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ONE HUNDRED THIRTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115

Majority (202) 225-2927
Minority (202) 225-3641

MEMORANDUM

January 30, 2015

To: Subcommittee on Oversight and Investigations Democratic Members and Staff

Fr: Committee on Energy and Commerce Democratic Staff

Re: Hearing on "Examining the U.S. Public Health Response to Seasonal Influenza"

On Tuesday, February 3, 2015, at 10:00 a.m. in room 2123 of the Rayburn House Office Building, the Subcommittee on Oversight and Investigations will hold a hearing titled "Examining the U.S. Public Health Response to Seasonal Influenza." The majority has indicated that the hearing will focus on this season's flu outbreak and the effectiveness of the flu vaccine.

I. BACKGROUND

Influenza, or the flu, is "a contagious respiratory illness caused by influenza viruses that infect the nose, throat, and lungs."[1] While typical symptoms include fever, cough, or sore throat, complications from the flu can lead to severe illnesses like bacterial pneumonia or even cause death. Children younger than age five, adults sixty-five years of age and older, pregnant women, residents of nursing homes and long-term care facilities, and others with medical conditions (e.g., weakened immune systems or heart disease) are at a higher risk for developing flu-related complications.[2]

The timing and duration of flu seasons vary but can begin in October and last as late as May. Peak activity generally occurs in January and February.[3] The severity of flu seasons are extremely unpredictable: "between 1976 and 2007, estimates of flu-associated deaths in the United States [ranged] from a low of about 3,000 to a high of about 49,000 people."

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[1] Centers for Disease Control and Prevention, *Key Facts About Influenza (Flu) and Flu Vaccine* (online at www.cdc.gov/flu/keyfacts.htm).

[2] Centers for Disease Control and Prevention, *People at High Risk of Developing Flu-Related Complications* (online at www.cdc.gov/flu/about/disease/high_risk.htm).

[3] *Id.*

Flu vaccines protect individuals against the flu by causing protective antibodies to develop in the body.[4] Traditional flu vaccines, called "trivalent" vaccines, are made to protect against three viruses: two influenza A viruses (an H1N1 and an H3N2 strain) and an influenza B virus. A quadrivalent vaccine, which protects against two influenza A viruses and two influenza B viruses, is also available. The Centers for Disease Control and Prevention (CDC) recommends that everyone six months of age and older receive a flu vaccine each year.

Because different strains of the flu can predominate in any given year, the flu vaccine must be modified annually.[5] In February, the Food and Drug Administration (FDA) convenes its Vaccine and Related Biological Products Advisory Committee and recommends strains for both the trivalent and quadrivalent vaccines. The viruses are then adapted for use in manufacturing the seasonal vaccine, which begins shipping at the end of the summer. Throughout the year, the World Health Organization (WHO) monitors worldwide influenza disease. At the beginning of each calendar year, FDA and WHO review data to recommend the composition of influenza virus vaccines for the next winter.

II. 2014-2015 FLU SEASON

The FDA Vaccine and Related Biological Products Advisory Committee met on February 28, 2014, to select the flu strains for this year's vaccine.[6] Seven manufacturers are producing vaccines: GlaxoSmithKline, Sanofi Pasteur, Novartis, CSL Limited, Protein Sciences Corp., ID Biomedical Corp., and MedImmune.

The most common flu virus this year is an H3N2 strain not targeted by the flu vaccine.[7] Nearly 70% of the H3N2 viruses seen in the United States have altered from the H3N2 strain used in vaccine production.[8] H3N2 years have typically resulted in more severe illness and mortality, especially in older people and young children, than years where the H1N1 or influenza

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[4] Centers for Disease Control and Prevention, *Key Facts About Seasonal Flu Vaccine* (online at www.cdc.gov/flu/protect/keyfacts.htm).

[5] Food and Drug Administration, *Vaccines and Related Biological Products Advisory Committee* (online at www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/VaccinesandRelatedBiologicalProductsAdvisoryCommittee/).

[6] Food and Drug Administration, *Influenza Virus Vaccine for the 2014-2015 Season* (online at www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/PostMarketActivities/LotReleases/ucm397090.htm).

[7] *H3N2 viruses fuel 'epidemic' levels of flu season deaths, CDC says*, Los Angeles Times (Dec. 30, 2014) (online at www.latimes.com/science/sciencenow/la-sci-sn-flu-season-epidemic-20141230-story.html).

[8] *A Universal Flu Vaccine May Be On the Horizon*, Smithsonian Magazine (Jan. 26, 2015) (online at www.smithsonianmag.com/science-nature/measles-vaccine-universal-flu-influenza-cdc-disease-outbreak-180954020/?no-ist).

B viruses dominated.[9] H3N2 years tend to see twice as many hospitalizations and deaths.[10] For the flu season thus far, CDC is reporting the highest proportion of deaths attributable to pneumonia and influenza in nearly a decade.[11]

On January 15, 2015, the CDC announced that this year's flu vaccine is 23% effective, meaning it reduces a person's risk of having to go a doctor because of the flu by 23%.[12] Since the CDC began monitoring effectiveness on a widespread scale in 2009, vaccines have typically shown approximately 50% to 60% effectiveness.[13] These statistics support the possibility -- if not the probability -- that the flu virus used in vaccine production and the flu virus actually circulating are thoroughly mismatched.

The CDC continues to recommend that individuals receive the flu vaccine.[14] Antibodies in the vaccine protect against different but related viruses and may decrease the severity of illness. CDC also recommends use of antiviral drugs for those who do become infected to reduce the length and severity of symptoms.[15]

III. VACCINE DEVELOPMENT: ALTERNATIVE TECHNOLOGIES

Traditional vaccine development uses egg-based technology, which involves a lengthy manufacturing process. In egg-based manufacturing, each virus strain is injected into eggs, which are then incubated. Once the viruses multiply, the fluid from the eggs is harvested, purified, and tested for potency and safety.[16]

Several new technologies have been developed in recent years to improve the manufacturing of flu vaccines, including cell-based vaccines, recombinant vaccines, and adjuvants. Cell-based technology uses cells infected with the influenza virus instead of

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[9] Centers for Disease Control and Prevention, *What You Should Know for the 2014-2015 Influenza Season* (online at www.cdc.gov/flu/about/season/flu-season-2014-2015.htm).

[10] *Flu shots only 23% effective this season*, USA Today (Jan. 15, 2015) (online at www.usatoday.com/story/news/2015/01/15/flu-shot-less-effective/21804187/).

[11] Centers for Disease Control and Prevention, *Situation Update: Summary of Weekly FluView* (Jan. 23, 2015) (online at www.cdc.gov/flu/weekly/summary.htm).

[12] Centers for Disease Control and Prevention, *Protection from Flu Vaccine Reduce this Season* (Jan. 15, 2015) (press release).

[13] Centers for Disease Control and Prevention, *Seasonal Influenza Vaccine Effectiveness, 2005-2015* (online at www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm).

[14] Centers for Disease Control and Prevention, *What You Should Know for the 2014-2015 Influenza Season* (online at www.cdc.gov/flu/about/season/flu-season-2014-2015.htm).

[15] Centers for Disease Control and Prevention, *What You Should Know About Flu Antiviral Drugs* (online at www.cdc.gov/flu/antivirals/whatyoushould.htm).

[16] Food and Drug Administration, *The Evolution, and Revolution, of Flu Vaccines* (online at www.fda.gov/ForConsumers/ConsumerUpdates/ucm336267.htm).

fertilized eggs. [17] This technology makes for faster start-up of vaccine manufacturing but it requires that an adequate supply of cells is readily available for production. In November 2012, the FDA approved Novartis' Flucelvax, the first vaccine using cell culture technology for individuals 18 and older.

Recombinant technology uses a similar technique, but uses specific proteins or genes from the virus instead of the entire virus, as the antigen. [18] While vaccines produced using this technology have a shorter shelf life, their manufacturing process is more truncated than the process for egg-based vaccines. These shorter timelines allow recombinant-based vaccines to be produced more quickly in the event of a pandemic or vaccine supply shortage. In January 2013, the FDA first approved Flublok made by Protein Sciences Corporation for individuals 18 or older. It is particularly recommended for those with egg allergies.

An adjuvant is an "antigen-sparing technology" that is added to a vaccine to enhance immune response, allowing smaller doses of vaccines to be used.[19] Adjuvants can be added to vaccines made with different production methods, including egg-based, cell-based, or recombinant technology. Currently, there are no seasonal flu vaccine adjuvants approved for use in the United States, but many labs at NIH's National Institute of Allergy and Infectious Disease are engaged in adjuvant research.

Scientists are also seeking to develop a universal influenza vaccine to protect against all flu strains.[20] Though there is promising data to support this idea, a universal vaccine is considered at least, five to seven years away.

IV. AGENCY RESPONSIBILITIES

CDC operates the U.S. seasonal flu surveillance systems, which track trends in the rate of illness and hospitalization.[21] CDC also monitors the types and subtypes of circulating flu viruses, the emergence of new strains, and the geographic spread of the flu virus. Additionally, CDC administers two programs that provide vaccines to uninsured and underinsured children, adolescents, and adults and invests in the infrastructure necessary to reach these populations

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[17] Centers for Disease Control and Prevention, *Cell-Based Flu Vaccines* (online at www.cdc.gov/flu/protect/vaccine/cell-based.htm).

[18] Centers for Disease Control and Prevention, *Flublok Seasonal Influenza (Flu) Vaccine* (online at www.cdc.gov/flu/protect/vaccine/qa_flublok-vaccine.htm).

[19] NIH National Institute of Allergy and Infectious Disease, *Vaccine Adjuvants* (online at www.niaid.nih.gov/topics/Adjuvants/Understanding/Pages/WhatIs.aspx).

[20] *A Universal Flu Vaccine May Be On the Horizon*, Smithsonian Magazine (Jan. 26, 2015) (online at www.smithsonianmag.com/science-nature/measles-vaccine-universal-flu-influenza-cdc-disease-outbreak-180954020/?no-ist).

[21] Centers for Disease Control and Prevention, *Overview of Influenza Surveillance in the United States* (online at www.cdc.gov/flu/weekly/overview.htm).

(the Vaccines for Children and Section 317 programs).[22] Finally, CDC maintains the Strategic National Stockpile (SNS), the nation's repository of flu vaccines and other critical pharmaceutical products and medical supplies for use during a public health emergency.

FDA is "responsible for the licensure and regulation of influenza vaccine — including the approval of facilities in which influenza vaccine is produced — for the U.S. market."[23] FDA issues guidance, consults with manufacturers, and regulates the vaccine's production and use. FDA also reviews and approves the composition of the seasonal vaccine annually.[24]

The Biomedical Advanced Research and Development Authority (BARDA), located within the Department of Health and Human Services (HHS), contracts with vaccine manufacturers for advanced research and development for vaccine technologies to respond to public health emergencies.[25] The National Institutes of Health (NIH) conducts research to prevent, diagnose, and treat seasonal and pandemic influenza.[26]

V. WITNESSES

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[22] Centers for Disease Control and Prevention, *Justification of Estimates for Appropriations Committees* (Fiscal Year 2015) (online at www.cdc.gov/fmo/topic/Budget%20Information/appropriations_budget_form_pdf/FY2015_CJ_CDC_FINAL.pdf).

[23] Government Accountability Office, *Influenza Vaccine: Federal Investments in Alternative Technologies and Challenges to Development and Licensure* (June 2011) (GAO-11-435).

[24] Food and Drug Administration, *Vaccines and Related Biological Products Advisory Committee* (online at www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/VaccinesandRelatedBiologicalProductsAdvisoryCommittee/).

[25] Office of the Assistant Secretary for Preparedness and Response, U.S. Department of Health and Human Services, *Influenza Division* (online at www.phe.gov/about/barda/Pages/influenza.aspx).

[26] NIH National Institute of Allergy and Infectious Diseases, *NIAID Role in Influenza Research* (online at www.niaid.nih.gov/topics/flu/Pages/default.aspx).

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