**Advisory Commission on Childhood Vaccines**
**March 3, 2016**

**99th Meeting**

Teleconference and Adobe Connect

**Members Present**

Kristen A. Feemster, M.D., Chair ('16)
Charlene Douglas, Ph.D. ('16)
Edward Kraus, J.D. ('16)
Karlen E. Luthy, D.N.P ('18)
Luisita dela Rosa, Ph.D. ('16)
Jason Smith, J.D. ('16)
Martha Toomey ('18)
Alexandra Stewart, J.D. ('18)

**Division of Injury Compensation Programs (DICP), Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services (HHS)**

Narayan Nair, MD., Acting Director, DICP
Andrea Herzog, Staff Liaison

**Welcome, Kristen A. Feemster, M.D., Chair**

Dr. Feemster called the meeting to order and completed a roll call, reflected above, for the record.

**Public Comment on Agenda Items**

Dr. Feemster invited public comment on the agenda. There were no comments.

**Approval of December 2015 Minutes**

Dr. Feemster invited approval of the December 3, 2015, meeting minutes. On motion duly made by Mr. Kraus and seconded by Ms. Toomey, the minutes were unanimously approved.

**Presentation and Remarks by Hon. Nora Beth Dorsey, Chief Special Master and Hon. Patricia Campbell-Smith, Chief Judge of the U.S. Court of Federal Claims**

Chief Special Master Dorsey noted that, at the last meeting, Dr. Avril Melissa Houston, former Director, DICP and Mr. Vince Matanoski, Assistant Director, Torts Branch, Civil Division, Department of Justice (DOJ) discussed the impact of the increasing number of claims filed with the National Vaccine Injury Compensation Program (VICP). She indicated that her presentation would be from the perspective of the Office of Special Masters (OSM). The OSM was established within the U.S. Court of Federal Claims (CFC) and, by statute, it may not consist

of more than eight special masters. Congressional legislation is required to provide authorization to increase the number of special masters, regardless of caseload. Chief Special Master Dorsey explained that when a petition is filed with the CFC, it is assigned to a special master who is responsible for all aspects of the claim, including hearing the testimony and evidence deciding whether the petitioner is entitled to compensation and, if so, how much.

There are two parts to each vaccine claim, the entitlement (petitioner's claim for compensation), and attorney's fees. In each case, if the parties to the case agree on the financial outcomes, the special master issues a written decision, usually affirming that agreement. However, if the parties to the case cannot reach an agreement, the case goes to hearing, which typically requires significant time and effort on the part of the OSM. In such cases, substantial additional testimony and evidence may be presented.

Chief Special Master Dorsey noted that her statistics would reflect a calendar year timeframe, which is different from the timeframes used by the DOJ and DICP. She presented a graphic showing the number of petitions filed for calendar years 2010 through 2015, which revealed relative stability for the first three years (about 400 each year), and a significantly increasing trend beginning in 2013, when the number of petitions increased to 525. The trend continued through 2014 (677) and 2015 (945). On a monthly basis, the graphics showed the increased trend, the number of petitions filed, the number of cases closed, and the sharp increase in petitions filed in the fall of each year (2014 through 2015). Particularly in 2015, the gap between petitions filed and cases closed was significant. There is a spike in filings each fall, which probably reflects an increase in claims related to the influenza vaccine and mainly related to the injuries, Guillain-Barré Syndrome and SIRVA (Shoulder Injury Related to Vaccine Administration). The widening gap between the number of filed cases and the number of cases closed each month is the crux of the increasing caseload problem. The gap represents the number of cases yet to be resolved, and this gap has steadily widened since April 2014.

Chief Special Master Dorsey described the Special Processing Unit (SPU) that was established in July 2014 to provide some relief through an expedited resolution process. That process involves a less formal approach to resolving claims which have historically been resolved through settlement or concession. Staff attorneys work under the supervision of Chief Special Master Dorsey and with petitioners' and DOJ's attorneys to reach a resolution. The approach has been effective. As of February 11, 2016, the SPU has handled 682 cases, resolving 254 of them in an average time of 319 days, and 96 of those cases resolved in less than 240 days. However, the overall picture is still challenging. Many of the claims that are filed cannot be assigned to the SPU because of the need for hearings, testimony, analyses of evidence, and written decisions, all of which must be performed by a special master.

Concerning the future, Chief Special Master Dorsey reported that the program anticipates over 1,200 cases to be filed in 2016. Unless there is legislation authorizing an increase in the number of special masters, the caseload backlog will continue to increase, which will result in petitioners having to wait longer for resolution of their claims.

Chief Special Master Dorsey introduced Chief Judge Campbell-Smith, who commended the OSM for its efficient handling of claims, including the support of the SPU, in spite of the

increasing caseload. It has become apparent that the statutory limit on the number of special masters is the choke point in the vaccine compensation program. Because that limit is fixed by legislation, the court cannot appoint additional special masters. But, the DOJ can hire additional attorneys to process the increasing number of claims, and on the petitioners' side, the number of attorneys currently identified as willing to represent petitioners has increased to 182. Judge Campbell-Smith concluded with the observation that the combination of these factors contributes to an exacerbation of the backlog, which could be further impacted if additional vaccines or conditions are added to the Vaccine Injury Table. She concluded by expressing appreciation for the opportunity to comment to the Commission.

Dr. Feemster invited questions from the Commission, and Ms. Toomey asked why there are more petitions being filed than before and what the Commission could do to address the limit on the number of special masters. Chief Special Master Dorsey responded that HHS has been effective in publicizing the program, and the petitioners' bar has been helpful in providing information to vaccine-injured individuals and parents. Although it is not clear whether there are more injuries or more claims because of program awareness. She invited Mr. Matanoski to comment, and he suggested that the petitioners' bar is becoming more effective at identifying vaccine injury cases and that the petitioners are more aware of the VICP. He noted that in the early days of the program there were fewer firms involved in vaccine litigation, and they typically drew their clients from the region in which they were situated. More recently, with greater use of the Internet by individuals who believed they were injured by a vaccine, the clients are coming from all over the country. Mr. Matanoski observed that greater awareness of the VICP might be more responsible for the increase in filings, rather than an increase in vaccine injuries.

Chief Special Master Dorsey commented on the Commission's options with regard to revising the legislative limitation on the number of special masters assigned to the OSM, noting the Commission would probably be limited to reviewing the issue and developing recommendations. Mr. Kraus observed that the Commission had taken that path several times since he has been a member and the recommendations were finalized, approved and forwarded to the Secretary of HHS. However, the Secretary has not responded to any of those recommendations. Dr. Feemster noted that the Commission had discussed this issue several times and has a current prospective agenda item to review the past recommendations to determine whether any or all should be revised and re-submitted.

Mr. Kraus posed a question about the number of special masters that should be authorized if legislation were to be revised. He also asked if the SPU, which could be a stopgap measure, might be made more permanent. Chief Judge Campbell-Smith responded that she felt a doubling of the present number of special masters would be appropriate and that perhaps the legislative language could be "up to 16" to provide sufficient latitude for budgeting purposes. She added that, unlike past omnibus proceedings that bundled certain types of claims, most claims now stand alone and proceed through the process independently of others. It was originally thought that most cases would be Vaccine Injury Table cases, which are more easily handled than claims that require individual evaluation. The cases that are most often referred to the SPU are claims that have few, if any, points of contention. Chief Special Master Dorsey

stated that the SPU should remain in place as long as the petitioners' bar, the DOJ and the CFC agree that it makes a positive contribution to handling the caseload.

Dr. Feemster expressed appreciation for the two comments and the discussion.

**Report from the DICP, Dr. Narayan Nair, Acting Director**

Dr. Nair briefly noted that the remaining agenda would include a report from the DOJ, a discussion of selected Vaccine Information Statements, and the usual reports from the ex officio members from the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the National Vaccine Program Office (NVPO).

Concerning the statistics through February 3, 2016, Dr. Nair reported that 408 petitions had been filed since the beginning of the fiscal year (FY) which started October 1, 2015. That number, nearly the same as for all of 2012, represented claims filed in about four months of FY 2016. There have been 146 cases adjudicated as compensable (two cases were dismissed), 36 conceded cases (25%), 18 cases decided by the special master (12%), and 92 cases resolved by settlement (63%). Petitioner awards have totaled $81 million to date, with $7.2 million paid for attorneys' fees and costs for FY 2016. Finally, the Vaccine Injury Compensation Trust Fund stands at $3.6 billion. Total income for the year to date was about $110 million, of which $91.5 million came from excise taxes and $18.4 million from interest income.

Dr. Nair noted that a public comment period on the Revisions to the Vaccine Injury Table Notice of Proposed Rulemaking (NPRM) ended on January 25, 2016. The public hearing was held on January 14, 2016.

Regarding outreach activities, presentations have been made to groups at universities, including one at Howard University in December 2015, and the Division is pursuing development of additional partnerships to disseminate information about the program. Staff has been working with the HRSA Office of Regional Operations to publicize the program.

Dr. Nair concluded with information about contacting Annie Herzog (aherzog@hrsa.gov) about meeting information, and the VICP web site: http://www.hrsa.gov/vaccine compensation/commissionchildhoodvaccines.html.

**Report from DOJ, Mr. Vincent Matanoski, Deputy Director, Torts Branch**

Mr. Matanoski welcomed the commissioners and referenced the DOJ Power Point materials ( DOJ PP), as part of his presentation for the three-month period from November 16, 2015 – February 15, 2016. During this reporting period, 237 petitions were filed. Of those, 47 were filed on behalf of children (20%) and 190 were filed by adults (80%). (DOJ PP at 2). The filings are far ahead of last year at this time-period with January 2016 showing a 70% increase in filings.

With regard to total cases adjudicated, Mr. Matanoski noted that 199 claims were adjudicated this quarter. (DOJ PP at 3). There were 162 cases compensated, which was up from 116 last quarter. Of those 162 cases, 57 were conceded cases by HHS. Of those 57 conceded cases, 54 were resolved by a decision adopting a proffer, and 3 were by a decision adopting a settlement stipulation. Mr. Matanoski noted the increase in concessions and adjudications from last quarter. Mr. Matanoski reported an improvement in the personnel situation with an increase in DOJ's budget allowing for additional attorney hiring. Also, the office has received volunteer attorneys from other sections of DOJ to handle cases, and an attorney from HHS Office of the General Counsel (OGC) has joined the office for a temporary six-month stint. There were 105 cases compensated, but not conceded by HHS. Of those, all 105 cases were resolved by a decision adopting a settlement stipulation. (DOJ PP at 3). There were 37 cases dismissed. Of those, 35 cases (non-OAP) were resolved by decisions dismissing the petition, and 2 were dismissed from the OAP. (DOJ PP at 3). There were 4 petitions voluntarily withdrawn. (DOJ PP at 4).

Turning to appeals, three cases filed by petitioners were decided by U.S. Court of Appeals for the Federal Circuit (CAFC). (DOJ PP at 5). In *Padmanabhan v. HHS*, which was discussed at the last meeting, the CAFC affirmed the dismissal of *pro se* (filed without the aid of counsel), petitioners' claim alleging injuries from an underlying mitochondrial disease that was significantly aggravated by the vaccination. Petitioners failed to comply with special master orders and the petition was dismissed for failure to prosecute. In *Rowan v. HHS*, the CAFC dismissed *pro se* petitioner's appeal for failure to prosecute and file a supporting brief after petitioner appealed decisions of the special master and CFC dismissing petitioner's claim alleging vaccine injuries from aluminum adjuvant in the human papillomavirus (HPV) vaccine. In *Scharfenberger v. HHS*, involving attorneys' fees and costs, petitioner appealed the CFC's affirmance of the special master's reduction of attorneys' fees from approximately $103,000.00 to approximately $80,000.00; however, petitioner withdrew his CAFC appeal before a decision issued despite incurring additional fees from the CFC appeal. No new appeals were filed at the CAFC. Mr. Matanoski noted that seven appeals filed by petitioners are pending, and these cases were discussed at prior meetings. (DOJ PP at 6).

Mr. Matanoski discussed appeals at the CFC, beginning with three recently decided cases brought by petitioners. (DOJ PP at 7). In *Tomberlin v. HHS*, the CFC denied as premature petitioner's appeal of an intermediate ruling by a special master, as opposed to a final decision. In *R.K v. HHS*, involving entitlement to compensation, the CFC affirmed the special master's dismissal finding petitioner's evidence to support causation insufficient. The case, which was discussed at the last meeting, involved a lengthy hearing with substantial expert testimony regarding whether or not the injuries of a child with preexisting mitochondrial illness were caused or substantially aggravated by vaccination. The second R.K. decision involved redaction of the case name. The CFC affirmed the special master's decision denying petitioner's request to rename the case, *Doe* and remove the case number, reasoning that the special master's use of initials and the case number in lieu of *Doe* afforded petitioner privacy protections consistent with the Act. (DOJ PP at 7). Mr. Matanoski noted that petitioners filed four new appeals to the CFC. (DOJ PP at 8). In *Cozart v. HHS*, petitioners appealed the special master's dismissal finding petitioners' experts' evidence insufficient to establish that the alleged vaccinations caused the death of a child from Sudden Infant Death Syndrome (SIDS). In *Godfrey v. HHS*, petitioner

appealed the special master's dismissal on remand from the CAFC finding petitioner's expert evidence insufficient to establish causation in a case involving juvenile ankylosing spondylitis. In *Canut*o v. HHS, *pro se* petitioners appealed the special master's dismissal finding no evidence that petitioner's autism spectrum disorder was caused by vaccination. Petitioners rejected the special master's offer to convene a hearing opting instead for a decision based on the record evidence consisting of expert reports. In *Marshall v. HHS, pro se* petitioner appealed the special master's dismissal for petitioner's failure to prosecute the claim. Four cases remain pending at the CFC. (DOJ PP 8).

There are two cases scheduled for oral argument at the CAFC - *Milek v. HHS*, on March 23, 2016 and *D'Angiolini v. HHS,* on April 8, 2016. (DOJ PP at 9).

Mr. Matanoski summarized the history of adjudicated settlements. (DOJ PP at 10-20). During the reporting period, 105 cases were resolved by settlement. The median processing time was 14 months - 45% of the cases were resolved within one year from filing the petition; 78% within two years; and, 91% within three years.

Mr. Matanoski addressed the SPU settlements discussed during the presentation about the impact of increased claims filed in the Program. He emphasized that any final decision issued in the SPU is approved by a special master and there is oversight by a special master in all SPU cases. Responding to a question about SPU case adjudication, Mr. Matanoski explained that DOJ considers settlements on a case by case basis evaluating an appropriate amount for each case based on the alleged vaccine and injury. Mr. Matanoski has not observed a difference in case valuation for SPU cases as DOJ always evaluates the facts and assesses risk in each individual case regardless of processing method.

Responding to a question from Mr. Kraus about the proportion of SIRVA cases conceded, Mr. Matanoski estimated that SIRVA accounts for a significant number of conceded cases. Mr. Matanoski did not anticipate a significant increase in SIRVA concessions when it is added to the Table as those cases are already processed consistent with the proposed Table criteria. Mr. Kraus agreed that case evaluation was not different in the SPU, but described a potential dilemma faced by petitioner if he/she does not agree with DOJ's damages assessment in those cases. If petitioner disagrees with a proposed settlement, the option is to schedule an entitlement and/or damages hearing, which adds delay as hearings are being scheduled nearly 15 months out because of case volume. Mr. Kraus pointed out that reasonable people can disagree about pain and suffering assessments, but the impact to petitioners in the SPU is that the alternative to rejecting a settlement is a lengthy adjudication process. Mr. Matanoski acknowledged that additional time may be involved if an SPU petitioner opts out of the SPU, but emphasized that there is no artificial reduction for settlement of SPU cases. The same settlement evaluation of risk/damages applies whether or not a case is processed in the SPU or is adjudicated by a special master outside of the SPU.

Dr. Feemster observed that it is important to recognize efficiencies from all perspectives. She acknowledged the benefits to settlement, open exchange of information between the parties, and efforts to increase case resolutions through SPU processing.

**Review of Vaccine Information Statements, Skip Wolfe and Suzanne Johnson-DeLeon, CDC**

***Chickenpox (Varicella) Vaccine***

Mr. Wolfe stated that the Commission would review two Vaccine Information Statements (VIS), one for chickenpox (varicella) vaccine and one for poliomyelitis. He added that the FDA had looked at the documents and made suggestions, which he would include in the discussion. The first VIS for review was for the varicella vaccine. In the first paragraph (Why get vaccinated?), the FDA had recommended including a brief statement about how the disease is transmitted. He invited further comments from the Commission members. Mr. Kraus suggested clarifying the statement in the same section concerning contracting shingles later in life. Mr. Wolfe agreed, proposing a sentence stating that infection with chickenpox can cause shingles. Ms. Toomey suggested that including the comment that shingles usually affects older individuals. Mr. Wolfe added that the FDA has noted that varicella vaccines do not necessarily prevent shingles. He added that the vaccine does not necessarily prevent shingles, but it does reduce the likelihood of shingles. Dr. Shimabukuro commented that shingles should be addressed in the zoster VIS rather than in any detail in the varicella VIS.

Mr. Wolfe noted that FDA had preferred a longer statement that had appeared in earlier VIS that, although the vaccine can prevent chickenpox, if one does get chicken pox after being vaccinated the condition is usually milder and resolves more quickly. Dr. Douglas commented that in her teaching experience, health care professionals have expressed a preference for fewer words and descriptions, which they feel enhances health literacy. Mr. Wolf agreed, suggesting that the additional detail might best be placed in the provider guidelines. He noted that the statement is actually located in the last sentence of Section 2. There was agreement to delete that sentence since the severity of the disease was addressed in the Section 1.

There was a brief discussion about the sentence in Section 2 (For anyone who has gotten only one dose, it is never too late to get the second dose) and there was agreement that the sentence should be revised to read that if an individual has received only one dose, he or she should consult a health care provider for counsel.

In Section 3, there was a suggestion to revise the first sentence to read, "Before you receive the vaccine tell your immunization provider:" Concerning the statement that live vaccines given too close together might not work as well refers to the efficacy of the vaccinations, not the safety. One live vaccine given together may affect the immunogenic effect of the other. There was a brief discussion about the caveat that if an individual is "not feeling well" the health care provider might reschedule the vaccination. There was concern that "not feeling well" was not clearly defined and Ms. DeLeon stated that new wording would be developed to the effect that "if you have a mild illness such as a cold, you can probably get the vaccine today; if you are moderately or severely ill you should probably wait until you recover. Your doctor can advise you."

Asked about getting the disease from the live virus vaccine, Dr. Shimabukuro commented that contracting chickenpox from the varicella vaccine is very unlikely, although there could be

adverse reactions, especially if the recipient's immune system is compromised. Mr. Wolfe noted that FDA had recommended including a warning not to take aspirin for six weeks post vaccination because of the risk of contracting Reye's syndrome.

Mr. Wolfe stated that Sections 5 through 7 are composed of standard phraseology that has been reviewed many times in the past.

***Polio Vaccine***

Mr. Wolfe indicated that the FDA recommended having a route of transmission explanation, but the Commission felt that, since polio has almost been eliminated in the U.S., there is no need to explain how it is transmitted to humans. In Section 2, the FDA recommended adding an explanation that individuals who began the polio vaccine series with oral polio vaccine (OPV) could complete the series with inactivated polio vaccine (IPV). Mr. Wolfe suggested that such an explanation would be most appropriate on the provider guidelines. Dr. Douglas agreed, commenting that that circumstance would probably only apply to individuals from other countries. In Section 2, there was a recommendation that since the term "wild poliovirus" may not be a common term in the U.S., the term polio disease would be more understandable.

Mr. Wolfe commented that the statement about "mild illness" (not feeling well) would be revised to reflect the wording agreed on previously for the Varicella VIS. Noting that Sections 5 through 7 had not changed since the last review, Mr. Wolfe thanked the Commission for their discussion of the two VIS.

**Update on the Immunization Safety Office (ISO), CDC, Dr. Tom Shimabukuro**

Dr. Shimabukuro stated that he would focus his update on the Vaccine Safety Datalink (VSD) White Paper (Glanz et al. White Paper on studying the safety of the childhood immunization schedule in the Vaccine Safety Datalink. Vaccine. 2016;34 Suppl 1:A1-A29).

In its 2013 report "Childhood Immunization Schedule and Safety: Stakeholder Concerns, Scientific Evidence, and Future Studies," the Institute of Medicine (IOM) concluded that the available evidence indicated the current U.S. childhood immunization schedule was safe; however, few published investigations had specifically examined the safety of the recommended childhood schedule as a whole. The IOM recommended that additional observational studies of the safety of the schedule were warranted, and stated that the VSD represents one of the best resources in the nation for conducting such studies. Guided by the IOM findings, CDC commissioned a white paper to assess how the VSD could be used to study the safety of the childhood immunization schedule. The objectives of the VSD white paper included:

- Define types of alternative immunization schedules and patterns of under vaccination that could be evaluated, focusing on the first 24 months of age.
- Identify plausible adverse event outcomes that could be related to the childhood immunization schedule, with an emphasis on long-term adverse events.
- Suggest methodological approaches that could be used to assess the safety of the recommended schedule as a whole.

- Propose next steps for studying the safety of the childhood immunization schedule within the VSD.

The VSD white paper defined different immunization schedules being employed within the participants of the VSD, identified health outcomes to study within the context of the immunization schedule, and described epidemiological and statistical methods for the study. The white paper described how the VSD could study the safety of the recommended childhood immunization schedule. Guided by subject matter experts, the paper outlies a 4-stage approach to identify groups of under-vaccinated children, and lists 20 prioritized outcomes, including study designs and statistical methods for analysis of safety. If studies are deemed appropriate, the white paper provides a guide to designing and conducting those studies.

Dr. Shimabukuro described the VSD as a collaboration between CDC and nine large integrated health care organizations that uses large-linked electronic health record databases to conduct monitoring and studies. Dr. Shimabukuro indicated he could invite the author of the VSD white paper to brief the Commission if that was deemed to be appropriate.

Dr. Shimabukuro mentioned several recent published papers:

- Glanz et al. Cumulative and episodic vaccine aluminum exposure in a population-based cohort of young children. Vaccine. 2015;33(48):6736-44. In this paper, up-to-date children were exposed to 11-26% more aluminum from vaccines than under vaccinated children. Power analyses demonstrated that safety studies of aluminum could detect relative risks ranging from 1.1 to 5.8 for a range of adverse event incidence. The safety of vaccine aluminum exposure can be feasibly studied in the VSD. However, possible biological mechanisms and confounding variables would need to be considered before conducting any studies.
- Groom et al. Influenza Vaccination During Pregnancy: Influenza Seasons 2002-2012, Vaccine Safety Datalink. Am J Prev Med. 2015 Oct 30. pii: S0749-3797(15)00505-X. The authors reported that influenza vaccination coverage among pregnant women increased between the 2002-2003 and 2011-2012 seasons, although it was still below the developmental Healthy People 2020 goal of 80%. The 2004 ACIP language change positively impacted first-trimester vaccination uptake. Vaccine Safety Datalink data estimates were consistent with U.S. estimates.
- Moro et al. Surveillance of adverse events after the first trivalent inactivated influenza vaccine produced in mammalian cell culture (Flucelvax(®)) reported to the Vaccine Adverse Event Reporting System (VAERS), United States, 2013-2015. Vaccine. 2015;33(48):6684-8. This review of VAERS reports did not identify any concerning pattern of AEs after cell culture IIV3 (ccIIV3). Injection site and systemic reactions were the most commonly reported AEs, similar to the pre-licensure clinical trials. Reports following ccIIV3 in persons <18 years highlight the need for education of healthcare providers regarding approved ccIIV3 use.
- McCarthy et al. Vaccination and 30-Day Mortality Risk in Children, Adolescents, and Young Adults. Pediatrics. 2016; 137(3):e2 0152970. This study of a cohort of individuals ages 9 to 26 years, of 1,100 deaths identified during the study period, 76 (7%) occurred 0 to 30 days after vaccination. Risk of death was not increased during the 30 days after vaccination, and in a causality assessment no deaths were found to be causally

associated with vaccination. McCarthy, et al analyzed cause of death in children, adolescents and young adults in a period 30 days after vaccination. The study revealed no increased risk of death in the cohort individuals 9 to 26 that could be attributed to the vaccinations. No deaths were deemed causally related to vaccines.

- Kharbanda et al. Maternal Tdap vaccination: Coverage and acute safety outcomes in the vaccine safety datalink, 2007-2013. Vaccine. 2016;34(7):968-73. In this study, Tdap coverage during pregnancy increased from 2007 through 2013, but was still below 50%. No acute maternal safety signals were detected in this large cohort. Outcomes included a composite outcome of medically attended acute adverse events within 3 days of vaccination, incident neurologic events, thrombotic events, new onset proteinuria, gestational diabetes, and cardiac events.

Dr. Shimabukuro noted that the Glanz et al. white paper previously discussed would normally have been included in this section of his report. He concluded his report, inviting question, if any. Dr. Feemster noted that the age range of the study involving young adults (9-26) was the same as that for recommended use of HPV vaccine. Dr. Shimabukuro agreed that it may have targeted vaccines given during that age range, including HPV vaccine.

**Update from the National Institute of Allergy and Infectious Diseases (NIAID), NIH, Ms. Claire Schuster**

Ms. Schuster reported that NIH, including the NIAID, is actively involved in Zika research. The mosquito-borne Zika virus can cause symptoms similar to dengue and chikungunya viruses. NIAID is involved in animal model research related to Zika virus, screening drug compounds for potential activity against Zika virus and developing rapid diagnostics to distinguish Zika from other similar viruses. NIAID, building on vaccine research for other similar viruses, has begun work on vaccine development, including a DNA-based vaccine, a live attenuated vaccine, and a vaccine that uses a genetically engineered vaccine version of vesicular stomatitis virus.

A large Phase III trial in Brazil is testing a candidate vaccine (TV003) for the prevention of dengue fever. The vaccine was developed by NIAID. The trial will enroll as many as 17,000 subjects, aged 2 to 59, and will last five years.

NIAID recently supported a clinical trial looking at sequential rotavirus vaccine schedules. Despite FDA-mandated testing of vaccine prior to licensing, there may be questions related to vaccine administration, especially when multiple products are licensed to prevent the same infection. Since children may receive different vaccines because of changes in their health care providers, or because the health care provider changes the products used, NIAID looked at this situation with regard to two such products, Rotateq and Rotarix, both licensed for use in infants. According to current recommendations and depending on which vaccine is used, infants receive a series of two or three vaccinations. Children in the study received either RotaTeq or Rotarix for the first dose, followed by 5 different combinations of the 2 vaccines to complete the vaccine series. The study found that for rotavirus vaccines, immunization with a mixed series of vaccines is safe and results in comparable immune responses to that generated by immunization with any single product.

Turning to the Environmental Influences on Child Health Outcomes (ECHO) program, Ms. Schuster reported that NIH has awarded $144 million through this program to investigate the effects of environmental exposure from conception to later years in a child's life. NIH's goal is to enroll 79,000 participants by the end of 2016 and one million by 2019.

For information, Ms. Schuster announced that a special edition of *Vaccine* (November 25, 2015) focused on advancing maternal immunization programs through research in low and middle income countries. Finally, Ms. Schuster identified a page on the NIAID web site that contains a discussion of selected NIAID research advances of 2015. The URL is http://www.niaid.nih.gov/about/pages/2015.aspx.

**Update from the Center for Biologics, Evaluation and Research (CBER), FDA, LCDR Valerie Marshall**

LCDR Marshall reported two recent vaccine supplement approvals. The first, human papillomavirus 9-valent vaccine, recombinant, trade name Gardasil 9, was approved in a supplement to the biologic license application (BLA) to extend the indication for use to boys and men age 16 to 26. This vaccine is intended to prevent: 1) anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58; 2) genital warts (condyloma acuminata) caused by HPV types 6 and 11; and 3) anal intraepithelial neoplasia (grades 1, 2 and 3) caused by HPV types 6, 11, 16, 18, 31, 33,45, 52, and 58. The vaccine was previously indicated for boys age 9 through 15 for the prevention of the same diseases.

The second approval was for haemophilus b conjugate vaccine (trade name Hiberix). The BLA was revised to include safety and effectiveness data to support the use of Hiberix for active immunization for the prevention of invasive disease caused by haemophilus influenza type b (Hib) in children 6 weeks to 14 months of age for the primary series. Hiberix was previously licensed for use as the booster (final) dose of the Hib vaccine series for children aged 15 months to 4 years who previously received the primary series of Hib vaccination.

LCDR Marshall provided a brief report on the November 13, 2015 meeting of the Vaccines and Related Biological Products Advisory Committee (VRBPAC), which convened to discuss considerations for evaluation of the safety and effectiveness of vaccines administered to pregnant women to protect the infant. The Committee discussed that serological markers may be acceptable to infer vaccine effectiveness to protect the infant from disease. The duration and safety follow-up of the infant and safety assessments in the mother will depend on the specific vaccine under consideration and disease targeted. The Committee noted challenges in the safety follow-up in infants given that infants may be seen by different health care providers. The need for clinical studies to assess potential immune interference with childhood vaccines depends on the vaccine antigen used for maternal immunization.

Finally, LCDR Marshall announced that the VRBPAC will meet on March 4, 2016 to make recommendations on the selection of strains that should be included in the seasonal influenza vaccine for the 2016-2017 influenza season.

**Update from the National Vaccine Program Office (NVPO), Dr. Karin Bok**

Dr. Bok discussed two significant items, the first related to adult immunization and the second to maternal immunizations. She described the National Adult Immunization Program (NAIP), which includes steps by federal and nonfederal stakeholders to achieve optimal disease prevention through immunizations. The NAIP also covers objectives and strategies to strengthen infrastructure, improve access, and stimulate demand for adult immunization. The goals include a focus on analysis of claims filed with the VICP to see if there is a link between vaccines received and adverse events. The goals also include enhancement of vaccine safety monitoring systems and development of methods to rapidly and accurately assess vaccine safety, especially in pregnant women.

Dr. Bok mentioned the National Vaccine Advisory Committee meeting at which there was a presentation on the Maternal Immunization Working Group. That working group is looking at identifying barriers to and opportunities for development of vaccines for pregnant women. Dr. Bok mentioned recommendations related to ethical issues, including development of an ethical framework that could apply to various venues, and acceptance of the premise that pregnant women are not a "vulnerable populations". They should be considered a complex population, and a proposal to standardize definitions of minimal risk to aid the institutional review board (IRB) review process should be developed.

The working group also considered a number of regulatory issues:

- Define the pregnancy and lactation labeling rules as it relates to vaccinations;
- Develop new Office of Human Research Protections guidelines for pregnant women in clinical trials;
- Look at models similar to the Best Pharmaceuticals for Children Act that would apply during pregnancy;
- Continue to support dialog between FDA and manufacturers on licensure requirements for vaccine for use by pregnant women;
- Encourage communication between HHS and manufacturers to encourage investment by manufacturers in maternal immunization; and
- Promote modification of the VICP to fully cover maternal immunizations.

The working group addressed safety monitoring issues:

- Development of standard definitions of maternal and neonatal outcomes;
- Support alignment of current safety systems for optimal output;
- Create an interface with international data systems;
- Promote education of providers about safety research;
- Develop guidance on newborn surveillance timeframes during trials and post-licensure; and
- Develop data on safety of antigen reparations, especially for flu and TDaP.

The working group also made proposals related to preclinical and clinical research:

- Address barriers to developing immunizations at the preclinical stage;
- Increase research focus by creating a Maternal Immunization Research Network;
- Standardize post-marketing surveillance for maternal immunization; and

- Encourage post-marketing effectiveness evaluation.

Finally, the working group expressed advocacy for provider education and support, noting that professional societies should be encouraged to partner in clinical research that includes pregnant women. Obstetricians should advocate for testing vaccines during pregnancy and for vaccine use during pregnancy. Obstetricians should be trained on the interpretation of new labeling to help them make more informed decisions.

**Public Comment**

Dr. Feemster noted that all of the agenda items had been completed for the meeting with the exception of public comment and consideration of future agenda items. She invited public to comments. She added that individuals could offer comments, but there would be no discussion after the comment.

***Theresa Wrangham, Executive Director, National Vaccine Information Center (NVIC)***

Ms. Wrangham offered the following comment, transcribed in their entirety:

My name is Theresa Wrangham. I am the Executive Director for the National Vaccine Information Center. Our mission is to prevent vaccine injury and death through public education and to defend the informed consent ethic, policy and laws. Our concerns today relate to the potential reclassification of pregnant women as a complex population for ethical reasons. What exactly would the definition of a complex population be? There was little information given today on this term. In addition, there is even less information on vaccine adverse effects on unborn children when vaccines are given during pregnancy, and the majority of this information is observational.

There also appears to be a lack of harmonization between the efforts of the maternal working groups within the National Vaccine Advisory Committee and the ACCV's maternal working group, and an apparent duplication of effort where injury compensation recommendations are concerned. The ACCV has spent considerable time on this matter and should be the lead committee in making recommendations to HHS.

In relation to the national adult immunization plan, there is also no language supporting the ongoing vaccine safety research mandate within the law to close IOM-acknowledged gaps, while there is a great focus on new vaccines and vaccine innovation. The plan would benefit from more input from the ACCV in that regard. A bottom line is there is a lack of balance within this plan that does not harmonize with the concerns normally expressed by the ACCV relating to vaccine injuries.

With regard to the VIS discussions today, there continues to be a general marketing of vaccines within the general language of the VIS, and more specifically a lack of background on diseases, incidence and severity as a matter of informed consent information to be given to the consumer. These documents are meant to disclose risks and benefits of vaccines and were much

longer and more informative than they are today, though there is no statutory limitation on their length.

I respectfully remind the ACCV that the Altarum report on VICP petitioner satisfaction noted that parents wanted more information up front on the risks of vaccination and the VICP program. Today's VIS is very brief and does little to balance this information against the necessity of also disclosing background information about the disease so that the risks and benefits of the vaccine are put into an appropriate context for consumers. There also seems to be a push to put things into the provider guidelines for VIS information, and wait for consumers to ask their provider questions.

As an organization of standing that receives many phone calls from the injured, and most who have questions about vaccination, many consumers do not know what questions to ask. And when they do ask their provide questions, they are threatened with being kicked out of medical practices and/or their questions are simply not welcome. In short, the VIS is not living up to what the spirit and intent that the law originally provided and amendments to the law have not supported informed decision making by consumers.

NVIC respectfully requests that the ACCV consider revisiting VIS content and statutory requirements, as well as possible recommendations that would promote informed decision making that does not rely on vaccine provider dialog, given the current hostility that parents face when they ask questions of providers about vaccines.

In closing, we would also appreciate the ACCV's consideration of requests that were made during December's meeting, and which were provided in writing to members. We appreciate the opportunity to comment today. Thank you.

Dr. Feemster stated that there were no other requests to participate in public comment.

**Future agenda items and new business**

Dr. Feemster commented that as a follow-up to discussion at the last meeting regarding whether prior recommendations should be re-submitted to the Secretary. One proposal is to reconvene the working group to address that issue. Mr. Kraus commented that, before that discussion, it would be helpful to receive a briefing on the possible new members that might be added in the future. Dr. Nair commented that his office is accepting nominations for a new member who is the parent of a vaccine-injured child. He added that he was in the process of filling vacancies on the Commission, but that he did not have a timeline for that process. Ms. Herzog added that there was no firm deadline for submission of nominations, noting that it can take 6 to 9 months for the whole approval process to be completed. Nominations in all other categories (not including parent) have been received. Dr. Douglas urged a continued focus on the process to ensure that it does not get bogged down, and Ms. Toomey endorsed the suggestion.

There was a suggestion that the Commission receive a list of recommendations considered by the Commission, identifying those that had been approved and forwarded to the

Secretary. As preparation for the next meeting, which will be in person, Dr. Feemster requested for a list of working group members and the charge to each group. Dr. Nair agreed to provide that information. Dr. Feemster also confirmed that inviting the author of the white paper would be helpful. There was a suggesting that a representative of the Secretary attend the next meeting to provide some background on how the recommendations are handled. However, there was agreement that the Commission should pursue its intent to review the recommendations already submitted before taking that step.

**Adjournment**

There being no further business, on motion duly made and seconded, the Commission unanimously approved adjournment.