



September 30, 2015

The Honorable Fred Upton
Chairman
Committee on Energy and Commerce
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

Thank you for your July 29, 2015, letter regarding the public health response to seasonal influenza. Enclosed are responses to the questions you posed in your letter.

I hope this information is helpful to you. Thank you for your continued commitment to public health preparedness.

Sincerely,

A handwritten signature in black ink that reads "Jim R. Esquea". The signature is written in a cursive style with a large initial "J".

Jim R. Esquea
Assistant Secretary for Legislation

cc: The Honorable Frank Pallone, Jr.
Ranking Member

Enclosure

Enclosure

1. What are the mismatch risks this year? What are the contingency plans for the upcoming 2015-2016 season in the event of a mismatch?

In June 2015, the Centers for Disease Control and Prevention (CDC) reported to the Committee via email that “through late May, more than 90% of the U.S. influenza viruses tested by CDC were characterized as being antigenically ‘like’ or ‘similar to’ the vaccine viruses recommended for the 2015-2016 Northern Hemisphere influenza vaccine. These proportions remain similar to those reported in late February/early March at the WHO [World Health Organization] Vaccine Consultation Meeting and the FDA’s [Food and Drug Administration] Vaccines and Related Biological Products Advisory Committee.”

The proportion of U.S. viruses collected since October 2014 that are antigenically similar to vaccine viruses recommended for the Northern Hemisphere influenza vaccine has remained constant and remains above 90 percent (93.7 percent as of July 30, 2015). This indicates U.S. A(H3N2) viruses from spring and early summer were antigenically similar to the 2015-2016 A(H3N2) vaccine virus. Influenza viruses, however, are notoriously unpredictable as they constantly undergo some degree of genetic change. These changes can be small and may accumulate over time (antigenic drift) or may be rapid and lead to a pandemic (antigenic shift). CDC cannot predict the exact timing, geography or severity of an upcoming influenza season, which types/subtypes of influenza viruses will predominate in a given year, or whether circulating viruses will undergo changes before or during a season that may result in antigenic differences between circulating and vaccine viruses. For these reasons, it is not possible to provide a “risk of mismatch” assessment for the season before it has begun.

Contingency plans in the event of the circulation of a virus that has undergone significant antigenic drift during the 2015-2016 influenza season include both those from previous years as well as new efforts. More frequent and comprehensive communication with Department of Health and Human Services (HHS) leadership and FDA has been implemented, and FDA has done likewise with the Chair of its Vaccines and Related Biological Products Advisory Committee regarding influenza virus surveillance data, including any evidence for viral antigenic drift and potential seasonal influenza vaccine.

In general, there are HHS-wide plans for a variety of influenza scenarios. CDC’s contingency plan in the event that a drifted strain emerges late, after the vaccine production and distribution process has begun, is to emphasize the use of other tools and strategies in the arsenal to fight the flu. As during the 2014-2015 influenza season, CDC emphasizes the use of antiviral medications as a “second line of defense,” promotes pneumococcal vaccination for seniors to help mitigate the complications of flu in the elderly, and stresses the importance of everyday preventive actions like covering coughs, social distancing, and frequent hand washing. CDC would expect to implement this same evidence-based approach if faced with a similar flu season in the future. During a “drift” season, CDC would continue to recommend influenza vaccination because the vaccine will likely still offer some protection, and it is likely that other influenza subtypes that the vaccine is well matched to will continue to circulate. For example, during the 2014-2015 influenza season (when the H3N2 component of the vaccine was antigenically different from

most circulating H3N2 viruses) there was a late season predominance of influenza B viruses, which were antigenically similar to viruses in the seasonal vaccine. CDC is working to strengthen antiviral treatment practices since these are not yet well implemented but can be of greater importance during years with substantial drift.

- 2. CDC has provided a 94 percent expected coverage estimate for the mammalian cell propagated parent of the egg-adapted H3N2 strain, which appears to have undergone significant antigenic change during egg passage. What is the expected coverage by the egg-adapted H3N2 strain in most of the vaccine supply for the 2015-16 influenza season?**

We assume that the question above relates to vaccine effectiveness. It is important to understand that there is a difference between antigenic match and vaccine effectiveness. As CDC reported to the Committee in writing in April, at least two factors play an important role in determining the likelihood that flu vaccine will protect a person from flu illness: the characteristics of the person being vaccinated (such as their age and health) and the similarity or "match" between the flu viruses contained in the vaccine and the flu viruses spreading in the community. CDC determines if circulating viruses are well-matched to the reference virus used to derive the vaccine virus through antigenic characterization using biological tests and genetic characterization.

The relationship between vaccine match, as determined by these laboratory methods, and vaccine effectiveness is not straightforward. Even when we identify a drifted strain via the methods above, we cannot predict how well the vaccine will work until the proper epidemiologic field studies are conducted once the influenza season has begun. We have accelerated the pace of these studies over the last several years so that we get interim results as quickly as possible during the season, but final estimates of how effective a vaccine actually was in people are not available until after the season is over.

CDC did not provide "coverage" estimates for the 2015-2016 season. As of July 30, 2015, the majority of U.S. viruses collected and tested since October 1, 2014, were antigenically similar to the respective influenza A and B vaccine viruses recommended for the 2015-16 Northern Hemisphere influenza vaccine, including 93.7 percent of the H3N2 viruses antigenically characterized during this period. CDC reports regularly during the year, and weekly during the influenza season, on the properties of the hemagglutinin protein of circulating influenza viruses and the level of antigenic similarity to reference viruses that are identified as suitable viruses from which to derive vaccine virus candidates. Seasonal influenza viruses are propagated primarily in mammalian cells as routine propagation in eggs is difficult and may introduce genetic changes that can alter the antigenic characteristics of the virus. Therefore, antigenic similarity for influenza A(H3N2) viruses is determined based on similarity with a reference virus also grown in mammalian cells. The antigenic similarity to A/Switzerland/9715293/2013 virus, the recommended A(H3N2) component for the 2015-16 Northern Hemisphere vaccine, is based on the virus propagated in mammalian cells. This provides the most accurate characterization of viruses circulating in humans.

The majority of influenza vaccines manufactured in the United States are grown in embryonated chicken eggs. As human influenza viruses adapt for high growth in eggs, which is typically

needed to produce enough antigen for large scale vaccine production, genetic changes can occur in the viruses. These are called “egg-adapted” changes. Some egg-adapted changes may have antigenic (or immunogenic) implications while others may not.

When characterizing influenza viruses as potential vaccine viruses, it is usual to compare the egg-propagated virus with its mammalian cell-propagated counterpart to ensure that the egg-adaptation has not introduced undesirable antigenic changes. The A/Switzerland/9715293/2013 virus used for the 2015-2016 season was evaluated in this way. While there are some egg-adaptations in the A/Switzerland/9715293/2013 vaccine viruses, WHO selected this virus as a candidate vaccine virus because it had egg adaptations that had the least impact compared to other candidates, and was antigenically similar to the majority of circulating viruses. Other egg-propagated viruses were also evaluated, but were found to be unsuitable.

- 3. Seasonal influenza has significant health and economic impacts, and in some cases greater impact than in a pandemic. For example, the 2009 H1N1 pandemic resulted in about 12,000 deaths, but close to 50,000 deaths have resulted from seasonal influenza when the H3N2 strain is dominant such as in the most recent influenza season. According to the World Health Organization (WHO), annual seasonal influenza epidemics resulted in about 3 million to 5 million cases of severe illness and about 250,000 to 500,000 deaths worldwide, which is likely an underestimation. As noted in a 2012 report by the Center for Infectious Diseases Research & Policy, “[T]hese figures indicate that the cumulative health impact of seasonal influenza over the last century rivals the potentially explosive, but time-limited, impact of the four pandemics of the past 100 years.”**

Given that the health and economic impacts of severe influenza outbreaks are significant, and arguably on par with other threats such as Ebola, MERS, H5N1 and H1N1 for which public health emergency declarations and Public Readiness and Emergency Preparedness (PREP) Act declarations have been used to support availability of medical countermeasures, should seasonal influenza outbreaks (for example, in the event of a vaccine mismatch) be considered public health emergencies?

The Secretary of HHS has discretionary authority to declare a public health emergency, issue a declaration under the PREP Act, or make other determinations regarding a public health emergency as warranted by the circumstances.

The Secretary may, under section 319 of the Public Health Service (PHS) Act determine, after consultation with such public health officials as may be necessary, that a) a disease or disorder presents a public health emergency; or b) that a public health emergency, including significant outbreaks of infectious disease or bioterrorist attacks, otherwise exists. Several legal authorities flow from a public health emergency declaration. For example, if the President has also declared an emergency or major disaster under the Stafford Act or National Emergencies Act, the Secretary may authorize the Centers for Medicare & Medicaid Services to waive certain conditions of participation or sanctions in accordance with section 1135 of the Social Security Act. However, many of the authorities the Secretary may employ during a response to a pandemic or infectious disease outbreak do not require a declaration of a public health emergency. For example, without declaring a public health emergency, the Secretary may

conduct research and clinical trials of countermeasures, deploy countermeasures from the Strategic National Stockpile, provide temporary assistance to States and localities, take actions to control the spread of communicable disease, and deploy the National Disaster Medical System. For more information on public health emergency declarations, please see <http://www.phe.gov/Preparedness/support/secauthority/Pages/default.aspx> and <http://www.phe.gov/Preparedness/legal/Pages/phedeclaration.aspx>.

The PREP Act authorizes the Secretary of HHS to issue a declaration that provides immunity from liability (except for willful misconduct) for claims of loss caused, arising out of, relating to, or resulting from administration or use of countermeasures to diseases, threats and conditions determined by the Secretary to constitute a present, or credible risk of a future public health emergency to entities and individuals involved in the development, manufacture, testing, distribution, administration, and use of such countermeasures. A PREP Act declaration is specifically for the purpose of providing immunity from liability, and is different from, and not dependent on, other emergency declarations. While the PREP Act states that a covered countermeasure must be a 'qualified pandemic or epidemic product' or 'security countermeasures,' current pandemic influenza PREP Act declarations provide liability immunity for countermeasures against pandemic influenza A viruses and influenza A viruses with pandemic potential. The current PREP Act declaration for pandemic influenza also specifies that liability immunity is available under the Act and the declaration for pandemic influenza vaccines until they are covered under the Department's National Vaccine Injury Compensation Program (VICP). The VICP provides a separate liability protection mechanism for vaccines that are recommended for use in children and for which Congress has passed an excise tax. Seasonal influenza vaccines generally are covered by the VCIP. For more information on the PREP Act, please see <http://www.phe.gov/Preparedness/legal/prepact/Pages/prepqa.aspx>. For more information on the VCIP, please see <http://www.hrsa.gov/vaccinecompensation/index.html>.

The Secretary may also determine under section 564 of the Federal Food, Drug, and Cosmetic Act that there is a public health emergency or a significant potential for a public health emergency that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that involves a biological, chemical, radiological or nuclear agent(s), or a disease or condition that may be attributable to such agent(s). She may then determine that the circumstances justify emergency authorization of unapproved products or unapproved uses of approved products, permitting FDA to issue Emergency Use Authorizations for such products. For more information about Emergency Use Authorizations, please see <http://www.fda.gov/emergencypreparedness/counterterrorism/medicalcountermeasures/mcmlegalregulatoryandpolicyframework/ucm182568.htm>.

- 4. According to the FDA response, a monovalent rescue vaccine was prepared in response to a possible vaccine mismatch because of a drifted (H1N1) strain for the 1986-1987 season in July 1986, even though there was very little information about the mismatch. In contrast, no action was taken in the early summer of 2014 for emerging evidence of a drifted strain in the 2014-2015 season, even though CDC testified that the mismatch was around 36 percent at that time. The CDC witness testified at the February 3 oversight hearing that by the time a 50 percent mismatch was determined in September 2014, it was too late to**

pursue a monovalent vaccine. However, CDC's acting influenza division director told committee staff in a briefing by telephone that a mismatch between 20-30 percent would be significant evidence of drift.

(a) What criteria will trigger action on pursuing a monovalent vaccine in the event of a mismatch?

The decision to produce an off-cycle monovalent seasonal influenza vaccine is not made based solely upon the percentages listed above. Instead, that decision would be made following a recommendation by FDA's Vaccines and Related Biological Products Advisory Committee and would be based on multiple factors that include:

- 1) Identification of a drifted virus that has been identified in multiple geographic regions worldwide and is increasing in its frequency of circulation with respect to other viruses within the subtype or lineage;
- 2) The availability of a candidate vaccine viruses (CVV) with suitable antigenic, genetic, and growth properties;
- 3) The availability of nucleotide sequences of circulating virus for vaccine development of a licensed recombinant vaccine or use of biosynthetic technologies;
- 4) Anticipated public health impact of the drifted strain, as determined by the magnitude of antigenic differences, subtype, and antiviral drug susceptibility, among other factors, and the ability of a monovalent vaccine to mitigate that impact;
- 5) Probability that drifted strain will become predominant in the coming flu season; and
- 6) Stakeholder consensus (including the Biomedical Advanced Research and Development Authority (BARDA), CDC, FDA, the National Institutes of Health (NIH), the Advisory Committee on Immunization Practices (ACIP), health care providers, and vaccine manufacturers) on the feasibility of an effective deployment, including capacity to produce enough vaccine in time to achieve high coverage before flu season.

In 2014, even if HHS had determined in July that a monovalent vaccine production should have been pursued, it would have been unable to do so because a suitable candidate vaccine virus (CVV) was not available despite CDC's early recognition of the emergence of a drifted H3N2 virus strain. To review the sequence of events that has previously been shared with the Committee:

- 1) In March 2014, CDC detected five A(H3N2) viruses that were antigenically distinct from the 2014-15 A(H3N2) vaccine component A/Texas/50/2012 and alerted other WHO collaborating centers to look for the antigenic drift variant in other regions of the world. In April and May 2014, CDC detected additional antigenically drifted viruses.
- 2) In May 2014, CDC began growing a potential candidate vaccine virus strain (A/Palau/6759/2014) that would be more antigenically similar to the drifted virus strain.
- 3) In June 2014, CDC isolated that candidate vaccine virus strain, and submitted it to New York Medical College (NYMC) for the generation of a high-yield reassortant vaccine virus candidate strain.

- 4) In July 2014, CDC received a new, egg-grown drifted H3N2 variant A/Switzerland/9715293/2013, and immediately forwarded it to the influenza reassorting lab at NYMC for creation of another potential vaccine candidate virus.
- 5) In August 2014, CDC performed the preliminary test on A/Palau/6759/2014 to determine whether it could qualify as a candidate vaccine virus. Unfortunately, testing indicated that this strain did not have the characteristics to qualify as a vaccine candidate virus.
- 6) In September 2014, CDC received a high yielding vaccine candidate virus (A/Switzerland/9715293/2013) from NYMC. CDC then performed its testing on the candidate virus and determined that it qualified as a candidate vaccine virus. On September 26, the WHO recommended the new H3N2 vaccine strain (A/Switzerland/9715293/2013) for inclusion in the Southern Hemisphere vaccine (for 2015).

(b) Under what circumstances would it be appropriate to pursue a monovalent rescue vaccine to respond to a drifted influenza strain?

As part of the efforts to improve public health emergency preparedness for seasonal and pandemic influenza, the Office of the Assistant Secretary for Preparedness and Response (ASPR) coordinates an inter-agency working group called the Flu Risk Management Meeting (FRMM). This group is comprised of HHS senior leaders and influenza subject matter experts. Participating agencies include HHS (ASPR, BARDA, the Assistant Secretary for Health's National Vaccine Program Office, FDA, NIH, and CDC), the Department of Homeland Security, and the Department of Veterans Affairs. The FRMM deliberates policy and programmatic issues regarding influenza medical countermeasures. Discussions include an end-to-end approach from basic research to the advanced development of new medical countermeasures to distribution and utilization strategies.

Recent discussions at the FRMM have included considerations to determine under what circumstances a monovalent rescue vaccine would be pursued due to a drifted seasonal influenza strain. Many factors have been identified that could impact that decision (e.g., manufacturing capabilities, disease severity, etc.) and discussions will continue into the fall to define the triggers for the decision to pursue a monovalent rescue vaccine. Meanwhile, HHS has taken a series of steps to increase the probability that a late season change to tri- or quadrivalent vaccine could be made. These changes would also enable faster production of a monovalent vaccine should it be needed. Newly implemented HHS actions include the following:

- 1) Enhanced global surveillance of circulating human and avian influenza viruses using existing WHO and CDC systems;
- 2) More frequent and comprehensive communication with HHS leadership and FDA, and between FDA and the Chair of its Vaccines and Related Biological Products Advisory Committee regarding influenza virus surveillance data, including any evidence for viral antigenic drift and potential seasonal influenza vaccine mismatch;

- 3) Greater availability of additional vaccine viruses from CDC and other WHO collaborating centers to vaccine manufacturers for seasonal influenza vaccine production; and
- 4) FDA will begin making potency reagents for new candidate vaccine viruses if surveillance data suggest antigenic drift may be a concern and provide these to vaccine manufacturers if antigenic drift emerges.

Implementation of these actions may reduce the timeline from identification of vaccine mismatch with the circulating virus strain to the availability of a well-matched vaccine. Expanded global surveillance will help identify antigenically drifted strains sooner. Frequent communication on the emergence of antigenic drifts and analysis of the circulating strain with candidate vaccine viruses will help inform decisions on making new vaccines sooner. The greater availability of potential vaccine viruses will help vaccine manufacturers to prepare virus stocks sooner and select those that are well-matched and best for vaccine production. The availability of more potency assay reagents will facilitate the production of new vaccines, if the decision is made to produce a new vaccine strain or new monovalent vaccine.

(c) Are there any contingency plans for a monovalent rescue vaccine in the event of a seasonal influenza vaccine mismatch?

Leadership from the FRMM is engaged in discussions with individual influenza vaccine manufacturers and international partners to solicit their thoughts on potential HHS contingency plans for development of a supplemental monovalent vaccine if antigenic drift and vaccine mismatch occur. HHS convened a meeting in June 2015 with vaccine manufacturers, international public health partners, and HHS representatives to solicit their individual opinions on HHS recommendations and potential plans to address potential seasonal influenza vaccine mismatches due to viral antigenic drift. Several initial proposed actions by HHS for immediate implementation included the following:

- 1) Work with the WHO to expand influenza strain surveillance capacity that ensures greater and earlier detection of emerging influenza viruses globally that may have drifted antigenically thereby informing decisions on generating more vaccine viruses sooner.
- 2) If antigenic drift in a particular virus strain is identified after the WHO and FDA's Vaccines and Related Biological Products Advisory Committee seasonal vaccine strain recommendations are communicated to the manufacturers in February or early March each year, CDC and FDA with WHO should notify the manufacturers of the situation as soon as possible and communicate to HHS senior leadership.
- 3) If there was evidence of antigenic drift, CDC would develop candidate vaccine seed strains (for egg and cell-based vaccines) that are antigenically similar to the drifted strain and provide the new candidate vaccine viruses to the manufacturers for production testing.
- 4) In the event of suspected antigenic drift, FDA would develop matched vaccine potency reagents for the new candidate vaccine viruses and make them available to manufacturers.

These and other steps will be tested and further refined in a tabletop exercise planned in November 2015 with HHS agencies and vaccine manufacturers, as individual participants, to solicit their individual opinions. The exercise outcome is expected to inform an HHS action plan for rapid development and manufacturing of a revised seasonal influenza vaccine as a strain change or a separate monovalent vaccine. The FRMM also recommends additional actions items to implement over the immediate, interim, and long-term horizons (18 months – five years) to address vaccine mismatch issues in the areas of virus surveillance and characterization, technologies, vaccine design, and vaccine distribution. Together with the influenza vaccine manufacturers, federal agencies, WHO and its collaborating laboratories, and regulatory authorities and public health leadership in other countries, a coordinated action plan may be adopted to address antigenic drift and vaccine mismatch problems.

- 5. A recent CDC study that examined clinician treatment practices for outpatients with influenza during the 2012-2013 season showed that only 16 percent of patients with laboratory-confirmed influenza were prescribed antiviral drugs, while as many as 30 percent were prescribed one of three common antibiotics. In light of such findings, should there be a greater emphasis and timeliness in federal public communications about the use of antiviral medications as a “second line of defense” against seasonal influenza?**

CDC recommendations emphasize that antiviral medication is recommended as early as possible for patients with confirmed or suspected influenza who have severe, complicated, or progressive illness; who require hospitalization; or who are at risk for influenza-related complications. Treatment is most effective when given early in the illness. CDC recommends that providers not delay treatment in these patients until test results become available and should not rely on insensitive assays such as rapid antigen detection influenza diagnostic tests to determine treatment decisions. In addition, because other reviews of randomized control trials (RCT) and observational studies have found consistent clinical benefit of early oseltamivir treatment in reducing the risk of lower respiratory tract complications such as those requiring antibiotics, CDC recommends that persons with uncomplicated influenza who are not in a high risk group and who present within 48 hours of illness onset can be treated with antiviral medications based upon clinical judgment.

Per CDC’s April 9, 2015, letter to the Committee, the agency maintains that communicating about antiviral drugs is already a core component of CDC’s annual seasonal influenza messaging and guidance. CDC’s research does indicate that antiviral drugs are underutilized, which is why it places very heavy emphasis on these communication efforts each year. Qualitative research is underway to better understand why this pattern of underutilization persists and target communications accordingly. While CDC continues to recommend vaccination as an important and still useful preventive measure during a season where there may be or there is reduced vaccine effectiveness, even more emphasis is placed on the use of influenza antiviral drugs for treatment of high risk persons in these seasons. Some of the ways in which CDC communicates about antivirals are as follows:

- 1) Direct outreach to clinicians (e.g., health alert network messages, clinician outreach and communication activity (COCA) calls);

- 2) Outreach to clinicians through professional organizations representing those patients at greatest risk (e.g., geriatricians, pediatricians etc.);
 - 3) Outreach to clinicians through mass media (e.g., traditional news media, specialized media like Medscape); and
 - 4) Outreach to public health partners (e.g., weekly situation and recommendation updates).
6. **According to the HHS website, flu.gov, 90 percent of influenza-related deaths and more than half of influenza-related hospitalizations occur in people age 65 and older. Last year's severe influenza season was reportedly the deadliest for seniors in five years. A recent study showed that a new high-dose vaccine was 24.2 percent more effective in preventing influenza in adults 65 years and older relative to a standard-dose vaccine. Another study based on data from more than 2 million Medicare beneficiaries suggests that the high-dose influenza vaccine works better than a standard-dose vaccine for preventing probable influenza illness and influenza-related hospital admissions in elderly people. The study, published by the journal *The Lancet Infectious Diseases*, was funded by the FDA and included authors from that agency as well as from the Centers for Medicare and Medicaid Services and the CDC. The CDC says it has not expressed a preference for either the high-dose or standard vaccine, but that the new findings will be considered in the future policy deliberations of the CDC's Advisory Committee on Immunization Practices (ACIP). CDC told committee staff in a briefing that the high-dose vaccine would not be on the CDC's ACIP agenda until February 2016. In light of these studies, is there any way to expedite consideration of these studies to see if CDC should express a preference on high-dose vaccines?**

The Advisory Committee on Immunization Practices (ACIP) has recommended high-dose inactivated vaccine (Fluzone HD, Sanofi Pasteur) since its licensure by FDA in 2009 and included the vaccine in the 2010-11 recommendations for use in persons 65 years of ages and older. Adopting ACIP's recommendation, CDC has included Fluzone HD, along with other flu vaccines, in the U.S. influenza vaccine recommendations each season since its approval. Data on the relative efficacy and safety of high-dose vaccine to standard dose vaccines has also been included in CDC outreach to clinicians. At the most recent ACIP meeting on June 24, 2015, a presentation was given which summarized evidence (including the studies referenced in the inquiry) concerning the relative efficacy and safety of high dose and standard dose vaccines for persons 65 years of age and older. Following discussion and consideration of this information, ACIP did not propose a preferential recommendation at that recent meeting. ACIP will continue to review emerging evidence for Fluzone HD as it becomes available. High dose inactivated influenza vaccine remains an appropriate option for persons 65 years of age and older, along with standard dose inactivated influenza vaccine.

7. **The Department's response stated that HHS/CDC purchases and distributes approximately 10 to 15 percent of the total seasonal influenza vaccines available in the United States each year through CDC's Vaccines for Children and Section 317 Immunization Programs. What are the total annual expenditures for seasonal influenza vaccines under these programs? Does HHS/CDC use its purchasing power to require measurement of outcomes for the seasonal influenza vaccines it purchases (i.e., vaccine effectiveness as measured by the degree of match of the vaccine to circulating seasonal**

strains or reductions in deaths or hospitalizations)? If so, what are the measurements, and what have they shown?

CDC's expenditures for seasonal influenza vaccines for the 2014-2015 influenza season were:

- 1) Vaccines for Children Program: \$284,662,004.88; and
- 2) Discretionary Immunization Program funds (Section 317): \$9,481,965.84.

CDC does not require measurement of outcomes as part of the vaccine purchase contracts. However, in addition to vaccine purchase, CDC used appropriated funds for programs that evaluate influenza vaccine effectiveness and influenza vaccine coverage. Vaccine effectiveness and coverage are two key metrics for evaluating and refining U.S. efforts to prevent influenza through vaccination. Through the U.S. Flu Vaccine Effectiveness (VE) Network, CDC has been working with researchers at universities and hospitals since the 2003-2004 flu season to estimate how well flu vaccine works through observational studies using laboratory-confirmed flu as the outcome. The U.S. Flu VE Network currently consists of five study sites across the United States that measure the flu vaccine's effectiveness at preventing outpatient medical visits due to laboratory-confirmed influenza. More information about the U.S. Flu VE Network can be found at <http://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm>. CDC estimates annual influenza vaccination coverage for the United States by utilizing data from several nationally representative surveys: the Behavioral Risk Factor Surveillance System (BRFSS), the National Health Interview Survey (NHIS), and the National Immunization Survey (NIS), and internet panel surveys of adults, health care providers, and pregnant women.

Adjusted vaccine effectiveness estimates for influenza seasons from 2005-2015 are available at: <http://www.cdc.gov/flu/pdf/professionals/vaccination/vaccine-effectiveness-table.pdf>. This page provides vaccination coverage estimates for 2014-2015: <http://www.cdc.gov/flu/fluview/1415season.htm>.

Additionally, for FY 2016, CDC has requested \$187,558,000 for influenza planning and response, which is level with the FY 2015 enacted level. CDC's influenza planning and response activities include both a comprehensive response for seasonal influenza as well as the ability to respond to an influenza pandemic. CDC's influenza program works to detect, respond to, and prevent influenza disease that can cause mild to severe illness, and at times, death. These annual activities improve preparedness by strengthening surveillance and diagnostic capacity, improving public awareness and provider knowledge about the importance of vaccination, prevention measures, and early treatment, and enhancing our international, federal, state, and local partnerships to respond quickly to influenza epidemics.

8. Has there ever been an emergency use authorization and/or expanded use authority to allow use of an unlicensed seasonal influenza vaccine?

An emergency use authorization or an expanded use authority has not been used to allow the use of an unlicensed seasonal influenza vaccine.