.m., in room 2318 of the Rayburn House Office Building, Hon. Eddie Bernice Johnson [Chairwoman of the Committee] presiding.

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

[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).

Chairwoman JOHNSON. This hearing will come to order. And without objection, the Chair is authorized to declare a recess at any time.

Let me say good morning and welcome our witnesses to today's hearing on vaccine science and innovation. Smallpox once plagued the world's population, killing approximately 300 million people in the 20th century alone. Smallpox is the only human disease to be eradicated, thanks to the development of the vaccine. Another devastating disease, polio, had just 33 cases reported worldwide in 2018, compared to 350,000 cases in 1988. Every day, vaccines are saving lives, especially the lives of children and other vulnerable populations. There is no such thing as healthy skepticism when it comes to vaccines.

Unfortunately, there is a well-funded, disinformation campaign targeting the public and weakening public health laws. School vaccination requirements have been commonplace in the U.S. for generations, and exemptions were granted only for legitimate medical reasons. However, in my home State of Texas, the number of unvaccinated children has spiked since 2003 when the Texas legislature expanded the exemptions to include nonmedical reasons. The number of exemptions rose from 2,000 in the year 2003 to 57,000 last year. We are seeing this replayed across the country, and innocent children are falling ill. Health officials have confirmed 21 measles cases in Texas this year and 1,261 nationwide, 61 of which led to serious complications.

As the first nurse elected to Congress, I have been dedicated to the improvement of public health my entire career. The Science Committee may not have jurisdiction over the Health and Human Services agencies, but we have long had a role in supporting improved public health through good science.

This morning, we will explore the science and innovation challenges for vaccine development through the lens of influenza. For the healthiest among us, the flu just lays us out for several days, with no lasting side effects. However, for the very young, the elderly, pregnant women, and other vulnerable groups, the flu can be deadly. The Centers for Disease Control and Prevention (CDC) recorded an estimated 48.8 million illnesses and 79,000 deaths during the 2017–2018 flu season. Approximately 600 of those deaths were children.

Each year, influenza vaccine production begins with the collection and analysis of data many months before the beginning of the flu season. The challenge with influenza is that the viruses change constantly, and by the time flu season begins, the vaccine may not fully match the circulating viruses. Scientists are working to develop viable and more effective alternatives to the current egg-based vaccine, as well as a universal vaccine that will not require annual update.

Yet another scientific challenge for influenza and many other infectious diseases is incomplete data and antiquated data systems. Through modernization of data systems and data analytic tools across the Federal and State levels, we will be able to accelerate vaccine research and development for many diseases.

We have two expert panels that will help us understand the full cycle from basic research to vaccine development, production and

deployment and surveillance. The witnesses will also describe the role of Federal agencies, State agencies, and the private sector, including the partnerships among all of the stakeholders. I want to extend my warm welcome to all of you this morning. And I want to thank the Vice Chair, Dr. Bera, for his leadership on this issue. I look forward to today's discussion.

[The prepared statement of Chairwoman Johnson follows:]

Good morning and welcome to today's hearing on vaccine science and innovation.

Smallpox once plagued the world's population, killing approximately 300 million people in the 20th century alone. Smallpox is the only human disease to be eradicated, thanks to the development of the vaccine. Another devastating disease, polio, had just 33 cases reported worldwide in 2018, compared to 350,000 cases in 1988. Every day, vaccines are saving lives, especially the lives of children and other vulnerable populations. There is no such thing as healthy skepticism when it comes to vaccines.

Unfortunately, there is a well-funded disinformation campaign targeting the public and weakening public health laws. School vaccination requirements have been commonplace in the U.S. for generations, and exemptions were granted only for legitimate medical reasons. However, in my home state of Texas, the number of unvaccinated children has spiked since 2003, when the Texas Legislature expanded the exemptions to include non-medical reasons. The number of exemptions rose from 2,000 in the year 2003 to 57,000 last year. We are seeing this replayed across the country, and innocent children are falling ill. Health officials have confirmed 21 measles cases in Texas this year, and 1,261 nationwide, 61 of which led to serious complications.

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We have two expert panels that will help us understand the full cycle from basic research to vaccine development, production, deployment, and surveillance. The witnesses will also describe the role of federal agencies, state agencies, and the private sector, including the partnerships among all of the stakeholders.

I want to extend a warm welcome to all of you this morning. And I want to thank the Vice-Chair Dr. Bera for his leadership on this issue. I look forward to today's important discussion.

Chairwoman JOHNSON. I might say that I have a markup in another Committee, so I will have to leave before we get through all of the deliberations.

The Chair now will recognize Mr. Lucas for an opening statement.

Mr. LUCAS. Good morning, Chairwoman Johnson. I would like to thank you and Vice Chairman Bera for holding this hearing, especially given that we are in the middle of flu season.

In the United States, nearly a million individuals are hospitalized for the flu every year, including more than 48,000 children. In

Oklahoma, since the 2019 flu season began on September 1, there has been one death and 73 hospitalizations from the flu. However, these numbers would be far worse if we did not have vaccines. Vaccination is, by far, the best flu prevention measure we can have today.

It's easy to forget that a little over 100 years ago the world faced one of the deadliest pandemics in history: The 1918 H1N1 pandemic, also known as Spanish flu. It killed an estimated 50 million people worldwide, including roughly 675,000 people in the United States. Medical technology and countermeasures at the time were limited to isolation and quarantine. Influenza vaccines did not exist, and antibiotics had not been fully developed yet.

Thankfully, due to basic research, advancements were made both in treatment and prevention of the flu. The development of vaccines has played an important role in reducing and eliminating deadly disease. I can still recall my father's stories about how late summer and fall were a terrifying time as a child because of the threat of polio during those seasons. Lucky for me, I did not have to experience this fear because of the first polio vaccine being available in the United States in 1955.

And thanks to widespread vaccination, polio has been nearly eradicated in the United States with just 33 cases reported in 2018. However, polio remains a threat in some countries. With the world becoming more connected through modern transportation, it only takes one traveler with polio to bring the disease into the United States. And as I'm sure we'll hear this morning from our witnesses, the best way to keep the United States polio-free is to maintain high immunity through vaccination.

Considerable advancements have been made in health technology, disease surveillance, medical care, medicines, drugs, vaccines, and pandemic planning. While significant progress has been made, gaps remain, and a severe pandemic could still be devastating to the global population.

As the human population has grown, so has the livestock, swine, and poultry populations to feed them. This expanded number of hosts provides increased opportunities for unique viruses from birds, cattle, and pigs to spread, evolve, and infect people.

As a Member of the House Agriculture Committee, I supported the creation of the National Animal Vaccine and Veterinary Countermeasures Bank, which was included in the last farm bill. This vaccine bank will maintain a sufficient quantity of animal vaccines and other countermeasures to provide a rapid response to an animal disease outbreak. If an outbreak were to occur and we were not prepared, our entire agricultural sector would suffer immense losses, causing long-term harm to the economic viability of the United States livestock, poultry, and swine production, not to mention the damaging to human health.

I look forward to hearing from our witnesses today about the current state of our stockpiles of human health vaccines to provide the capacity for rapid responses to emergency situations. I particularly look forward to hearing how BARDA (Biomedical Advanced Research and Development Authority) Influenza Vaccine Manufacturing Infrastructure is supporting the public-private partnerships with domestic vaccine manufacturers to increase preparedness lev-

els and response capacities for potential pandemic flu events in the United States.

Last, I would just like to say how pleased I was to see the President's recent executive order to address modernizing flu vaccines. The executive order recognizes influenza as a public health and national security priority with the potential to inflict harm on the United States through large-scale illness and death. Most importantly, it establishes a national task force to explore alternative vaccine production methods and new technologies, including a plan to accelerate the development of a universal flu vaccine. I look forward to seeing what recommendations come from the task force.

I would again like to thank Chairwoman Johnson and Vice Chair Bera for holding this hearing. I would also like to thank both witness panels for taking the time to share your expertise, your insights with us this morning.

And I yield back the balance of my time, Madam Chair.

[The prepared statement of Mr. Lucas follows:]

Good morning Chairwoman Johnson. I would like to thank you and Vice Chairman Bera for holding this hearing, especially given we are in the middle of flu season.

In the United States, nearly a million individuals are hospitalized for the flu every year, including more than 48,000 children. In Oklahoma, since the 2019 flu season began on September 1st, there has been one death and 73 hospitalizations from the flu. However, these numbers would be far worse if we did not have vaccines. Vaccination is, by far, the best flu prevention measure we have today.

It is easy to forget that a little over a hundred years ago the world faced one of the deadliest pandemics in history - the 1918 H1N1 pandemic, also known as the "Spanish flu." It killed an estimated 50 million people worldwide, including roughly 675,000 people in the United States. Medical technology and countermeasures at the time were limited to isolation and quarantine. Influenza vaccines did not exist, and antibiotics had not been fully developed yet.

Thankfully, due to basic research, advancements were made both in treatment and prevention of the flu. The development of vaccines has played an important role in reducing or eliminating deadly disease. I can still recall my father's old stories about how late summer and fall was a terrifying time as a child because of the threat of polio during those seasons. Lucky for me, I did not have to experience living with this fear because the first polio vaccine became available in the United States in 1955.

And thanks to widespread vaccination, polio has been nearly eradicated in the United States, with just 33 cases reported in 2018. However, polio remains a threat in some countries. With the world becoming more connected through modern transportation, it only takes one traveler with polio to bring the disease into the United States. As I'm sure we will hear this morning from our witnesses, the best way to keep the United States polio-free is to maintain high immunity through vaccination.

Considerable advancements have been made in health technology, disease surveillance, medical care, medicines and drugs, vaccines and pandemic planning. While significant progress has been made, gaps remain, and a severe pandemic could still be devastating to the global population.

As the human population has grown, so has the livestock, swine and poultry populations to feed them. This expanded number of hosts provides increased opportunities for unique viruses from birds, cattle, and pigs to spread, evolve and infect people.

As a Member of the House Agriculture Committee, I supported the creation of the National Animal Vaccine and Veterinary Countermeasures Bank, which was included in the last Farm Bill. This vaccine bank will maintain sufficient quantities of animal vaccines and other countermeasures to provide a rapid response to an animal disease outbreak. If an outbreak were to occur and we were not prepared, our entire agricultural sector would suffer immense losses, causing long-term harm to the economic viability of U.S. livestock, poultry and swine production - not to mention the damaging effect on human health.

I look forward to hearing from our witnesses today about the current state of our stockpiles of human health vaccines to provide the capacity for rapid response in emergency situations. I particularly look forward to hearing how BARDA's Influenza

Vaccine Manufacturing Infrastructure is supporting public-private partnerships with domestic vaccine manufacturers to increase preparedness levels and response capabilities for potential pandemic flu events in the United States.

Lastly, I would just like to say how pleased I was to see the President's recent Executive Order to address modernizing flu vaccines. The Executive Order recognizes influenza as a public health and national security priority with the potential to inflict harm on the United States through large-scale illness and death.

Most importantly, it establishes a national task force to explore alternative vaccine production methods and new technologies - including a plan for accelerating the development of a universal flu vaccine. I look forward to seeing what recommendations come from the task force.

I would again like to thank Chairwoman Johnson and Vice-Chairman Bera for holding this hearing. I would also like to thank both witness panels for taking the time to be here to share your expertise and insights with us this morning.

I yield back the balance of my time.

Chairwoman JOHNSON. Thank you very much.

If there are Members who wish to submit additional opening statements, your statements will be added to the record at this point.

At this time I will introduce our witnesses. Our first witness on the panel is Dr. Daniel Jernigan. Dr. Jernigan is the Director of Influenza Division for the National Center for Immunization and Respiratory Diseases at CDC. Dr. Jernigan is responsible for oversight and direction of a broad scientific program to improve detection, prevention, treatment, and response to seasonal, novel, and pandemic influenza. The Influenza Division is responsible for national and global surveillance of influenza and serves as a World Health Organization collaborating center for the surveillance, epidemiology, and control of influenza. Dr. Jernigan entered the CDC in 1994 and is a retired Captain of the U.S. Public Health Service and was the recipient of the 2019 Service to America Medal.

The next witness on this panel is Dr. Anthony Fauci. Dr. Fauci is the Director of the National Institute of Allergy and Infectious Diseases (NIAID), a position he's held since 1984. He oversees an extensive research portfolio of basic and applied research to prevent, diagnose, and treat established infectious diseases such as HIV/AIDS, respiratory infections, diarrhea diseases, tuberculosis, and malaria, as well as emerging diseases such as Ebola and Zika. He also supports research on the transplantation and immune-related illnesses, including the anti-immune disorders, asthma, and allergies. He has advised six Presidents on HIV/AIDS and many other domestic and global health issues. He was one of the principal architects of the President's Emergency Plan for AIDS Relief, a program that has saved millions of lives throughout the developing world.

As our witnesses should know, you will each have 5 minutes for your spoken testimony. Your written testimony will be included in the record for the hearing. When you've completed your spoken testimony, we will begin with questions. Each Member will have 5 minutes to question the panel. We will start with Dr. Jernigan.

TESTIMONY OF DR. DANIEL B. JERNIGAN, M.D., MPH, DIRECTOR, INFLUENZA DIVISION, NATIONAL CENTER FOR IMMUNIZATION AND RESPIRATORY DISEASES, CENTERS FOR DISEASE CONTROL AND PREVENTION

Dr. JERNIGAN. Well, thank you very much. Good morning, Chairwoman Johnson, Ranking Member Lucas, and distinguished Mem-

bers of the Committee. I am Dr. Dan Jernigan, Director of the Influenza Division of the Centers for Disease Control and Prevention. I want to thank the Committee for the opportunity to discuss CDC's work supporting vaccine innovations to improve prevention of influenza.

Each year, influenza causes a significant health burden in the United States with many millions of Americans becoming ill, hundreds of thousands requiring hospitalization, and tens of thousands dying. Influenza viruses are constantly changing, requiring us to update the vaccine components every year. Sometimes, these changes can be sudden and significant, resulting in flu strains that can lead to devastating pandemics. Hospitalization and death can happen in any flu season, and each year, flu vaccination prevents millions of illnesses and thousands of severe and sometimes tragic outcomes.

Influenza vaccines are very safe, and they remain the single best way for people to fight the flu. Despite the significant benefits, the effectiveness of the flu vaccine, and the numbers of Americans being vaccinated are not optimal. We at CDC are working with NIH (National Institutes of Health) and other Federal and State government partners and with the private sector to use cutting-edge science to make influenza vaccines better.

The long-lasting broadly protective universal vaccines that Dr. Fauci will talk about are the ultimate goal for flu prevention. However, these vaccines are still years away. In the near term, we can save millions of Americans from the flu by making incremental improvements to vaccines that can be produced using already available production platforms and by getting more Americans vaccinated each flu season.

CDC has a central role in every part of the seasonal influenza vaccine development and administration cycle, including continuous virus tracking around the globe, preparation of vaccine viruses, purchasing 10 percent of flu vaccines used in the United States, and monitoring vaccine coverage, safety, and effectiveness.

To improve flu vaccines, CDC has implemented innovations throughout the vaccine lifecycle. CDC has invested in and collaborated with every State public health department on flu surveillance. This investment has resulted in automated real-time electronic laboratory reporting of influenza test results to CDC using cloud-based messaging.

CDC has transformed flu virus surveillance by using next-generation genomic sequencing to characterize all influenza specimens received at CDC. This means we can identify and track viruses much more quickly and accurately, leading to more timely selection of candidate vaccine viruses and earlier detection of viruses with pandemic potential.

Genomic sequencing equipment, which once filled a room, now fits in the palm of your hand. We now have a mobile mini lab that can be taken on the plane as a carry-on and set up almost anywhere in the world, including rural resource-constrained settings.

CDC has implemented innovations for supporting newer vaccines by developing candidate vaccine viruses for the cell-based vaccine and by providing genomic sequences used to make the recombinant protein vaccine. Both of these newer vaccines have the potential to

be manufactured more quickly and may be more effective than traditional vaccines that are grown in eggs.

CDC now also routinely generates vaccine viruses using a technique called reverse genetics. This allows us to build a vaccine in a matter of days or weeks, much faster than traditional methods, making the U.S. more prepared to respond quickly to a pandemic.

CDC was the first to establish a national system for the routine monitoring of influenza vaccine effectiveness, and that vaccine effectiveness network provides critical information for manufacturers and researchers in developing enhanced vaccines by collecting more specific data about how well the vaccine works each season. Recently, we have expanded the network and are planning to add new immunity testing and conduct more studies to better evaluate vaccine effectiveness.

Finally, a major component of improving influenza vaccine impact is getting more people vaccinated. Fewer than half of adults in the U.S. receive their influenza vaccines. And despite all of our successes and our global leadership in influenza detection and prevention, there is still more we need to be able to do. Each of the topics I mentioned today from working with domestic public health partners to track and characterize viruses to developing vaccine candidates and studying vaccine effectiveness will benefit from investments in generating more precise and timely data. I believe we can harness this data to make vaccines work better.

I want to close today by reminding you all to make sure that you and your families are vaccinated before the holiday travel begins. And thank you for the opportunity to talk about CDC's influenza work, and I look forward to your questions. Thanks.

[The prepared statement of Dr. Jernigan follows:]

Statement of Daniel B. Jernigan, M.D., M.P.H.
Director, Influenza Division,
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services

House Committee on Science, Space, and Technology
U.S. House of Representatives

Good morning Chairwoman Johnson, Ranking Member Lucas, and distinguished members of the committee. I am Dr. Dan Jernigan, the director of the Influenza Division at the Centers for Disease Control and Prevention. I want to thank the committee for the opportunity to discuss innovations in influenza vaccine technology and for bringing attention to influenza as an ongoing and very serious public health threat.

Each year, influenza (also commonly known as "flu") causes a significant health burden in this country with many millions of Americans becoming ill, hundreds of thousands requiring hospitalization, and tens of thousands dying. The recent 2017-2018 influenza season was particularly severe, causing thousands of flu-related deaths, including 186 children. The 2018-2019 season, while less severe, was record breaking in length at 21 weeks of elevated influenza activity. Influenza pandemics occur less frequently than seasonal epidemics, but their impacts can be even more devastating and result in millions of deaths around the globe.

Influenza vaccination remains the single best way for Americans to protect themselves. Current influenza vaccines are the best protection available, however, there is more work to be done to increase the effectiveness at preventing influenza-related illness, healthcare visits, and death. CDC, and other components of the Department of Health and Humans Services (HHS), including the National Institutes of Health (NIH), Food and Drug Administration (FDA), and Biomedical Advanced Research and Development Authority (BARDA), are working together other Federal partners to use cutting edge science to make influenza vaccines better. But this is a complicated, multi-year process that must be

both stepwise and iterative. In order to improve the prevention and control of influenza, we need to increase both vaccine effectiveness and the number of Americans receiving their influenza vaccinations.

CDC has a central role in every part of the seasonal influenza vaccine development and administration cycle including: virologic surveillance and tracking, strain selection, production of candidate vaccine viruses (which are influenza viruses that are prepared by CDC or another public health partner to be used by vaccine manufacturers to produce a flu vaccine) vaccine distribution, public education, determining vaccine effectiveness and monitoring safety. The resulting data are used to provide feedback and inform policy and recommendations for new and better vaccines. CDC is the global leader in tracking and studying influenza disease and flu viruses. We have some of the world's very best scientists working on flu 24/7, and have used innovative surveillance, diagnostic, and sequencing approaches to dramatically advance what we know. However, influenza viruses are incredibly difficult to track because they constantly change. These changes are why we select new vaccine components every year and they are also why new flu strains can emerge and lead to devastating pandemics.

CDC believes that long-lasting, broadly protective "universal" vaccines are the ultimate goal for flu prevention. We are still years away from having a universal vaccine. The good news is that we think in the much-nearer future, we can save millions of Americans from the flu by making incremental improvements to vaccines that can be produced using already available production platforms and by improving the immunization infrastructure necessary to get more Americans vaccinated each flu season. In the Executive Order on Modernizing flu vaccines recently signed by the president, CDC is called upon to focus on these nearer-term gains. Today I will talk about some innovative things we have already implemented in influenza prevention, as well as areas where we would like to implement further improvements.

Influenza viruses travel around the world with great speed and require innovative approaches to detection and tracking. Our surveillance systems provide the scientific basis for vaccine virus selection – for each year's seasonal flu vaccine, as well as for pandemic vaccine stockpiling. We diligently monitor for genetic changes in the flu virus around the world and identify how those genetic changes affect disease transmission and severity. CDC continues to work to enhance and expand its data systems to provide vital information for public and private sector decisions about new vaccine innovation and immunization recommendations. We are working to modernize our data systems to not only track disease and viruses in near-real time, but also to obtain greater depth and precision of data.

Over the last decade, CDC has significantly improved worldwide surveillance and characterization of influenza viruses in support of more effective vaccines. Globally coordinated epidemiologic and virologic surveillance is the foundation of the influenza vaccine virus selection and development process. CDC serves as one of six World Health Organization (WHO) Collaborating Centers that receive and characterize thousands of influenza viruses each year and support core influenza staff at the WHO. CDC contributes a large amount of virus characterization and genomic sequencing data for both the U.S. and global viruses and is an innovator in new methods for the strain selection process. This process involves working across the United States and with countries all around the world to characterize many thousands of influenza viruses, which are used to inform vaccine strain selection and to develop the vaccines. CDC partnerships with more than 50 Ministries of Health and other health agencies have strengthened global influenza surveillance and created the capacities to analyze and characterize flu viruses more quickly and to increase the number of candidate vaccine viruses CDC produces to expand options for suitable vaccine development.

We develop diagnostic assays for public health laboratories in the United States and globally, and through our International Reagent Resource, we ship them around the world to help stop the spread of flu at its source. CDC continues to increase our ability to sequence viruses around the world –

we use next generation sequencing to gather and analyze genomic data and share those data with other stakeholders. Genomic data help us make better decisions about what goes in each year's flu vaccine, and also help us evaluate viruses for their pandemic potential. We would like to be able to move completely to a domestic and global flu surveillance model that is "sequence-first," a method that uses Next Generation Sequencing (NGS) for all specimens sent to CDC for virologic surveillance. Next Generation Sequencing reveals the genetic variation among different virus particles in a single specimen and allows public health laboratorians to confirm the genetic identity of circulating viruses. These sequence data are also now a vital component of the twice-yearly WHO influenza vaccine virus selection process and are used in molecular modeling and forecasting. As the cost of Next Generation Sequencing drops and the availability of more rapid sequencing platforms increases, this technique may begin to serve as a routine approach for influenza virologic surveillance.

Additionally, CDC has developed and deployed a mobile mini-lab that can be carried on a plane, set up in remote, resource-limited settings to process and test specimens, and send the genomic data up to a cloud platform for further analysis and action. What was once a room full of equipment is now a device that can fit in the palm of your hand. Particularly in an outbreak setting, we can even more rapidly characterize viruses and improve detection of influenza viruses with pandemic potential. CDC can use this technology to detect other pathogens beyond flu, making it a valuable tool in resource challenged outbreak settings.

Over the last few years, CDC has transformed its ability to make influenza vaccine viruses for use in vaccine manufacturing. We have established high-containment laboratories that are dedicated to generating vaccine viruses that adhere to FDA standards of quality. We also now routinely use reverse genetics to very rapidly design and build vaccine viruses. By combining the data from our expansive global flu surveillance, we can quickly detect an emerging influenza virus with pandemic potential, and within hours start the process of synthesizing the vaccine. Most recently, we demonstrated this

approach using the mobile mini-labs to rapidly detect and characterize swine influenza viruses. Within hours, CDC staff pulled the genomic sequence of the swine influenza virus from the cloud platform and using the sequence synthesized a vaccine virus that met all GLP quality standards for use in manufacturing if the emerging swine influenza virus were to pose a higher pandemic threat. Having this capability to rapidly make influenza vaccine viruses could allow the U.S. to respond more quickly in the case of a pandemic. Using these methods, CDC will continue to work to expand the production capability of non-egg-based vaccine candidates by using cell-based and recombinant platforms.

CDC has developed and maintains one of the nation's system for monitoring the effectiveness of influenza vaccines, the U.S. Vaccine Effectiveness Network (U.S. VE Network). The U.S. VE Network currently consists of five study sites across the United States that measure the flu vaccine's effectiveness in reducing outpatient medical visits due to laboratory-confirmed influenza. This system provides critical information for manufacturers and researchers in developing enhanced vaccines by collecting more specific data about how well the vaccine works each season. Data collected through the network are instrumental in making recommendations for vaccine use, selection of new viruses for updating vaccines, and communication to the public on the performance of the vaccines. These data are more specific and are not available through other surveillance systems. Examples include: the type of vaccine received by the patient, the influenza virus subtype, and age group. Sustained increases in our vaccine effectiveness studies are needed to improve our understanding of how well different vaccine products work, and factors that influence how individuals respond to influenza vaccination and infection. Last year, CDC funded a randomized control trial to look at comparative effectiveness of cell-based vaccines. In future years, CDC would like to continue to expand the U.S. VE Network to allow for more enrollees and greater granularity of studies regarding specific vaccine products, and clinical outcomes for subpopulations and age cohorts.

CDC recommends an annual flu vaccine for everyone six months of age and older. However, even with this recommendation, fewer than half of adults in the United States receive their influenza vaccinations. Research indicates that part of the reason people choose not to get the flu vaccine is their perception that flu vaccine isn't effective. While CDC is working to improve vaccine effectiveness of flu vaccines, Americans also need to understand that the current vaccines still avert millions of cases of flu, and thousands of hospitalizations and deaths. We also want to assure Americans that the vaccine is safe. Hundreds of millions of Americans have safely received seasonal flu vaccines over the 50-year history of U.S. flu vaccination. We have been working with our partners, such as pharmacies, to make sure that vaccines are readily available in a variety of healthcare settings. The healthy choice to get vaccinated should also be an easy choice. Also, through health communication campaigns and working with our partners, CDC helps to inform healthcare providers and the general public on the benefits and safety of flu vaccine.

CDC supports the Federal, state and local public health workforce comprising the nation's immunization infrastructure. Through its vaccine contracts and distribution systems, CDC is the largest public purchaser of routinely recommended vaccines, including approximately 10 percent of the seasonal influenza vaccines distributed in the United States each year. In addition, ensuring access to vaccination is a key strategy in improving influenza vaccination coverage rates. Purchase and delivery of vaccines for vulnerable populations, including uninsured adults and pregnant women, will strengthen the safety net for those otherwise unable to access vaccine. In order to improve the prevention and control of influenza through vaccination, CDC will expand its data systems to provide essential information for public and private sector decisions about new vaccine innovation and immunization recommendations. CDC supports states in the development and maintenance of immunization information systems for tracking vaccinations in the United States; however, significant improvements in

interoperability of these systems are needed. CDC will continue to modernize these information systems to achieve greater capabilities for monitoring child and adult vaccination.

In the coming years, CDC will continue its collaboration with FDA, NIH, and BARDA, and other Federal partners to fight influenza through improvements in the vaccine production process, better detection and tracking of influenza illness and viruses, the development of new influenza vaccines and monitoring of vaccine effectiveness, and improvements in influenza treatment and control.

I want to take this opportunity to urge everybody to make sure you and your families are vaccinated and protected from the flu before the holiday season begins. Thank you for the opportunity to talk about CDC's important role of using science and innovation to fight influenza. I am happy to answer any questions you may have.

Daniel B. Jernigan, MD MPH

Daniel B. Jernigan, MD MPH is the Director of the Influenza Division in the National Center for Immunization and Respiratory Diseases at CDC where he is responsible for oversight and direction of over 300 people executing a broad scientific program to improve the detection, prevention, treatment, and response to seasonal, novel, and pandemic influenza. The Influenza Division is responsible for national and global surveillance of influenza and serves as a World Health Organization Collaborating Center for the Surveillance, Epidemiology and Control of Influenza. Dr. Jernigan completed training at Duke University and Baylor College of Medicine and has completed residencies in Internal Medicine and Preventive Medicine. He entered the CDC in 1994 as an Epidemic Intelligence Officer, and has been studying respiratory and emerging diseases since that time. He is a retired Captain in the U.S. Public Health Service and was the recipient of the 2019 Service to America Medal.

Updated September 1, 2019

Chairwoman JOHNSON. Thank you, Dr. Jernigan. Dr. Fauci.

TESTIMONY OF DR. ANTHONY S. FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTION DISEASE, NATIONAL INSTITUTES OF HEALTH

Dr. FAUCI. Thank you very much, Madam Chairwoman, Members of the Committee. Thank you for giving me the opportunity to testify before you today. I am Dr. Anthony Fauci, the Director of the National Institute of Allergy and Infectious Diseases at the NIH, and I'm going to talk to you over the next couple of minutes about the NIH's efforts to improve the influenza vaccines and to ultimately develop a universal flu vaccine.

As shown on this slide, although, as Dr. Jernigan had mentioned, it's very important to get vaccinated because even if a vaccine is not 100 percent effective or even 50 percent effective, the benefit to the individual to get vaccinated and to the community is profound. However, we can do better because seasonal influenza vaccines are not consistently optimally effective. In addition, we know through history that pandemics occur, but we usually are too late in our response, as we were in the 2009 H1N1.

And finally, we spend considerable time what I call chasing after pandemics, as we had with the H5N1 and H7N1, in which we made significant investments. We needed to do that, but those pandemics never occurred.

This slide shows a journal, the *Journal of Infectious Diseases*, containing a number of papers in which my colleague and I gave the introduction emphasizing the point that I just made that although influenza vaccines are good and important and should be utilized, we can do better. By doing better, we need to improve the seasonal influenza vaccines, which would lead to a better capability to respond to pandemic influenza, which ultimately will get us to the goal that we'll speak about over the next minute or 2, and that is the development of a universal influenza vaccine.

In the summer of 2017, we brought a group together to develop a plan, which we published in 2018, for the strategic plan and the research agenda to mobilize scientists throughout the country and the world to develop a universal flu vaccine.

So let me explain what we mean by a universal flu vaccine. This is somewhat of a complicated slide, but it really does make the point. We will not get a universal flu vaccine overnight. I use the word iterative, which means it will be a step-wise process in which we go from improvement, the broad capability of responding to a particular type of a strain, versus the ability to respond to all strains. Note on the lower left-hand part of the slide it is divided into two major groups of influenza: Group 1 and group 2.

On the right-hand part of the slide, the tip of that triangle is what we do today. We make a vaccine for this season that's highly specific to the strains that are circulating this season. However, those strains change. They mutate. They drift. What we want to do is go to the next step, is to make a vaccine that would cover all the H3N2's or all the H1N1's, and then next step would be to get one that would do all the group 1's and all the groups 2's until ultimately we have a universal vaccine that essentially covers all of these.

We're going to do that with new technologies, as you are well aware. We currently have a technique of growing the virus in eggs to develop a vaccine. Although that's tried and true and time-honored, it's inefficient and has many areas of going wrong. So we're using new platforms, as shown here on the slide, such as recombinant proteins, viral vectors, nanoparticles, and others.

This is a blowup of the influenza virus. And to the right is an important protein called the hemagglutinin. It is important to note that the hemagglutinin has two components, what we call a head and the stem. The head is the part that the body makes an immune response against. However, it mutates often, changes leading to the ineffectiveness. However, the dark blue is the stem, which doesn't change much at all.

So the strategy now, one of several strategies is to develop a vaccine in which you cut off that head, as shown there, take the stem, and put it on a nanoparticle, which is highly immunogenic, which will ultimately serve as the vaccine.

So if I could show you this, this is a 4-million-times blowup of what the first universal flu vaccine would look like, and these dark blue areas are the stems.

We have started a phase 1 trial, as shown here, in the spring of this year. It will end at the end of this year, and then next year, we will do a group 2 universal flu vaccine.

So as the President said in the executive order, the purpose of what we're doing is to go ahead and improve little by little until we get vaccines to protect us in the most efficient way possible. Thank you.

[The prepared statement of Dr. Fauci follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

The Role of the National Institute of Allergy and Infectious Diseases in Research on Influenza Vaccine Innovation

Testimony before the

House Committee on Science, Space, and Technology

Anthony S. Fauci, M.D.

Director

National Institute of Allergy and Infectious Diseases

National Institutes of Health

November 20, 2019

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 broadly reactive or "universal" influenza vaccines that could protect individuals over many years against multiple types of influenza viruses, both seasonal and pandemic. NIAID efforts in this regard are bolstered by ongoing collaborations with academia, philanthropic organizations, and biotechnology and pharmaceutical companies. NIAID conducts this work alongside key U.S. government partners, particularly the Department of Defense, the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), and the Department of Health and Human Services Office of the Assistant Secretary for Preparedness and Response (ASPR), including the Biomedical Advanced Research and Development Authority (BARDA).

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" of an influenza virus from an animal population to humans, who lack existing immunity to that virus. If these novel viruses can efficiently transmit from person to person, the risk of a potential influenza pandemic is high.

The mainstay of influenza prevention is vaccination. Seasonal influenza vaccination can protect an individual from illness, hospitalization, and death due to influenza. Current influenza vaccines are designed to protect against a few influenza strains. These vaccines result in highly "strain-specific" immunity. This means that updated influenza vaccines must be developed each year against the specific viruses that are predicted to circulate in the upcoming season. The effectiveness of seasonal influenza vaccines – a measure of how well the vaccines work to prevent influenza illness – has ranged from 10 to 60 percent in the last 15 years. This rate is

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.

In addition, due to the long time-frame for egg-based influenza vaccine production, vaccines likely would not be readily available if an antigenic shift occurs and a previously unidentified strain of pandemic influenza suddenly emerges. Currently, an updated – and sometimes a novel – influenza vaccine is needed for each new strain of influenza with pandemic potential. During the H1N1 influenza pandemic in 2009, a vaccine against the emergent virus strain was not available to the public until well after the peak of the pandemic had occurred. Continually "chasing" influenza viruses that jump from animals to humans comes at a substantial economic cost and can leave public health at risk. It is essential that we move beyond the current strain-specific influenza vaccine development strategy to address both seasonal and pandemic influenza.

THE NEED FOR INNOVATIONS IN INFLUENZA VACCINOLOGY

The optimal influenza vaccination strategy would deploy universal influenza vaccines that protect broadly and durably against seasonal influenza strains and those with pandemic

potential. NIAID has prioritized the development of universal influenza vaccines and has outlined its research strategy toward this goal in our *Strategic Plan for a Universal Influenza Vaccine. The Strategic Plan* focuses on three research areas: improving knowledge of the transmission, natural history, and pathogenesis of influenza infection; characterizing influenza immunity and immune factors that correlate with protection against influenza; and supporting the rational design of universal influenza vaccines. NIH will continue targeted investments in each of these research areas to generate critical information for the development of universal vaccines effective against both seasonal and pandemic influenza. Currently, we face two main challenges when designing such innovative influenza vaccines: improving vaccine production strategies and moving beyond strain-specific vaccines to vaccines with universal influenza strain coverage.

Improving Vaccine Production Strategies

Most existing influenza vaccines are produced by growing the virus in eggs. This is a time-honored, but time-consuming process. Furthermore, the vaccine undergoes a process of adaptation to grow in eggs that may in itself lead to mutations that make the resulting vaccine less effective. In recognition of these limitations, the President signed the *Executive Order on Modernizing Influenza Vaccines in the United States to Promote National Security and Public Health* on September 19, 2019. Broadly, the Executive Order directs BARDA, CDC, NIH, and FDA to accelerate the adoption of improved influenza vaccine technologies. In alignment with the goals of the Executive Order, NIAID is conducting and supporting research to develop state-of-the-art vaccine platform technologies that could be used to develop universal influenza vaccines as well as to improve the speed and agility of the influenza vaccine manufacturing process. These platform technologies include DNA, messenger RNA (mRNA), virus-like

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 stage of development will focus on vaccines against all versions of a single subtype. For example, one vaccine may target all strains of subtype H3N2, whereas another vaccine may target all strains of subtype H1N1. All influenza A viruses fall within two broad groups. Following the initial stage, efforts would progress toward development of vaccines against all subtypes within a specific group. These vaccines would target influenza A viruses throughout either "group 1" (which includes subtypes H1N1 and H5N1, among others) or "group 2" (which includes subtypes H3N2 and H7N9, among others). The final iteration of development would provide a truly universal vaccine that would protect against all influenza A viruses.

STRATEGIES FOR DEVELOPING UNIVERSAL INFLUENZA VACCINES

NIAID is pursuing multiple strategies for the development of universal influenza vaccines that target common parts of the influenza virus in order to elicit a protective immune response against diverse influenza viruses. The NIAID Vaccine Research Center (VRC) is conducting a Phase 1 clinical trial of a universal influenza vaccine that uses a nanoparticle-based platform technology to display the stem region of the HA protein. Proteins displayed on nanoparticles are highly immunogenic. The vaccine candidate incorporates the stem region of an H1 influenza virus subtype that in animal models provided protection against influenza viruses from other subtypes within "group 1." These results suggest that vaccines targeting the stem of the HA protein could offer broader protection than existing strain-specific influenza vaccines. In 2020, VRC scientists plan to evaluate a similar nanoparticle-based vaccine candidate designed to protect against "group 2" influenza viruses. Additionally, the NIAID Division of Intramural

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 studies, clinical trials, and human challenge studies to explore approaches to improve seasonal and universal influenza vaccines, such as alternative vaccine platforms or new adjuvants (substances added to vaccines to boost immunity). In addition, NIAID is supporting research to examine how the immune systems of young children respond over time to their initial influenza infection and their first vaccination. These long-term cohort studies will help us understand how repeat vaccinations and immune memory affect the ability to mount an immune response to different influenza subtypes. Insights from this research will inform the design of more effective influenza vaccines and vaccination strategies.

CONCLUSION

Recent NIAID-supported advances in the areas of influenza virology, structural biology, protein engineering, immunology, and vaccinology have made possible the goal of advancing beyond strain-specific vaccines toward a universal influenza vaccine. The recent Executive Order has helped to focus and reinvigorate NIAID's longstanding partnerships with government, academic, and industry partners dedicated to the improvement of vaccines that protect against influenza. In support of the objectives of the Executive Order and guided by *the Strategic Plan for a Universal Influenza Vaccine*, NIAID will continue to accelerate research toward the development of modern vaccines that can protect against both seasonal and pandemic influenza.

Anthony S. Fauci, M.D.
Director, National Institute of Allergy and Infectious Diseases (NIAID)

Dr. Fauci was appointed Director of NIAID in 1984. He oversees an extensive research portfolio of basic and applied research to prevent, diagnose, and treat established infectious diseases such as HIV/AIDS, respiratory infections, diarrheal diseases, tuberculosis and malaria as well as emerging diseases such as Ebola and Zika. NIAID also supports research on transplantation and immune-related illnesses, including autoimmune disorders, asthma and allergies. The NIAID budget for fiscal year 2019 was approximately $5.5 billion.

Dr. Fauci has advised six Presidents on HIV/AIDS and many other domestic and global health issues. He was one of the principal architects of the President's Emergency Plan for AIDS Relief (PEPFAR), a program that has saved millions of lives throughout the developing world.

Chairwoman JOHNSON. Thank you, Dr. Fauci.

At this point we will begin our first round of questions, and the Chair will recognize herself for 5 minutes.

Dr. Jernigan, as you well know, there is a well-funded disinformation campaign sowing confusion and fear in the public. This campaign carefully targets and preys on different populations with different belief systems. Innocent children are falling ill today with diseases we once thought were eradicated in the U.S. Young women are unnecessarily being put at increased risk for cancer. And these anti-science forces are creating a major challenge in future vaccination efforts.

How big of a role does social media play in this resurgence, and how can we overcome these tactics? And what is CDC doing specifically to combat these efforts?

Dr. JERNIGAN. Yes, so certainly at CDC we want to do everything we can to get more people vaccinated. We know with influenza that only about half of Americans actually get a vaccine. Another half still need to get vaccinated. A lot of the reasons why they don't get that vaccinated for influenza is because they're worried about the effectiveness of the vaccine. So with regard to our discussion here, improving the effectiveness of the flu vaccine certainly would actually I think get more people to be vaccinated.

Your question is really around the role of misinformation and social media participating in that. We do think that there is a lot of information out there. Parents have lots of different places that they can get information, and a lot of times they don't know which of it is science-based, which of it is evidence-based, et cetera.

So I think at CDC our plan is really to try and strengthen public trust in vaccines by truly trying to get people to be more confident in the vaccines, getting the information out there about how effective they are. And that really comes down to three things: Protecting the community; helping to understand the differences in these different pockets, these different communities, what makes them not have as much confidence in vaccine as they should; and to identify and develop materials that we can use for those specific communities, reaching out to key opinion leaders within those communities.

A second thing would be to empower the parents, that is, get with the very young parents when they first have children or with pregnant women. Get them the right information that they could understand better about the benefits of vaccine and understand why it is so important to get vaccinated and work with clinicians so that they have the tools to talk with those family members as well.

And then finally to stop the myths as much as possible, and so we do that I think by providing the scientific-based, evidence-based information that's out there, that's on our website, and then working to make sure that that can be reused on multiple different platforms so that people can get that science-based or evidence-based information.

Chairwoman JOHNSON. Thank you very much. Dr. Fauci, would you like to comment on that?

Dr. FAUCI. Yes, just to underscore what Dr. Jernigan said. You know, if you do a survey and find out what is the most important

reason why people don't get vaccinated for influenza, and it's because of the so-called misperception that it—it really doesn't work. And I think we need to emphasize that even though it isn't 100-percent effective, even a modestly effective vaccine will prevent you from getting infected, will prevent individuals, particularly those who are susceptible to complications, will prevent them from getting hospitalized and may ultimately save their lives. So this perception that the vaccine doesn't work, really we need to put that aside because everyone, as Dr. Jernigan said, should get vaccinated.

Chairwoman JOHNSON. Thank you very much. I'm going to ask Mr. Lucas to ask his questions.

Mr. LUCAS. Thank you, Madam Chair.

Dr. Jernigan, in Oklahoma the State Department of Health has reported that influenza has already claimed one life and hospitalized 70 others. Continuing on the comments that you and Dr. Fauci have made, when I look my constituents in the eye back home to stress the importance of getting vaccinated and to prevent the hospitalizations and deaths, can you expand on that? You're in a town meeting with me, you're looking my neighbors in the eye, this is rural Oklahoma, you're talking about things that are to the point.

Dr. JERNIGAN. Well, certainly we know the burden of influenza is very high. That is the illnesses and deaths that occur because of influenza. There are tens of millions of cases every year, hundreds of thousands of hospitalizations, and tens of thousands of deaths that occur every year. We know that with the vaccine that we have you can prevent thousands of deaths every year and tens of thousands of hospitalizations. It's important to get vaccinated and not just for yourself because it also helps protect the community around you.

There are a number of benefits that the vaccine has. It prevents you from getting sick. It reduces you from having to be hospitalized with flu. For people with underlying chronic diseases, it's actually like a prevention tool. It's like something you should take every year because it can keep you from getting a second heart attack. So people with underlying conditions, it helps them as well. It protects pregnant women and their babies so that those that are born but not 6 months, ineligible for vaccine, getting the pregnant mother vaccinated actually helps the baby during that period of time before they can get vaccinated.

There's data that shows that it's lifesaving in children. You can actually reduce the chance of death with influenza by 65 percent. So there are a number of things that are important about it.

Even if it's not 100-percent effective like Dr. Fauci mentioned, it can reduce the severity of illness that you have during the flu season if you were to get infected.

Mr. LUCAS. Dr. Fauci, my background is in agriculture, and in that world of course we have the robust National Veterinary Stockpile, which is prepared to provide farmers and ranchers with countermeasures against damaging animal diseases such as avian influenza and swine flu within 24 hours. Could you speak to the current state of the human vaccine stockpile management and what we could do to better prepare to address potential pandemic emergencies?

Dr. FAUCI. I would love to do that except that the CDC is the one who's responsible for the stockpile, so I'll pass that to Dr. Jernigan.

Mr. LUCAS. I flip over to you then, Doc.

Dr. JERNIGAN. Not to keep passing this, but actually BARDA is the one that manages the vaccine stockpile——

Mr. LUCAS. With the great insight that both of you have——

Dr. JERNIGAN. Yes.

Mr. LUCAS [continuing]. Enlighten us as to what's going on so we can reassure the folks back home——

Dr. JERNIGAN. Sure.

Mr. LUCAS [continuing]. We're paying attention, that is, you and your entities are taking care of their best interest.

Dr. JERNIGAN. Absolutely. So I think in terms of what we do at CDC, we monitor influenza around the globe, especially the avian influenza and the swine influenza viruses that are emerging around the globe. We do that through 143 laboratories where we detect those. We take that information and use it in a thing called the influenza risk assessment tool or the IRAT. You can actually get on your browser and put in IRAT CDC and see a graph of where we have ranked these different concerning potential pandemic viruses in that graph.

With that information, we work with the rest of the interagency to determine which of those should be made into vaccine candidates, which of them should actually be made into vaccines and stockpiled, which ones should undergo trials. And so with that we have made decisions about things to put into that stockpile so that the U.S. is prepared.

Many of those vaccines, say, for instance, the H5N1 vaccine, it's in the vaccine stockpile. It may be enough to vaccinate first responders and a few small risk groups. However, these viruses continue to change, and so it's actually very important for us to find new vaccine technologies so that the vaccine stockpile isn't something that just has to keep getting more and more vaccines put into it but rather upstream we have fast technologies and be able to make vaccines quickly. And then ultimately, once there is a universal vaccine, that may be the best thing for us to prevent pandemics is to have that available.

Mr. LUCAS. In my final moments before I yield back I eluded in my opening statement to my father's observations in the 1940s and 1950s prior to the development of the polio vaccine in 1955 how the outbreaks kept seemingly getting worse and worse and the sheer terror that it brought in the communities in that late summer season and early fall. My generation was not alive for that, did not experience that, but it was truly terrifying.

My first off-farm job when I was 14 was mowing a little country cemetery, and I had a great-aunt who was the family historian. And I remember asking her why in one section of the cemetery, why are all these babies buried? Why are all these young women buried? She said look at the tombstones. They say 1918 and 1919. The Spanish flu took them all, took them all and brought, even in rural Oklahoma, society to a grinding halt for weeks and weeks as this passed through.

My generation, having not experienced any of that, sometimes doesn't necessarily understand what the potential downside is and why you gentlemen and all of your colleagues work so hard.

And thank you, Dr. Bera, for giving us this opportunity to focus on these issues. And with that, I yield back.

Mr. BERA [presiding]. Yes, thank you to the Ranking Member. Also thank you to Chairwoman Johnson for allowing me to be a doctor today.

And, yes, there are a couple hearings happening on the Hill today. I think this is the most important hearing that's taking place actually today, and I think that's why all the cameras are out in Longworth.

You know, just thinking about it, to both Dr. Fauci and Dr. Jernigan, you know, my home district and my home State senator is Dr. Richard Pan, a colleague of mine and, you know, we're on the frontlines of trying to combat some of the disinformation that is out there.

And I just want to run through a couple quick yes/no questions. Is there any scientific evidence that vaccines lead to increased risk of autism, Dr. Fauci?

Dr. FAUCI. Absolutely not.

Mr. BERA. Dr. Jernigan?

Dr. JERNIGAN. No.

Mr. BERA. You know, when I was practicing, I would talk to some of my patients. They would often come back at me and say, well, I don't want to get the flu vaccine because I had it before and it caused the flu. Dr. Fauci, is there any evidence that the flu vaccine causes the flu?

Dr. FAUCI. The flu vaccine does not cause the flu.

Mr. BERA. Dr. Jernigan?

Dr. JERNIGAN. I agree the flu vaccine does not cause the flu.

Mr. BERA. Great. And, you know, the whole point of science is to pursue the truth, and I think it's important for us to dispel some of these myths. There are legitimate reasons for a small cohort of individuals, you know, if they have allergies to eggs, et cetera, to opt out of the vaccine.

But, you know, one of the most important things about why it is important—let's use measles as an example to vaccinate a large population of folks—is the concept of herd immunity. And I think it's important for the public to understand that particular concept. Dr. Fauci or Dr. Jernigan, whoever—would you, you know——

Dr. FAUCI. It's a very important concept not only for flu but, I mean, our recent unfortunate experience that we had in this country particularly in New York City in the Williamsburg section was a classic example of what happens when the umbrella of herd immunity goes down below a certain level because you had a community in which the level of vaccination was somewhere between 70 and 80 percent. For measles you need somewhere between 91 and 93 or more percent of the community so that when someone inevitably comes in from the outside or someone travels and brings back measles, if the community isn't protected by that herd immunity, you get the very unfortunate situation which we saw in the Williamsburg section of Brooklyn.

Mr. BERA. What are current measles vaccination rates in America?

Dr. FAUCI. It's over 90 percent.

Mr. BERA. OK. So we want to keep that. And measles was a disease that, you know, for the most part we had eradicated in America, and now we're starting to see the incidence starting to pop up again.

I guess for Dr. Jernigan, you know, I'll often hear individuals say, well, you know, we don't really need these vaccines or the flu vaccine because we haven't had a pandemic like the Spanish flu for 100 years. Can you talk a little bit about why we've been so lucky?

Dr. JERNIGAN. Yes. So I think with the pandemic influenza, this is a situation where the flu viruses that are actually circulating in animals can actually mix with those flu viruses that are in humans. And when they do that, they share their genes and can create a flu virus that has not been seen before. That means that it can spread very quickly through the community, and often it can cause severe deaths and illnesses and hospitalizations. The 1918, like was mentioned, was one of the worst. That one clearly caused at least probably 675,000 deaths in the United States.

We've had three other pandemics in the last 100 years. Those were with changes in the vaccine that were not as bad. We at CDC have looked at the 1918 virus and found that there are particular changes in that virus that really made it severe. So there's nothing preventing that from happening again, so for us it's important to maintain the vigilance so that we can see what's happening, maintain the ability to have vaccine available quickly so that we can get it and be able to prevent influenza and severe influenza if we were to have another pandemic.

Mr. BERA. And in today's interconnected world where people move across boundaries, having two big oceans are not necessarily protective for us.

Dr. Fauci, you and I had the opportunity to work together around the 2014 Ebola outbreak in West Africa. Can you talk a little bit about the evolution and development of an Ebola vaccine and how that's helped us, you know, in the 2017 outbreak in Western Congo and, you know, and giving us an ability to better manage Ebola?

Dr. FAUCI. Well, back in the 2014 to 2016 outbreak in West Africa of Ebola, during that period of time we, together with a variety of other agencies, including the CDC and other international agencies, began the testing of a vaccine called VSV, which now is ultimately made by the company Merck. So at that time we did phase 1 studies right here in the United States. We did it at the NIH in our campus. Some were done in Europe, and then we did it in West Africa. We advanced to phase 2. The CDC did a study in Sierra Leone. We did one in Liberia, and then ultimately it was shown in a ring vaccination study in Guinea to actually be effective in preventing infection, particularly those who were exposed. That vaccine has now been used in the Democratic Republic of the Congo (DRC), and over 245,000 doses have been given in a contact ring vaccination approach.

It is very clear that if in fact we didn't have that vaccine, we would be in a much worse situation than we found ourselves in in

the Democratic Republic of the Congo. And, as you well know from the reports coming out from the CDC, the number of cases per week of Ebola have gone down and down and down. We're not through with it yet. It's still there, but the vaccine has played a major role in being able to prevent the explosion that we saw in West Africa.

Mr. BERA. Well, Dr. Fauci, Dr. Jernigan, thank you for your service to our country. And just in closing, vaccines are safe, vaccines are effective, and vaccines save lives.

So with that, Mr. Posey.

Mr. POSEY. Thank you. And I'm grateful to the Chair for holding this hearing.

Flu shots can play a very important role in protecting the public from the flu and reducing its spread. I want to focus my comments on a 90-year-old policy which should have ended decades ago. Why do we still have mercury in millions of flu vaccines that are given to infants, toddlers, and pregnant women?

In July 1999 the Public Health Service, the American Academy of Pediatrics, and vaccine manufacturers issued a joint statement agreeing that thimerosal-containing vaccines should be removed as soon as possible.

And at this point I have a number of documents that I would like to include in the record by unanimous consent. First is a bibliography of studies raising safety concerns about thimerosal, which is vaccine mercury; second, a report from the Children's Health Defense outlining some of the misconceptions about mercury in vaccines, clearing up some misconceptions; third, a 1999 joint statement of the American Academy of Pediatrics and the U.S. Public Health Service calling for the immediate removal of mercury from all vaccines.

In 2004 the Institute of Medicine recommended removing mercury from all vaccines administered to pregnant women and children. By 2003 mercury was removed from vaccines in the United States. Yet a year later the CDC recommended the flu vaccine for children 6 months to 36 months of age but refused to state a preference for mercury-free vaccines, thus reintroducing mercury to the childhood vaccine schedule.

In 2006 California passed a law banning mercury-containing flu vaccines for pregnant women and children under 3. In 2009, much to the credit of Chairwoman Johnson, a bill was introduced banning mercury from power plants, and I think what she said then is even more pertinent to vaccinations, that mercury is a neurotoxin. Even at low levels, mercury can have an adverse health effect, particularly on women of childbearing age and on developing fetuses.

Dr. Fauci, you worked with my predecessor Dr. Dave Weldon, and I reviewed your testimony from October 5, 2004. That hearing was on removing mercury from flu vaccines. During that hearing, CDC Director Gerberding, the FDA's (Food and Drug Administration's) Dr. Egan, and you all agreed and you stated repeatedly, "We are moving rapidly to thimerosal-free vaccines." And you also said, "The better part of it is that if you can move to a vaccine preparation that is absolutely risk-free with regard to mercury, then you should do it."

The public concerns are still there. Mercury is in fact a neurotoxin. Babies, unborn and newborn, are at a critical stage of neurodevelopment. The one change is when the flu vaccine became a recommended shot. Manufacturers were automatically protected from all liability and accountability by lawsuits. Now they have no incentive to remove mercury.

I read over the flu vaccine package insert for flu vaccine, and each one says it has not been tested for safety in pregnant women. Common sense said that we should err on the side of safety.

Dr. Fauci, you testified to that 15 years ago. The failure to completely remove mercury feeds the fear and takes a backseat to saving a few bucks each shot. What steps are being taken by you as a leader in the public health community to move, quote, "rapidly to mercury-free vaccines," close quote? Or is it no longer a priority? And when can we expect it to be completed?

Dr. FAUCI. I don't think I can answer directly the question of when it will be completed. Just getting back to the discussions that we had years ago in the Committee, I said then and I would say it again that the optimal situation would be to have thimerosal-free vaccines, mostly as I mentioned at that hearing, which you didn't say, was that was mostly for the peace of mind of people, but the scientific evidence that that is a harmful amount of this material in the vaccine does not indicate that.

The issue with the thimerosal—and I'll let Dr. Jernigan also comment on that with regard to the CDC—is that it is in very, very few vaccines and only in multidose components. In the multidose component, the balance of the risk of getting a contamination of a bacteria, which we know can occur if you don't put something like thimerosal into the vaccine, versus the risk of a deleterious effect of thimerosal, which is really ethylmercury and not methylmercury, clearly balances the favor of making sure you protect from infection the multidose vials.

Dan, maybe you can amplify that a bit.

Dr. JERNIGAN. Yes, I think it's important to know that CDC is committed to assuring that vaccines in the United States are safe. Currently, this year there's projected to be 169 million doses of influenza vaccine, and we understand that only about 15 percent of that is the thimerosal-containing multidose vials. So those that would like to have a thimerosal-free vaccine, actually the vast majority of vaccine that is available are the prefilled syringes, the single-dose vials.

Mr. POSEY. My time is expired. Thank you.

Mr. BERA. Thank you. Before I recognize Mr. McNerney, just a quick question.

Mr. Posey raised a couple issues and maybe just yes/no answers. Is the flu vaccine safe for pregnant women?

Dr. FAUCI. Yes.

Dr. JERNIGAN. Yes, absolutely.

Mr. BERA. Is the flu vaccine safe for infants and children?

Dr. FAUCI. Yes.

Dr. JERNIGAN. Yes.

Mr. BERA. Great. With that, I'd like to recognize the gentleman from California, Mr. McNerney.

Mr. MCNERNEY. The neighbor from California. Thank you, Chairman. I thank the witnesses this morning.

Dr. Fauci, how can computational data scientists partner better with microbiologists to accelerate the research?

Dr. FAUCI. Well, I mean, computational biology is a discipline that essentially impacts on virtually all of the biological issues we do, so we can do computational biology when we do the sequencing of various strains of virus that come in and that you want to make a vaccine for. In fact, I think in his opening statement Dr. Jernigan had mentioned the fact that the capability both of the CDC and the NIH to do mass sequencing of a variety of quasi-species of any virus, including influenza, relies on computational biology to be able to get to the next step in developing a vaccine.

Mr. MCNERNEY. Is the symmetry pattern of this nanoparticle significant in any way?

Dr. FAUCI. Yes, I mean, actually what it is is that the display of multiple components of that stem create the ability to engage what we call the B cell repertoire of the immune system so that the chances of it hitting the B cells that will ultimately respond to give you the kind of an antibody response you want, that's a highly immunogenic approach. And nanoparticle approaches to any vaccine is really the wave of the future.

And that's what we're trying to do to get away from the situation of having to grow a complete virus and use that as the vaccine the way we're doing in eggs. Here, you use recombinant DNA technology, and you show the immune system only that part of the virus that you want it to respond to and you avoid all of the other distracting immune responses. That's why the scientific community is so excited about those new technologies.

Mr. MCNERNEY. Thank you. Dr. Jernigan, following up on Dr. Bera's question, if we find ourselves in a pandemic outbreak, how quickly with existing technology can vaccines be produced to catch up with the outbreak?

Dr. JERNIGAN. An example I think is in 2017 when there was the identification of a very bad H7N9 influenza virus that started to circulate among poultry in China. It ended up having almost 2,000 human cases that were exposed to them. We were able to receive the virus sequence directly from colleagues in China. And with that, we were able to use reverse genetics like I mentioned before to actually build the vaccine virus. CDC has the capability to do that under good laboratory practices conditions at CDC and then be able to hand that vaccine virus to the manufacturers. We can do that very quickly, within a matter of days to weeks.

However, once we hand it off to the manufacturers, they are bound by the existing manufacturing capabilities that they have. About 18 percent of all manufacturing right now is in non-egg-based manufacturing. The rest is egg-based manufacturing, which takes at least 6 months. And so getting things to be quicker is going to be an important national security thing for us to be able to respond more quickly.

Mr. MCNERNEY. Thank you. Can you address the autoimmune reaction to influenza vaccines—and forgive my pronunciation—such as Guillain-Barre syndrome?

Dr. JERNIGAN. I'll let you do that if you want.

Dr. FAUCI. So there has been a rare association of cross-reactivity between some of the antigenic components of a vaccine and certain tissues in the body. Again, and this has not been clearly proven yet, but in one of the vaccines that were available for the H1N1 flu of 2009, there was the suggestion that one of the peptides that's associated, which is part of a protein that was associated with the vaccine, induced the response that cross-react with a substance—I hate to use these big words for you—we use a substance called hypocretin, which is one of the neuropeptides that's involved in narcolepsy. So the autoimmune phenomenon of that has been discussed, disputed, but not really definitively proven. So what it is is that when you expose the body to a protein, it recognizes it as something that's similar to what's in your body and makes an autoimmune response against it.

Mr. MCNERNEY. Well, my son had a pretty scary reaction to his second DPT injection. Can you speak to that? It was a seizure that was pretty scary, maybe not dangerous but scared the hell out of us.

Dr. JERNIGAN. Certainly. I mean, febrile seizures is a known reaction just to a number of different vaccines, and I don't know the particulars, but that is something that is possible.

Mr. MCNERNEY. Is it dangerous?

Dr. JERNIGAN. No. For the most part it's something that does not have a lasting impact.

Mr. MCNERNEY. OK. Thank you. I yield back.

Mr. BERA. I recognize Mr. Baird.

Mr. BAIRD. Thank you, Mr. Chairman. And we appreciate you witnesses being here and sharing your expertise.

So my first question, Dr. Jernigan, deals with, in your testimony you mentioned the development of a mobile mini lab cloud-based platform that can be set in a remote resource-limited settings to process test virus specimens and to send that genomic data up to a cloud for further analysis and action. So could you elaborate on how this cloud-based platform would allow public health officials to address outbreaks quicker and more effectively in a largely rural area like my 4th congressional District in Indiana?

Dr. JERNIGAN. So, yes, I think we were referring to the use of these micro-technologies like this one here, which actually is a sequencer. And so you actually take the specimen, prepare it in some little boxes that we take that fit into a carry-on on a plane. You prepare them, and then you just simply inject it in you. There's a way that you can actually do what's called barcoding of the specimens and do multiple specimens at one time. And with that, you get a sequence. And the sequence just tells you the genes of the influenza viruses.

So this is something that we have demonstrated in various different settings. We actually did take it to Iowa to a swine fair where we actually swabbed a number of the show pigs and that we were able to quickly determine if they had influenza, the swine influenza that was circulating among that group.

That data plugs into a laptop through this little USB port, and then on the laptop it runs a lot of the information and prepares the signal that gets sent up to the cloud where we have a process called IRMA. IRMA is a tool, a pipeline tool that actually takes the

data and uses machine learning and artificial intelligence to try and determine which of the flu viruses are actually in the sequences. That information then gets pulled down by our bioinformatics staff at CDC where they can then, if needed, generate a vaccine virus. And so this allows us to take the tool to the place where the problem is occurring rather than having to try and figure out how to get viruses to the CDC.

Mr. BAIRD. So to take that one step farther, you could regionalize or wherever you collected your data, then you could develop a vaccine specific for that area is what——

Dr. JERNIGAN. It's possible.

Mr. BAIRD [continuing]. More quickly——

Dr. JERNIGAN. The manufacturing process would let you probably not be able to do that, but yes, you can tailor what you know about in certain regions. I think Dr. Watkins will probably get into some of the data issues in the subsequent testimony.

Mr. BAIRD. So you mentioned pigs, and I have a background in agriculture, so when you were swabbing those pigs, any thoughts on the African swine fever?

Dr. JERNIGAN. Yes, so African swine fever is something that's different than the swine influenza, and so I'm not an expert in the swine fever, but certainly these same kinds of technologies could be used anywhere in the world to do that kind of detection.

Mr. BAIRD. Thank you. Dr. Fauci, do you have any thoughts on that area?

Dr. FAUCI. Yes. The point that Dr. Jernigan made, it's interesting. I'm in some respects glad you brought that up because we constantly get people confused between African swine fever and influenza that's in pigs that could recombine with an influenza to give us a pandemic. It has absolutely nothing to do with that, but sometimes people get confused when they hear the word African swine fever, which is really completely unrelated to influenza.

Mr. BAIRD. And I appreciate that. That's part of the reason I mentioned that. So I thank you. I yield back.

Mr. BERA. Thank you. Let me recognize Mr. Foster.

Mr. FOSTER. Thank you, Mr. Chairman. And thank you to our witnesses.

Let's see. Back to the nanoparticle universal influenza—can you, I guess, Dr. Fauci, say a little bit about the nature of the nanoparticle and how you actually bond the stem sections to the nanoparticle?

Dr. FAUCI. Yes, it's very interesting. It's a beauty of nature. It's a self-assembling ferritin particle, the ferritin protein from a bacteria. And what it does is that when you combine the genes of both, when they express themselves, they express themselves as the nanoparticle, which symmetrically has the——

Mr. FOSTER. Bonding site, so——

Dr. FAUCI [continuing]. Stem of the hemagglutinin——

Mr. FOSTER. So they just fit properly?

Dr. FAUCI. They just fit properly.

Mr. FOSTER. They fit in the—OK.

Dr. FAUCI. You know, it's—I hate to use this word, but it's almost like a miracle of the natural selection——

Mr. FOSTER. All right.

Dr. FAUCI [continuing]. Becoming——

Mr. FOSTER. So the nanoparticle is actually just a larger protein——

Dr. FAUCI. Exactly.

Mr. FOSTER [continuing]. Folded in the specific——

Dr. FAUCI. Precisely.

Mr. FOSTER [continuing]. Geometry.

Dr. FAUCI. Right.

Mr. FOSTER. OK. And now, if I was reading your slides correctly, the stem section is highly preserved but not absolutely preserved?

Dr. FAUCI. Right.

Mr. FOSTER. And so are you then going to need several versions of this or are there dozens of versions or—just in terms of the stem variability?

Dr. FAUCI. We don't know, but we believe that we will not need very much because even though it's not completely preserved, we don't believe that the mutations that occur in the stem have a functional relevance in making it different from one to the other. So everything we've done so far where we've looked at the stem and we just recently completed a series of experiments where you made antibody against multiple components of the stem, and then you uses antibodies to screen the entire group of the group 1, which contains 10 of those H's, and it just neutralized every one of them. So we think—not 100-percent sure—that if we get a series of antibodies against multiple components of the stem, we could probably knock out an entire group. And there are two major groups. So I think we're going to need at least two, but I don't think we're going to need 10.

Mr. FOSTER. OK. Fascinating. And you mentioned—this is in phase 1 clinical trials at NIAID Vaccine Research Center, which is——

Dr. FAUCI. Yes.

Mr. FOSTER [continuing]. And that's human safety?

Dr. FAUCI. Yes.

Mr. FOSTER. And has it proven effective in animals?

Dr. FAUCI. Yes. Yes. Yes.

Mr. FOSTER. OK. And so it's all the way through safety and effectiveness in animals and is at safety in humans right now?

Dr. FAUCI. Right. What we showed in animals is that when you injected it into the animal, you got a complete array of antibodies against the whole panel of the flu. You don't challenge them with every single one, but you know you have a protective level of antibody.

Mr. FOSTER. Fascinating. OK. Changing the subject a little bit, Dr. Jernigan, can you say a little bit about the unique challenge of achieving high rates of immunization in immigrant populations where they very often have a lot of reticence to connect to anything official because of the demonization of immigrant communities?

Dr. JERNIGAN. Relative to my earlier comments about ways to protect the community as a form of increasing vaccine confidence, certainly there are communities that don't value the vaccine, and so I think the better way to get at those groups is to really identify what are the factors that are leading them not to get vaccinated.

Mr. FOSTER. In the case of immigrant communities, you know, frankly, following the 2016 election, I talked to principals in minority communities in my district who were turning kids away from school because they were not being immunized because they were terrified that ICE (Immigration and Customs Enforcement) was going to come get them if they got their kids immunized. And these are kids that are U.S. citizens, but they have someone in their family who might be undocumented. And is that something you see? Do you monitor the rates of non-immunization in different populations, and do you see an effect?

Dr. JERNIGAN. I don't know if we have that information. We do look at immunization coverage and look at it by race and ethnicity. But in terms of the specifics around immigrant communities, I don't know that we have that information.

Mr. FOSTER. OK. Yes, if you could do a little——

Dr. JERNIGAN. I can get back to you on that.

Mr. FOSTER [continuing]. And get back to us, I'd appreciate it.

Let's see. Finally, you had mentioned that it was the meat industry in various forms that was a major player in the spreading pandemics and having the viruses. Now, in a world where you had artificial vegetable-based meat, which is one that a lot of people dream about, is that something where you'd be intrinsically less prone to pandemics?

Dr. JERNIGAN. So influenza viruses are in reservoirs, and so humans are one of those reservoirs, and there's, you know, human-specific influenzas that circulate among humans. The biggest reservoir is among birds, and the biggest reservoir among birds is migratory waterfowl, and so ducks and geese——

Mr. FOSTER. OK. So we're without——

Dr. JERNIGAN. So——

Mr. FOSTER [continuing]. Migratory——

Dr. JERNIGAN. Yes.

Mr. FOSTER. That's not something anyone really wants.

Dr. JERNIGAN. That would be very difficult to try and get rid of, yes.

Mr. FOSTER. OK. Thank you. I yield back.

Mr. LUCAS. Would the gentleman yield?

Mr. FOSTER. Absolutely, I'll yield my negative 2 seconds.

Mr. LUCAS. That's wonderful. One of the great challenges those of us in the agriculture industry deal with are migratory birds and migratory animals who move around from Canada to Central and South America. They are the thing that we're most frightened about because in their overflights they deposit little presents as they go along.

Which then are subject to consumption by other forms of livestock that have similar characteristics to the rest of us. So that's an issue that causes us great angst not—maybe that's just the best place to leave it.

Mr. BERA. Great. Let me recognize Mr. Gonzalez.

Mr. GONZALEZ. Thank you. Thank you for calling this hearing, and thank you to our panel for all your work. I'm a somewhat new father, 19-month-old son, and obviously the flu with respect to our children is something that's near and dear to my heart and many hearts in this room and across the country.

According to a *Wall Street Journal* article, CDC estimated that over 27,000 children ages 4 and younger were hospitalized with the virus and 118 died in the 2017 to 2018 flu season. Clearly, these are troubling for any parent, I think the uncertainty maybe more than anything. And while immunization levels in the U.S. are relatively high, gaps still do exist. And providers can do more to increase immunization rates among their patients and their colleagues.

According to the CDC, fewer than 70 percent of healthcare providers receive the influenza vaccine each year. How does the CDC engage with healthcare providers to promote vaccination?

Dr. JERNIGAN. So certainly through a number of different studies CDC has identified that the one way to get patients vaccinated is to make sure that the healthcare providers are promoting the vaccine as well. If you look at the coverage among healthcare providers, it falls into different kinds of categories. The more you are at an academic hospital, the more likely you're to be vaccinated as a healthcare provider. The more training you have—physicians have upwards of 90 percent. The farther you get away from a hospital and the lower the training like an aide at a long-term care facility——

Mr. GONZALEZ. Got it.

Dr. JERNIGAN [continuing]. Those are the ones that are not being vaccinated. We clearly want to get the message out that those folks really need to get vaccinated.

Mr. GONZALEZ. Great. And then additionally, in the last decade it's predicted that fewer than 50 percent of Americans actually get the shot. What research has been done or are you all doing just to get a sense of why folks aren't actually getting vaccinated?

Dr. JERNIGAN. So——

Mr. GONZALEZ. I'm trying to identify root causes here.

Dr. JERNIGAN. Yes, so there are periodically focus-group testing that gets done on different groups to try and find out what the reasons are. The main reason that we've identified in the last few years is the effectiveness of the vaccine. People don't think it's as effective as it should be, and that's keeping them from getting vaccinated.

We know now that there are more places to get vaccinated than ever, so access is one of those things that may have been a problem but certainly we're getting over with now.

Mr. GONZALEZ. OK. And then NIAID has prioritized the development of universal influenza vaccines and has highlighted its research strategy toward this goal in the Strategic Plan For a Universal Influenza Vaccine. In your testimony you highlight that one of the main challenges facing the goal of producing universal vaccines is improving vaccine production strategies. Could you tell us about plans to address this challenge and keep working toward a universal vaccine?

Dr. FAUCI. Yes. Thank you for that question, Mr. Gonzalez. Yes, that was the point I was trying to make, that we really need to switch into different what I call vaccine platforms. In other words——

Mr. GONZALEZ. Yes.

Dr. FAUCI [continuing]. Not to require to having to decide on a strain in February and then take 6-1/2 to 7 months to get it grown and processed to be able to put it in a vaccine, whereas if you do the kind of platform such as the nanoparticle, which is one of several platforms.

So as part of our strategic plan that I articulated in that document that you mentioned is to try and develop and perfect various platforms so that we can get away from the burden of having to grow the virus.

Mr. GONZALEZ. Thank you. And I will yield my remaining time.

Mr. BERA. Let me recognize Ms. Stevens.

Ms. STEVENS. Thank you so much for this insightful panel, and thank you, Dr. Bera, as well for bringing us all here together.

We heard a little bit today that despite strong efforts in both the public and private sector that a universal flu vaccine remains elusive. What scientific advances do you see on the horizon to improve the flu vaccine?

Dr. FAUCI. Yes. I believe the scientific advances will be what I was showing on one of the slides of ultimately being able to develop a vaccine that would induce a response that would have broader coverage. You know, I was just actually speaking to one of the scientists who made a breakthrough discovery yesterday when he visited the NIH, Dr. Ian Wilson from the Scripps Clinic. And in 2009 he developed an antibody from a person who was infected with flu, and it bound very, very clearly to a particular component of the stem antibody, which was interesting. And then he found out that not only did it neutralize the virus that the person was infected with, it neutralized all of the viruses in that particular group, which is the group 1, 10 viruses. That was the scientific breakthrough that allowed us to go to the next step of a universal flu vaccine. So it's breakthroughs like that that I predict over the next few years will make it easier and easier to get to the ultimate goal of a universal flu vaccine.

Ms. STEVENS. Dr. Jernigan, did you have any——

Dr. JERNIGAN. Yes, I think in terms of the near-term kinds of things, I think what we've been looking at, the main problem in the influenza vaccine right now is one of the virus components. We can only put four different components in the vaccine and one of them called H3N2, that's the problem child of the vaccine. And so that one we know that when you put it into eggs to manufacture, which is 85 percent of all manufacturing, it ends up changing that influenza virus so that it no longer looks as much like the circulating viruses that are infecting people. So the use of the egg-based manufacturing is introducing some changes that may be having an effect on the effectiveness of the vaccine itself. So moving to cell-based vaccines, moving to recombinant vaccines may be quicker and may actually make the vaccine to be looking more like the H3N2 viruses that are actually circulating.

Ms. STEVENS. Can the Federal Government play a role particularly in terms of the tools that are being developed to monitor the effectiveness and safety of our vaccines?

Dr. JERNIGAN. Absolutely. I think at CDC we have a vaccine effectiveness network that we manage. And that one we've been able to expand some, but I think expanding that much greater would

allow us to be able to get information about how the vaccine is working better or worse in certain age groups, certain parts of the country, certain types of individuals. It would give us a lot more information to know how to make the current vaccines better.

Ms. STEVENS. Yes. And then in your testimony, Dr. Watkins, you mentioned that public health data infrastructure is a little outdated and it hinders our ability to prevent outbreaks before they occur and it hinders our ability to respond rapidly when they do occur. And it also hinders, you know, just our overall ability around surveillance data. Could you just speak a little bit about—or tell us a little bit about the—and Dr. Watkins isn't here—sorry. I'm so eager for Dr. Watkins, and you're both looking at me like Dr. Watkins isn't here. But one of you could talk about data infrastructure and, you know, we will also pay note to Dr. Watkins when she arrives.

Dr. JERNIGAN. I think that over time we have seen that there's been an improvement in the use of data at healthcare facilities through electronic health records, et cetera, but the public health establishment has to receive information from multiple different sources. And right now there's not a really standardized or common way that that information can come in. Plus, it's hard for a State health department to be able to quickly get the information they need to know, is this a case of whatever particular reportable disease? Do I need to intervene quickly? Has this person been vaccinated?

From a flu perspective, we currently get real-time information about influenza-like illness from a number of different sources, but only about half of that is real-time. The other is doctors filling out forms and things. If we were able to get real-time information from all of those providers regularly, we would be able to know exactly what's happening with flu at a much more local level, more precise data, more actionable data for decisionmaking.

Ms. STEVENS. Thank you, Dr. Jernigan. And, yes, it is the race for information and data in this modern age. Thank you, Mr. Chairman. I yield back the remainder of my time.

Mr. BERA. Thank you. Let me recognize Dr. Babin.

Mr. BABIN. Thank you. Dr. Chairman. I appreciate you.

And thank you two gentlemen for being here, your expert testimony.

I just wanted to ask you, Dr. Jernigan, first, what are some of the emerging technologies and practices being developed to identify different pathogens, targets, and modernize the delivery of vaccines? And pardon me if you've already answered questions like this, but I have a markup on a different floor in the same building, so I just came in.

I'm a dentist, and one of my colleagues down here asked me if there were vaccines to eliminate cavities and would I be against those. He said that in jest, of course, but we encourage Halloween and things like that for.

Dr. JERNIGAN. So with regard to the diagnostics—I'm not going to address the cavity issue, but in terms of diagnostics, so CDC currently maintains a thing called the International Reagent Resource, which is an online storefront that all of the public health departments in the United States and 143 laboratories around the

globe are able to go on and order standard reagents that CDC makes so that we know that the globe is actually doing the same kind of testing for influenza so that we can use that information quickly. That uses a process called PCR or polymerase chain reaction, which is a common way. We're currently updating that to get to some newer kinds of PCR devices. But what's really been game-changing is the ability of genomic sequencing.

Mr. BABIN. Right.

Dr. JERNIGAN. And so CDC has established three national influenza reference centers at three public health labs in the United States where they do all of that genomic testing so that we can pick up emerging antiviral resistance, viruses that might be a pandemic, a virus that's emerging, those kinds of things so that we can act more quickly.

Mr. BABIN. Thank you very much. That's very fascinating.

And what are the main scientific and technological hurdles that stand in the way of the development of a universal influenza vaccine? I caught the tail end of somebody's question that had a similar one like that. And how are you working to overcome these, Dr. Jernigan, if you would. I'm going to ask him one here in just a second.

Dr. JERNIGAN. Well, certainly. I'll let Dr. Fauci talk about all the various different hurdles that are out there. For us the influenza virus has been able to evade human immunity forever, and so you can get influenza every year. So the task we have at hand is a very difficult one in that the body itself is not able to have long-lasting immunity. So we're trying to find something that the body itself is not very good at.

Mr. BABIN. All right. Now, Dr. Fauci, if you would just go ahead and elaborate on that as well then.

Dr. FAUCI. Yes. Well, there's one hurdle that I think is really a serious hurdle. Even if we get a universal vaccine that would induce a response against a wide array of influenzas, and that is a phenomenon that's really very interesting. It's called imprinting. And what it is is that your body tends to make a response against the first influenza or the first antigen that it was exposed to when you were a youngster so that even later on in life when you get exposed to that organism, that microorganism again from an evolutionary standpoint, that was a good thing because that means that your immune system is primed so that if you see that micro begin, you make a really good response.

That's great for something like measles or mumps or rubella, which doesn't change. It stays the same. With influenza it works against you——

Mr. BABIN. Yes.

Dr. FAUCI [continuing]. So that what you will do is that if the first—I'm an H1N1 person in the sense that I was born at a time when H1N1 was around. So my immune system is primed to make a response against H1N1. So if I get exposed to an H3N2 or even get vaccinated with that, even though I'll make a reasonable response, my body will revert to wanting to make a response to H1N1. It's referred to sometimes as original antigenic sin.

So the real problem is how do you get around that so that you can vaccinate somebody and overcome that tendency to make a re-

sponse against something that you were originally exposed to? That's going to be an important obstacle.

Mr. BABIN. Well, and that was the question I was saving for you, and you've actually mostly answered it because this is why measles, mumps, and rubella vaccines have a 97-percent effectiveness where influenza is only, what is it, 10 percent up to 60?

Dr. FAUCI. No, no, that was a very bad year.

Mr. BABIN. Up to 60 percent, though, right, 10 to 60 percent.

Dr. FAUCI. Yes, 40 to 60 percent is——

Mr. BABIN. Yes.

Dr. FAUCI [continuing]. What it is, yes.

Mr. BABIN. So that's the biggest hurdle we have.

Dr. FAUCI. Exactly.

Mr. BABIN. Yes. OK.

Dr. FAUCI. You hit the nail on the head exactly.

Mr. BABIN. All right. Thank you very much, and I yield back.

Mr. BERA. Let me recognize Mr. Casten.

Mr. CASTEN. Thank you, Mr. Chair. Thank you both so much. I am just totally intrigued by this universal vaccine idea, and I want to start if you'll just humor me as a biology nerd.

I want to just follow on Congressman Foster's question. So the fact that the stem has been so preserved, how confident are you that that's because there is something fundamentally that the bug just can't change that protein versus the fact that statistically the antigens were on the surface and so, as we start developing antibodies to go after the stem, are you confident that the stem won't start evolving into something else?

Dr. FAUCI. You know, it could. It could evolve under immunological pressure, but from the standpoint of conserved components—we call them epitopes, parts of proteins—when something is conserved throughout evolution, it's usually because it's critical for that particular thing to survive whether it's a species, an animal, or a protein, so there must be something about that stem that's absolutely critical to the function of the virus. So we think it's not going to change, but we better be careful. We don't want to make an assumption that is going to turn out to be wrong.

Mr. CASTEN. And have the animal studies been of a long enough duration to give you some confidence that there is no—I forgot what the word that you used was, that immunological——

Dr. FAUCI. Yes, no, to be honest with you, no. We haven't done it for a decade and shown that over a period of time if you keep vaccinating an animal and making a response against stem and then years later it's going to evolve, we haven't proven that yet. So, I mean, obviously, it needs to be done.

Mr. CASTEN. OK. So what if anything can we do to accelerate—we on, you know, this side of the room to accelerate the development of these universal vaccines? Is it the time to just get through phase 2 trials at this point or is there something else that you need?

Dr. FAUCI. No, actually, what it is that—we thankfully have gotten very good support from the Congress to do the kind of work that we're doing for the universal flu vaccine. In fact, in our last appropriation there was a set-aside that was put in order to stimu-

late the research in that area. So we are very appreciative of the Congress for what you already are doing.

Mr. CASTEN. OK. I want to pivot—and this is—I'm going to take a chance here just because I get the sense, Dr. Fauci, that you and I may share a sense of humor. Do you know what you call alternative medicine when it works? Medicine.

I raise that because we are in a moment where there's this rise in anti-scientific thinking from climate science denial to the anti-vax movement to, you know, I think *The New Yorker* last week had this article about the rise in people who think that the—where the stars were when they were born has an impact on their future.

As you think about the concerns to public health, there's one set of concerns that is, you know, the anti-vax movement, people consciously choosing not to take proven medicine. There's a separate risk of people who are consciously choosing to take bogus medicine. Which of those—and maybe I'm phrasing this the wrong way, but are those comparable concerns, and are we doing enough to combat both?

Dr. FAUCI. I think they are comparable. I think there's danger in both of those. I think you brought up two very important points. There really is an obvious concern about people who are anti-science and don't want to believe the clear-cut science facts, and there is a danger to actually having deleterious effects of assuming the efficacy of things that are bogus and going ahead and doing that.

We have, several years ago, established first a center and now an institute for an alternative and complementary medicine to be able to look at some of these things that society and people in the community are convinced work to prove whether they either do or do not work, so we are doing something about trying to put some scientific rigor to some of these things that are potentially bogus. So that's what we're trying to do on that end.

On the anti-science end, the only thing that we can do is to continue to do what Dr. Jernigan and his colleagues at the CDC and what we do at the NIH is to continue to try and get out the message and the evidence-based proof of what works. There's nothing like evidence to be able to convince someone that something works, and you have to keep coming in with evidence over and over again.

Mr. CASTEN. So are we doing enough to keep bogus science off the shelves? Because when I go to Walmart and I look down the flu medicine, there's some homeopathy up there as well, and I don't know that the average person knows the difference. So should we be doing more to make sure that we——

Dr. FAUCI. Yes, I think as a society we should be. I'm not sure that there's much that we at the NIH or that—with Dan at the CDC can do, but clearly there's stuff out there that really doesn't really do anything except potentially harm people.

Mr. CASTEN. Thank you. I yield back my time.

Mr. BERA. Let me recognize Mr. Murphy.

Mr. MURPHY. Thank you, Mr. Chairman. I just want to say thank you actually professionally to both of you gentlemen. Dr. Fauci, I followed your career since the early 1980s when you made such fantastic and landmark discoveries with HIV, and it's really

put forward something today now that's manageable, so thank you from our community.

Being the last one to speak, I always have to figure out which questions that folks have already asked, but let me go back to one of the things that my colleague pointed out, the anti-scientific movement these days, and I actually think that's a major problem. I saw last week that people are now starting back on the flat Earth agenda.

And I want to go back to the anti-vaccine movement that's going back in our country. I wonder if you could really speak to that, what it's done as far as populations at risk, and where do you see that going in the future? Because it is a major issue these days.

Dr. JERNIGAN. Well, certainly, I think there are pockets where individuals are talking with one another, some schools, that kind of a setting where folks are actually hearing from each other rather than looking to see what the science space is or listening to physicians. And so those pockets I think can lead to more and more children, for instance, not getting vaccinated, to get into school.

I think it's important for us also to recognize that people get their information multiple different ways now, and so for us to be nimble on how it is that we get the science-based information, the evidence-based information to those folks, identify what their needs are, and then provide them the information that they need. But until you address those specific groups, I think with information that is valid to them, I think it's going to be actually very difficult.

Mr. MURPHY. Thank you. One other issue I'd like us to revisit is Ebola. I don't think people in the United States really understood the gravity of what would have happened if that had gotten into Lagos or any of the other places in the future. And I was wondering if you could talk a little bit more just about the vaccine with Ebola. Does it mutate on the level that the other ones do? And can you, just for edification, just explain to folks the infectivity rate of the Ebola virus versus the HIV virus, for example? I know it's a multitude-scale more infective, but I think giving an example would be helpful.

Dr. FAUCI. Well, Ebola, unlike influenza, which drifts and mutates, is pretty stable. It's an RNA virus, so there's always mutations. But the mutations have not proven to be functionally relevant. So if you do a sequence of Ebola in a strain in West Africa, which was Ebola Zaire, the Ebola that's now in DRC is still Ebola Zaire. There are different types of Ebola. There's Ebola Sudan, Ebola Zaire, and others. But within Ebola Zaire, which is the one we're dealing with right now, it really has not been a problem that it has mutated to the point of being functionally relevant. So you can measure point mutations, but they don't change anything about it.

I think the question you ask is, what is the relationship with the vaccine. The relationship with the vaccine is that the vaccine has worked, and any change in the virus has not had any impact on the vaccine, so it looks pretty good. So as I mentioned a little bit earlier in the testimony, we've now distributed over 250,000 vaccinations in the outbreak in the DRC.

The second part of your question is the issue of how it's transmitted. In an untreated, unvaccinated arena such as what's going

on in the DRC right now, the mortality of that is about 67, 70 percent. It's transmitted only by direct contact with a contaminated bodily fluid.

Mr. MURPHY. Right.

Dr. FAUCI. And that was really important, so if someone gets Ebola and they're incubating it and they get a fever but they're not having diarrhea, they're not having bleeding, they're not vomiting, that person is really quite noncontagious. And that's the reason why there wasn't a concern of people back when the patients in Texas got infected. There was a concern that those two nurses were infecting people, and they were not.

Whereas when you get something like influenza, influenza is transmitted by the respiratory route, and there's a window of when you're actually not really very sick when you can actually transmit it because you're shedding virus for a period of time before you get sick and after. So there really is a rather substantial difference in transmissibility. It is tough to get infected with Ebola unless you have direct contact with a really sick person, whereas you can get influenza on an elevator when the person next to you sneezes——

Mr. MURPHY. Right.

Dr. FAUCI [continuing]. So there's a big difference.

Mr. MURPHY. Thank you. I thank you, Mr. Chairman. I'm going to yield back the remainder of my time to Mr. Posey.

Mr. POSEY. I thank the gentleman for yielding.

Mr. Chairman, I'd like to add one more document to the documents.

It clearly indicates that while these vaccinations are safe for most people, there are some for whom it's not safe. The Vaccine Injury Trust Fund has paid out over $4 billion, with a B, which they did not mention. Forty-six percent of those were for influenza-based vaccinations. So I didn't want to ruin the love in here, but I think we should not be cavalier about those for whom it's inappropriate and that we do try and identify who it might not be appropriate to receive those shots for public safety in the future. Thank you very much.

Mr. BERA. Great. Let me recognize Ms. Bonamici.

Ms. BONAMICI. Thank you, Dr. Chairman. And thank you, Dr. Fauci, for reminding us that we can get flu in elevators, which we ride in all the time in this building, and I'm really glad I got my flu shot.

And thank you to the witnesses for being here today. You know, when we reflect over what happened last century, we made such astounding success developing vaccines to eradicate pernicious diseases. In the United States we essentially eliminated polio and smallpox and diphtheria and in the rest of the world largely defeated those. The World Health Organization (WHO) estimates that vaccines have prevented at least 10 million deaths between 2010 and 2015. That's pretty remarkable.

But in this hearing today we're acknowledging that there's still a great deal of work to do, especially with influenza, one of the most pervasive infectious diseases globally, yet, despite all the efforts, we're still struggling to effectively predict or respond to those annual epidemics because of the rapidly changing nature of the flu, as you both discussed.

The good news, as our witnesses indicated, is this exciting cutting-edge research that's being conducted throughout the country to develop new approaches. Thank you, Dr. Fauci, for bringing your model. Thank you, Dr. Jernigan, for bringing your mobile lab.

And a lot of that work is federally funded or supported, which is why I'm glad we're having this hearing today. Some of that innovative research is happening at the Oregon Health Sciences University in Portland. Dr. Jonah Sacha and his team are working on a novel method of long-term flu vaccination that inserts pieces of target pathogens into cytomegalovirus, or CMV, to trigger a response by the immune system's T cells when the body encounters flu virus. I don't understand what that means, and I'm hoping you will explain it.

Dr. Fauci, are you familiar with this approach? Can you briefly explain how it functionally differs from the one you described in your testimony or more traditional efforts that rely on antibodies, as well as comment on the importance of pursuing varied methods in search of a breakthrough? And, Dr. Jernigan, if you're familiar as well.

Dr. FAUCI. Right. So the person you're referring to is named Dr. Louis Picker, and he has established the vaccine platform, which uses a cytomegalovirus, which is highly immunogenic. And what that platform is, it's called a vector platform. So he takes a virus that we know and have experience with, cytomegalovirus. He inserts into the virus the gene of a particular protein that he wants to make. He's done it with tuberculosis, he's done it with HIV, and he's doing it with other pathogens.

So what happens is that if you wanted to make a vaccine, which he's trying to do, against HIV, he takes the gene that codes for the outer protein of the HIV called the envelope. He sticks it into the cytomegalovirus, and he injects it first into an animal. He hasn't done it into a human yet because there were some safety issues there. Cytomegalovirus is not a benign virus, so it needs to get big scrutiny from the FDA. But in the animals, it's been very effective. He injects it into the animals. It starts to replicate, and it starts pumping out this protein, which is the HIV protein, and he's created in the animals at least a pretty good HIV vaccine.

Ms. BONAMICI. Fascinating. The project I was mentioning was at the Oregon Health Sciences University Vaccine and Gene Therapy Institute.

Dr. FAUCI. Correct.

Ms. BONAMICI [continuing]. In Oregon. So also I wanted to ask about Dr. Jernigan, about the FluSight website. Since 2013 the CDC has engaged in efforts to use its predictive data analytics. How's that working and, you know, the public-facing website? What are you learning from that?

Dr. JERNIGAN. Yes, so this is a network where we have over 25 different academic modelers. These are individuals that use various different sources of information—social media, weather, all kinds of different information. We provide them some inputs each week, and then they have to tell us what they think is going to happen in terms of, is the flu going to peak this week—when's it going to start, et cetera, so it's a way that we are trying to get not what's happening with flu now but what is flu going to do. We think that's

important so that when we have a pandemic, we can use that information to inform folks. But during regular seasons, that information can be quite helpful for an outpatient clinic, knowing when they need to increase the amount of staff, for a hospital in knowing if they need to have more beds in the ICU, even for pharmacies to know when they move things around——

Ms. BONAMICI. Right. Right.

Dr. JERNIGAN [continuing]. At the pharmacy.

Ms. BONAMICI. And some places run out of flu vaccines.

Dr. Jernigan, data from more than 100 countries is used to determine which viruses—and influence the viruses that are recommended for inclusion in the annual vaccine. What challenges exist for collaborating with so many countries to share data and make sure that that's usable by everyone? What can be done to improve the international disease surveillance and data sharing so that we can better prepare?

Dr. JERNIGAN. Right. So in the United States we have a very good view of what's happening with influenza with thousands of viruses that we characterize here. We work with 143 other laboratories, receive viruses from them, but there are blank spots on the globe where we don't know what's going on. So the more we can get improved surveillance, better genomic surveillance in that setting, more timely information from them, that helps that country, but also helps the rest of us to know what's going on with flu, know if pandemics are showing up, and to make better vaccines.

Ms. BONAMICI. Thank you. I see my time is expired. I yield back.

Mr. BERA. Thank you. Let me recognize Ms. Wexton.

Ms. WEXTON. Thank you, Mr. Chairman. And thank you, Dr. Jernigan and Dr. Fauci, for joining us here today.

In October the CDC released some new statistics about maternal vaccinations. And I was kind of surprised to see that only one in three pregnant women receive both flu and whooping cough vaccines because women with the flu are more than twice as likely to be hospitalized if they're pregnant and nearly 70 percent of whipping cough deaths occur in children who are younger than 2 months of age.

However, flu vaccinations during pregnancy reduce hospitalization of babies less than 6 months old by an average of 72 percent, and whooping cough vaccinations will lower the hospitalization of babies by 91 percent. I hope we can agree that vaccinations are a critical part of prenatal care for expectant mothers.

And I understand that, Dr. Jernigan, you mentioned in your testimony that fewer than half of adults in the United States will get their flu shot because they have a perception that the flu vaccine is not effective. And I know that you've already talked a little bit about misperceptions and false information that's out there, but how can we more effectively communicate the benefits of flu vaccine?

Dr. JERNIGAN. With regard to pregnant women, I think it's currently around half are getting vaccinated for flu, and so that's a real success story. Over the last several years we've seen it really rise to that level. Clearly, we need to do more, and clearly we need to do more with the other vaccines that are for pregnant women.

If you look at who's getting vaccinated, while only half of Americans are getting vaccinated, you can actually see that the most vaccinations are happening among the old and the very young. And so trying to get at those groups that are late in their teens, 18 to 49 years of age, that's the group that we really need to get at to start increasing the amount of vaccinations. So that's going to take targeted efforts, really using social media and other approaches to get to them.

Ms. WEXTON. And just get them used to getting a vaccine every year——

Dr. JERNIGAN. Yes, and——

Ms. WEXTON [continuing]. Just make it an annual thing.

Dr. JERNIGAN. Part of the problem is that you have to get a vaccine to flu every year, plus that's a group of people that probably don't avail themselves of a lot of preventative health care and don't go to the doctor a lot, so I think getting that group in is a challenge but one that we need to work on.

Ms. WEXTON. And I'm glad you brought up social media because, you know, we have seen a lot of how social media can impact lives in a good way or a bad way. And one of the issues with social media is that information spreads so quickly. The viral nature of it allows people to communicate in a bubble without external sources that point out when something is just plain false or something is true, has withstood peer review and all that. So it's something that we've seen across Committees in other contexts as well, but here in this issue we're talking about lives are at stake.

And earlier this year, the American Academy of Pediatrics sent letters to the CEOs of major social media platforms, including Google, Facebook, and Pinterest, and highlighted the growing harm to children from vaccine misinformation that's spread across their sites. And I understand that you have already spoken in some of your testimony about the misinformation and how it spreads, but can you—do you—and this is for both witnesses. Do you think that these platforms are doing enough, given that lives are on the line?

Dr. JERNIGAN. I certainly think people access their information multiple different ways than they used to, and so making sure that we get our information that is scientific-based, evidence-based in the format that is going to be reused, reusable in that setting I think is an important thing. I don't know if you want to talk on that.

Dr. FAUCI. I agree. I think we can do more, and we can do better, but I think that the platforms that we have now to get the message out I think are having some positive effect. But clearly it's a challenge that's not going to go away. We're going to have to keep on it. It's not going to be a problem you'll solve and it's over. We have to keep at it over and over again.

Ms. WEXTON. Very good. Thank you so much. I'll yield back.

Mr. BERA. Well, in closing, just two other questions that come up repeatedly. Folks will say it's almost the end of November, I've already made it this far, I don't need the flu shot this year. Is that correct?

Dr. JERNIGAN. So our recommendation from the Advisory Committee on the Immunization Practices and CDC is that we recommend you get your vaccine if possible by the end of October, but

as long as influenza virus is circulating, we recommend you get a vaccine. So it is not too late to get a vaccine. Our goal is to try and get people vaccinated prior to the season start so that there's 2 weeks of time before—allow their immune systems to build up so that if they get exposed, but clearly we recommend that you continue to get vaccinated now.

Mr. BERA. So since I know most of America is watching this hearing and not another hearing, it is not too late to get the flu shot?

Dr. JERNIGAN. It is not too late to get vaccinated.

Mr. BERA. And then another question that comes up occasionally is nasal flu vaccine versus flu shot, any recommendations or equally effective?

Dr. JERNIGAN. So currently CDC does not have any preference for any one vaccine over another. There are personal preferences and parental preferences with regard to the live attenuated influenza vaccine, the nasal vaccine, so there's no preference for one over the other. They're all listed as effective as each other.

Mr. BERA. Great. Well, I once again want to thank both of you for your service to this country and service to medicine. And again for those watching at home, vaccines are safe, vaccines are effective, and vaccines save lives. Thank you.

And we'll recess for a few moments and allow the second panel to get seated. Thank you.

Dr. JERNIGAN. Thank you.

Dr. FAUCI. Thank you.

[Recess.]

Mr. BERA. Welcome back. At this time I would like to introduce our second panel of witnesses. The first witness in our second panel is Dr. Sharon Watkins. Dr. Watkins is the Director for the Bureau of Epidemiology and the State Epidemiologist for the Pennsylvania Department of Health. She is also the President of the Council of State and Territorial Epidemiologists. Dr. Watkins is responsible for management and oversight of the Bureau of Epidemiology, which includes the Division of Infectious Disease, Environmental Health, and Community Health. Dr. Watkins has led disease surveillance and outbreak response efforts, including those related to Zika, healthcare-associated infections, measles, and hepatitis A. Dr. Watkins has over 40 peer-reviewed publications and over 20 years of experience in applied public health and epidemiology. Thank you for being here, Dr. Watkins.

Our second witness is Dr. Robin Robinson. Dr. Robinson is currently Vice President of Scientific Affairs for RenovaCare, Incorporated, directing development of cellular therapies for wound healing. Previously, he served as the first Director of the Biomedical Advanced Research and Development Authority, BARDA, and Deputy Assistant Secretary for Preparedness and Response from 2008 to 2016. He also served as BARDA's Influenza and Emerging Disease Program Director from 2004 to 2008. Dr. Robinson was the recipient of the Department of Defense Clay Dalrymple Award in 2008, the HHS (Department of Health and Human Services) Distinguished Service Award 3 times, and a finalist for the

Service to America Medal in 2009. Thank you for being here, Dr. Robinson.

As our witnesses should know, you will each have 5 minutes for your spoken testimony. Your written testimony will be included in the record for the hearing. When you have completed your spoken testimony, we will begin with questions. Each Member will have 5 minutes to question the panel. We'll start with Dr. Watkins.

TESTIMONY OF DR. SHARON M. WATKINS, PH.D., STATE EPIDEMIOLOGIST, DIRECTOR, BUREAU OF EPIDEMIOLOGY, PENNSYLVANIA DEPARTMENT OF HEALTH, AND PRESIDENT, COUNCIL OF STATE AND TERRITORIAL EPIDEMIOLOGISTS

Dr. WATKINS. Dr. Bera, Ranking Member Lucas, and Members of the Committee, thank you for the privilege to appear before you today. My name is Dr. Sharon Watkins, President of the Council of State and Territorial Epidemiologists, CSTE, and State Epidemiologist for the Pennsylvania Department of Health.

CSTE is an organization of 56 member States and territories representing applied public health epidemiologists or disease detectives. We work every day in partnership with CDC to detect and respond to influenza outbreaks, gain an understanding of potential changes in the virus, and deliver lifesaving vaccines. I have witnessed the devastating impact of seasonal influenza, the 2009 H1N1 pandemic, measles, and many other vaccine-preventable diseases in the communities I serve.

Public health threats require efficient, timely responses that rely on a network of public health agencies at all levels of government in coordination with healthcare providers. Response to outbreaks happens at the local level. Data on the age group affected, vaccination status, underlying illness, pregnancy status, and whether the outbreak is in a school or a long-term care facility, for example, are all needed to be able to rapidly identify where to respond and what is needed.

Unfortunately, this public health network is choked by antiquated data systems that rely on obsolete and sluggish data-sharing methods. Faxes and phone calls are still in widespread use. The system is in dire need of security upgrades. Lack of interoperability, reporting consistency, and data standards lead to errors in quality and completeness, timeliness, and communication.

I have stood before communities in crisis who are justifiably bewildered and angered that public health cannot access disease data or access it faster. "How is it that I can simply log into a portal and get my medical test results in a matter of minutes and you, who are charged with protecting public health don't have access to today's health data?"

It shocks people to learn that we do not have national coverage connecting hospital emergency departments (EDs) with public health surveillance systems. About 40 percent of all ED visits are not submitted to public health departments, leaving us flat-footed in identifying and responding to severe flu infections among high-risk groups, including pregnant women, children, and the elderly.

We are now entering flu season and are challenged by the concurrent outbreak of lung illness associated with e-cigarettes. Public

health is urgently deciphering faxed medical records to distinguish e-cigarette-related cases from flu cases. This information arrives piecemeal at different times through different channels. Try to decipher addendum 1 in my written testimony. It's a 4-page sample of a 350-page faxed medical record received by the Pennsylvania Department of Health on one of our e-cigarette cases. Providers already have this data shared and collected in electronic health records but cannot rapidly share these data with public health, who have no way to receive them electronically.

Death certificates are still filed on paper in some states, and only 63 percent of all death certificates are submitted to CDC for national aggregation within 10 days. Regrettably, most influenza-associated deaths occur in unvaccinated children, and it takes weeks to uncover and link the flu death with vaccination history, causing lags in communication to stakeholders who need answers to these questions.

CSTE and our partners, the Association for Public Health Laboratories, NAPHSIS (National Association for Public Health Statistics and Information Systems), and HIMSS (Healthcare Information and Management Systems Society), together with more than 90 other institutions, believe the time is now to step up and take a coordinated approach to building a 21st century public health data superhighway. The superhighway will collect health data from healthcare providers and report it automatically to public health departments and link it to other key data, including birth and death records and immunization registries and share that data seamlessly and securely with CDC.

The technology is here. What we really need are resources. That is why the proposed funding of $100 million that was included in the House Labor, Health, and Human Services appropriation bill to support data infrastructure at the CDC is urgently needed. During your ongoing deliberations, CSTE hopes you will consider the need for a modernized electronic interoperable public health data system and skilled public data health scientists to strengthen public health's best prevention strategy—vaccination. We recognize this effort must be funded with new money rather than cut already-underfunded public health. Without Federal support, public health surveillance modernization will remain unattainable, and the Nation will suffer.

We look forward to working with you, and I thank you for the opportunity to testify before you today.

[The prepared statement of Dr. Watkins follows:]

Written Testimony
House Committee on Science, Space, and Technology
Hearing on Fighting Flu, Saving Lives: Vaccine Science and Innovation
November 20, 2019

Statement of Sharon M. Watkins, PhD
President, Council of State and Territorial Epidemiologists
State Epidemiologist, Pennsylvania Department of Health

Chair Johnson, Ranking Member Lucas, and other members of the committee, thank you for the privilege to appear before you today. I am Sharon Watkins, President of the Council of State and Territorial Epidemiologists (CSTE) and State Epidemiologist for the Pennsylvania Department of Health. Thank you for the opportunity to testify before the Committee regarding "Fighting Flu, Saving Lives: Vaccine Science and Innovation." CSTE is an organization of 56 member states and territories representing applied public health epidemiology and serves as the professional home for 2,000 applied public health epidemiologists or "disease detectives" nationwide working tirelessly to respond to and protect the public's health. In my over 20 years as a public health professional I have witnessed the devastating impact of seasonal influenza, the 2009 H1N1 pandemic, measles, pertussis, and many other vaccine preventable disease (VPD) in the communities I serve. Throughout influenza seasons, state, local, tribal, and territorial health departments partner with clinical stakeholders and the Centers for Disease Control and Prevention (CDC), to conduct disease surveillance and gain a comprehensive understanding of when and where influenza is circulating, any potential changes in the virus that may lead to health disparities, work to contain outbreaks and deliver life-saving vaccine.

Whether it's influenza, measles, pertussis, Ebola, dengue, Zika, lead, hepatitis A, human papillomavirus (HPV), wildfires, tornados, or now the use of e-cigarettes, public health threats are persistent and constantly evolving here at home and overseas. Effective prevention and efficient, timely responses rely on an interactive network of governmental public health agencies

at the federal, state, local, tribal, and territorial levels working with health care providers and the public and private sector. Every day, this cooperative network saves lives by detecting and responding to influenza and other health threats, like *E. coli* contaminated lettuce, mumps, varicella, meningococcal meningitis, opioid overdoses, Zika, and more.

Unfortunately, this essential public health network is seriously disadvantaged by an antiquated public health data system that relies on obsolete information sharing methods including faxes and phone calls, and is in dire need of security upgrades. Lack of interoperability, reporting consistency, and data standards lead to errors in quality, completeness, timeliness, and communication. Sluggish, manual processes—paper records, phone calls, spreadsheets, and faxes requiring manual data entry—are *still in widespread use* and have important consequences, most notably delayed detection and response to influenza and public health threats of all types: chronic, emerging, and urgent. For reference, every week, the Pennsylvania Department of Health Bureau of Epidemiology that I direct receives over 250 faxed or paper case reports of disease requiring immediate review and processing before being sent on to the appropriate front line staff who contact impacted individuals to conduct interviews, implement control measures (like excluding children from daycares and schools to prevent others from becoming sick), identify risk factors for how they may have gotten sick, and compile and communicate the information to inform the public and policy makers. These 250 paper case reports are many pages long translating to 1000s of pages per week—critical test results including those for hepatitis A, STDs, HIV, childhood lead, and other diseases being communicated slowly and requiring multiple steps to process. Rapid advances in data science and evolving cybersecurity threats demand public health professionals stay up to date with current skills and tools to protect, defend privacy, and securely integrate health data.

In my experience on the front lines of public health emergency detection, prevention, and response as a public health epidemiologist in Florida during the 2009 H1N1 influenza pandemic, and now here in Pennsylvania, I have seen first-hand and heard from colleagues about the challenges and frustrations with the current data infrastructure to respond to influenza, VPDs, and other public health threats. I will share a few recent examples of those experiences with you.

Amid the outbreak of lung illness associated with e-cigarettes, distinguishing e-cigarette, or vaping, product use-associated lung injury (EVALI) cases from influenza infection as the virus begins to circulate widely is becoming increasingly challenging. Not to mention the added challenge of determining the impact of influenza co-infections among EVALI cases. Complicating the response around the country, is obtaining near-real time information about influenza vaccination status of suspected cases to further evaluate illness and impact of the vaccine among these now high-risk patients for influenza infection complications. Not only are our public health surveillance data systems not receiving information seamlessly from our immunization registries, but they are not operating in seamless interoperable ways with the healthcare community. Deciphering faxed reports and sifting through medical records to identify critical pieces of medical information like influenza vaccination status is time consuming. Review of radiographic imaging to distinguish injury from flu infection and other critical information is even more time-consuming, and all of these steps are frequently done in a piece meal approach as different bits of paper information arrive at different times and leads to lost opportunity and sometimes death. As evidence, I submit to you, and ask you to decipher as my disease detectives are doing daily, ADDENDUM 1, a typical sample four pages of an average 350-page medical record fax received by the Pennsylvania Department of Health on one of our EVALI cases.

Nationally, there is limited coverage and lack of full participation of emergency departments (ED) in public health syndromic surveillance systems, which inhibits our ability to rapidly identify changes in the severity of the influenza season. Unfortunately, approximately 40 percent of all ED visits are *not* submitted to public health departments and key information like pregnancy status is not systematically recorded or provided to public health; leaving public health professionals flat-footed in identifying and responding to severe influenza infections among high risk groups for influenza complications, including pregnant women—where despite the science, we see increased vaccine hesitancy. While the influenza vaccine isn't "perfect," it does significantly reduce severe complications—hospitalizations and deaths—especially among high risk groups like pregnant women, children, and the elderly. Hourly, real-time information about the number of people presenting to the ED for care as a result of an influenza infection can be powerful in communicating with the public to encourage vaccination. Additionally, key data sources like death data are not always electronically available to public health staff and are not available to be visualized in the national syndromic surveillance system alongside other data (e.g. ED data) further limiting the ability of public health to identify the severity of the season or outbreak early, even before final coding of death certificate data (which can take months). This gap in real-time ED data and limited use of advanced descriptive and predictive analytic tools, including artificial intelligence and machine learning to identify outbreaks early, as soon severe illnesses are occurring and well before thousands of deaths occur, is devastating, and demonstrates that the underlying obstruction to effective public health surveillance in magnitude and scope is not a technical limitation, rather it is a resource problem.

Death certificates were one of the first sources of public health surveillance data. When we look at influenza mortality data, every death certificate tells a story. Influenza mortality data

when viewed collectively, uncover health disparities, inform policy and funding decisions, and improve outbreak and disaster response efforts. Sadly, in some states, death certificates are still filed on paper, and nationally only 63 percent of all death certificates are submitted to CDC for national aggregation within 10 days (https://www.cdc.gov/surveillance/pdfs/Tracking-Deaths-protects-healthh.pdf); and while improved, 10 days is still too long, and it typically takes weeks to months to have final influenza season death estimates. Then, even after the data are received, it is fragmented and unconnected to vaccination information, leading to missed opportunities to understand and evaluate vaccine effectiveness. Tragically, each year, most pediatric influenza deaths occur in unvaccinated children, but it can take weeks to uncover and link the influenza death information with vaccination history (or medical examiner information which is not linked with death registration systems) in order to communicate meaningful information to policymakers, the media, the public, and providers who need answers to questions—where did the deaths occur and what populations are most vulnerable? What immediate steps can be taken to prevent more deaths based on today's data? Unfortunately, because of the lag in paper-based data systems and lags caused by the non-integration of key public health data systems, public health officials are hampered to provide fast, high-quality answers the public wants, needs, and expects in our technologically capable world.

Nationally, there have already been dozens of influenza outbreaks in skilled nursing and long-term care facilities this influenza season already. Despite clear public health recommendations to vaccinate staff and residents in these facilities, when investigating outbreaks, unfortunately we consistently find under vaccination among residents, staff, and their family member visitors. In Pennsylvania, our population is aging, and we have over 80,000 citizens residing in over 700 nursing homes. In the 2018-19 flu season, we had 284 outbreaks

among these facilities impacting more than 3400 residents and staff and our data indicated that only 69 percent of staff and 78 percent of residents were vaccinated among those long-term care facilities (for which data were available). Much of the data related to these outbreaks required significant back and forth follow-up to obtain the data needed to understand the outbreak. Making these investigations more challenging is the time needed to collect vaccination information from the facility—often provided on hand-written line-lists or paper records which may be faxed to public health or sent as pdfs, if at all, and the make recommendations. Obtaining and linking the vaccination information delays administration of life-saving vaccine given as prophylactic treatment following an outbreak. Time spent in finding records, review of paper records, and manual and duplicate entry of data is time that public health could be spending addressing recommendations to the facility, their residents, and visitors; and this is true across all outbreak types.

During the 2009 H1N1 influenza pandemic or any of the hundreds of influenza related outbreaks that occur each year in schools, assisted living or nursing facilities, samples must be collected for specialized testing at the state laboratories. Influenza viral strain surveillance is a key component of our public health surveillance and vaccine development approach to determine if key changes or mutations to the virus have occurred. These highly specialized laboratory tests are only able to be performed in state public health laboratories or at the CDC due to availability of necessary reagents and state of the art diagnostics. Unfortunately, the CDC and nearly all state public health laboratories have no data system to order a laboratory test electronically. Thus, when samples are sent for specialized testing, they are accompanied only by paper order forms – there is no electronic method to track the process: if the sample has been sent, for submitters or epidemiologists to know if the state or the CDC laboratories received it, the quality and viability

of the sample on arrival, where the sample is located prior to testing, or when testing and results are anticipated. And once results are available, there is no electronic process to rapidly communicate those results back to submitters.

- Laboratories are often not notified of incoming orders and samples. Laboratories cannot anticipate or plan for staffing capacity, surge, or what types of tests will need to be completed until the sample arrives. Staff are unaware when a specimen is lost or does not arrive.
- Thousands of samples come through a laboratory, and each must be manually accepted and entered by staff. During the 2018-19 moderate influenza season US public health laboratories collectively tested 80,993 specimens (https://www.cdc.gov/mmwr/volumes/68/wr/mm6824a3.htm). When data are missing, staff must contact submitters to complete or verify the information— which is time-consuming and error-prone.
- Order information is not linked to vaccine histories or epidemiologic surveillance systems, where risk factor information about persons under investigation is stored.

These processes and modes of data sharing are slow, cumbersome, and make it logistically impossible to respond effectively to the speed and intensity with which the influenza seasons or the 2009 H1N1 pandemic hit.

In August of this year, Pennsylvania experienced its 14th measles case of 2019 (https://www.media.pa.gov/Pages/Health-Details.aspx?newsid=642) with over 1250 measles cases reported nationally this year and the most since 1992 (https://www.cdc.gov/measles/cases-outbreaks.html). As of November, we have had 17 cases in Pennsylvania. In response to these

cases, we have identified 1,000s of close contacts and exposures, and for each contact or exposed person, needed to rapidly determine vaccination status in an unconnected world where health data is not shared or easily accessible to public health. Hundreds of exposures are common for each case and gathering vaccination history or rapidly testing for immune status, must all be done quickly, before prophylaxis is no longer possible and quarantine is considered. We collect and review detailed travel and location histories for cases (see timeline for potential exposure locations (https://www.media.pa.gov/Pages/Health-Details.aspx?newsid=642), and then collect and manually connect lists of hundreds of individuals potentially exposed by being at the same location or venue. Why? Because key electronic data systems storing health care visits, epidemiologic, laboratory and immunization data had no way to seamlessly share the information and speed the response. When vaccine status or immune status cannot be confirmed, or confirmed in time, quarantine occurs. Without rapid access and connectivity of health data, unnecessary testing and quarantine can occur, leading to strains on public health resources and budgets, potential lost wages for citizens, and lost productivity for the community and workplace.

Clear information about availability of influenza vaccine becomes paramount during flu season and especially during seasons of more severe activity or when supply chain issues impact delivery. In Pennsylvania and across public health we work vigorously to respond, activating our emergency operations center, conducting frequent calls with public health and the health care community, issuing health advisory notices to providers, and issuing press releases to keep the public informed about influenza disease occurrence, vaccine availability and uptake. It is confusing to the public about when and where to get vaccinated with differing options for convenience or coverage. Parents may delay getting children vaccinated due to the increased

challenge of scheduling a specific provider office visit, but our public health messaging, driven by science and data should provide clear messages and motivation. However, with disease data dragging, our fragmented public health surveillance system constricts our ability to implement timely life-saving interventions.

Finally, our focus today is on influenza and vaccination innovation, but as a public health professional who works across disciplines, I must reflect these public health data challenges are broad and systemic and hamper our public health responses beyond influenza and vaccine development to other critical but non-infectious disease threats. When I reflect upon some of the recent public health emergencies, such as Zika, the opioid epidemic, and now e-cigarettes and EVALI, one of the common critical stumbling blocks to rapid response has centered on data collection, data management, and data sharing. I fear that this will continue and worsen, unless investment in data infrastructure occurs across all of public health. To provide one such example, in Pennsylvania, we were working in concert with CDC and the Agency for Toxic Substances and Disease Registry (ATSDR), responding to a manufacturing plant that had released lead into the air in a community that understandably wants answers about their health: What are our blood levels? How many people and children have been tested? How do they compare to other communities? Does my child need to be tested? Unfortunately, those questions couldn't be quickly or adequately answered with today's data, because, like with influenza, while health care facilities have data stored in electronic medical records, data are sent on paper to the public health department and the stacks take time to enter and process. Included as ADDENDUM 2 are examples of the millions of hand-written, paper lead lab reports that I received while in Florida and now in Pennsylvania.

These modes of data sharing are slow and cumbersome. They are also vulnerable. With sophisticated cybersecurity threats, it is critical that public health systems are equipped to prevent and respond to cyberattacks. Health care providers are *required* to report diseases and conditions to public health departments. These health records contain sensitive personal information—required to be reported and protected by state laws—and they demand significant care in handling to protect the privacy and safety of patients, particularly since such systems are frequently the target of hackers.

The nation's public health infrastructure is so fragmented and antiquated that health care providers who *already have the data stored and collected in electronic health records* cannot rapidly share these health data because public health departments cannot receive them electronically. This environment leads to an increased burden on providers to report—or delays and failures to report—and inefficiency and frustration on the part of patients, care providers and public health professionals. It leads to lost time, lost opportunities, and lost lives. In any outbreak, time matters—whether the issue is vaccine and prophylactic treatment following meningococcal exposure, which needs to be rapidly disseminated, or measles cases who need to be isolated to prevent others from becoming infected, or where vaccine effectiveness to prevent pertussis needs to be evaluated for both children and adults, or where influenza threatens the lives of pregnant mothers and their babies. Most importantly, data matters. I have stood before communities who are justifiably bewildered and angered that public health cannot access data or access it faster. "Why can I simply log into a portal and get my medical test results and history in a matter of minutes and you, who are charged with protecting public health, don't seem to have access to or the systems to get today's health data?"

Public health professionals, providers, policymakers, and the public will all agree that to halt influenza and foster vaccine development and innovation (be it Zika, dengue, malaria, Lyme or Ebola), we need more, better, faster, and secure data to protect the public's health. To date, in the demand for better data, we have taken a piecemeal, fragmented approach to funding our public health data infrastructure. When a new disease emerges, such as 2009 H1N1, Congress has funded standalone data systems at CDC to support the response. But this funding approach is inconsistent and does not support an invested, sustainable enterprise approach in detection and prevention *before* an event occurs. While Congress's support and funding during emergencies is critical to support a response, a well-planned, long-term, optimal data collection and data system management are necessary and cannot be approached as 'one and done.'

CSTE and our partners—the Association for Public Health Laboratories (APHL), the National Association for Public Health Statistics and Information System (NAPHSIS), and the Healthcare Information and Management Systems Society (HIMSS)—together with more than 90 other institutions representing patients and consumers, public health professionals, health care providers, and health systems believe the time has come to step up and take a coordinated, comprehensive, strategic approach to building a public health data super highway of the 21st Century to speed the seamless exchange of data for all diseases and conditions, to *predict* and *prevent* public health threats before they occur and to allow rapid response when they do occur. This interstate system of systems will seamlessly and securely collect sensitive data about diseases and conditions from health care providers and report it automatically to public health departments, link it to other key data—including birth and death records and immunization registries—and where required to be reported nationally, share that data seamlessly and securely with CDC.

And while our proposed *approach to funding* this IT modernization is new, what we're proposing isn't. The data systems that feed this public health information superhighway already exist, have demonstrated value, and are used to varying degrees in all state and local public health departments. What we need is to bring all jurisdictions online with all of these systems, and to modernize receiving, sharing, and connecting data that exists in silos. In addition, CDC needs its own secure data platform to receive data electronically from the states via the National Notifiable Disease Surveillance System. For further information about the need to modernize the public health data systems and workforce, please see CSTE's newly released a new report, "Driving Public Health in the Fast Lane: The Urgent Need for a 21st Century Data Superhighway" at http://resources.cste.org/data-superhighway/mobile/index.html.

To support this essential infrastructure and modernize public health data, several Congressional initiatives have been introduced. H.R.2741 the *Leading Infrastructure for Tomorrow's America Act,* includes Section 45001 on public health data system transformation. In the Senate, S. 1793, the *Saving Lives Through Better Data Act* and Section 405 of S. 1895 the *Lowering Health Care Costs Act* would give CDC the authority to expand and modernize public health data systems and allow for more, better, faster, secure data to track public health events like influenza outbreaks, vaccination rates, and e-cigarette illness. This modernization of CDC's data systems is essential for public health departments like mine to be able to share and report data in a timely and practical manor.

However, what we really need to make this happen are resources. This is why the proposed funding of $100 million to support better data infrastructure at the CDC that was included in the House Labor, Health and Human Services Appropriations bill is urgently needed.

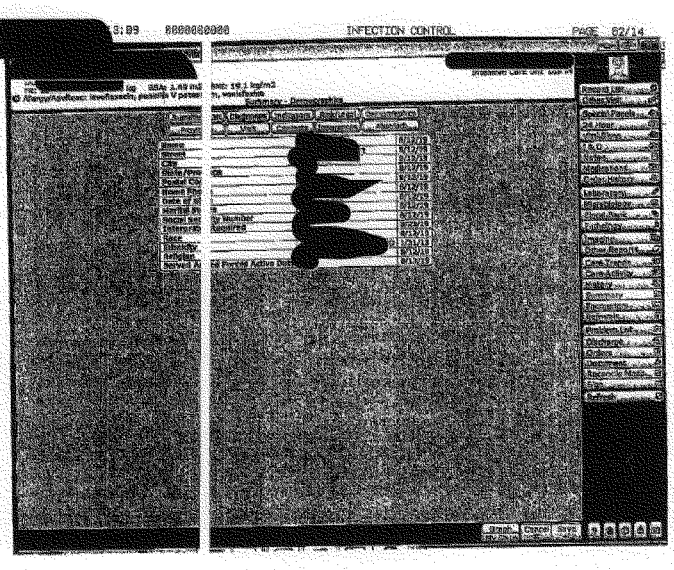
This is an essential first installment towards a more robust and effective data superhighway in the US.

Our nation requires a modernized, electronic, interoperable, enterprise public health data system and a new generation of skilled public health data scientists. We strongly urge you to prioritize and support a public health surveillance enterprise that will speed the data collection and response for current and future public health threats.

In a world where travel across the globe can be accomplished within 36 hours, the demands for public health surveillance have changed dramatically over the past several decades and we need to ensure we are protecting the public's health in the way the public wants and needs to be protected. Diseases can have infectious and non-infectious consequences (Zika), old diseases re-emerge (measles), life threatening genetic changes or mutations (influenza), and common behaviors can have sudden and devastating impacts (EVALI) and public health must be able to rapidly respond. Aging data infrastructure is hampering our responses and it cannot be improved without widespread investment. CSTE hopes in your ongoing deliberations about fostering the critical science of vaccine development and use, you will consider the foundational need for a modernized, electronic, interoperable public health data system, a new generation of skilled public health data scientists, and their necessity to optimally evaluate one of public health's best prevention and control strategies (vaccination). We recognize this effort must be funded with *new* money, rather than cut already underfunded public health programs. Without federal support, public health surveillance modernization will remain unattainable and the health of the nation will suffer. The technology is available to develop the enterprise public health data superhighway, but new, consistent, reliable and sustained investments are needed to improve the health of the nation. A robust, sustained commitment to transform today's public health data

system will ultimately improve Americans' health. We look forward to working with the Committee in these endeavors and hope you will turn to the CSTE as a resource in the future. Thank you very much for the opportunity to testify before you today.

ADDENDUM 1: Redacted Example of Typical 350-page Fax Received by PA Public Health Officials



Example faxes of medical records received by public health officials in Pennsylvania for individuals under investigation for severe lung illness associated with e cigarettes; these medical records are individually reviewed by public health disease detectives to determine if the ill indivdual is part of the outbreak associated with e cigarettes.

Note records have been redacted here to protect patient confentiality.

[redacted]

apprec ortho
"**Addendum**[redacted] or [redacted]

EXAM: MR [redacted]

HISTORY: Weakness

TECHNIQUE: MRI of the [redacted] utilizing the following sequences: axial T2, coronal oblique T1, coronal oblique T2 with fat saturation, and sagittal T with fat saturation.

COMPARISON: Plain films dat 08[redacted]/2019

FINDINGS: No fracture or destr tive bony lesion. No significant arthropathy of the glenohumeral joint with AC joint. There is a tubular T2 hyperinten finding measuring about 2.4 x 0.6 x 0.7 cm along the anterior supraspinatus myotendinous area. This is nonspecific howev may reflect the sequela of myotendinous injury. More distally however no tearing of the rotator cuff tendon insertions or thology otherwise is clearly identified. Long head of biceps appears to be in normal anatomical patient. There is inst sically limited evaluation of the glenoid labrum without performing an arthrogram however no labral pathology is clearly su ected..

IMPRESSION:
Area of T2 hyperintensity in the upraspinatus myotendinous area as outlined suspicious for the sequelae of a myotendinous injury noting the actual rotator c f tendon insertions themselves appear to be within normal limits.
Workstation ID : [redacted]

After review of MRI findings w [redacted] we make the following changes to our recommendations:

1. Continue with neurology co sult as recommended previously.
2. No need for sling immobiliz ion as there are no signs of [redacted] instability on MRI today. Recommend PT for the left shoulder while she rer ains inpatient and as an outpatient as well. Increase shoulder movement as tolerated.
3. Follow-up with us in 2-3 we ks after discharge for ongoing evaluation.

Please contact us with any qu stions or concerns. I did discuss this plan with [redacted] at [redacted] pm today. "

apprec ID
"**Impression and Plan**
Problem List:
(1) Hypoxemia
(2) Multilobar lung infiltrate
Impression and Plan: clinic y better, Ct neg for abscesses
Leucocytosis and thrombocyt sis improving
Stable off of antibiotics, rash l ely acneform, as she says she gets them
Will sign off
Pl call us if we can help
Thank you

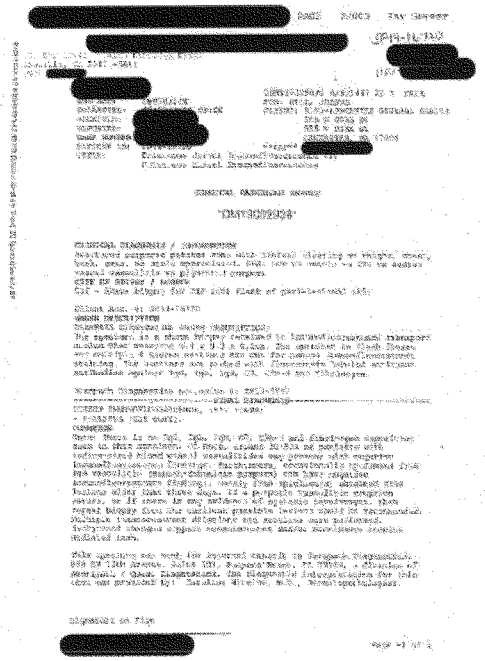
[redacted] [redacted]

[redacted] [redacted] PAGE 2/130 Fax Server

[redacted] Encounter Date: [redacted]

Order-Level Scanned Encounter Result(s) - [redacted]

Scan on [redacted] - PATHOLOGY RESULTS (below)



[redacted] Page 1 of 6

PM

[redacted] Encounter Date: [redacted]

Order-Level Scanned Encounter Result(s) [redacted] (continued)

[redacted]

Patient Name: [redacted] Procedure Date: [redacted]
MRN: Date of Birth:
Procedure Date No Time: [redacted]

Procedure Name: Bronchoscopy
Indications/Preoperative Diagnosis: Atelectasis of the left upper lobe, Atelectasis of the left lower lobe, Atelectasis of the right middle lobe, Atelectasis of the right lower lobe, Bilateral atelectasis
Providers: [redacted] (Doctor)
Referring MD:
Requesting Physician:
Complications: No immediate complications

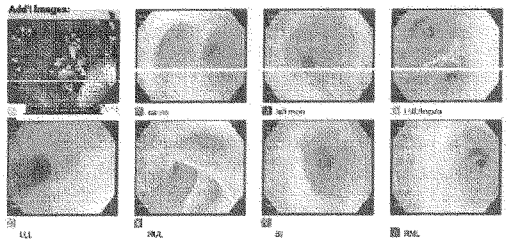
Impression/Postoperative Diagnosis: Bilateral infiltrates, FUO
Recommendation: - Await BAL, biopsy, brushing, culture and cytology results.
Procedure: Pre-Anesthesia Assessment:
- The anesthesia plan was to use general anesthesia.
After obtaining informed consent, the Bronchoscope was introduced through the mouth, via laryngeal mask airway and advanced to the tracheobronchial tree of both lungs. The procedure was accomplished without difficulty. The patient tolerated the procedure well.

Findings:

Vocal cords appeared normal. Mucosa appeared normal without any cobblestoning or lesions. No endobronchial lesions, minimal clear secretions. BAL done in all lobes, Return was clear. Brushings done in RML and RLL. Transbronchial biopsies done in RML and RLL. No bleeding, patient tolerated procedure well

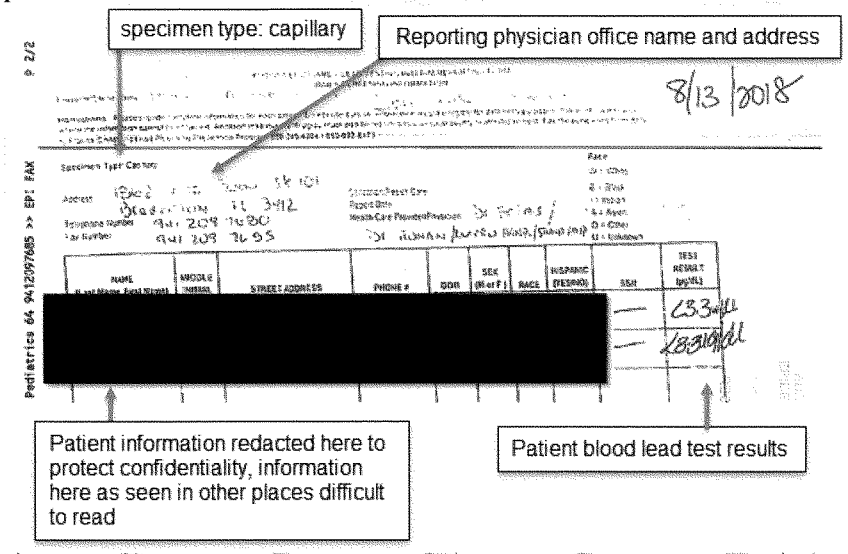
Estimated Blood Loss: Estimated blood loss: none.

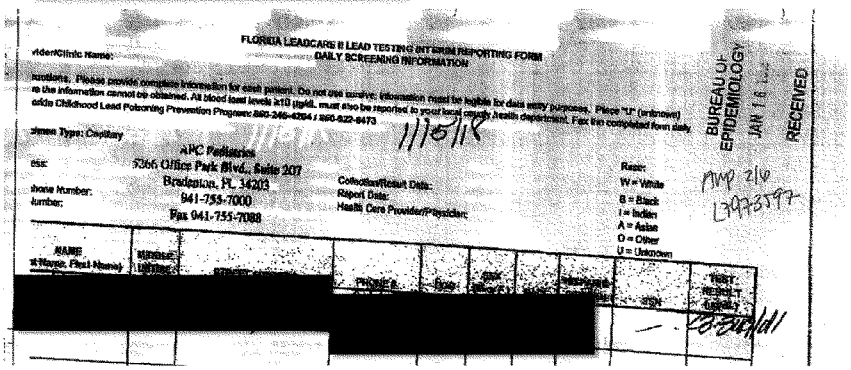
Add'l Images:



ADDENDUM 2

Example: Lead test results received by the Florida Department of Health as submitted by a private provider to fulfill required lead test result reporting, August 2018, January 2019. Patient information, test results, and reporting provider information difficult to read and creates delays in identifying the patient as well as recording the data in the health departments data system necessary to identify any community increases in blood lead, respond and implement control measures. **While these examples are lead data, data across all diseases and conditions including influenza are regularly submitted and received via paper by private providers to public health.**





Sharon Watkins, PhD
Director, Bureau of Epidemiology and State Epidemiologist
Pennsylvania Department of Health
President, Council of State and Territorial Epidemiologists

Dr. Sharon Watkins joined the Pennsylvania Department of Health in November 2015. She is the Director for the Bureau of Epidemiology and the State Epidemiologist and is responsible for the management and oversight of the Bureau which includes the Division of Infectious Disease, Environmental Health, and Community Health. Dr. Watkins is a graduate of Ohio State University and specialized in Epidemiology, Environmental Epidemiology, and Perinatal/Maternal & Child Epidemiology. Prior to joining Pennsylvania, she has served as Chief for the Bureau of Epidemiology and as Director of Public Health Research for the Florida Department of Health.

Since coming to Pennsylvania, she has led disease surveillance and outbreak response efforts including those related to Zika virus, healthcare associated infections, measles, hepatitis A and many others. Noninfectious efforts underway in the bureau being led by Dr. Watkins include neonatal abstinence syndrome surveillance, Zika related birth defects registry, surveillance of childhood and adult blood lead levels, public health response to water contamination with Per- and polyfluoroalkyl substances (PFAS), community cancer concerns, and the current response to severe lung injuries related to vaping. Dr. Watkins has over 40 peer reviewed publications and over 20 years of experience in Applied Public Health and Epidemiology. She has served as an elected Executive Board member of the Council of State and Territorial Epidemiologists since 2012 and is the current president.

Mr. BERA. Thank you. Dr. Robinson.

TESTIMONY OF DR. ROBIN ROBINSON, PH.D., VICE PRESIDENT OF SCIENTIFIC AFFAIRS, RENOVACARE, AND FORMER DIRECTOR, BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. ROBINSON. Good morning. Thank you, acting Chairman and Ranking Member Lucas and distinguished Members of the Committee. Thank you for the opportunity to speak with you today. I'm Dr. Robin Robinson, currently the Vice President of Scientific Affairs at RenovaCare, the former Director of BARDA, and the DAS (Deputy Assistant Secretary) at ASPR (Assistant Secretary for Preparedness and Response), and a developer of influenza vaccines in industry.

Four years ago I testified as the BARDA Director before the House on the state of affairs for seasonal influenza during a harsh season and what we could do to remedy mismatched flu vaccines. Since that time, seasonal influenza has returned each year and brought illness and death despite our medicine cabinet full of vaccines and antivirals.

New influenza vaccines with adjuvants and a fourth strain of influenza vaccines and a new class of antivirals were added since 2015. Yet we still have not solved the chief issue with influenza vaccines—poor effectiveness.

Our domestic capacity to produce pandemic influenza vaccines has quadrupled since 2005 thanks to our investments in new cell and recombinant-based production technologies. However, our ability to manufacture and make available pandemic influenza vaccines are not fast enough to preempt pandemic peak effects.

Last, many universal influenza vaccine candidates have emerged over the past 40 years but none have crossed the finish line. Today, I wish to address poor vaccine effectiveness, slow vaccine production, and elusiveness of universal influenza vaccines.

Vaccine effectiveness and universal influenza vaccines are both dependent on the selection of viral antigens that can elicit long-lasting, broad, and strong immuno-protective responses across many different influenza virus subtypes. An ideal universal influenza vaccine would elicit strong and lasting immunity against currently circulating and drifted strains of seasonal influenza viruses to obviate the need for annual immunization against seasonal influenza and serve as a vaccine primer for pandemics.

The story of universal influenza vaccine development is long and woeful. For the past 40 years, multiple ways of innovation have driven universal influenza vaccine development. One of the earliest and most expensive efforts was by Merck in the 1980s and 1990s focusing on vaccines comprised of the highly conserved influenza M2 matrix protein. However, the M2 vaccine candidates were poorly immunogenic. Next, vaccine candidates targeted the highly conserved MP, and NS2 proteins were developed and shown to be poorly immunogenic as well.

The story changed with two discoveries, one of which Dr. Fauci mentioned earlier, made this decade. Antibodies were discovered in 2011 to specific epitopes on the conserved stem portion of the viral

hemagglutinin protein and shown to bind and neutralize widely diverse influenza viruses. This discovery has led to a new development wave of chimeric hemagglutinin and hemagglutinin stem vaccine candidates that are undergoing clinical evaluation presently.

The other discovery, which occurred this year, was the finding of antibodies to conserve epitopes on the viral neuraminidase protein, which has been a target for antivirals for many years. These antibodies bind and neutralize widely diverse influenza viruses. This discovery will likely initiate another wave of vaccines that scientists will likely include this specific neuraminidase protein in their next generation of flu vaccine candidates.

On the issue of more rapid production of influenza vaccines, new synthetic messenger RNA (mRNA) vaccine technology may expedite vaccine production. Since mRNA vaccines do not require the isolation, adaption, and production of viral vaccine stocks like the current egg and cell-based influenza vaccines, weeks to months may be saved in vaccine production. This time savings may allow the late production of seasonal influenza vaccine strains when a mismatch occurs between circulating influenza viruses and seasonal influenza vaccines.

Similarly, the production time for 600 million doses of pandemic influenza vaccine may be reduced from 6 months to 3 months and become available before the pandemic peaks. As added value of messenger RNA vaccines may be a faster and easier way to distribute and administer these vaccines. Many messenger RNA vaccines are encapsulated in liposomes or nanoparticles, as Dr. Fauci stated, and which may intrinsically have adjuvant properties and the ability to administer vaccines transdermally, hence trading a syringe and needle for a self-administered patch.

None of these innovations and discoveries will make it into the influenza vaccines of the 2020s without immediate and sustained multiyear funding and authorities to NIH, BARDA, FDA, and CDC to execute with industry partners the pandemic plans of yesterday and today. Your continued wisdom, generosity, and support have carried us this far. Help us finish the journey. Thank you.

[The prepared statement of Dr. Robinson follows:]

	Written Testimony **Committee on Science, Space, and Technology** **United States House of Representatives**

"Fighting Flu, Saving Lives: Vaccine Science and Innovation"

Statement of

Robin A. Robinson, Ph.D.

Vice President, Scientific Affairs, RenovaCare, Inc.
Former Deputy Assistant Secretary and BARDA Director
Office of the Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services

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Introduction

Good morning Chairwoman Johnson, Ranking Member Lucas, and distinguished Members of the Committee. Thank you for the invitation to opine on medical countermeasure (MCM) preparedness and response efforts for seasonal and pandemic influenza. I am Dr. Robin Robinson, current Vice President of Scientific Affairs at RenovaCare, Inc. and former Director of the Biomedical Advanced Research and Development Authority (BARDA) and Deputy Assistant Secretary to the Assistant Secretary for Preparedness and Response (ASPR) at the Department of Health and Human Services (HHS). I look forward to talking with you about our technological advancements, prospects, and challenges with influenza vaccines and their effects on seasonal and pandemic influenza preparedness.

Over the past 27 years I have devoted my professional career to the development, improvement, innovation, and production of vaccines for existing and emerging infectious diseases. Much of that effort spent in the private sector and federal government service was devoted to inventing new influenza vaccines; stimulating vaccine innovations; providing resources for the development and commercialization of new cell-and recombinant-based seasonal and pandemic influenza vaccines and new seasonal and pandemic influenza vaccines containing adjuvants; building national stockpiles of pre-pandemic influenza vaccines ensuring national and public health security; and expanding domestic and international influenza vaccine manufacturing capacity for pandemics.

Vaccines are one on man's greatest achievements and a cornerstone to today's public health preparedness and response. Without vaccines and public health programs, catastrophic diseases

such as smallpox would continue to wipe out large populations upon introduction to the virus; childhood diseases such as diphtheria, pertussis, tetanus, measles, mumps, rubella, Hemophilus influenza, and others would decimate our youngest and most vulnerable populations; and our elderly population would suffer and decline more rapidly without vaccines for pneumococcal, zoster, and influenza vaccines. However, there are still glaring gaps in our vaccine armory against existing major diseases such as human immunodeficiency virus, hepatitis C virus, malaria, and respiratory syncytial virus. Additionally, more effective vaccines delivering longer lasting immunity for influenza remain elusive. Lastly vaccines for newly emerging pathogens such as Zika virus and other pathogens are only reaching clinical development.

Seasonal influenza epidemics occur every year. However, periodically a novel influenza virus strain, for which there is little human immunity, will emerge and cause a global pandemic like the 2009 H1N1 pandemic, or worse, the pandemic of 1918. Because influenza viruses mutate as they spread and reassort primarily among birds, swine, and humans, achieving protection against seasonal influenza viruses is a significant challenge. Means to control and address the medical and public health consequences of influenza include social distancing, proper hygiene practices, vaccination, antiviral drugs, and diagnostics. In the last decade, we have been repeatedly reminded about the complexity of managing seasonal and pandemic influenza both globally and nationally. The most recent examples include the seasonal influenza vaccine mismatch to the antigenically drifted H3N2 virus during the 2014-2015 influenza season and the avian influenza H5 viruses that killed millions of domestic birds in the Midwest in 2015.

The evolution of influenza vaccines over the past 50 years has witnessed many vaccines starting with inactivated whole virion influenza virus vaccines produced in eggs in the 1970s to a less reactogenic and more purified inactivated egg-based split, subunit influenza vaccines in the 1980s that enriched for the major immunodominant viral hemagglutinin protein. By the end of the millennium, the influenza vaccine industry had compressed from as many as 12 manufacturers to less than four in the U.S. The emergence of highly lethal H5N1 avian influenza viruses from Asia in 1999-2004 for man and birds, including chickens used for vaccine manufacturing highlighted the vulnerability of the influenza vaccine infrastructure and public health preparedness to address potential influenza pandemics. The potential devastation was brought into better focus y 2005 as we understood the catastrophic socio-economic and medical effects of the 1918 influenza pandemic and our the poor immunogenicity of candidate H5N1 vaccine candidates produced by the usual means. These results informed the *National Strategy for Pandemic Influenza* (2005) that laid the game plan to stimulate the development new influenza vaccines using modern technologies; establishment of pre-pandemic influenza vaccine stockpiles for high risk individuals; and expansion of domestic influenza vaccine manufacturing capacity. Through the enactment of $5.6 billion appropriated (2005) to carry out the *HHS Pandemic Influenza Plan* and All Hazards Preparedness Act (2006), this strategic plan became operational with the necessary funding and authorizations, including the creation of the BARDA within HHS to carry out these programs.

Before results of these new influenza vaccine programs could even be realized, the H1N1 influenza pandemic emerged (2009). Dependence on egg-based influenza vaccines, their associated manufacturing infrastructure, and newly implemented pandemic preparedness

capabilities were tested and received mixed marks. Lessons learned from the H1N1 pandemic resulted in the President's Council of Advisors on Science and Technology's (PCAST) *Report to the President on Reengineering the Influenza Vaccine Production Enterprise to Meet the Challenges of Pandemic Influenza* (2010), which recommended improvements in virus surveillance, in vaccine research and development, and in influenza vaccine manufacturing. As a call to action, HHS reviewed and revised existing plans to develop new influenza vaccines, antiviral drugs, and diagnostics; to assess the size, composition, and usage of influenza vaccine and antiviral drug stockpiles; and to expand our domestic influenza vaccine manufacturing infrastructure and capacity. The common thread throughout these revised preparedness and response plans was that seasonal and pandemic influenza are inextricably interwoven; what we do in one area directly affects what we do in the other.

Following the release of the Department's 2010 *PHEMCE Review* and the PCAST report (2010), HHS adjusted and took steps to execute the pandemic influenza preparedness priorities enumerated in the review and report. Significant progress improving vaccines and manufacturing technologies occurred in the first half of this decade. Specifically, the federal government has partnered with industry to achieve the following:

- Modernization of influenza vaccine manufacturing systems through the development and licensure of new cell- and recombinant-based influenza vaccines as well as antigen-sparing vaccines using adjuvants.
    - Flucelvax (2012), the first cell-based seasonal influenza vaccine in the U.S.

- FluBlok (2013), the first recombinant-based seasonal influenza vaccine in the U.S.,
- Q-Pan H5N1 vaccine (2013), the first adjuvanted pandemic influenza vaccine in the U.S.
- Fluad seasonal influenza vaccine (2015), an adjuvanted seasonal influenza vaccine for seniors in the U.S.;

- With NIH, CDC, and FDA, BARDA launched the Influenza Vaccine Manufacturing Improvement (IVMI) initiative, as recommended by PCAST to optimize the generation of high yielding vaccine seed strains and alternative potency and sterility assays, to expedite influenza vaccine availability. The IVMI initiative improvements cut weeks off the vaccine manufacturing process and increased production yields;
- Establishment and maintenance of pre-pandemic influenza vaccine stockpiles for H5N1 and H7N9 viruses with pandemic potential to rapidly immunize the critical workforce at the onset of an influenza pandemic. Clinical trials showed that vaccine stockpiles remained highly immunogenic even those stored for ten years. In parallel, BARDA and CDC developed and implemented the Influenza Risk Assessment Tool (IRAT) in 2010 to inform the composition and prioritization of vaccines in these stockpiles;
- Multi-fold expansion of domestic influenza vaccine production for pandemic preparedness was afforded by retrofitting older egg-based vaccine manufacturing plants (2007-2011 and 2017) and the building new state-of-the art, award-winning cell-based vaccine manufacturing facilities (2009-2012) through public-private partnerships with industry leading to a domestic vaccine manufacturing capacity able to produce enough pandemic influenza vaccine for the U.S. in six months;

- Establishment of a national infrastructure including the Centers for Innovation and Advanced Development and Manufacturing (CIADM) to rapidly develop, manufacture, and test new influenza vaccines and medical countermeasures for emerging infectious diseases, such as Ebola. This infrastructure responded in 2013 and 2018 with the development, production, testing, and stockpiling of H7N9 influenza vaccines and more recently Ebola vaccine and monoclonal antibody therapeutic candidates in 2014-2015; and
- Establishment of a global vaccine manufacturing infrastructure with the World Health Organization (WHO) in 2006 in eleven (11) developing countries to make pandemic influenza vaccines and vaccines for other diseases. This initiative has resulted in the establishment of manufacturing facilities making more than four licensed influenza vaccines with a current capacity to produce more than billion doses of pandemic influenza vaccine.

On the seasonal influenza front, HHS responded to the H3N2 antigenic drift and seasonal influenza vaccine mismatch in 2014-2015 by tasking the Department's senior influenza leaders and experts to provide a comprehensive set of recommendations to the former HHS Secretary on how to address the issue of vaccine mismatch in the near and long term. HHS convened numerous meetings from December 2014 through May 2015 with internal and external influenza and vaccine experts from government, industry, and academia to understand the complexities of virus antigenic drift, vaccine mismatch, and influenza vaccine manufacturing and how seasonal vaccines and their manufacturing may be changed to accommodate this type of virus variance. In May 2015, senior HHS influenza leaders provided a set of twenty (20) recommendations to

HHS leadership that may improve virus surveillance and characterization, vaccine design, vaccine manufacturing, vaccine availability and distribution, and ultimately vaccine effectiveness. In June 2015, BARDA hosted a meeting with the influenza vaccine manufacturers constituting the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) and with representatives from the WHO, the government of the United Kingdom, HHS agencies, and others to review current influenza epidemiology. This review recommended improving responses to seasonal influenza vaccine mismatches, exercises simulating the 2014-2015 seasonal influenza antigenic drift and vaccine mismatch, and ways to reduce timelines for production of a new seasonal influenza vaccine. Many of these recommendations were adopted, implemented, and assimilated into the way influenza vaccine manufacturers and federal agencies deal with the late emergence of seasonal influenza viruses mismatched to newly produced influenza vaccines.

While the recent introduction of quadrivalent, high-dose, and novel seasonal influenza vaccines by vaccine manufacturers represents incremental progress towards more effective influenza vaccines, the efficacy of seasonal influenza vaccines remains much lower than our expectations and needs. Significant technical challenges before a substantially more effective influenza vaccine is available. Despite the best efforts of the influenza scientists, the vaccine industry and the government, especially at NIH, CDC, and BARDA, the "holy grail" of influenza vaccines – a universal influenza vaccine- remains elusive.

The discovery of antibodies in 2011 to conserved epitopes on the stem region of the influenza hemagglutinin protein the major immunodominant viral protein responsible for virus attachment

and the major component of influenza vaccines, has led to the development of many chimeric and headless influenza vaccine candidates using different platform expression technologies and their clinical evaluation presently. The discovery of antibodies this year to the influenza neuraminidase protein, which enables virus budding from infected cells and serves as a major target for influenza antiviral drugs, showed neutralization against a broad spectrum of different influenza subtypes; the inclusion of both HA and NA that include these special conserved epitopes will likely serve as a new source of influenza vaccine candidates that may be more effective and provide longer immunity.

BARDA and NIH are working together to foster collaborations with academia and industry in pursuit of more effective influenza vaccines. New evolutionary biology methods such as antigen cartography may be able to predict influenza virus evolution better and understand immune responses to the influenza viral hemagglutinin (HA) proteins from genetically distinct viruses better. By generating specific and random influenza virus mutants to seasonal and pandemic influenza viruses, the evolutionary trend for new virus strains may be understood better and thus may inform vaccine strain selection. With these results, future vaccine candidates may be designed using this forward-looking information and may provide more effective vaccines through what is called "back-boost" vaccine immunity.

Other waves of innovations and technologies since the start of the millennium have provided already started to fill some vaccine gaps. Contemporary vaccine innovations over the past 20 years have included the usage of new adjuvants in vaccines for human papillomavirus and

influenza to enhance and expand protective immunity; making new influenza vaccines in tissue culture cells and by recombinant technologies rather than in embryonated hen's eggs; bacterial glycoprotein conjugation delivering new vaccines to meningococcal and pneumococcal infections; and usage of new viral-vector technologies to produce Ebola and dengue vaccines.

On the horizon are new vaccine innovations that are being evaluated in clinical trials today. These include expansion of viral vector-based and adjuvants for development of vaccines against emerging and re-emerging pathogens including Lassa Fever, Zika virus, Human Immunodeficiency virus, and influenza. Utilization of synthetic mRNA technologies and development of liposome and nanoparticle carriers as carriers for these vaccines into the body are at the forefront of vaccine development against viral diseases and cancer. Structural examination of antigenic epitopes at the atomic level using new imaging technologies are helping to understand the physical properties of antibody and cell receptor binding to antigenic epitopes and to determine which epitopes may be best to target for greater vaccine efficacy, broader vaccine specificity, and longer duration. Innovations in drug delivery technologies may allow transdermal vaccine administration, obviate the need for syringes and needles, and afford rapid distribution and administration of vaccines.

The recent Executive Order (2019) provides a revised plan to modernize influenza vaccine manufacturing and pandemic preparedness. In addition to the continuation of on-going programs on seasonal and pandemic influenza vaccines recommended by previous pandemic plans and the convening a new Task Force to prepare a new pandemic plan, an emphasis was placed on the development of technologies that enable faster production and availability of seasonal and

pandemic influenza vaccines and the development of universal influenza vaccines to coincide with expanded domestic influenza vaccine manufacturing capacity. Potential recommendations will require funding at the multi-billion level through the 2020 decade for NIH, CDC, FDA, and BARDA to successfully implement and achieve these proposed seasonal and seasonal and pandemic influenza vaccine goals.

Even with these advances in vaccines and proposals to reinvigorate influenza vaccine development and preparedness, major challenges still await our efforts going forward into 2020. These include the resurgence of vaccine hesitancy by anti-vaccine advocacy groups with new cyberterrorist-like tactics that contributed to the recent unprecedented outbreaks of measles; competition for resources at large multi-national pharmaceutical companies between vaccines and other drugs products that have smaller cost of goods to manufacture and larger returns on investments; rapidity and availability of vaccines to quell the severity and even spread of catastrophic pathogens such as pandemic influenza viruses and others; the sheer difficulty in translating our basic understanding of immunity into successful vaccines; and last but most importantly, our continued inability to follow through in the many lessons learned reports over the past 50 years on pandemics that have cited the same deficiencies and recommendations with only incremental progress and questioned sustainability.

Conclusion

Influenza and other emerging infectious diseases with pandemic potential continue to mutate, evolve, and infect animals and humans, posing significant threats to global public health and to the United States. Together federal and industry partners have made great strides towards

pandemic influenza preparedness. While we have made progress in leveraging the improvements achieved for pandemic influenza vaccine manufacturing to benefit our seasonal vaccine needs, overall success in improving influenza vaccine effectiveness and duration have not been achieved. Success is dependent on the introduction and implementation of new innovations and technologies into new vaccines as public-private partners. Private industry partnered with U.S. government agencies and NGOs are poised to renew efforts to address seasonal and pandemic influenza challenges and provide the necessary resources, expertise, and technical assistance to attack pandemics with the wisdom and generosity of the U.S. Congress.

Biosketch

ROBIN ROBINSON, Ph.D.

Dr. Robin Robinson currently serves as Vice President of Scientific Affairs for RenovaCare, Inc. directing development of cellular therapies for wound healing. Concurrently he is a Fellow for Regenerative Medicine and Biomedical Research at the Thought Leadership and Innovation (TLI) Foundation on regenerative medicines and independent consultant on vaccines and biodefense matters.

He reentered the biopharmaceutical business sector after retiring in 2016 from federal public service at the U.S. Department of Health and Human Services, where he served from 2008 - 2016 as the first director of the Biomedical Advanced Research and Development Authority (BARDA) and Deputy Assistant Secretary for Preparedness and Response and as BARDA's Influenza and Emerging Disease program director (2004-2008). Dr. Robinson brought BARDA into prominence as one of the top 10 fully integrated R&D organizations worldwide supporting advanced development and acquisition of drugs, vaccines, diagnostics, and medical devices to address the deleterious outcomes of man-made biodefense threats, pandemic influenza, and emerging infectious diseases including Ebola and Zika viruses. 32 of its 250+ medical countermeasure products that BARDA supported since 2008 were fully approved and licensed by the FDA during his tenure; today that total is 52. Dr. Robinson established a pandemic influenza program with scientific and technical experts to implement the national and global strategic plans and policies for the development of new influenza antiviral drugs, vaccines, and diagnostics outlined in the *National Strategy for Pandemic Influenza*. For his leadership in this role, Dr. Robinson was the recipient of the Department of Defense's Clay Dalrymple Award in 2008, the HHS Distinguished Service Award three times, and a finalist for the Service to America Medal in 2009. In 2013-2015 Dr. Robinson was recognized as one of the top 50 most influential persons worldwide in vaccines by Vaccine Nation. In 2018 Dr. Robinson was recognized by Medicine Maker as one of the top 100 innovators in medicine.

Dr. Robinson received a Bachelor of Sciences degree in Biology from Millsaps College in 1976, a Doctoral degree in 1981 from the University of Mississippi Medical School in medical microbiology under Dr. Dennis O'Callaghan on herpesvirus oncogenesis, and completed in 1983 a NIH postdoctoral fellowship at the State University of New York at Stony Brook under Dr. Arnold Levine on molecular mechanisms in oncology. Dr. Robinson pursued his own research as a faculty member in the Department of Microbiology and Immunology at the University of Texas Southwestern Medical School from 1983-1992 on the molecular pathogenesis of herpesviruses and HIV. Prior to federal public service, Dr. Robinson served as the Director of Vaccines at Novavax, Inc. (Rockville, MD) from 1995-2004, where he led the development of 20+ vaccines to hepatitis B and E, influenza, HIV, noroviruses, and human papilloma viruses from early development, clinical trials, manufacturing scale-up, and commercialization through FDA licensure. While at Novavax, he developed patented platform vaccine technologies including virus-like particles and subunit protein vaccines for human pathogens including malaria, human papilloma, hepatitis, and influenza and for prostate, melanoma, and cervical cancers.

Dr. Robinson also served on the Senior Advisory Group for the World Health Organization (WHO) on emerging infectious diseases and pandemic influenza. Additionally, he continues to serve as an editorial board member and reviewer for several professional scientific and technical journals on virology, vaccines, public health, and biotechnology.

Mr. BERA. Thank you, Dr. Robinson.

At this point we'll begin our first round of questions. The Chair recognizes himself for 5 minutes.

Dr. Robinson, thank you for your service at BARDA. I've had the chance to meet with the top folks at BARDA, but another international organization that I've also had the chance to meet with is CEPI (Coalition for Epidemic Preparedness Innovations) and, you know, it is an organization that is looking at bringing the international community together, along with the private sector to look at vaccines for emerging diseases and so forth.

If you could elaborate a little bit more on the mission of CEPI. And, you know, one of the big disappointments for me is that the United States currently doesn't participate in CEPI, and I'd be curious about your opinion as to whether the U.S. should participate and, you know, if you want to elaborate on that.

Dr. ROBINSON. Thank you for the question. I always smile when CEPI is brought up because my former deputy at BARDA was Richard Hatchett, and he is the current CEO of CEPI.

Should the U.S. participate in the activities of CEPI against emerging infectious diseases and the development of vaccines? And the answer is that we already are. The inception of CEPI occurred back around 2014, and it actually became a reality in 2017, and that the NIH and BARDA specifically had investments in emerging infectious disease and specifically on vaccines such as Ebola, Zika, and others, and that that was part of our contribution and we will continue as the U.S. Government's efforts in these specific areas. So we do actually support what they do. In many cases we have contracts and grants that actually are supporting these same projects that they're working on but not on—so—but without duplication of exactly what they're doing.

Mr. BERA. You know, if we play off of that for a moment—and, again, my interest in pandemic preparedness and some of the threats, if we look at emerging diseases and some of those pandemic threats, what is our capacity to, you know—within the private sector to quickly ramp if we see an emerging pathogen, quickly identify it, identify a potential vaccine to mitigate that pathogen, you know, just from your perspective as an expert in the field?

Dr. ROBINSON. So I'll give it in the context of when I started my public service in 2004 in which it would take months to years to be able to respond to a new emerging pathogen. My first assignment was on H5N1, avian influenza viruses, and how we could actually make a vaccine toward that.

Since that time, we actually had a real live test in 2013 with the emergence of H7N1 viruses. What normally would take about 6 months to actually produce those vaccines, we actually brought that down to closer to 3 months. There was a specific reason why. First, as you heard from Dr. Fauci and Dr. Jernigan, we were able to get the sequence of that virus immediately. And actually it was on April Fools' Day of 2015 it actually moved forward within weeks to actually have that sequence distributed not only to the vaccine manufacturers of egg and cell-based producers but also for recombinant products. By the summer we actually had those vaccines in clinical trials. And so in record time we were able to do that. Many of the innovations that we are talking about today would even ex-

pedite that further. And our goal of course is to actually have pandemic vaccine not only produced but available within 12 weeks.

Mr. BERA. Great. And, Dr. Watkins, you know, in a prior life I was Chief Medical Officer for Sacramento County, so did a lot of public health work and, you know, it makes me chuckle because we would get information faxed to us and, you know, most of the public wouldn't believe that in this day and age in 2019 a lot of public health records and information is faxed-based.

So you talk about interoperability. You talk about collecting data and creating big data sets. Could you just elaborate a little bit more on what that would allow you to do in terms of more rapidly identifying potential outbreaks, et cetera, and why a more robust interoperable electronic public health record would allow you to do your job better?

Dr. WATKINS. Sure. You know, when I think about medical delivery of the healthcare system today, I mean, it's amazing the advancements that have been made, but I think public health has been left behind a little bit. And we are still dealing with faxes, and we are still dealing with phone calls and spreadsheets, handwritten spreadsheets. And it really does impact our ability to quickly respond to a situation.

So if immunization records were able to be quickly linked to our disease reporting system, if we were able to get electronic case reports and see data as it's coming in and digest that in the health department, we would really be able to respond much faster.

Much of what we do in many of the pandemics or the emerging threats that we have today is scratch our heads, and we're really struggling with the data sharing and the data management of so much big data. Public health needs to have our systems renewed and reinvested in.

And CSTE has produced this book in conjunction with stakeholders. There are a lot of stakeholder stories in this that talk about why public health is important and the time is now to invest money in our data systems.

Mr. BERA. Great. The Chair now recognizes Ranking Member, Mr. Lucas, for 5 minutes.

Mr. LUCAS. Thank you, Mr. Chair.

Dr. Robinson, in your testimony you highlight that clinical trials have shown that vaccines that are stockpiled remain highly effective even after 10 years in storage. How has BARDA worked with the industry to improve the shelf life of stockpiled vaccines and other countermeasures in the event of a pandemic emergency?

Dr. ROBINSON. Thank you for the question, sir. We started in 2005 building our stockpiles for pandemic influenza. These would be to treat those individuals that are highly vulnerable, at high risk, and our critical workforce to make sure the country still operates in a severe pandemic, so around 27 million doses. And that was actually for all the different strains that have been shown to have pandemic potential from the H5N1 viruses to the H7N1 I just described a moment ago to the new waves of H7N9 viruses. Through the IRAT (Influenza Risk Assessment Tool) process that the CDC has with BARDA, FDA, and NIH, we actually meet twice a year, go over these strains to see which ones are available.

But in 2015 we said that—and it was a question that actually came up from the Members here. Is the vaccine that you have stockpiled in these companies, is it still good? And the answer was, well, we know that the potency assays look really good, but we said that's not enough. So we went and actually did a clinical study using newly made H5N1 virus vaccine against a vaccine that had been made 10 years before. And the results of that in the Bright study, which have been published, show that they were equal and they were still highly immunogenic and could be used without or with an adjuvant to protect those individuals.

Mr. LUCAS. Thank you, Doctor.

Dr. Watkins, you suggest that the use of artificial intelligence or machine learning could be useful to identify outbreaks early and encourage individuals to get vaccinated. Can you elaborate further on how this technology can be utilized?

Dr. WATKINS. Sure. Thank you for that question. Public health does have a lot of data. It's not interconnected, and I think that the ability to look at birth and death certificates and immunization rates and existing comorbidities and combine that with census-tracked information and behavior information and information on poverty and immigration status, all of those other data sets helps us better understand at the community level what are the hesitations or what are the limitations to vaccination or access to health care or maybe language barriers. And when we're able to use all the data that Google has at their hands and we don't, I think we're better able to target where efforts should go.

As an example, during the opioid crisis, we and other states funded by CDC have been looking at vulnerability assessments. So we're looking at where are our deaths happening due to overdose. Where are babies being born with neonatal abstinence syndrome? Where are rates of hepatitis C and HIV increasing? And where does that overlay with poverty and some other statistics? That's use of big data in a state to really look at vulnerabilities and target where we should be working. We could be doing that with many more things had we the technology and interconnection.

Mr. LUCAS. Thank you, Doctor. I yield back.

Mr. BERA. Let me recognize Dr. Murphy.

Mr. MURPHY. Thank you, Mr. Chairman. Thank you guys for coming this afternoon, and I appreciate your expertise.

The first question I'm going to have is for Dr. Watkins because I was looking through some of the copies that you have of medical records and everything and having experienced the explosion of the electronic medical record just in my own practice in the last 25 years I see the challenges for it. If you could wave a magic wand, you know, there is a way to pull data out of these reports and quantify it, what would it look like? Because I preface it by saying we have so many different medical record systems in our country, most of which don't talk to one another. And unless we have literally a single system, I'm not sure of what this would look like. So I'm just interested in your thoughts about reality of this, how we do this because I think the purpose is altogether a great one, but the devil's in the details. What does that look like?

Dr. WATKINS. Thank you for that question. I would also refer you to this report that has been done. And we can get you a copy of

that. But what we're talking about is modernizing systems we already have, so our laboratory system, which is called LIMS (laboratory information management system), and its ability to rapidly transmit data between us and the provider and CDC, and handle those results needs to be modernized and made more interoperable.

Our death and birth certificate registries need to be more rapid. I mean, we shouldn't be having paper records of these important documents. Our immunization registries should be interconnected with our other disease reports. And our electronic disease collection system should be able to know if you've gotten influenza when a death certificate comes in. I shouldn't have to wait weeks. I should be able to see that within real time.

So looking at being able to bring those and CDC is doing a lot of work on electronic case records and modernizing all of these systems. What we're talking about is bringing all states up to a better level. Some states are really far behind, and some states are behind in some things but not in others.

And when I think about a pandemic or the next emerging issue, I mean, we don't want public health to be the weak link in the chain. We want public health to protect your family, my family, and the public's health with the same tools that private medicine has and the same speed. So that's what we're talking about.

Mr. MURPHY. All right. Thank you for the question. It's a daunting task. I think it's a good idea. I will tell you just it adds an entirely additional level of just data entry, but then again, that's what we do. We work on data.

Dr. WATKINS. We'd like to get out of the data entry. You know, I have some analogies for you if I may, I'm sure we all have private physicians. We have healthcare providers. And, you know, they're not sharing information handwritten on you. They're not walking your lab test results in a spreadsheet. I mean, they're working in a modern world with modern technology and modern informatics. And public health is the frontline for pandemics. We should be working with that same speed. It's like building a space probe and forgetting to put in the advanced communication and data-sharing aspect of it.

And I feel like in this modernization of health care and we're talking about vaccine innovation, we're thinking about all that, but we need to think about modernization of public health data sharing so that we can be the frontline of public health and not be the weak link in the chain.

Mr. MURPHY. Great, thank you. Because I agree. Those are the issues. It's not cancer, it's not other things that you need the connectivity.

Just one other quick question just, Dr. Robinson. I was wondering if you could speak to—we've talked a little bit about the vaccines that come primarily from eggs versus the cell-based and the recombinant. Can you speak to really why you don't believe that the technology of the latter really is taking up or are we making good progress toward moving away from the egg-based vaccines?

Dr. ROBINSON. So because of the efforts we had at HHS and primarily through BARDA we actually made a paradigm shift where we were 100 percent egg-based to, as Dan Jernigan said today, 85 percent.

Now, how are we going to move to at least having greater adoption of recombinant cell-based when we don't have some of the problems with mismatches? First of all, we have to realize that the influenza vaccine industry is a commodity-driven industry, and that the way that we were able to move the needle to begin with, it was interacting with them as public-private partnerships. That has to be revived and continue to go forward with these new discoveries to make it worthwhile for them to have a product so they can get out of the egg-based vaccine business.

I will say that there's promising progress that companies that are solely egg-based have actually either bought recombinant vaccine candidates and that are actually licensed now or they're internally developing new influenza vaccine candidates. So we need to expedite that and facilitate it with the continued efforts that we've had with a good formula before.

Mr. MURPHY. I have just one follow-up. Do you think that the recalcitrance to doing that really is regulatory or is it the economies of the cost?

Dr. ROBINSON. It's regulatory. I mean, they—industry and that—I am now part of that industry—will—may say, well, we don't want to do that because the—we have to go through the entire process of getting a new vaccine license from the FDA, but that's the normal course of vaccine development.

The real problem is, why spend money and we don't have to?

Mr. MURPHY. Right. Sure.

Dr. ROBINSON. And that's a reality.

Mr. MURPHY. Sure. Thank you very much. I yield back my time.

Mr. BERA. All right. Let me recognize Mr. Cohen.

Mr. COHEN. Thank you, Mr. Chair.

Dr. Robinson—and you may have—this probably have been—may have been touched on in the first panel, but the whole public media, social media conspiracy theories about vaccinations causing autism, how much of an effect has this had on people getting vaccinated? And how much of an effect of people not getting vaccinated have on public health?

Dr. ROBINSON. So there's two parts to that question. The first part is, what was the effect of anti-vaccine groups for autism? And we fought this battle during the last decade, and I will say that to a great extent that battle has been won, and so scientific data was actually shown that there's no link between vaccination and autism.

The second part of that——

Mr. COHEN. Let me ask you a follow-up on that.

Dr. ROBINSON. Yes.

Mr. COHEN. You say it's been won.

Dr. ROBINSON. I'm going to answer that because we have a new wave of anti-vaccination, and I'm very concerned about this because they don't have as their true agenda vaccination. They could care less whether it works or doesn't work because they have a hidden agenda for other things of anarchy and other things. And the tactics that they're using are ones that cyber terrorists have been using over the past several years, and I'm very alarmed by that because, again, the vaccination is not their real issue here.

Mr. COHEN. Well, there are some that I think—you know, for instance, my friend Robert Kennedy, Jr., he's a major anti-vaxer, and he's not for anarchy.

Dr. ROBINSON. No.

Mr. COHEN. I think his issue was thinking that mercury as a preservative was the cause. Is that correct?

Dr. ROBINSON. That is one of the platforms that they have espoused.

Mr. COHEN. Has there been studies to show that that is wrong?

Dr. ROBINSON. So that was said by Dr. Fauci earlier, one is it's not methylmercury, it's ethylmercury that is in some multidose vials of some vaccines. I will say that we made a pointed effort in 2008 with influenza vaccines to remove that, and the manufacturers did this without being mandated to do so and so that there are single-dose syringes without the mercury in those vaccines and those are primarily given to children and to pregnant women. And so there has been major progress on this. And as Dr. Jernigan said in his testimony earlier that CDC and FDA are mounting efforts to be able to minimize that. But again, the amounts that are there and the kind of mercury there are not the kind that Mr. Kennedy has been talking about.

Mr. COHEN. Dr. Watkins, do you have any perspective on this as well, anything you can add?

Dr. WATKINS. Thank you. I mean, I think public health is clearly worried about these sentiments and that we need to do a better job in communicating the efficacy of the vaccine and the benefits that it does. In addition to preventing disease, it also lessens the severity and complications and particularly for those most at risk, so it prevents death and hospitalization.

I think, you know, public health thinks a lot about where people get their health information and how do they communicate with each other? And we need to do a better job of producing convincing messages that are shared on different platforms.

Mr. COHEN. How many people do you know—or if you can give us a round figure—die annually from the flu?

Dr. WATKINS. I don't have the figure in my head, but we can get it for you.

Mr. COHEN. Well, Dr. Robinson, do you have a clue?

Dr. ROBINSON. Yes, sir. At the low end, 10,000, upwards to 48,000 a year, sir.

Mr. COHEN. So those people more likely than not, if they had the flu vaccine—and you don't know that some of them might not have gotten the flu vaccine and not been that particular strain—but more likely than not, that would have and reduced greatly if all those people had been inoculated?

Dr. ROBINSON. That's correct.

Mr. COHEN. Yes. Thank you. I'm a big proponent of vaccinations. My father was a pediatrician. He gave vaccines. In 1954 he gave the Salk vaccine to second-grade students in the test trials. I had a brother that was in second grade. He gave him the Salk vaccine. I was in kindergarten. He brought it home to give to me, and he had second thoughts because it was outside of his charge. Within 2 months I got polio. Vaccines are good.

I yield back the balance of my time.

Mr. BERA. Thank you. We'll open it up to additional questions from the Members, and I'll start by recognizing myself.

And my interests are in pandemic preparedness, Dr. Watkins. You know, we've been having conversations with companies like Google. And I know Google has been doing some work in identifying particular search words that may pop up that would then allow us to rapidly say, you know, people are searching the term fever or, et cetera, to try to quickly go into, let's say, a country in Africa or someplace else. Are you familiar with any of those trials and, you know, have they been successful, not successful, et cetera?

Dr. WATKINS. Well, public health is aware of those kind of crowdsourcing tools that look at G.I. symptoms or they look at fever, but we've not been using them in public health, most jurisdictions. I think some may have. What we are interested in because we are system that uses case-based surveillance—I mean, we know your name if you're sick. We're counting you as an individual. But we have expanded a little past that into syndromic surveillance where we are looking at deidentified emergency department visits and really gaining a lot of information that way.

So I can't say whether Google has been validated through public health methods, that is crowdsourcing. I can say that looking at emergency departments, just, you know, are you seeing a spike in this, that, or the other, has been incredibly effective, not just in identifying the uptick of flu, but of many other diseases, including being able to identify clusters of illnesses.

Mr. BERA. Dr. Robinson, would you want to add anything?

Dr. ROBINSON. No, I think Dr. Watkins——

Mr. BERA. Yes.

Dr. ROBINSON [continuing]. Has said it.

Mr. BERA. And yet I still think it's worth—as we're looking at global health and, you know, pandemic preparedness, to continue to work with these technology companies that, you know—because part of rapidly responding and getting ahead of pandemics is quickly saying, hey, let's get someone out there, let's identify what that pathogen is, and let's see if we can't mitigate it at the source. Is that correct?

Dr. WATKINS. Absolutely. But with all due respect, I think public health is under-sourced and under-resourced in the informatics world. So our ability to really be doing that is contingent on us being able to modernize.

Mr. BERA. Do public health information systems speak across State lines?

Dr. WATKINS. No, not necessarily. No.

Mr. BERA. OK. And that's not because of any regulatory issues that we've placed as Congress? That's just under-resourcing or——

Dr. WATKINS. Well, it's both. I mean, Ohio doesn't have the jurisdiction to see that John Smith in Pennsylvania has influenza. It's my jurisdiction. But we could do a better job of sharing, not identified data, across State lines.

Mr. BERA. Right.

Dr. WATKINS. And when there is an outbreak and we need to share that information, we do so securely.

Mr. BERA. OK.

Dr. WATKINS. But, no, for example, in my state, Philadelphia is on a different surveillance system than the state is, and it does really matter. We have to really work hard to share data. And when CDC wants to see Statewide data, we have to work with Philadelphia to harmonize it. It's inefficient.

Mr. BERA. You know, as a public health expert, let me ask another question about vaccination rates and—I guess let me put it this—when I was a child, I got a lot of my vaccines at school. And it's how—I'm an internist by training, not a pediatrician, but it's always occurred to me that, you know, for efficiency's sake, especially for multidose vaccines, you've got a captive audience in that school. The kids are going there. But the overhead if you had school-based nurses or public health nurses that were able to go into those schools to vaccinate their kids, it would be more effective, more efficient, and I'd just be curious from your perspective, Dr. Watkins, if that's something that we made a mistake of moving away from?

Dr. WATKINS. Well, we certainly do school-based vaccinations in outbreak settings. That's a perfect setting, and we do use that venue. I think school-based nurses are a resource that is shrinking, and so not all schools have access to that. I think that looping schools into immunization and other kinds of issues is always a goal of public health, and I do think that we've done it broader but have shrunk that footprint, yes.

Mr. BERA. I mean, I understand that there's probably concerns about liability issues——

Dr. WATKINS. There are.

Mr. BERA [continuing]. And, et cetera, that have moved us away from that, but just from a pure cost perspective and efficacy perspective, I think those investments in public health nurses or school-based nurses, the overhead and, et cetera, and again the efficiency, particularly with multidose vaccines because you lose a lot of kids. They don't come in for a month later for that second vaccine. And, again, I believe you could rapidly boost the number of children that are getting vaccinated, you know, if we were to utilize tools like that.

And I guess I'd ask one last question with regards to measles, et cetera. Just I'd be curious from your perspective as a public health professional, how Pennsylvania and others around the country are trying to address the periodic outbreaks.

Dr. WATKINS. Sure. I mean, we're exhausted. I'll just be honest. I was just at a conference in New York, and I can't even imagine what they've had to go through to be able to address those thousands of cases.

You know, in Pennsylvania, I think we're at 17 cases. What I think you don't realize is that for every case, hundreds of people are likely exposed. And if it's been close-contact exposure, if you were infectious with measles right now, everyone in this room and everyone in this room for the 2 hours after you have left it would have been exposed.

Public health notifies you. We track you down when we can. We assess your immunity. We work to make sure that not only are you taken care of but everyone you've exposed is notified and properly treated. Either you're immune or you're not, and if you're not and

we can't get—we can't get you prophylaxis in time, you may be quarantined. There are a lot of steps that go into measles. And it's an enormous resource drain. It's been difficult for New York and for any of us who have had cases of measles.

Mr. BERA. Well, Dr. Watkins, thank you for your work and all those public health professionals. And, Dr. Murphy, if you have any additional questions.

Mr. MURPHY. Thank you, Mr. Chairman. Again, thank you guys for coming.

Dr. Watkins, let me ask a question just because we're looking at this in one level of the problems that you face with interconnectivity and challenges by all means. My question is what have you done in the State of Pennsylvania to talk to the other counties because public health departments at least in North Carolina are run by counties? What have you guys done on a State level to develop interconnectivity?

And just on a corollary, I did a lot of work in the North Carolina legislature with the opioid epidemic. And we had people on the border of North Carolina going into Virginia getting prescriptions, vice versa. So we worked close by with our State neighbors to develop a system that somebody in Virginia could know if somebody's jumping across a line and getting prescriptions in North Carolina.

It's the same thing. It's State interconnectivity, not necessarily a Federal pushdown approach. When we look at the Nation as a whole of pandemics that are going on, by all means we need to know that information. But these tend to be localized. And so what have you guys done on the State level to address this problem?

Dr. WATKINS. So let me just say that Pennsylvania is structured differently than North Carolina. I mean, we have 10 county and municipal jurisdictions. We're home rule, commonwealth, so they are on our same system of disease surveillance, and so we are able to share that. So what happens are lab reports come in or a report from a physician comes into the State health office, and we push it to the jurisdiction or to the district office.

Mostly if you're in a home rule system, if you're in Pittsburgh, for example, Pittsburgh is seeing their own records. But we do collect it all in the same data system. Philadelphia is large, and they're able to have their own data in a different system. So we work with them. We work with them both from a disease perspective. We share outbreak information all the time. We work with them from an IT perspective to try to harmonize what we do.

And of course we're always working with our neighbors, whether it be on hepatitis A outbreaks or measles or sharing of—I mean, patients don't have borders. I mean, you could be hospitalized in New Jersey and go into a long-term care facility in Pennsylvania. It happens all the time. So we keep in touch, but we could do it better, faster, and without loss of information or misinformation if we were better electronically suited.

Mr. MURPHY. All right. Well, let me just follow up then. Are you not electronically suited in these different counties? And why would you not appeal to your State rather than the Federal Government to make that happen?

Dr. WATKINS. So what I'm talking about is the sharing of laboratory information with disease surveillance, and that is happening

at the State level, but it's not an easy connection. We've really not invested money in this in a long time. For example, our immunization record is not connected to our disease surveillance record. And I'm speaking from the national perspective, CSTE. You've asked me a Pennsylvania question, but I could be answering for many states. I don't know if your immunization record in North Carolina is connected to your disease registry. For many states it's not. So those are the kind of things that would help us get data and respond faster.

You know, in a measles exposure situation, who's been immunized? You know, that's a hard question. It shouldn't be a hard question, but it is a hard question. And we've resorted to actually going to high schools, the old high school who's stored records who've looked them up for us because the physician had gone out of practice or—you know, I mean, public health is a make-it-work kind of a system, and we just do what we need to do. But we're getting further and further behind.

Mr. MURPHY. I see. Thank you. Thank you. And one other quick question just with Dr. Robinson. In the success that we've seen with the cervical cancer vaccine against the HPV virus—here I am a physician trying to put myself out of business. Where are we and where do you see us as far as other malignancy vaccines? I'm going to give you prostate cancer, for example, because I've seen literature for that for 15 years. I just don't see the door being knocked down. So can you just speak to that briefly and what your experience is and thoughts?

Dr. ROBINSON. Yes. Twenty years ago when I was in industry we actually worked on a prostate cancer vaccine and a melanoma vaccine. What has driven the oncology vaccine has been supplanted by the monoclonal antibodies that have been developed with great, great success over the last 15 years. So that has somewhat moved the vaccine programs and especially in companies to a lesser degree.

Some of those vaccines were extremely promising as we and others were evaluating those in the clinic, and I would suspect that once we reach the peak of the monoclonal antibodies for oncology purposes, that we will actually see a resurgence of vaccines for different types of cancer reappear probably in the next decade in fact.

Mr. MURPHY. Thank you.

Mr. BERA. Great. Before we bring the hearing to a close, I want to thank both of our witnesses for testifying before the Committee today.

The record will remain open for 2 weeks for additional statements from the Members and for any additional questions the Committee may ask of the witnesses. The witnesses are excused, and the hearing is now adjourned.

[Whereupon, at 12:31 p.m., the Committee was adjourned.]

Appendix I

Answers to Post-Hearing Questions

ANSWERS TO POST-HEARING QUESTIONS

Responses by Dr. Daniel B. Jernigan, MD

Questions for the Record (QFR) – Fighting Flu, Saving Lives: Flu Vaccine Science and Innovation hearing

November 20, 2019

From Rep. Bill Posey:

Q1. For the 2019-2020 season, how many individual doses are (will be) available in mercury free doses? How many individual doses are provided in multidose vials? Please provide similar breakdown for 2018/19, 2017/18, 2016/17, 2015/16, 1014/15 flu seasons. What is CDC's best estimate of the number of doses of mercury preserved flu vaccine administered to the following groups: pregnant women, children, and the elderly, during each of these flu seasons?

The Centers for Disease Control and Prevention (CDC) receives information from manufacturers each spring about the doses they anticipate distributing. The table below summarizes the total doses projected to NOT contain thimerosal as a preservative, and the percentage projected to contain thimerosal as a preservative.

Annual Vaccine Projections from Manufacturers

Season	Doses projected	% Projected to NOT Contain Thimerosal Preservative	% Projected to Contain Thimerosal Preservative
2014-15	151-146M doses	68%	32%
2015-16	171-179M doses	67%	33%
2016-17	157-168M doses	74%	26%
2017-18	151-166M doses	82%	18%
2018-19	163-168M doses	82%	18%
2019-20	162-169M doses	85%	15%

*As of Dec 6, 2019.

While CDC does not have specific estimates on which populations receive thimerosal-containing vaccines, CDC is aware that a majority of children receive thimerosal-free flu vaccine.

Q2. Removal of mercury from flu vaccines will build public confidence as it would re-enforce the notion that public health officials place safety over all other considerations. What specific initiatives is the CDC taking to encourage manufacturers to fulfill their commitment to fully remove mercury from the annual flu vaccines? If there is not such effort, please share that as well.

In 1999, the U.S. Public Health Service and the American Academy of Pediatrics issued a joint recommendation for removing thimerosal from childhood vaccines. With the exception of flu vaccines in multi-dose vials, thimerosal was completely removed from all other childhood vaccines in 2001. Even though there was no evidence that thimerosal in vaccines was dangerous, the decision to remove it was a made as a precautionary measure to decrease overall exposure to mercury among young infants. The amount of thimerosal-containing flu vaccine used in the United States has decreased over time, with only 15 percent of this season's vaccine containing the preservative. Flu vaccine in multi-dose vials contain thimerosal to prevent contamination.

Multidose vials are still used to ensure adequate supply of flu vaccine for the American public, and are an important tool for vaccinating during an influenza pandemic

Q3. As a nation, we have established a 'safety first' standard, especially as it relates to babies born and unborn. The FDA regulates manufacturers of drug and biologics and makes informed judgement decisions regarding the information which must be included in package inserts of products, such as vaccines. Each of the flu vaccines currently on the marketplace has a package insert in which the information regarding the proof of safety for pregnant and lactating women includes statements such as "Available data are insufficient to inform vaccine-associated risks in pregnant women," and "its is not known if '[X] vaccine' is excreted in human milk. Data are not available to assess the effects on the breastfed infant or on milk production/excretion." There is an incongruence between the package inserts and the CDC's recommendations. Please compare and contrast the standard which the CDC uses to establish the safety of flu vaccines for babies and fetuses with that of the FDA.

CDC response:

Questions regarding the content of vaccine package inserts are best directed to the Food and Drug Administration (FDA). CDC is committed to ensuring that the vaccines administered to children and adults in the United States are safe and effective. CDC has conducted vaccine safety studies for decades. These vaccine safety studies cover the entire human lifespan, including infants, young children, adolescents, adults, pregnant women, and the elderly. CDC continuously monitors the safety of U.S.-licensed vaccines to rapidly identify and address potential safety concerns that are detected during post-licensure monitoring. Data accumulated over decades of monitoring and research overwhelmingly support the safety of childhood immunizations. Safety monitoring and studies of the two vaccines routinely recommended during pregnancy – inactivated influenza vaccine and tetanus, diphtheria, and pertussis vaccine – strongly support their safety in pregnancy.

Additional information on the safety of the childhood immunization schedule, the safety of vaccination during pregnancy, and the safety of vaccinations during breastfeeding is available at:

http://www.nationalacademies.org/hmd/Reports/2013/The-Childhood-Immunization-Schedule-and-Safety.aspx

https://www.cdc.gov/vaccinesafety/concerns/vaccines-during-pregnancy.html,

https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/vaccinations-medications-drugs/vaccinations.html.

Q4: Mercury, at some level of exposure, is commonly known to pose a risk to fetuses, infants and young children in all its forms. While public health authorities have produced major campaigns to raise awareness for pregnant women to avoid certain types of fish due to mercury content; and have moved to eliminate mercury in research laboratories and in over-the-counter FDA approved products, the initial call 20 years ago to completely remove mercury from vaccines has not been fulfilled. During the hearing it was stated that only 15% of this year's flu vaccine is preserved with thimerosal, the mercury preservative. What is the scientifically validated known safe exposure level for injected thimerosal for infants and pregnant women (and their unborn children)? What is the safe exposure level for adults? Please provide the documentation to support this standard. If no safe exposure level has been determined, how can this mercury-containing product remain in the marketplace when there are safer alternatives?

CDC Response:

There is no evidence to suggest that the amount of thiomersal used in vaccines and other medical products poses a health risk. Data from many studies show no evidence of harm caused by the low doses of thimerosal in

vaccines. Additionally, reputable vaccine safety research does not show any link between thimerosal in vaccines and autism, a neurodevelopmental disorder, or other neurodevelopmental problems. As a precaution, thimerosal was removed from U.S. vaccines routinely recommended for children by 2001, with the exception of multidose vial formulations of inactivated influenza vaccine. The majority of influenza vaccine used in the United States today does not contain thimerosal preservative.

Measles, mumps, and rubella (MMR) vaccines do not and never did contain thimerosal. Varicella (chickenpox), inactivated polio (IPV), and pneumococcal conjugate vaccines have also never contained thimerosal. Other questions on this topic are best directed to FDA.

Q5: Dr. George Lucier, Associate Director National Toxicology Program from 1969- 2000, said "The developing fetus should NEVER be exposed to any amount of mercury period!" Dr. Jernigan, do you agree with Dr. Lucier on this? If not, why not? Please explain.

CDC Response:

Not all types of mercury are the same. Some types of mercury, like methylmercury in some kinds of fish, stay in the human body and can make people sick. High amounts of methylmercury can harm the nervous system. This has been found in studies of some populations that have long-term exposure to methylmercury in foods at levels that are far higher than the U.S. population. Thus, in the United States, Federal guidelines keep as much methylmercury as possible out of the environment and food, but over a lifetime, everyone is exposed to some methylmercury.

On the other hand, thimerosal is a different kind of mercury, ethylmercury. Ethylmercury does not accumulate in the body the same way that methylmercury does and there is no evidence to suggest that the amount of thiomersal used in vaccines and other medical products poses a health risk.

Q6: If a six-month old infant is given a flu shot from a multi-dose vial preserved with thimerosal, does the mercury from thimerosal enter the brain of that infant? NIH-funded research on primates by Dr. Thomas Burbacher (2004) found that it does cross the blood-brain barrier (thereby entering the brain). Do you disagree with Dr. Burbacher's findings? Please provide evidence to support your response

CDC Response:

It is important to understand the difference between the two compounds that contain mercury: ethylmercury and methylmercury, which are totally different materials. Thimerosal is an ethylmercury-based preservative used in vaccine vials that contain more than one dose of a vaccine (multi-dose vials) to prevent germs, bacteria and/or fungi from contaminating the vaccine. There is no evidence to suggest that the amount of thiomersal used in vaccines poses a health risk. Low-level ethylmercury exposures from vaccines are very different from long-term methylmercury exposures because ethylmercury is broken down by the body differently and clears out of the blood more quickly. Additionally, reputable vaccine safety research does not show any link between thimerosal in vaccines and autism, a neurodevelopmental disorder, or other neurodevelopmental problems. As a precaution, thimerosal was removed from U.S. vaccines routinely recommended for children by 2001, with the exception of multidose vial formulations of inactivated influenza vaccine. The majority of influenza vaccine used in the United States today does not contain thimerosal preservative

A 2004 external scientific review by The National Academies of Sciences, Engineering, and Medicine concluded that "the evidence favors rejection of a causal relationship between thimerosal–containing vaccines and

autism." Additionally, CDC scientists have been studying the use of thimerosal in vaccines for many years and have not found any evidence that thimerosal causes harm. A list of CDC studies on thimerosal in vaccines can be found on CDC's website at: https://www.cdc.gov/vaccinesafety/pdf/cdcstudiesonvaccinesandautism.pdf

Q7: Being mindful of the rapid neurodevelopment early in life, if thimerosal crosses the blood-brain barrier, what might be the results of that exposure for a six-month old or an unborn fetus?

CDC Response:

As noted in the responses above, there is no evidence to suggest that the amount of thiomersal used in vaccines poses a health risk. Data from CDC as well as other reputable sources show no evidence of harm caused from the low doses of thimerosal in vaccines. Most people do not have any side effects from thimerosal. It is also very unlikely that someone will have an allergic reaction to thimerosal. In addition, thimerosal has not been used in vaccines for children since 2001, with the exception of influenza vaccines in multi-dose vials and thimerosal-free preparations of influenza vaccine are widely available for both children and adults.

Q8: It is known in science that human exposure to mercury has effects on the kidney, heart and brain. What might be the result on the kidneys, heart and brain of exposure to mercury? At what level of exposure would these effects be realized?

As stated in question 6, thimerosal is a different kind of mercury, ethylmercury. Ethylmercury does not accumulate in the body the same way that methylmercury does. There is no evidence to suggest that the amount of thiomersal used in vaccines and other medical products poses a health risk. Furthermore, low-level ethylmercury exposures from vaccines are very different from long-term methylmercury exposures because ethylmercury is broken down by the body differently and clears out of the blood more quickly.

Q.9 Is there any scientific reason related to the efficacy of flu vaccine for the continued use of thimerosal in flu vaccine, other than having it in multi-dose vials as a preservative?

Thimerosal is used in multi-dose vials to prevent germs, bacteria and/or fungi from contaminating the vaccine. Thimerosal does not impact vaccine efficacy, other than safeguarding multi-dose vials from contamination which can cause illness or death.

Q. 10 The flu vaccine, which was introduced to the Vaccine Injury Compensation Program (VICP) in 2006, accounts for over 27% of the total number of vaccine injury petitions filed for the entire 31 years of the program? It accounts for more than 13% of the death claims. Please provide a list and copies of the studies and projects which NIAID has undertaken to specifically as a result of vaccine injuries compensated by the federal government through the VICP injury and death claims and the results of those studies.

CDC has referred this question to the National Institutes of Health (NIH) National Institute of Allergy and Infectious Disease (NIAID). Their response is provided below:

NIAID is committed to the development of safe and effective vaccines, including those aimed at preventing influenza infection. NIAID's longstanding efforts to develop new and improved vaccines and vaccine technologies are independent of the VICP, which is administered by the Health Resources and Services Administration. It is important to note that all NIAID-supported vaccine research includes a focus on safety as an integral part of the research. In addition, any further information about vaccines identified after their licensure may inform studies conducted or supported by agencies comprising the vaccine safety enterprise.

In addition to NIH's ongoing commitment to biomedical research activities on vaccine safety and efficacy, NIH renewed two research funding initiatives in 2018 to encourage studies that address scientific areas potentially relevant to vaccine safety. These scientific areas include: 1) responses to vaccines and vaccine components, including adjuvants; 2) genetic variations that may impact vaccine safety; 3) risk factors that may be used to assess whether there is a relationship between certain diseases or disorders and licensed vaccines; 4) statistical methodologies for analyzing data on vaccine safety, including data available from existing data sources, such as passive reporting systems or healthcare databases; or 5) genomic/molecular technologies and systems biology approaches to evaluate vaccine safety. Currently, NIAID is supporting three research studies pertaining to the safety of influenza vaccines submitted in response to these funding opportunity announcements. Results are not yet available for these ongoing studies, which aim to: generate prediction models for risk of severe adverse events post vaccination; advance vaccine safety and efficacy through the development of an innovative vaccine delivery technology; and develop a more effective influenza vaccine for the elderly. The projects are listed in the table below.

Ongoing NIAID-supported Vaccine Safety Studies Relevant to Influenza		
Project Title	Project Number	Institution
Dynamic learning for post-vaccine event prediction using temporal information in VAERS	R01AI130460	University of Texas Health Science Center Houston
Fusion: Vaccine conjugate technology to advance vaccine safety and efficacy	R01AI137146	University of Montana
Effectiveness of R848 conjugated IPR8 as a vaccine for the elderly	R21AI137741	Wake Forest University Health Sciences

Responses by Dr. Anthony S. Fauci, MD
HOUSE COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

"Fighting Flu, Saving Lives: Vaccine Science and Innovation"

Questions for the Record to:

Dr. Anthony S. Fauci

Director, National Institute of Allergy and Infectious Diseases

National Institutes of Health

Submitted by Congressman Bill Posey

As I stated at the hearing, I am supportive of vaccination as we know that vaccines play an important role in protecting the public from infectious disease. It is important that we take every step possible to ensure that vaccines are as safe as possible - which will only serve to further boost public confidence in the safety of vaccines. We know that a small number of people suffer vaccine injuries as the federal government's vaccine injury compensation program has paid out more than $4 billion in injury claims to several thousand Americans. It is incumbent upon us to take every step we can to reduce the risk of vaccine injury. I would appreciate answers to the following questions.

1. How long has NIAID (and the US Government) been pursuing, and how much in taxpayer funding, has been expended for researching and developing a Universal Flu Vaccine?

NIAID Response:
The National Institute of Allergy and Infectious Diseases (NIAID) supports a comprehensive portfolio of basic, translational, and clinical research on influenza, including the development of broadly protective or "universal" influenza vaccines that could protect individuals over many years against multiple types of influenza viruses, both seasonal and pandemic. Longstanding NIAID-supported research on influenza, particularly research to improve seasonal and pandemic influenza vaccines, has stimulated tremendous progress in the development of more broadly protective influenza vaccines. Since fiscal year (FY) 2009, NIAID has provided $2.9 billion in funding for influenza research, which includes $1.3 billion for research on influenza vaccines. Achieving the goal of a universal influenza

vaccine has become more feasible in recent years due to significant advances in atomic level structural information for vaccine design, gene-based vaccine platforms, modern protein engineering, and potent adjuvants.

NIAID has prioritized the development of universal influenza vaccines and outlined a research agenda toward this goal in our *Strategic Plan for a Universal Influenza Vaccine* issued in 2018. *The Strategic Plan* focuses on three research areas: improving knowledge of the transmission, natural history, and pathogenesis of influenza infection; characterizing influenza immunity and immune factors that correlate with protection against influenza; and supporting the rational design of universal influenza vaccines. NIAID funding for universal influenza vaccine research guided by the 2018 *Strategic Plan* for fiscal years (FY) 2018-2020 is provided in the table below.

	FY 2018 (actual)	FY 2019 (estimate)	FY 2020 (estimated)
NIAID	$113.2M	$140.2M	$200M

NIAID will continue targeted investments in each of these research areas to generate critical information for the development of universal vaccines effective against both seasonal and pandemic influenza.

For information on funding from other Department of Health and Human Services Operating Divisions, please contact the Office of the Assistant Secretary for Financial Resources.

2. In March you testified that the NIAID and the Vaccine Research Center at the NIH is testing universal flu vaccines and that you have products in Phase III trials. What is the status of these studies now? What is the' standard that will need to be met to see a universal flu shot approved for safety and efficacy in order to enter the marketplace?

NIAID Response:

NIAID is pursuing multiple strategies for the development of universal influenza vaccines that target common parts of the influenza virus in order to elicit protective immunity against diverse influenza viruses. NIAID is building on decades of basic and translational research in influenza virology, immunology, and vaccine development to design broader, highly immunogenic influenza vaccines. Development of a universal influenza

vaccine will be iterative and progressive. All influenza A viruses fall within two broad groups, with multiple subtypes in each. The initial stage of development will focus on vaccines against all versions of a single subtype. For example, one vaccine may target all strains of subtype H3N2, whereas another vaccine may target all strains of subtype H1N1. Following the initial stage, efforts would progress toward development of vaccines against all subtypes within a specific group. These vaccines would target influenza A viruses throughout either "group 1" (which includes subtypes H1N1 and H5N1, among others) or "group 2" (which includes subtypes H3N2 and H7N9, among others). The final iteration of development would provide a universal vaccine that would protect against all influenza A viruses. It is important to note that each universal influenza vaccine candidate will need to be evaluated over several influenza seasons to determine the level and durability of protection that is induced. While clinical trials are underway to evaluate the first iteration of universal influenza vaccine candidates, a truly universal influenza vaccine is still many years away.

Currently, there is one universal influenza vaccine candidate in an industry-sponsored Phase 3 clinical trial. This M-001 vaccine candidate, developed by the company BiondVax, contains several influenza fragments common among multiple influenza virus strains. NIAID, using its Vaccine and Treatment Evaluation Units (VTEUs), supported a separate Phase 2 clinical trial to evaluate the M-001 vaccine candidate.

NIAID also is supporting the development of several universal influenza vaccine candidates in ongoing or planned clinical trials. 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 booster dose with a licensed, quadrivalent inactivated seasonal influenza vaccine. The NIAID Vaccine Research Center (VRC) also is conducting a Phase 1 clinical trial of a universal influenza vaccine candidate that uses a nanoparticle-based platform technology to display the stem region of the hemagglutinin (HA) protein. Proteins displayed on nanoparticles are capable of creating a robust immune response. The vaccine candidate developed by VRC scientists incorporates the stem region, a relatively conserved area of an H1 influenza virus subtype that in animal models provided protection against influenza viruses from other subtypes within "group 1." In 2020, VRC scientists plan to evaluate a similar nanoparticle-based vaccine candidate designed to protect against "group 2" influenza viruses.

The NIAID Division of Intramural 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 vaccine candidate in a human influenza challenge model. DIR investigators also plan to launch two Phase 1 clinical 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 neuraminidase influenza surface protein.

Standards for universal influenza vaccine approval for safety and efficacy are determined by the United States Food and Drug Administration (FDA). The FDA is responsible for evaluating the scientific and clinical data submitted by manufacturers to determine whether the product meets standards for approval/licensure.

3. You stated during the hearing that giving the flu vaccine to pregnant women is "perfectly safe." Each of the flu vaccines currently in the marketplace has a package insert in which the information regarding the proof of safety for pregnant and lactating women includes statements such as 'Available data are insufficient to inform vaccine-associated risks in pregnant women, and "It is not known if ' [x] vaccine' is excreted in human milk. Data are not available to assess the effects on the breastfed infant or on milk production/excretion'." There is an incongruence between the package inserts and your statement. Please explain the standard the NIAID and you use to establish the safety for babies both born and unborn for receipt of flu vaccines and compare and contrast that to the FDA standard. How do you reconcile your statement that the flu vaccine is perfectly safe with the package inserts which indicate it has not been tested for safety in pregnant women?

NIAID Response:

When I was asked by Representative Bera, "is the flu vaccine safe for pregnant women?", I responded, "Yes." The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices and the American College of Obstetricians and Gynecologists recommend that women who are or will be pregnant during influenza season receive an inactivated influenza vaccine as soon as it is available. This recommendation is based on a large body of scientific studies that supports the safety of influenza vaccines in these populations. Any of the licensed, recommended, age-appropriate, inactivated influenza vaccines can be given

safely during any trimester of pregnancy. The FDA also has made public statements highlighting the importance of influenza vaccination for people in high-risk groups, including pregnant women. Additional information on influenza vaccine safety and monitoring is available from the CDC and the FDA.

4. The flu vaccine, which was only introduced to the Vaccine Injury Compensation Program (VICP) in 2006, accounts for over 27% of the total number of vaccine injury petitions filed for the entire 31 years of the program. It also accounts for more than 13% of the death claims. What is NIAID and the NIH doing to improve the safety of the flu vaccines? Please provide a list of these NIH-funded studies and projects which NIAID has undertaken specifically as a result of vaccine injuries compensated by the federal government through the VICP injury and death claims and the results of those studies.

NIAID Response:

NIAID is committed to the development of safe and effective vaccines, including those aimed at preventing influenza infection. NIAID's longstanding efforts to develop new and improved vaccines and vaccine technologies are independent of the VICP, which is administered by the Health Resources and Services Administration. It is important to note that all NIAID-supported vaccine research includes a focus on safety as an integral part of the research. In addition, any further information about vaccines identified after their licensure may inform studies conducted or supported by agencies comprising the vaccine safety enterprise.

In addition to the National Institutes of Health's (NIH) ongoing commitment to biomedical research activities on vaccine safety and efficacy, NIH renewed two research funding initiatives in 2018 to encourage studies that address scientific areas potentially relevant to vaccine safety. These scientific areas include: 1) responses to vaccines and vaccine components, including adjuvants; 2) genetic variations that may impact vaccine safety; 3) risk factors that may be used to assess whether there is a relationship between certain diseases or disorders and licensed vaccines; 4) statistical methodologies for analyzing data on vaccine safety, including data available from existing data sources, such as passive reporting systems or healthcare databases; or 5) genomic/molecular technologies and systems biology approaches to evaluate vaccine safety. Currently, NIAID is supporting three

research studies pertaining to the safety of influenza vaccines submitted in response to these funding opportunity announcements. Results are not yet available for these ongoing studies, which aim to: generate prediction models for risk of severe adverse events post vaccination; advance vaccine safety and efficacy through the development of an innovative vaccine delivery technology; and develop a more effective influenza vaccine for the elderly. The projects are listed in the table below.

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Effectiveness of R848 conjugated IPR8 as a vaccine for the elderly	R21AI137741	Wake Forest University Health Sciences

5. One concern which has contributed to individuals refusing the MMR vaccine is the fact that this vaccine is made using cell lines from aborted fetal tissues. This will continue to be a concern for some with whom this violates their religious or philosophical beliefs. As a step toward addressing this issue and to enhancing uptake of the MMR and future vaccines, has NIAID implemented a policy of (a) developing or encouraging the licensing of an MMR vaccine which does not utilize these cell lines, including already licensed measles vaccines from other countries such as Japan or (b) ensuring that future vaccines avoid utilizing these and similar cell lines in vaccines under development to avoid these controversies and enhance vaccine uptake? If so, please provide details.

NIAID Response:

1 1 Vaccine Adverse Event Reporting System (VAERS) is a spontaneous reporting system for adverse events following vaccination that is co-managed by CDC and FDA

NIAID works in partnership with vaccine researchers in academia and industry to support the development of new and improved vaccines, including novel development and production processes that may be needed in certain populations for health or other reasons. In doing so, NIAID requires that scientists receiving NIAID funding follow all applicable Federal regulations and policies for such research. NIAID has supported the development of vaccine platforms that do not require the use of fetal tissue.

Submitted by Congressman Michael Waltz

1. Dr. Fauci: As you know, the Federal government has set a goal of delivering pandemic vaccines within 12 weeks of a declaration. In achieving that goal:

a. How important is the speed with which we respond to a pandemic determine our ability to effectively combat it?

NIAID Response:
When novel influenza viruses have the capacity to spread efficiently among humans, the risk of a potential influenza pandemic is high. The speed with which we are able to respond to a potential pandemic is crucial to minimizing potential mortality and morbidity. Our best tool to prevent the next influenza pandemic is a safe and effective vaccine. Unfortunately, a vaccine likely would not be immediately available if a previously unidentified strain of pandemic influenza suddenly emerges, as has been the case in previous influenza pandemics.

It is essential that we move beyond the current strain-specific influenza vaccine development strategy to get ahead of future outbreaks of pandemic influenza. Most existing influenza vaccines are produced by growing the virus in eggs. Currently, an updated – and sometimes a novel – influenza vaccine is needed for each new strain of influenza with pandemic potential. During the H1N1 influenza pandemic in 2009, a vaccine against the emergent virus strain was not available to the public until well after the peak of the pandemic had occurred. Development of a universal vaccine capable of protecting against a wide range of different influenza strains would decrease the potential of a pandemic when a novel strain emerges.

b. Do you think it's important to support pursuing multiple, novel technologies to ensure we can produce vaccines rapidly following a pandemic declaration?

NIAID Response:
NIAID has prioritized research to develop state-of-the-art vaccine platform technologies that could be used to develop universal influenza vaccines, as well as to improve the speed and agility of the influenza vaccine manufacturing process. These platform technologies include DNA, messenger RNA (mRNA), virus-like particles, vector-based, and self-assembling nanoparticle vaccines. 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. NIAID's development of vaccine platform technologies that significantly reduce the time to production for novel vaccines, including development of a universal influenza vaccine, are crucial to decreasing the response time in the event of a future pandemic.

c. Is there value in pursing multi-modal technologies capable of responding not only to influenza but additional biological threats such as Ebola?

NIAID Response:
A critical component of preparedness is biomedical research to develop medical countermeasures that could be rapidly deployed in response to a naturally occurring or deliberately introduced infectious disease outbreak. This includes NIAID-supported research to develop multi-modal, or platform-based, technologies.

Novel vaccine platforms that have been intensively studied employ recombinant DNA technology that bypasses the need to grow the virus. These platforms include recombinant proteins, viral vectors containing genes that express specific viral proteins, virus-like particles that can be manufactured, nanoparticles with high immunogenicity, and genetic approaches such as DNA and RNA that code for viral proteins. These platforms can be rapidly deployed against a variety of pathogens.

NIAID scientists used newly identified Zika virus genetic information to rapidly develop a Zika vaccine candidate using a DNA vaccine platform that progressed from sequence selection to a first-in-human clinical trial in less than four months. The NIAID Zika vaccine candidate was developed with a readily deployable DNA vaccine platform that was previously used by

NIAID to develop a West Nile virus experimental vaccine. Using this broadly applicable platform technology, NIAID was able to accelerate its response to a previously unrecognized public health threat. This particular platform, or a similar multi-modal technology, could be used to address other public health threats in the future.

NIAID will continue to support the development of multi-modal, or platform, technologies to enhance pandemic preparedness and response efforts.

Responses by Dr. Robin Robinson

Questions from Congresswoman Mikie Sherrill (D-NJ 11th District)

BARDA successes in influenza vaccines

Among the 250+ medical countermeasures whose development and procurement have been supported by BARDA from 2004 to 2019, influenza vaccines have been among its most extraordinary accomplishments with its industry partners in vaccine development, stockpiling, domestic and international manufacturing capacity, and national and global pandemic strategic planning.

BARDA supported the development of 14 new cell- and recombinant-based seasonal, pandemic, and universal influenza vaccines starting in 2006, resulting in the FDA licensure of the following first-in-class seasonal and pandemic influenza vaccines:

- Flucelvax, a cell-based seasonal influenza vaccine licensed in 2012 to Novartis and later acquired in 2015 by Commonwealth Serum Laboratories' subsidiary, Seqirus.
- Pandemrix, an adjuvant-containing pandemic H5N1 pandemic influenza vaccine in 2013 to GlaxoSmithKline.
- FluBlOk, a recombinant-based seasonal influenza vaccine licensed in 2015 to Protein Sciences, Inc. and later acquired in 2016 by sanofi pasteur
- Fluad, an adjuvant-containing seasonal influenza vaccine licensed in 2019 by Seqirus in the U.S. for prevention of influenza in senior citizens $\geq$ 65 years old

BARDA began in 2006 and maintains today the first and largest pre-pandemic H5N1 and H7N9 influenza vaccine and adjuvant stockpiles with its industry partners in the world that is able to protect more than 200 million Americans. BARDA led the national immediate vaccine manufacturing and stockpiling responses to the multiple waves of H5N1 avian influenza viruses from 2004-2011 and H7N9 viruses from 2013-2019.

BARDA through public-private partnerships with industry expanded domestic pandemic vaccine manufacturing capacity from 100 million doses in 2006 to more than 600 million doses in 2016 through development of new influenza vaccine classes and the building of new and renovated manufacturing plants as follows:

- sanofi pasteur (Swiftwater, PA), completed expansion from two to four bulk influenza vaccine manufacturing lines in 2009 and 2018 and most recently has help to fund the building of a new recombinant-based influenza vaccine manufacturing facility.
- Novartis, acquired by Seqirus (Holly Springs, NC), completed the building of a new state-of-the art and award-winning cell-based influenza vaccine and adjuvant manufacturing plant in 2012
- MedImmune, acquired by AstraZeneca (Red Line, PA), completed a second fill finish manufacturing line in 2009 for production of their live, attenuated influenza vaccine, FluMist

BARDA with its sister HHS agencies led policy discussions and implemented a strategic plan in 2015 to expedite production of seasonal influenza vaccines during vaccine mismatched seasons and helped construct the basic vaccine principles forming the ***National Strategy for Pandemic Influenza*** (2005).

BARDA, starting in 2006 through its technical and financial support of the WHO Global Action Plan for influenza vaccines, has helped more than 15 companies in countries without influenza vaccines in 2006 to develop and produce influenza vaccines for the first time. Today licensed influenza vaccines are available in Viet Nam, India, South Africa, Brazil, Mexico, and Thailand thanks to BARDA's technical assistance and funding that has been leveraged nearly nine-fold with other donors.

BARDA, since its inception to now, has been an integral player in the U.S. Government's pandemic vaccine role, with worldwide industry partners to develop and produce more and better influenza vaccines sooner, and as advisors to the World Health organization on the role of vaccines to address global seasonal and pandemic influenza issues.

Temperature-monitoring of Vaccines

Temperature monitoring is an essential element in the manufacturing, storage, and distribution of vaccines by vaccine industry manufacturers, temperature-sensitive transportation carriers, the CDC through its Vaccine for Children's Program, and BARDA through its vaccine stockpiling and manufacturing programs. The technology for temperature-monitoring has evolved over the past 20 years to afford reliable and robust precise environmental monitoring at the facility, pallet, case, carton, and dose level. Evaluation and adoption of these state-of-the-art temperature monitoring systems have been integrated into overall vaccine manufacturing, storage, and distribution systems by industry and government agencies.

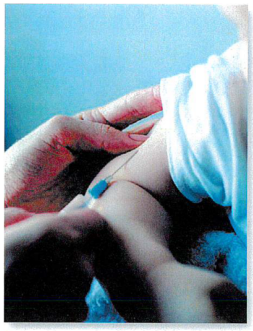
As partners with the vaccine manufacturers and distributors, CDC, FDA, and BARDA are at the forefront of supporting the development of new environmental monitoring technologies and systems and for ensuring these new methods are disseminated to and adopted by industry vaccine manufacturers and others in the supply chain. BARDA has adopted these new methods from highly sophisticated domestic vaccine manufacturing facilities for influenza vaccine stockpiles to remote areas in Sierra Leone for vaccine storage and distribution during the Ebola epidemic in 2014-2015, where large refrigeration facilities were sparse and limited in function.

Appendix II

Additional Material for the Record

Dispelling Myths Regarding the Use of Thimerosal in Vaccines

Lyn Redwood, RN, MSN
Executive Director
World Mercury Project



POWERFUL POISON—Exposure to ethylmercury can cause irreversible damage to the central nervous system.

Earlier this week, entertainer John Oliver discussed vaccines on his weekly HBO program Last Week with John Oliver. In doing so, he exposed viewers to several inaccuracies about vaccine safety, including those regarding the use and toxicity of the mercury-based preservative thimerosal. In developing his monologue, it appears that Mr. Oliver—like numerous other news outlets who promote vaccines as universally safe and effective—relied solely on information from the Centers for Disease Control and Prevention (CDC) which continues efforts to persuade the American public that injecting mercury into pregnant women and children with thimerosal-containing flu vaccines is safe.

The talking points reviewed below were derived from a recently published article by CNN titled *Thimerosal: Everything You Need To Know About This Vaccine Preservative*. These talking points are at best misleading, and at worse, patently false. The World Mercury Project has responded to each of the CNN/CDC talking points with factual information in our effort to educate consumers to avoid this completely unnecessary and dangerous neurotoxin.

CNN Statement: Thimerosal is best known as a preservative used in some vaccines to keep them from becoming contaminated. The preservative has gotten a lot of attention over the years, particularly since it was removed from childhood vaccines in 2001. Several studies have shown that the preservative is safe, but not everyone has been convinced. (Note, there is no link provided to the to support the statement thimerosal is safe)

WMP Fact: Although thimerosal was slated for removal from childhood vaccines in 1999, the reformulation process took several years. Products containing thimerosal were not recalled and the manufacturers were allowed to continue to distribute thimerosal containing vaccines well into 2001 that had a two year expiration date. In 2003 when all the residual stock of thimerosal containing vaccines was almost distributed, the CDC Advisory Committee

for Immunization Practices (ACIP) made the new recommendation that all pregnant women, infants starting at six months of age and children receive flu vaccines annually.

This recommendation was contradictory to the fact that the prestigious Institute of Medicine made the recommendation in 2001 that pregnant women, infants and children NOT receive thimerosal preserved vaccines. At the time, the vast majority of flu vaccines contained thimerosal. Pregnant women are especially vulnerable to mercury exposure because the fetus accumulates mercury at a higher rate than the mother. This flu season approximately 48 million doses of flu vaccine containing thimerosal were distributed and administered to pregnant women, infants and children in the U.S.

Here's what you need to know about what it is (and what it isn't).

CNN Statement: Thimerosal is the most widely used preservative in vials of vaccines used multiple times, a mercury-based organic compound that can prevent bacteria and fungus from growing.

WMP Fact: While it is true that thimerosal is a widely used preservative, it is not necessarily an effective preservative. In 1975 the FDA convened a panel of experts to review the use of thimerosal as a preservative. The agency issued a report of the panel's findings in the Federal Register where they concluded that "some mercury-containing preparations are not effective and others are not safe and effective" for antimicrobial use.

With respect to thimerosal in particular, the panel found evidence from 1950 which concluded that "thimerosal was no better than water in protecting mice from potential fatal streptococcal infections." and "35.3 times more toxic for embryonic chick heart tissue than for *Staphylococcus aureus*." The panel concluded that "thimerosal was not safe for OTC topical use and not effective as a topical antimicrobial because its bacteriostatic action can be reversed."

Most of the literature reviewed addressed mercury's lack of antibacterial properties. One study reviewed published in 1970 titled, "Three thousand years of mercury. A plea for abandonment of a dangerous, unproven therapy," addressed mercury's lack of effectiveness regarding anti-fungal properties.

Why do vaccines need preservatives?

CNN Statement: Vaccine makers started using preservatives in the 1930s after they found that contamination could become a problem with multi-dose vaccines. Doctors learned that the hard way in 1928, when 12 children died after getting vaccinated for diphtheria. An investigation found that the multi-dose vaccine had been contaminated with living staphylococci. The children had been injected with the diphtheria vaccine and a staph infection.

WMP Fact: While it is true that preservatives are used to prevent bacterial contamination in multi-dose vials of vaccines, there is ample evidence provided by federal agencies and independent scientists that spans the last 80 years which documents that thimerosal is not an effective or safe vaccine preservative.

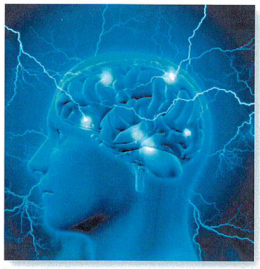
In a study published in the *Journal of the American Medical Association* in 1948 titled "The bacteriostatic and bactericidal actions of some mercurial compounds on

...thimerosal was no better than water in protecting mice from potential fatal streptococcal infections

and 35.3 times more toxic for embryonic chick heart tissue than for Staphylococcus aureus.

hemolytic streptococci," the authors vigorously argued that thimerosal was ineffective as a "disinfectant, germicide and antiseptic." In the review of the literature in this paper, the authors cited eight studies from 1928, 1935, 1937, 1938, and 1944 all of which drew similar conclusions.

There are several recent reports of thimerosal's failure as a preservative as well. Clusters of disease from *Group A streptococcus* infections were traced back to multi-dose vials of diphtheria toxoid, pertussis, and tetanus toxoid (DPT) vaccine which were contaminated after being opened. Additionally, in 2004, a Chiron plant that manufactured Fluvirin was forced to close because its vaccine was contaminated with *Serratia marcescens*. This vaccine used thimerosal as a preservative in its product. In this case and others, thimerosal failed to prevent bacterial growth which resulted in dangerous infections.



TOXIC PATHWAY—Ethylmercury is more persistent in the brain than methylmercury.

What happens to the preservative in your body?

CNN Statement: Your body easily eliminates the thimerosal. Unlike chemicals that might stay in your body for a long time, it is quickly removed from the blood and excreted in your waste. Thimerosal does not build up in your system like other mercury-based compounds can. (Note, this link takes you to the CDC website where this statement is repeated, but with no references or resources to support the claim)

WMP Fact: This statement is patently false. Thimerosal does leave the blood stream faster than methylmercury, but that is because it more quickly moves into the tissue and organs in the body than methylmercury. A 2005 study funded by the National Institutes of Health compared brain mercury levels in infant monkeys exposed to injected ethylmercury (thimerosal) and equal amounts of ingested methylmercury. In this study, ethylmercury exposure resulted in twice as much inorganic mercury in the brains of the infant monkeys compared to those exposed to methylmercury. Specifically, the relative concentrations in monkeys with detectable levels of inorganic mercury were 16 ng/g in thimerosal-treated monkeys and 7 ng/g in the methylmercury-treated monkeys in which inorganic mercury levels were detectable. Inorganic mercury was below detectable levels in 8 out of 17 of the methylmercury-treated monkeys. Inorganic mercury has an estimated half-life in the brain of 27 years. Exposures to mercury during these critical periods of development disrupt the growth and migration of neurons, with the potential to cause irreversible damage to the central nervous system.

Is it safe?

CNN Statement: Hundreds of studies have shown that it is extremely safe for humans. Several comprehensive reviews have shown there is no evidence of harm caused by low doses. (This links to the CDC website, but there is no data to support this claim on the site) In animals, some studies have shown central nervous problems, coma and death, although the same has not been found in humans.

WMP Fact: There are several reports of deaths in the medical literature from exposure to thimerosal. In April of 2001 thimerosal was nominated by the FDA to be reviewed by the National Toxicology Program (NTP) due to the lack of toxicity and safety data. In the nomination, several cases of acute mercury poisoning from thimerosal-containing products were documented. These reports included the

exposure to thimerosal from immune globulin (Matheson 1980) hepatitis B immune globulin (Lowell 1996), thimerosal ear irrigations in a children with tympanostomy tubes (Royhans 1994), thimerosal treatment of omphaloceles in infants (Fagan 1977), and a suicide attempt with thimerosal (Pfab 1996). These studies reported local necrosis, acute hemolysis, disseminated intravascular coagulation, acute renal tubular necrosis, and central nervous system injury including obtundation, coma, and death resulting from the exposures.

Are there any side effects?

CNN Statement: The most common side effect is a mild rash or redness at the injection site. There may also be a little swelling. All of these symptoms disappear quickly. On rare occasions, some people have had allergic reactions to the preservative.

WMP Fact: What CNN fails to acknowledge are the thousands of families who have reported developmental regression of their children after exposure to thimerosal containing vaccines. One such case was actually covered by CNN in 2007 when a child who received multiple thimerosal-containing vaccines regressed developmentally within 48 hours after receiving the vaccines and was later diagnosed with autism.

Do children get vaccines with thimerosal?

CNN Statement: All routinely recommended vaccines for children in the US are available in a thimerosal-free formulation or contain only a trace amount.

WMP Fact: Flu vaccines are universally recommended for infants and children. Approximately 1/3 of all flu vaccines contain thimerosal. According to the CDC 48 million doses of flu vaccine manufactured this year contained thimerosal. A trace amount is defined as being 1 microgram (mcg) or less. Flu vaccines contain 25 mcg of mercury. According to EPA mercury exposure guidelines of 0.1 mcg per kilogram of body weight, a baby would need to weigh 550 lbs to be able to safely process the amount of mercury in a thimerosal containing flu vaccine. State and Federal guidelines require that any product that contains more than 0.2 milligrams per liter (200 PPB) of mercury must be disposed of as a hazardous waste. All flu vaccines preserved with mercury that are not used must be disposed of as hazardous waste because they contain 50,000 PPB mercury.

What makes it different from other mercury-based products?

CNN Statement: Thimerosal is an ethylmercury; the mercury that can be found in fish is a methylmercury. Though they are only one letter apart, the substances are different. Mercury is an element found in the Earth's crust. We are all exposed to mercury as we live on the surface of the planet. It's in our water, in our soil and in the air. Methylmercury is created when mercury comes into contact with some bacteria. Doctors warn pregnant women to avoid some fish because it can be contaminated with this form. Unlike ethylmercury, which can pass through your body quickly, methylmercury can linger and accumulate. If enough accumulates, it can be toxic.

In 1999, the National Vaccine Advisory Committee held a meeting to discuss the safety of thimerosal. Some who testified worried that babies were unable to eliminate the mercury from their systems. Follow-up studies of infants showed that they "excreted significant amounts of mercury in stool after thimerosal exposure," meaning it was removed from the body quickly, compared with methylmercury.

According to the CDC, 48 million doses of flu vaccine manufactured this year contained thimerosal.

A trace amount is defined as being 1 microgram (mcg) or less. Flu vaccines contain 25 mcg of mercury.

WMP Fact: Evidence that ethylmercury is quickly passes through the body is not supported by scientific research which documents that ethylmercury accumulates in the kidneys and brain tissue. Although infants have been found to excrete some mercury in their stool after exposure to thimerosal containing vaccines, the amount excreted does not account for the amount injected. Michael Pichichero, a pediatrician, measured mercury concentrations in stool of 22 normal infants exposed to thimerosal in vaccines, ages two and six months, and found a range of 23-141 *nanograms* of mercury per gram of stool (dry weight). The authors interpreted these levels, mere parts per billion, as positive evidence of mercury elimination. But these mercury levels are extremely low and not nearly enough to allow for rapid excretion as the authors propose.

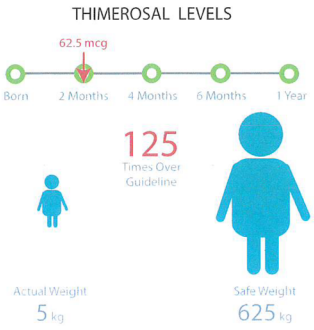
One of the few researchers who studies the effects of ethylmercury is Thomas Burbacher, PhD, professor of environmental and occupational health sciences and director of the infant primate research lab at the National Primate Research Center, University of Washington, Seattle. Burbacher says that just because ethylmercury is gone from an infant's blood soon after it receives a dose of thimerosal — a half-life of just 3.7 days in the Pichichero study — doesn't mean it's gone from the body. It could have gone to the brain," Burbacher tells WebMD. "Although total mercury levels in the blood are lower following thimerosal exposure [than following methyl mercury exposure], mercury in the blood from thimerosal has an easier time getting to the brain than methylmercury."

GRIM GUIDELINES—The CDC currently recommends the flu shot for pregnant women and annually for children aged six months and older.

If it is safe, why was it removed from kids' shots?

CNN Statement: Based on the recommended childhood vaccination schedule, there was concern that some babies could be exposed to a higher cumulative level of mercury in the first six months of life from these shots. At the time, babies got diphtheria-tetanus-acellular pertussis, Haemophilus influenza type b and hepatitis B shots. If an infant got all three, the accumulation went beyond the EPA guidelines for methylmercury.

WMP Fact: This is actually a factual statement. WMP would like to add that the amount that infants received from thimerosal containing vaccines was far in excess of EPA guidelines. An average 5 KG infant at 2 months of age could receive 62.5 mcg of mercury from vaccines. According to EPA guidelines the allowable exposure levels would be .5 mcg. Infants were routinely exposure to 125 times EPA allowable guidelines based on weight.



A study published in *Pediatrics* in 2000 measured blood mercury levels in newborns administered the Hepatitis B vaccine, containing 12.5 mcg of ethyl mercury. The investigation documented elevated post-immunization concentrations relative to pre-immunization levels in all neonates studied. One infant was found to have developed a mercury level of 23.6 mcg/L, thus meeting the CDC criteria as a case of chemical poisoning from mercury.

Experts contend that there are "windows of vulnerability" which occur during neurological development and that specific types of developmental outcomes may have separate windows of vulnerability. These critical periods of development have not been established and may be relatively short in duration. The fact that thimerosal from vaccines has been documented to raise blood mercury levels over known thresholds where developmental effects have been documented to occur during the first few months of life means that particular "windows of vulnerability" may have been breached. Even minor neurological impairment can have profound societal effects when amortized across the entire population and life span.

For more information regarding the use of mercury in vaccines see click here.

For more information about the use of thimerosal in vaccines see World Mercury Projects FAQ

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MMWR

Weekly

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Notice to Readers: Thimerosal in Vaccines: A Joint Statement of the American Academy of Pediatrics and the Public Health Service

The Food and Drug Administration (FDA) Modernization Act of 1997 called for FDA to review and assess the risk of all mercury-containing food and drugs. In line with this review, U.S. vaccine manufacturers responded to a December 1998 and April 1999 FDA request to provide more detailed information about the thimerosal content of their preparations that include this compound as a preservative. Thimerosal has been used as an additive to biologics and vaccines since the 1930s because it is very effective in killing bacteria used in several vaccines and in preventing bacterial contamination, particularly in opened multidose containers. Some but not all of the vaccines recommended routinely for children in the United States contain thimerosal.

There is a significant safety margin incorporated into all the acceptable mercury exposure limits. Furthermore, there are no data or evidence of any harm caused by the level of exposure that some children may have encountered in following the existing immunization schedule. Infants and children who have received thimerosal-containing vaccines do not need to be tested for mercury exposure.

The recognition that some children could be exposed to a cumulative level of mercury over the first 6 months of life that exceeds one of the federal guidelines on methyl mercury now requires a weighing of two different types of risks when vaccinating infants. On the one hand, there is the known serious risk of diseases and deaths caused by failure to immunize our infants against vaccine-preventable infectious diseases; on the

other, there is the unknown and probably much smaller risk, if any, of neurodevelopmental effects posed by exposure to thimerosal. The large risks of not vaccinating children far outweigh the unknown and probably much smaller risk, if any, of cumulative exposure to thimerosal-containing vaccines over the first 6 months of life.

Nevertheless, because any potential risk is of concern, the Public Health Service (PHS), the American Academy of Pediatrics (AAP), and vaccine manufacturers agree that thimerosal-containing vaccines should be removed as soon as possible. Similar conclusions were reached this year in a meeting attended by European regulatory agencies, European vaccine manufacturers, and FDA, which examined the use of thimerosal-containing vaccines produced or sold in European countries.

PHS and AAP are working collaboratively to assure that the replacement of thimerosal-containing vaccines takes place as expeditiously as possible while at the same time ensuring that our high vaccination coverage levels and their associated low disease levels throughout our entire childhood population are maintained.

The key actions being taken are

1. A formal request to manufacturers for a clear commitment and a plan to eliminate or reduce as expeditiously as possible the mercury content of their vaccines.
2. A review of pertinent data in a public workshop.
3. Expedited FDA review of manufacturers' supplements to their product license applications to eliminate or reduce the mercury content of a vaccine.
4. Provide information to clinicians and public health professionals to enable them to communicate effectively with parents and consumer groups.
5. Monitoring immunization practices, future immunization coverage, and vaccine-preventable disease levels.
6. Studies to better understand the risks and benefits of this safety assessment.

PHS and AAP continue to recommend that all children should be immunized against the diseases indicated in the recommended immunization schedule. Given that the risks of not vaccinating children far outweigh the unknown and much smaller risk, if any, of exposure to thimerosal-containing vaccines over the first 6 months of life, clinicians and parents are encouraged to immunize all infants even if the choice of individual vaccine products is limited for any reason.

While there is a margin of safety with existing vaccines containing thimerosal, there are steps that can be taken to increase that margin even further. Clinicians and parents can take advantage of the flexibility within the existing schedule for infants born to hepatitis B surface antigen (HBsAg)-negative women to postpone the first dose of hepatitis B vaccine from birth until 2 to 6 months of age when the infant is considerably larger. Preterm infants born to HBsAg-negative mothers should similarly receive hepatitis B vaccine, but ideally not until they reach term gestational age and a weight of at least 5.5 lbs (2.5 kg). Because of the substantial risk of disease, there is no change in the recommendations for infants of HBsAg-positive mothers or of mothers whose status is

not known. Also, in populations where HBsAg screening of pregnant women is not routinely performed, vaccination of all infants at birth should be maintained, as is currently recommended. In addition to the key actions mentioned above, the PHS Advisory Committee on Immunization Practices and the AAP Committee on Infectious Diseases will be reviewing these issues and may make additional statements.

Reported by: Public Health Service, US Dept of Health and Human Services. American Academy of Pediatrics, Elk Grove Village, Illinois.

DOCUMENTS SUBMITTED BY REPRESENTATIVE BILL POSEY

A Small Sampling of Peer Reviewed Publications on Thimerosal

Thimerosal and Adverse Effect

Hypersensitivity Reports in Letters to Journals (1970s) [1-4]

Concerns About Thimerosal in Ocular Solutions (1980s)
Ocular inflammatory process, delayed hypersensitivity to thimerosal demonstrated.[5]
Ocular irritation and keratoconjunctivitis clinically resembling superior limbic
Light and transmission electron microscopic examination of conjunctival specimens disclosed intercellular epithelial edema, pseudoepitheliomatous hyperplasia, acute and chronic inflammation, and decreased numbers of goblet cells. Exposure to thimerosal is implicated in the etiology of contact lens-superior limbic keratoconjunctivitis (CL-SLK).[6]
Thimerosal sometimes triggers a sensitivity reaction.[7]

Blood Brain Barrier

A comparison of topical and subcutaneous administration of thimerosal to rabbits shows that a substantial concentration of mercury was present in blood and tissues of the treated animals and their offspring. In 1975, **thimerosal was found to cross the blood-brain and placenta barriers**.[8]

Animal Studies with Thimerosal

From Japan, a Mouse study, as a result of the present findings, in combination with the brain pathology observed in patients diagnosed with autism, the present study helps to support the possible biological plausibility for how low-dose exposure to mercury from thimerosal-containing vaccines may be associated with autism.[9]

From Iran, an inert placebo-controlled study in rats, immune cells [mast cells (MCs) and microglia] and pro-neuroinflammation cytokines (interleukin-1b and tumor necrosis factor-α) were assessed in the prefrontal lobe of rat brains exposed to thimerosal in different timeframes. A total of 108 neonatal Wistar rats were divided into three groups having three subgroups. The experimental groups received a single dose of thimerosal (300 μg/kg) postnatally at 7, 9, 11, and 15 days. The vehicle groups received similar injections of phosphate-buffered saline in a similar manner. The control groups received nothing. Samples of the prefrontal cortex were collected and prepared for stereological, immunohistochemical, and molecular studies at timeframes of 12 or 48 h (acute phase) and 8 days (subchronic phase) after the last injection. The average density of the microglia and MCs increased significantly in the experimental groups. This increase was more evident in the 48-h group. At 8 days after the last injection, there was a significant decrease in the density of the MCs compared to the 12 and 48 h groups. Alterations in pro-inflammatory cytokines were significant for all timeframes. This increase was more evident in the 48-h group after the last injection. There was a significant decrease in both neuroinflammatory cytokines at 8 days after the last injection. It was found that ethylmercury caused abnormal neurogenic inflammatory reactions and alterations in the neuroimmune cells that remained for a longer period in the brain than in the blood.[10]

Also, from Iran a study looking at the protective effects of Alpha Lipoic Acid (ALA), an organosulfur compound derived from Octanoic Acid, on Thimerosal-induced behavioral abnormalities in rat. The data showed that Thimerosal at all doses (30, 300 and 3000 µg Hg/kg) significantly impacted locomotor activity. Thimerosal at doses of 300 and 3000 but not 30 µg Hg/kg impaired social and stereotyped behaviors. The results of this preclinical study, consistent with previous studies on mice and rats, reveals that neonatal dose-dependent exposure to Thimerosal mimicking the childhood vaccine schedule can induce abnormal social interactions and stereotyped behaviors similar to those observed in neurodevelopmental disorders such as autism, and, for the first time, revealed that these abnormalities may be ameliorated by ALA. This indicates that ALA may protect against mercurial-induced abnormal behaviors.[11]

Our of Brazil, a study aimed to evaluate the kinetics of mercury species in mice found through injecting mice with thimerosal that the kidney must be considered a potential target for ethylmercury (etHg) toxicity (a component of thimerosal).[12]

From Japan, an inert placebo-controlled study of premature rats injected with thimerosal on postnatal day 1 found, that 48 days later, in those receiving the highest dose (131.2 ug/kg) the expression of dopamine D4 receptor (DRD4) and serotonin 2A receptor (5-HT2AR), and learning function decreased, and apoptosis (cell death) increased significantly. In 3 of the 4 thimerosal exposure levels memory function was significantly impaired. The authors conclude, that the negative adverse consequences on neurodevelopment observed in the present study are consistent with previous studies; this study raised serious concerns about adverse neurodevelopmental disorder such as autism in humans following the ongoing worldwide routine administration of thimerosal containing vaccines to infants.[13] **Why do dopamine and serotonin expression matter**?: NIEHS funded study on Dopamine expression raises concerns about loss of midbrain dopamine neurons, neuronal loss, accompanied by oxidative stress and fine motor deficits.[14] Serotonin expression linked to gene expression as detailed in NIDA-funded study.[15] Dr. Francis Collins noted in discussing this article, "Serotonin is best known for its role as a chemical messenger in the brain, helping to regulate mood, appetite, sleep, and many other functions. It exerts these influences by binding to its receptor on the surface of neural cells… the molecule also can enter a cell's nucleus and directly switch on genes."[1]

From Croatia, due to the facts that thiomersal-containing vaccine is still in use in many developing countries, and all forms of mercury have recognized neurotoxic, nephrotoxic, and other toxic effects, studies on disposition of ethylmercury and other mercury forms are still justified, especially at young age. Our investigation aimed at comparing mercury distribution and rate of excretion in the early period of life following exposure to either thiomersal (TM) or mercuric chloride (HgCl2) in suckling rats. Three experimental groups were studied: control, TM, andHgCl2, with 12 to18 pups in each. Both forms of mercury were administered to mimic the vaccination regimen in infants. After the last administration of TM or HgCl2, total mercury retention and excretion was assessed during following six days. In TM-exposed group mercury retention was higher in the brain, enteral excretion was similar, and urinary excretion was much lower compared to HgCl2-exposed sucklings. This work has provided a considerable contribution to the evidence that all forms of mercury are more toxic when administered to infant

[1] (https://directorsblog.nih.gov/2019/03/19/mood-altering-messenger-goes-nuclear/)

than adult mammals by showing that under same exposure conditions higher mercury retention is found in the gut and the brain of young compared to adult experimental animals.[16]

Follow on rat study out of Poland, concluded, this study documents that parenteral administration of THIM to suckling rats at doses equivalent to those used in pediatric vaccines or higher produces lasting alterations of l-opioid receptors (MORs) in several brain regions and damage to neurons. If analogous changes occur in the brains of some children, they are likely to have profound neurological, physiological and behavioral consequences, which may be relevant for certain neurodevelopmental disorders. These data argue for removal of THIM from all infant vaccines. The earlier study showed that thimerosal administered to suckling rats causes persistent, endogenous opioid-mediated hypoalgesia. Citations provided in paper document that centuries of human experience and a large body of scientific data document that all forms of Hg are highly toxic. Considerable amounts of Hg have been found in the blood of human infants after the injection of THIM-containing vaccines and studies conducted with infant monkeys showed that Hg from THIM-vaccine injections accumulates in the brain at concentrations many times higher than those in the blood, and that it stays there for months or years. Post vaccination levels of Hg in infant brains may reach medium nanomolar concentrations, which are neurotoxic and kill neurons in vitro. THIM doses equivalent to those used in vaccines have been shown to harm the brains of developing mice. [17]

Primate Studies

From the US: The macaque infant is a relevant animal model in which to investigate specific environmental exposures and structural/functional neuroimaging during neurodevelopment. In this pilot study, infant macaques receiving the recommended pediatric vaccine regimen from the 1990's displayed a different pattern of maturational changes in amygdala volume and differences in amygdala-binding of [11C]DPN following the MMR/DTaP/Hib vaccinations between T1 and T2 compared with non-exposed animals. There was also evidence of greater total brain volume in the exposed group prior to these vaccinations suggesting a possible effect of previous vaccinations to which these animals had been exposed. Because primate testing is an important aspect of pre-clinical vaccine safety assessment prior to approval for human use the results of this pilot study warrant additional research into the potential impact of an interaction between the MMR and thimerosal-containing vaccines on brain structure and function. Additional studies are underway in the primate model to investigate the mechanistic basis for this apparent interaction.[18]

From the US – A study of whether acquisition of neonatal reflexes in newborn rhesus macaques was influenced by receipt of a single neonatal dose of hepatitis B vaccine containing the preservative thimerosal (Th). Hepatitis B vaccine containing a weight-adjusted Th dose was administered to male macaques within 24 h of birth (n = 13). Unexposed animals received saline placebo (n = 4) or no injection (n = 3). Infants were tested daily for acquisition of nine survival, motor, and sensorimotor reflexes. In exposed animals there was a significant delay in the acquisition of root, snout, and suck reflexes, compared with unexposed animals. No neonatal responses were significantly delayed in unexposed animals. Lower birth weight and lower gestational age exacerbated the adverse effects following vaccine exposure.[19]

A Small Sampling of Peer Reviewed Publications on Thimerosal

The 2005 Burbacher primate study comparing topical methylmercury and injected thimerosal (ethylmercury) study (often misquoted) found notable similarities and differences in the kinetics of Hg after oral administration of MeHg and im injection of thimerosal in vaccines. The absorption rate and initial distribution volume of total Hg appear to be similar between im thimerosal and oral MeHg. This means approximately equal peak total blood Hg levels after a single exposure to either MeHg or thimerosal or after episodic exposures that are apart by longer than four elimination half-lives (i.e., > 80 days for MeHg or > 28 days for thimerosal). Studies in preterm and term human infants have reported similar results. It is relevant to note that the kidney-to-blood concentration gradient of total Hg is much higher in the thimerosal monkeys than in the MeHg monkeys. The large difference in the blood Hg half-life compared with the brain half-life for the thimerosal-exposed monkeys (6.9 days vs. 24 days) indicates that blood Hg may not be a good indicator of risk of adverse effects on the brain, particularly under conditions of rapidly changing blood levels such as those observed after vaccinations. The blood concentrations of the thimerosal-exposed monkeys in the present study are within the range of those reported for human infants after vaccination (Stajich et al. 2000). Data from the present study support the prediction that, although little accumulation of Hg in the blood occurs over time with repeated vaccinations, accumulation of Hg in the brain of infants will occur. Thus, conclusion regarding the safety of thimerosal drawn from blood Hg clearance data in human infants receiving vaccines may not be valid, given the significantly slower half-life of Hg in the brain as observed in the infant macaques. There was a much higher proportion of inorganic Hg in the brain of thimerosal monkeys than in the brains of MeHg monkeys (up to 71% vs. 10%). Absolute inorganic Hg concentrations in the brains of the thimerosal exposed monkeys were approximately twice that of the MeHg monkeys. The author concluded, "Knowledge of the biotransformation of thimerosal, the chemical identity of the Hg-containing species in the blood and brain, and the neurotoxic potential of intact thimerosal and its various biotransformation products, including ethylmercury, is urgently needed to afford a meaningful interpretation of the potential developmental effects of immunization with thimerosal-containing vaccines in newborns and infants. This information is critical if we are to respond to public concerns regarding the safety of childhood immunizations."[20]

Laboratory Research

Study evaluating a chelating agent confirms exposure to Hg is emerging as a risk factor associated with the cardiovascular diseases (CVDs) in humans. Levels of Hg in toenail and urine have been directly correlated with the elevated risk of myocardial infarction and coronary heart disease. Mercury exposure has also been linked to asthma and hypertension. Regardless of the reported association of exposure to Hg with CVD in humans, the role of vascular endothelial cells (ECs) in the Hg-mediated CVD is not known. Vascular endothelium is crucial for the structure and function of the blood vessels toward maintaining the homeostasis of the circulatory system. The dysfunction of EC has been shown to cause vascular damage and leak and the breakdown of the cardiovascular system. Hence, Hg-induced vasculotoxicity at the EC level appears to be involved in the Hg-induced CVDs. Phospholipase D (PLD) is a crucial signaling enzyme ubiquitous in mammalian cells, including vascular ECs, which generates the bioactive lipid signal mediators, phosphatidic acid (PA), diacylglycerol (DAG), and lysophosphatidic acid (LPA) from the hydrolysis of membrane phospholipids. These bioactive lipids regulate important cellular functions such as cell proliferation and differentiation.[21]

A Small Sampling of Peer Reviewed Publications on Thimerosal

Thimerosal (aka Merthiolate) Sensitivity and Patch Testing

Positive and negative patch tests to merthiolate occur with the same frequency in monozygotic and dizygotic twin pairs. There is no correlation to strong or weak reactions to primary irritants. Consequently, the positive merthiolate reactions should be considered allergic rather than irritant.[22]

A patient treated his slight score-throat with a thiomersal first aid spray. The next day, because of continued discomfort, he repeated its use. Laryngeal obstruction followed within hours. Emergency tracheostomy produced prompt improvement. Patch testing revealed an extreme spreading reaction to thiomersal. It is our interpretation that the acute laryngeal obstruction was delayed hypersensitivity to this first aid spray.[23]

2% of Eczema patients have sensitivity to thimerosal.[24] 4.9% of infants tested sensitive to thimerosal in patch testing.[25] 1% of individuals attending the Contact Dermatitis Investigation Unit in UK tested were positive patch tests to thiomersal. Individual cases of severe reactions to thiomersal demonstrate a need for vaccines with an alternative preservative.[26]

Swedish Study showed the methyl analogue of the preservative merthiolate [thimerosal], tested for its sensitizing capacity in the guinea pig, induced delayed allergy to a similar degree as merthiolate.[27]

Recommendation to replace thimerosal in vaccines due to high percentage of thimerosal sensitive persons Marked reaction in young patients.[28] Another study reports thimerosal reaction as adverse event vaccination. Confirmed through testing. [29]

Systemic Reactions to Thimerosal May Not Be Rare.[30]

Adverse Reaction to Thimerosal Containing Vaccine

Within 30 minutes of Hepatitis B Vaccine (2nd dose) generalized pruritus, dyspnea, urticaria and infraorbital edema developed. On questioning, she revealed that she had experienced a similar but less severe reaction to the vaccine's first dose four weeks earlier, when dyspnea and generalized itching developed, which were relieved by an injection of diphenhydramine by her personal physician. She had totally forgotten the link between the vaccine and the reaction. No other allergens present. The patient has not been given the third dose of vaccine.[31]

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"VICP Settlements Chart" submitted by Representative Bill Posey

VICP Adjudication Categories, by Alleged Vaccine For Petitions Filed Since the Inclusion of Influenza as an Eligible Vaccine for Filings 01/01/2006 through 12/31/2017							
Name of Vaccine Listed First in a Petition (other vaccines may be alleged or basis for compensation)	Number of Doses Distributed in the U.S., 01/01/2006 through 12/31/2017 (Source: CDC)	Compensable Concession	Compensable Court Decision	Compensable Settlement	Compensable Total	Dismissed/NonCompensable Total	Grand Total
Influenza	1,518,400,000	658	168	2,262	3,088	529	3,617
The flu vaccine, which was only introduced the Vaccine Injury Compensation Program in 2006 accounts for over 27% of the total number of vaccine injury petitions filed for the entire 31 years of the program. It accounts for more than 13% of the death claims. It also accounts for 46% of the cases that have been compensated.							
Petitions Filed, Compensated and Dismissed, by Alleged Vaccine, Since the Beginning of VICP, 10/01/1988 through 11/01/2019							
Vaccine	Filed Injury	Filed Death	Filed Grand Total	Compensated	Dismissed		
Influenza	5,592	176	5,798	3,251	524		
Grand Total of All filings	19,991	1,312	21,303	6,941	11,411		
Research funded by the FDA notes that less than 1% of adverse events are reported for all vaccines.							
https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/data-statistics-november-2019.pdf							

Hearing of the House Committee on Science, Space, and Technology

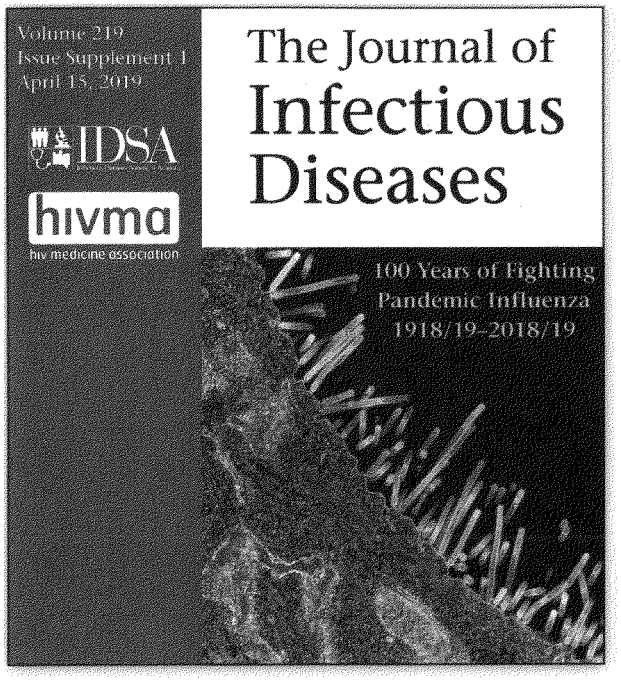
Innovations in Influenza Vaccinology: A View from NIAID

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health

November 20, 2019

NIH National Institute of Allergy and Infectious Diseases

- Current seasonal influenza vaccines are not consistently effective
- Pandemics do occur and response after the fact is not effective
- "Chasing after" potential pandemic outbreaks (pre-pandemic viruses) is costly and ineffective



Influenza Vaccines: Good, but We Can Do Better

CI Paules and AS Fauci

- **15 articles discuss research toward goal of developing a universal influenza vaccine**

Improving seasonal influenza vaccines
Pandemic influenza vaccines
Universal influenza vaccines

Published online
February 28, 2018

IDSA

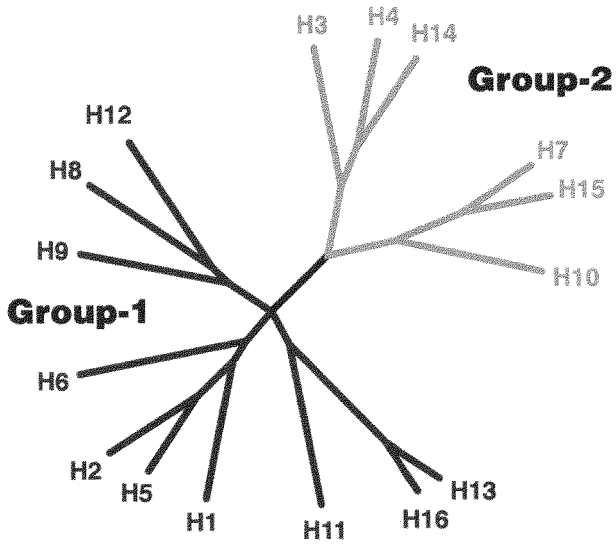
hivma
hiv medicine association

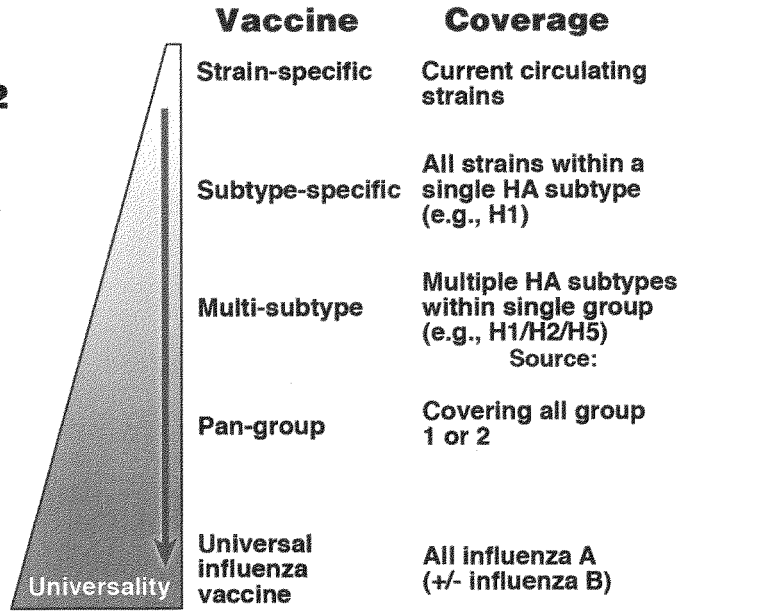
The Journal of
Infectious
Diseases

A Universal Influenza Vaccine: The Strategic Plan for the National Institute of Allergy and Infectious Diseases

EJ Erbelding, D Post, E Stemmy, PC Roberts, A Deckhut Augustine, S Ferguson, CI Paules, BS Graham, AS Fauci

Iterative Expansion of Breadth on the Path to a Universal Influenza Vaccine



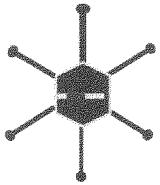


Source: Russell et al. *PNAS* 105(46), 2008; Paules et al. *Immunity* 47(4), 2017.

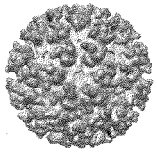
Courtesy Gary Nabel

New Platforms for Seasonal and Pandemic Influenza Vaccines

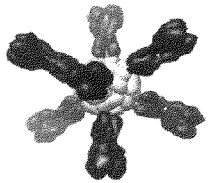
Recombinant protein



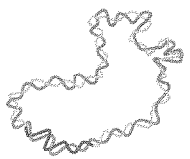
Viral vector (e.g., adenovirus)



Virus-like particle (VLP) (no RNA; non-infectious)

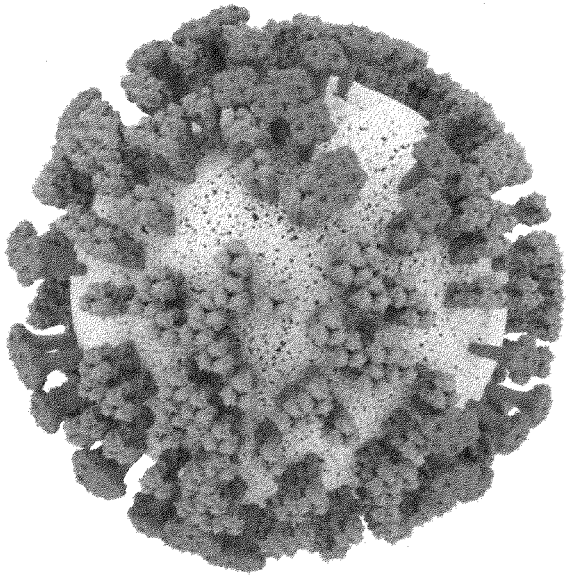


Nanoparticles (protein on particle)

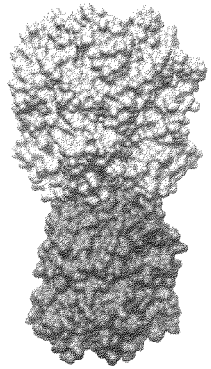


Genetic immunization (DNA and RNA vaccines)

Hemagglutinin Protein: Major Target of Influenza Vaccines



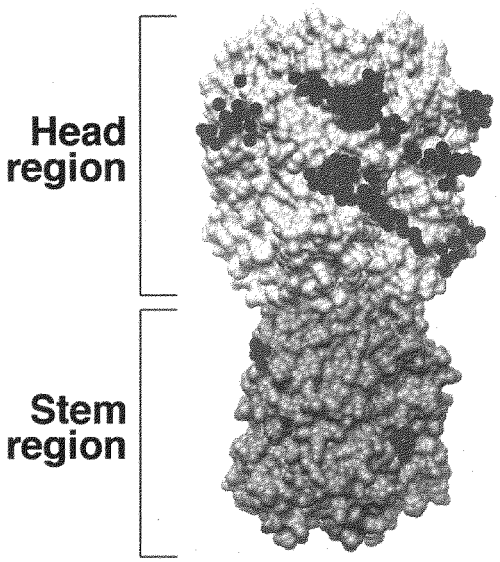
Influenza Virus



Hemagglutinin (HA) Protein

Courtesy of VRC

Influenza A Hemagglutinin (HA)



Head region

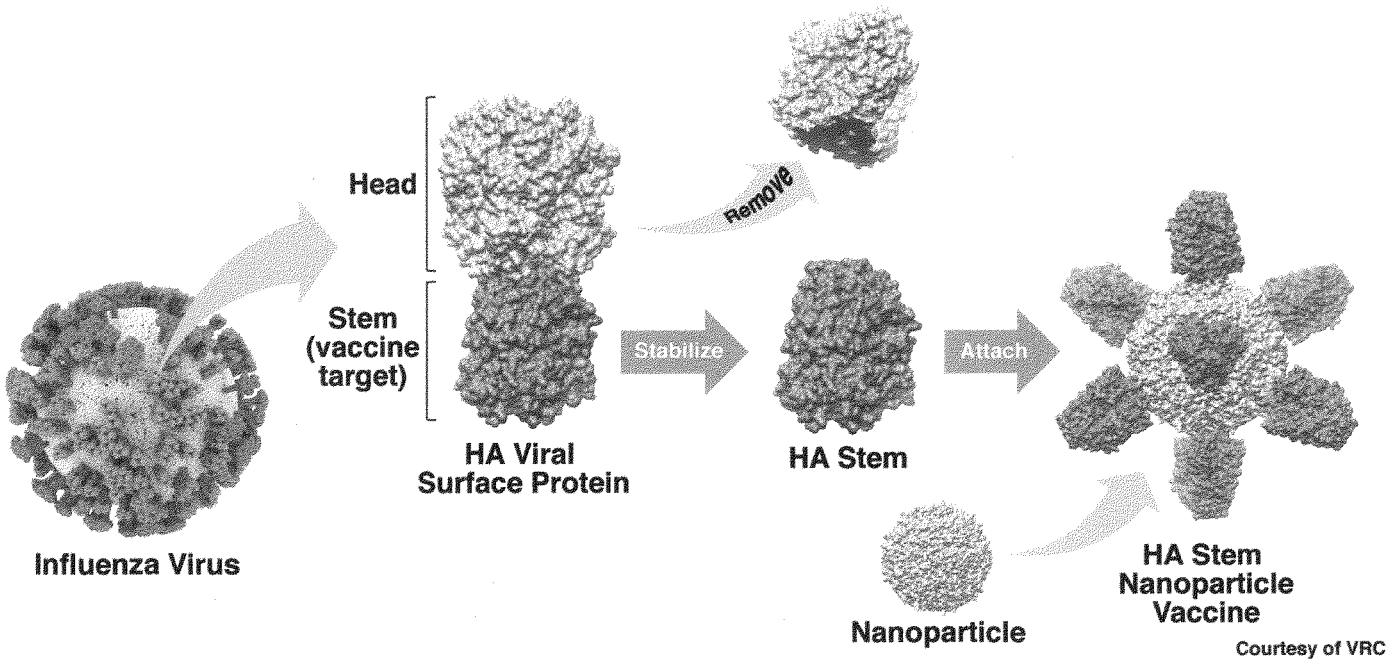
- Target of current influenza vaccines
- Differs among influenza strains
- Many mutations (●) each season

Stem region

- Target of universal influenza vaccines
- Similar among influenza strains
- Few mutations each season

Courtesy of VRC

Representative Approach to the Development of a Universal Influenza Vaccine



Courtesy of VRC

National Institute of Allergy and Infectious Diseases

April 3, 2019

News Release

NIH Begins First-in-Human Trial of a Universal Influenza Vaccine Candidate

Investigational vaccine designed to provide durable protection from Group 1 influenza strains