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# Update From the Advisory Committee on Immunization Practices

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The Advisory Committee on Immunization Practices (ACIP) consists of medical and public health experts who develop recommendations on vaccine use in the United States. The ACIP meets 3 times per year, and members and Centers for Disease Control (CDC) staff present findings and discuss vaccine research, vaccine effectiveness (VE) and safety, clinical trial results, and labeling/package insert information. Outbreaks of vaccine-preventable diseases and vaccine shortages are also discussed. Nonvoting representatives from the American Academy of Pediatrics and the Pediatric Infectious Diseases Society are present. The ACIP met on June 22–23, 2016 to discuss proposed recommendations for influenza vaccination, for human papillomavirus (HPV) vaccine dosing schedules, for the cholera vaccine (CVD 103-HgR), and for the use of MenACWY in human immunodeficiency virus (HIV)-infected persons, as well as an overview of respiratory syncytial virus (RSV) vaccines, safety of maternal tetanus, diphtheria, acellular pertussis (Tdap) immunization, and laboratory containment of poliovirus type 2.

**Key words.** ACIP; CDC; immunization.

## INFLUENZA VACCINES

### Background

The Influenza Working Group's (WG) discussions have focused on new vaccines, vaccine safety updates for the 2015–16 season, and VE data for the 2015–16 season in the United States. Dr Bruce Innis of GSK and Dr James Mansi of Seqirus presented data on FluLaval and FLUCELVAX, respectively. Dr Tom Shimabukuro of the CDC provided an update on vaccine safety. Drs. Brendan Flannery of the CDC and Chris Ambrose of MedImmune gave a VE update for live-attenuated influenza vaccine (LAIV). Dr Lisa Grohskopf of the CDC discussed the possible recommendations for the use of inactivated influenza vaccine (IIV) and LAIV, and the ACIP voted on the 2015–16 recommendations.

### FluLaval Quadrivalent and FLUCELVAX Quadrivalent

Fluzone is currently the only IIV licensed for children ages 6–35 months. Other influenza vaccines have not been licensed in this young age group due to lack of immunogenic noninferiority or unacceptable reactogenicity. FluLaval Quadrivalent received US Food and Drug Administration (FDA) approval in August 2013 for use in persons  $\geq 3$

years. Subsequent studies in children ages 6–35 months demonstrated FluLaval Quadrivalent to be immunogenically noninferior to Fluzone Quadrivalent for all 4 strains as determined by geometric mean titers (GMTs) and seroconversion response (SCR) 28 days after completion of dosing. FluLaval met the Center for Biologics Evaluation and Research's SCR and seroprotective (SPR) criteria for all strains except the SPR for B/Victoria. The vaccine was immunogenically superior to Fluzone Quadrivalent for B strains in 6- to 17-month-old children and all 6- to 35-month-old, unprimed children (children with no prior history of influenza vaccination). Reactogenicity and safety profile between the 2 vaccines are similar. A supplemental biologic license application (BLA) was submitted in January 2016 to extend the indication for FluLaval Quadrivalent to 6–35 months of age. The FDA will make a decision by November 26, 2016.

FLUCELVAX Quadrivalent (cell culture IIV; ccIIV4), a subunit influenza vaccine prepared from virus propagated in a system where cells grow freely in suspension in culture medium, is licensed for persons  $\geq 4$  years old. The ccIIV4 was noninferior to 2 ccIIV3 vaccines, each containing an

alternate influenza B strain. The safety profile between the vaccines was similar. The ccIIV4 is thought to be a potential alternative to overcome issues associated with egg-based production, particularly in a pandemic.

### Influenza Vaccine Safety

No new safety concerns for IIV, LAIV4, ccIIV3, or recombinant influenza vaccine (RIV3) were identified from the Vaccine Adverse Event Reporting System (VAERS). Surveillance for the 2016–17 influenza season will include monitoring for adjuvanted influenza vaccine (Fluad), IIV4-ID (Fluzone Intradermal Quadrivalent), pregnancy reports, and anaphylaxis reports in persons with a history of egg allergy. Near real-time surveillance in the United States in the 2015–16 season demonstrated an increase in Guillain-Barré syndrome (GBS) rates after IIV with 7.25 cases per million IIV vaccines compared with an average of 5.45 cases per million IIV vaccines from the prior 3 seasons. The Vaccine Safety Datalink (VSD) identified a significantly elevated relative risk for GBS of 3.67 with an attributable risk after IIV3 of 2.6 additional cases per million doses administered. Further investigation, including chart review of cases and adjustment for seasonality and other confounders, is being performed. Guillain-Barré syndrome risk estimate appears to be consistent with that observed in some previous influenza seasons.

### Influenza Vaccine Effectiveness

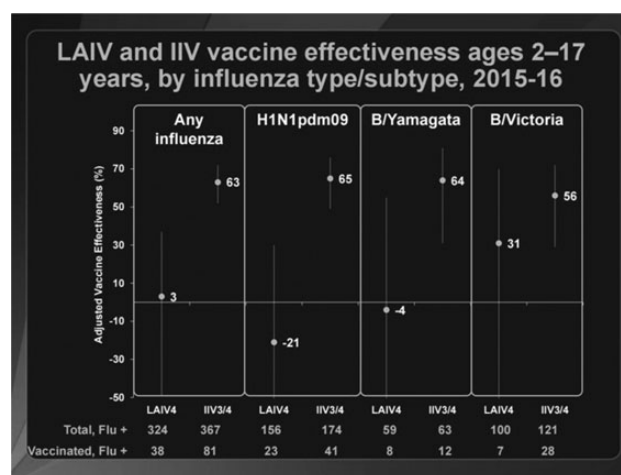
The US Flu VE Network consists of 5 sites, enrolling outpatients >6 months of age with acute respiratory illness and cough ≤7 days duration. The network utilizes a test-negative design to determine VE in influenza reverse transcription-polymerase chain reaction (RT-PCR)-confirmed patients. Receipt of at least 1 dose of any 2015–16 seasonal influenza vaccine was assessed based on medical records, immunization registries, and by self-report. A total of 1341 of 7563 (18%) enrolled subjects were influenza positive. The majority, 772 (58%), were influenza A(H1N1)pdm09 (pH1N1) positive. Influenza A H3N2 (6%), B/Yamagata (19%), and B/Victoria (15%) were detected with the remainder being unsubtypeable A, unknown lineage B, or coinfection. Overall adjusted VE for any influenza virus was 47%. Adjusted VE for specific vaccine strains across all ages was as follows: pH1N1, 41%; H3N2, 45%; B/Yamagata, 55%; and B/Victoria, 55%.

Of children ages 2–17 years, 411 of 2286 (18%) were influenza RT-PCR positive during the 2015–16 season. The majority (47%) were positive for pH1N1, followed by H3N2 (3%), B/Yamagata (16%), B/Victoria (31%), with the remainder unsubtypeable A, unknown lineage B, or coinfection. In children, overall VE was 48% and 64% in children 6 months–8 years and 9–17 years, respectively.

The VE for LAIV was significantly lower than IIV, with no effectiveness at all of LAIV for prevention of infection by pH1N1 or B viruses (Figure 1). The LAIV recipients were 3.67-fold and 1.62-fold more likely to get pH1N1 and B, respectively, compared with IIV recipients. Overall, IIV VE in children aged 2–17 years was 63%, showing that the poor effectiveness was limited to LAIV. A US Department of Defense study of children aged 2–17 years also noted no LAIV effectiveness against pH1N1, and a MedImmune study had a VE estimate against pH1N1 that was not statistically significant but with a higher point estimate. Both studies demonstrated significant VE for IIV.

Data from the AstraZeneca Influenza Clinical Investigation for Children study were presented. During 2015–16, children ages 2–17 years from 8 US sites with influenza-like illness were enrolled in an observational, test-negative design, similar to the CDC VE study. The VE for LAIV was 46% compared with an IIV VE of 65%. However, adjusted LAIV VE estimates for pH1N1 and B crossed 0. In a MedImmune study from the United Kingdom, LAIV4 VE was 57.6%, but no specific VE for pH1N1 was reported.

Prior VE data were reported and reviewed for LAIV and IIV VE. Since 2009, LAIV VE has been poor. In 2013–14, studies from the US Flu VE Network, AstraZeneca, and Department of Defense noted no significant VE for LAIV against pH1N1 despite significant VE for IIV3 against pH1N1. The reason for the poor LAIV VE is unknown, although hypotheses include the suboptimal performance of the pH1N1 hemagglutinin vaccine component, potential interference among viruses in the quadrivalent vaccine, or reduced immunogenicity due to a population more highly vaccinated with LAIV in recent years. The FDA is



**Figure 1.** Influenza vaccine effectiveness by type/subtype, 2015–16. Abbreviations: IIV, inactivated influenza vaccine; LAIV, live-attenuated influenza vaccine.

concerned and is working with MedImmune to gather more information; at this time, they have determined that specific regulatory action is not warranted.

#### **Working Group Recommendations and Advisory Committee on Immunization Practices Discussion**

The WG considered multiple different recommendations with the goal of conveying that the latest data suggest that IIV is more effective than LAIV against pH1N1 and that VE for LAIV against AH3N2 and B viruses is uncertain. The WG noted that policy should encourage the use of the most effective vaccine, and recommendations would be interim for the 2016–17 season. It is expected that LAIV represents 14 million (8%) of the total 171–176 million doses of influenza vaccine. The WG recognized that not recommending LAIV may impact school-based immunization programs, persons who refuse injectable vaccine, and future evaluation of LAIV effectiveness.

The WG proposed 2 options: LAIV should not be used or LAIV use should be limited. After lengthy discussion, ACIP voted to approve the recommendation that LAIV should not be used for the 2016–17 seasons based on poor VE for the last 3 influenza seasons. The ACIP also approved removal of LAIV from Vaccines for Children (VFC) coverage.

### **HUMAN PAPILLOMAVIRUS VACCINES**

#### **Background**

The WG reviewed evidence for a 2-dose HPV vaccine schedule. Dr Allison Kempe, WG chair, reviewed background information on the 2-dose schedule presented at the previous ACIP meeting and noted that a supplemental BLA supporting a 2-dose schedule was submitted to the FDA in early 2016. Dr Lauri Markowitz of the CDC reviewed data on duration of protection after HPV vaccination. Dr Marc Brisson of Laval University discussed cost-effectiveness of a 2-dose vaccination schedule, and Dr Sara Oliver of the CDC discussed HPV VE after 2-dose schedules. Dr Elissa Meites presented Grading of Recommendations Assessment, Development, and Evaluation (GRADE) for 2-dose schedules, and Dr Lauri Markowitz reviewed the recommendation options.

#### **Noninferiority and Maintenance of Antibody in a Two-Dose Schedule**

The WG reviewed data demonstrating noninferiority between a 2-dose schedule (0, 6 months or 0, 12 months) in children aged 9–14 years compared with a 3-dose series (0, 2, 6 months) in persons 15–26 year olds. Follow-ups from bivalent (2vHPV) and quadrivalent HPV (4vHPV) vaccine studies demonstrate maintenance of antibody responses for as long as 14 years. Waning antibody response was not associated with loss of protection for HPV type 18.

Although long-term protection data are not available for the 2-dose series, the 2-dose schedule for 2vHPV and 4vHPV seems to generate similar antibody kinetics in adolescents compared with a 3-dose schedule in women.

#### **Cost-Effectiveness of a Two-Dose Schedule**

Using a vaccine cost of \$158 per 9-valent HPV (9vHPV) administration, 2 doses must protect for more than 20 years for the third dose to be cost-ineffective. This was not adjusted for a higher per-dose cost for the 2-dose series. Therefore, cost-effectiveness depends on the relative duration of efficacy of the 2- and 3-dose schedules, the additional vaccination coverage achieved through a reduced vaccine schedule, and the cost per dose. A 2-dose schedule will provide similar population-level health benefits as a 3-dose schedule unless the 2-dose schedule provides a shorter duration of protection and does not enable higher vaccination coverage. Conclusions are similar with the 4vHPV effectiveness and cost-effectiveness analyses in Canada and the United Kingdom.

#### **Human Papillomavirus Vaccine Effectiveness**

Thirteen studies with VE data for the 2-dose schedule were reviewed. Four studies included evaluations of 0- and 6-month intervals, with 3 of these reporting similar outcomes between a 2- and 3-dose series. All were post hoc analyses of clinical trials. Ten studies found that 2 doses were not as effective as 3 doses. However, all of these studies were post-licensure effectiveness studies performed within the setting of a recommended 3-dose schedule, so most of the subjects received the HPV immunization at 0 and 1 month or 0 and 2 months, as opposed to 0 and 6 or 0 and 12 months. Persons receiving the 2-dose schedule were different from those receiving the 3-dose schedule in regards to age, socioeconomic status, and timing of cervical screening, all factors that have implications on HPV exposure. The GRADE for the 2-dose schedule is overall evidence type 3.

#### **Working Group Recommendations**

Draft recommendations were presented. New recommendations included a 2-dose schedule with the second dose being administered 6 to 12 months after the first dose. For persons initiating the vaccine series after their 15th birthday or immunocompromised persons of any age, the WG is considering its recommendation for a 3-dose series with a schedule of 0, 1–2, and 6 months. No vote was taken by the ACIP at this meeting, although there was general support for a 2-dose schedule. A vote will likely to place at the October 2016 meeting.

### **CHOLERA VACCINE**

Dr Karen Wong of the CDC provided an update on cholera epidemiology, at-risk populations, the recently licensed

vaccine, and the proposed recommendations for vaccine use from the WG. There was discussion among the ACIP members and others before a vote regarding the proposed recommendations.

### Background

The Cholera Vaccine WG was formed in August 2015. Since the February 2016 meeting, the WG has reviewed data in special populations, including pregnant and breast-feeding women, immunocompromised persons, and children. The WG has also reviewed data regarding shedding and transmission of the vaccine strain and duration of protection. On June 10, 2016, CVD 103-HgR vaccine (Vaxchora) was licensed by the FDA to prevent cholera in adults, ages 18–64 years, traveling to cholera-affected areas. Although cholera is rare in the United States, most cases occur among travelers to affected areas, and an increase in cases in travelers from Haiti was recognized after a Haitian epidemic in 2010. High-risk individuals include the following: travelers visiting friends and relatives; long-term travelers; travelers who do not follow safe food, water, and hygienic practices; and healthcare workers with direct exposure to bodily fluids from cholera patients.

### Cholera Vaccine Update

The vaccine is a live-attenuated single-dose oral cholera vaccine that protects against toxigenic *Vibrio cholerae* O1. A previous formulation had formerly been licensed, but after its removal from the US market, it was redeveloped as Vaxchora. The vaccine is immunogenic and protective against cholera challenge. The GRADE evidence type is 2, with safety evidence type 2 and efficacy evidence type 1. Vibriocidal antibody response from the vaccine ranged from 29% to 98% in children ages 3 months–17 years in 3 countries based on available data from the previous formulation. No systemic adverse events were noted after the use of the older vaccine in the pediatric population. Cumulative shedding data of the new vaccine range from 3.3% to 12.5% in 2 studies, although the new vaccine was not isolated from stools of household contacts cultured 7 days postvaccination. The older vaccine was isolated in <1% of household contacts 5 days postvaccination with seroconversion of 3.7% of family contacts at 9 or 28 days. In challenge studies, VE of the new formulation against severe (>3 liters) diarrhea was 90.3% at 10 days and 79.5% at 3 months. The older formulation had a VE of approximately 100% against diarrhea of any severity at 4–6 months. There are no data on reimmunization with the new formulation.

### Work Group Recommendations

Safe food and water precautions, proper sanitation, and proper hygiene measures were reviewed as the primary

preventive strategies against cholera infection. Travelers with severe diarrhea should seek prompt medical attention and rehydration therapy. The WG recommended that the decision to vaccinate be based on the traveler's risk of exposure and risk of severe outcomes if infected. Risk of exposure is increased in travelers unable to follow preventive strategies while visiting friends and relatives in areas of active toxigenic *V. cholerae* O1 exposure as well as healthcare workers with direct contact with body fluids from patients with cholera. Travelers at risk of poor outcomes include those without rapid access to rehydration and medical care, low gastric acidity, blood type O, and travelers with chronic medical conditions. The vaccine is anticipated to cost \$200–\$300 and should be given  $\geq 10$  days before travel. The ACIP and others discussed the complexity of the language describing the 2 groups; eg, does a patient have to know their blood type to receive the vaccine? The ACIP decided against specifying high-risk subpopulations (those at high risk of exposure and those at risk of severe outcomes) and voted to recommend use of the vaccine in adults traveling to an area of active toxigenic *V. cholerae* O1 transmission as a category A recommendation. A pediatric study in children 2–18 years is planned to start next year.

## MENINGOCOCCAL VACCINES

### Background

Dr Laura York of Pfizer gave an update on the new MenB-FHbp (Trumemba) label, which allows for a 2-dose schedule, and Ms. Jessica MacNeil of the CDC presented the WG discussions on the 2-dose schedule. Dr Ismael Ortega-Sanchez of the CDC presented data on the cost-effectiveness of MenACWY in HIV-infected persons. Ms. Jessica MacNeil presented the WG's considerations for the use of MenACWY in HIV-infected persons and the proposed recommendations. The ACIP then voted on the use of MenACWY in HIV-infected persons.

### MenB-FHbp (Trumemba) Two-Dose Schedule

In April 2016, the FDA approved a 2-dose schedule (0, 6 months) for MenB-FHbp. This is in addition to the already approved 3-dose schedule (0, 1–2, and 6 months) for MenB-FHbp. The FDA recommended that the dosing schedule should be based on risk of exposure and susceptibility to disease. The current ACIP recommendation going into the meeting was a 3-dose series for MenB-FHbp and a 2-dose series for MenB-4C.

The WG reviewed immunogenicity data for MenB-FHbp. Of the 2-dose schedules evaluated, the 0 and 6 months schedule had the highest percentage of responders

with GMTs most similar to the 3-dose schedule. However, GMTs and the proportion of subjects with a  $\geq 4$ -fold rise in human complement serum bactericidal assay (hSBA) titers both were lower. Safety and tolerability are similar between the 2- and 3-dose schedules, with injection site pain being the most common adverse event. Policy options discussed by the WG include a preference for the 3-dose schedule for at-risk persons, which would include outbreaks, due to early protection and maximization of the immune response. However, a preference for the 3-dose schedule in healthy adolescents was also expressed. At the October 2016 ACIP meeting, data will be presented on antibody persistence after the 2-dose schedule, evaluation of hSBA data for MenB-FHbp and MenB-4C against US outbreak strains, and the impact of MenB-FHbp on carriage among college students.

#### **Cost-Effectiveness of MenACWY and Rates of Meningococcal Disease in Human Immunodeficiency Virus-Infected Persons**

Cost per quality-adjusted life year (QALY) gained by recommending MenACWY in HIV-infected persons is approximately \$723,000. This figure was compared with various other vaccine recommendations and noted to have a much higher cost per QALY. Routine vaccination of HIV-infected persons against MenACWY, including primary series and periodic boosting, is costly due to low rates of disease cases and deaths as well as the high cost of repeated boosting.

From 1995 to 2014, 62 cases of meningococcal disease among HIV-infected persons, or 2% of total meningococcal cases, were reported in the Active Bacterial Core (ABC) surveillance program. Disease was primarily due to serogroups C, W, and Y. The relative risk of meningococcal disease was 12.9 in HIV-infected persons meeting the CDC/acquired immune deficiency syndrome (AIDS) surveillance case definition (referent to uninfected and HIV-positive but not meeting AIDS case definition). Meningococcal disease risk in HIV-infected persons compared with HIV-uninfected persons, previously presented at the February 2016 meeting, was reviewed. There was only 1 case of meningococcal disease among children under 10 years of age recorded in the ABC data. In summary, HIV-infected adults and adolescents have an increased rate of meningococcal disease ranging from 5- to 24-fold. The risk of meningococcal disease in HIV-infected persons increases with low CD4 count or high viral load. The seroresponse to MenACWY-D conjugate vaccine is lower in HIV-infected adolescents than healthy adolescents and HIV-infected 2- to 10-year-olds. Immune response to the vaccine wanes rapidly although an increased response occurs with boosting.

#### **Work Group Recommendations**

Only MenACWY conjugate vaccine recommendations were discussed because disease in HIV-infected persons is primarily due to serogroups C, W, and Y, and no safety or immunogenicity data exist for serogroup B meningococcal vaccines in HIV-infected persons. Considerations for the recommendation included the requirement of regular booster doses because the risk of meningococcal disease with HIV infection is lifelong. The WG, recognizing the suboptimal vaccine response and duration of protection, supported the inclusion of HIV-infected persons into the group at increased risk of meningococcal disease. The ACIP and liaisons discussed 2 policy options that differed regarding the age, 2 months or 11 years, at which vaccination should begin. The pros of initiating vaccination at 2 months included harmonization with current ACIP recommendations for the use of the vaccine in asplenic- and complement-deficient patients, a low financial and burdensome recommendation due to the small number of HIV-infected children, a presumed increased risk of meningococcal disease similar to older children and adults, and higher hSBA titers postvaccine in HIV-infected children ages 2–10 years compared with HIV-infected adolescents. The pros of initiating vaccine at age 11 years included decreasing the number of booster doses over a lifetime.

The ACIP reviewed both policy options and voted to approve the recommendation for routine receipt of MenACWY in HIV-infected persons aged  $\geq 2$  months. Additional recommendations include the use of a 2-dose (0, 2 months) primary series with MenACWY in HIV-infected persons aged  $\geq 2$  years who have not been previously vaccinated and the use of a multidose schedule for children aged  $< 2$  years. HIV-infected persons previously vaccinated with one dose of MenACWY should receive a second dose at the earliest opportunity with an 8 week minimum interval between doses. Human immunodeficiency-infected persons should receive booster doses every 3 years if age  $< 7$  years at previous dose and every 5 years if age  $\geq 7$  years at previous dose. The VFC coverage also was approved.

#### **HEPATITIS**

The ACIP provided comprehensive recommendations for hepatitis A in 2006 and for hepatitis B in 2005 and 2006. These recommendations will be updated in the near future, with a revision to the hepatitis B statement expected by October 2016. Current WG considerations include hepatitis A disease burden, population protection, catch-up vaccination for children 2–18 years, and

immunogenicity and safety of HEPLISAV-B (a 2-dose hepatitis B vaccine in adults).

## RESPIRATORY SYNCYTIAL VIRUS VACCINES

### Background

The current goal of the RSV Vaccine WG is to consider recommendations for the use of a vaccine in adults  $\geq 60$  years old and those with underlying medical conditions. Dr Lindsay Kim of the CDC presented an overview of RSV and RSV vaccines.

### Respiratory Syncytial Virus Burden of Disease and Vaccines

Respiratory syncytial virus causes 177 000 hospitalizations and 14 000 deaths annually. The goal of RSV vaccine development is to safely induce sufficient immunity to protect against serious RSV infections (eg, lower respiratory tract infection [LRTI] and apnea in infants). Respiratory syncytial virus vaccine development has been complicated. A formalin-inactivated vaccine tested in children in the 1960s had significant unexpected adverse events. When subsequently infected with RSV, seronegative vaccine recipients had more severe LRTI compared with vaccine non-recipients; vaccine recipients had hospitalization rates of 80%, including 2 deaths, compared with 5% of controls. This vaccine-enhanced disease syndrome in RSV-naïve vaccine recipients is thought to be related to poor vaccine-induced neutralizing antibody as well as a Th2 biased immune response with enhanced cytokine release upon subsequent infection. Potential new vaccine strategies include replicating or vectored vaccines, subunit vaccines, and maternal immunization to protect young infants. Novavax's RSV fusion protein subunit nanoparticle vaccine will be the first RSV vaccine considered for FDA licensure. Over the next 1–2 years, the RSV WG will assess the epidemiology and burden of RSV in older adults, review vaccine manufacturer presentations, consider correlates of protection and immunogenicity, and assess cost-effectiveness. Implementation considerations and a potential vote are anticipated in 2018.

## TETANUS, DIPHTHERIA, ACELLULAR PERTUSSIS VACCINE SAFETY DURING PREGNANCY

### Background

Since October 24, 2012, ACIP has recommended the use of Tdap during every pregnancy, irrespective of prior Tdap receipt, with optimal immunization timing between 27 and 36 weeks gestation. The ACIP acknowledged the need for enhanced monitoring and safety studies for Tdap given during pregnancy. Dr Pedro Moro of the CDC presented data on enhanced surveillance of Tdap vaccine safety in pregnancy from VAERS. Dr Lakshmi Sukumaran of the CDC provided data from the VSD on maternal vaccination and structural

birth defects in offspring. Dr Kathryn Edwards of Vanderbilt University School of Medicine presented data on the reactogenicity and immunogenicity of Tdap in pregnant women, and Dr Art Reingold, chair of the WG, provided an update from the WG.

### Tetanus, Diphtheria, Acellular Pertussis Vaccine Safety from the Vaccine Adverse Event Reporting System and Vaccine Safety Datalink

The Tdap vaccination coverage has increased from 27% in 2014 to 42.1% in 2015. The VAERS surveillance from October 2011 to June 2015 demonstrated no new or unexpected safety concerns among Tdap-immunized pregnant women or their infants. A limited number of pregnancy reports with repeat Tdap doses have been received by VAERS, and these will continue to be monitored by the CDC. Data from the VSD suggest that maternal Tdap vaccination during pregnancy was not associated with an increased risk for birth defects.

### Reactogenicity and Immunogenicity of Tetanus, Diphtheria, Acellular Pertussis in Pregnant Women

The vaccine was well tolerated in pregnant women. Moderate/severe injection-site pain occurred more frequently in pregnant than nonpregnant women, but the rates were consistent with clinically reported rates and did not lead to medical visits. Approximately one half of women had received a prior Tdap, and rates of moderate/severe reactions were similar between women who had and had not received a prior Tdap. All women had significantly higher antigen-specific antibody titers after vaccination.

### Timing of Tetanus, Diphtheria, Acellular Pertussis Immunization During Pregnancy

The WG reviewed 3 studies that demonstrated equal or higher antibody concentrations among infants born to mothers with second trimester Tdap vaccination compared with third trimester vaccination. No differences in neonatal antibody titers were noted between mothers vaccinated in the late second trimester and during the third trimester. In February 2016, the United Kingdom's Joint Committee on Vaccination and Immunization recommended that maternal Tdap vaccination be given as early as 16 weeks gestation but after the mid-pregnancy ultrasound, generally approximately 18–21 weeks. The WG will review new data and current guidance on Tdap vaccination in pregnant women. At the October ACIP meeting, the timing of maternal Tdap vaccination will be summarized with a draft statement prepared.

## LABORATORY CONTAINMENT OF POLIOVIRUS TYPE 2

The last wild-type poliovirus type 2 and 3 cases occurred in India in 1999 and in Nigeria in 2012, respectively. In 2016,

17 wild-type poliovirus type 1 cases occurred in 2 endemic countries, Pakistan and Afghanistan. The World Health Organization (WHO) Global Action Plan minimizes poliovirus facility-associated risk after type-specific eradication of wild polioviruses and cessation of oral poliovirus vaccine (OPV) use. The goal of the program is not absolute poliovirus containment but rather a major risk reduction. It is a phased plan with containment of poliovirus type 2 being implemented first in 2016. Laboratory containment means destroying, and documenting, specimens by autoclave or incineration or transfer to an “essential” laboratory facility that works within an appropriate containment space. The CDC is the largest WHO Global Polio Reference Laboratory. In 2015–16, 9 US laboratories reported possession of a wild-type or vaccine-derived poliovirus potentially infectious materials, and 8 US laboratories reported possession of OPV/Sabin potentially infectious materials. It is likely that some laboratories may not be aware of poliovirus containment and may be unknowingly storing potentially infectious materials (for example, frozen stool specimens from periods when

poliovirus was endemic in the United States, or when OPV was in use).

## VACCINE SUPPLY

Sanofi Pasteur is experiencing a manufacturing delay of diphtheria-tetanus-acellular pertussis-inactivated poliovirus/*Haemophilus influenzae* type b (DTaP-IPV/Hib) (Pentacel) with a supply for only 70% of historical demand. Individual vaccines are in adequate supply, and resolution is expected during the second half of this year. Merck is experiencing a shortage of prefilled syringes for HPV, hepatitis B, and hepatitis A vaccines, with anticipation of availability in the second quarter of calendar year 2017. Vial formulations are available in adequate supply. Up-to-the-minute information can be found at <http://www.cdc.gov/vaccines/vac-gen/shortages/>.

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**Potential conflicts of interest.** All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.