Advisory Commission on Childhood Vaccines
December 3, 2015
98th Meeting
Teleconference and Adobe Connect

Members Present

Kristen A. Feemster, M.D., ('15)
Charlene Douglas, Ph.D. ('15)
Edward Kraus, J.D. ('15)
Karlen E. Luthy, ('18)
Luisita dela Rosa, Ph.D. ('15)
Jason Smith, J.D. ('15)
Martha Toomey ('18)
Alexandra Stewart, (18)
Sylvia Fernandez Villarreal, M.D. ('15)

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

Melissa Houston, MD., Director, DICP
Andrea Herzog, Staff Liaison

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

Dr. Feemster invited commissioners to announce their presence on the phone after which she invited public comment on the meeting agenda.

Public Comment on Agenda Items

Janet Cakir noted that she was submitting a PowerPoint presentation to support of comments that she would be making during the public comment period. She requested that they be made available on the web during her presentation.

Approval of September 3, 2015 minutes

Dr. Feemster invited approval of the minutes of the September 3, 2015 ACCV meeting. On motion duly made by Ms. Douglas, seconded by Mr. Smith, the minutes of the September 3, 2015 meeting were approved without corrections or revisions. Dr. Feemster then turned to the agenda and invited Dr. Houston to provide her report.

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Report from the Division of Injury Compensation Programs (DICP), Dr. A. Melissa Houston, Director

Dr. Houston welcomed those present and briefly reviewed the agenda. The agenda includes an update from the Department of Justice (DOJ), a report from the ACCV Adult Immunization Workgroup, Presentations on Impact of Increased Claims Filed (DICP and DOJ) and finally updates from the ex officio members from the Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH) and the National Vaccine Program Office (NVPO).

Looking at petitions and adjudications, Dr. Houston stated, as of November 5, 2015, the Division had received 133 petitions and the projection, based on that number is about 1,500 petitions may be filed before the end of this fiscal year (FY). The total adjudications for the current report period is 12, 75% of them were settled and 25% were due to concession. In the first month of FY 16, awards to petitioners totaled $18.5 million and $2 million to petitioners' attorneys for fees and costs. The Vaccine Injury Trust Fund stands at $3.6 billion as of September 30, 2015. Of the $3.6 billion $275 million was derived from excise tax payments and $59 million from interest on the Trust Fund balance.

Dr. Houston announced that the Revisions to the Vaccine Injury Table Notice of Proposed Rulemaking was published in the Federal Register on July 29, 2015, and the 180-day public period extends through January 25, 2016. There will also be a public hearing to provide further opportunity for public comment, and the date of that hearing will be published in the Federal Register. The commissioners will be informed when that date is known.

Dr. Houston described the National Vaccine Injury Compensation (VICP) outreach activities one of which is a partnership with the Food and Drug Administration, which distributes VICP materials at various meetings such as the November 18, 2015 meeting of 24 National Nurses Associations. In addition to meetings, an article written by the VICP was posted to the National Association of County & City Health Officials blog at http://essentialelements.naccho.org/archives/1319 and went live on November 10, 2015.

Dr. Houston stated she attended the Advisory Committee on Immunization Practices (ACIP) in Atlanta on October 21, 2015. Information on ACCV meetings, including minutes and presentations, can be found on the web at http://www.hrsa.gov/vaccinecompensation/commissionchildhoodvaccines.html

Report from DOJ, Vince Matanoski, Assistant Director, Torts Branch

Mr. Matanoski welcomed commissioners and referenced the Department of Justice Power Point materials (DOJ PP), as part of his presentation for the three-month period from August 16 - November 15, 2015. During this reporting period, 337 petitions were filed. Of those, 32 were filed on behalf of children and 305 were filed by adults. Last year there were about 800 petitions filed and this year the Department is expecting over a 1,000. He explained that, since flu accounts for the majority of vaccinations, and there is a seasonal effect on when vaccinations are given for flu, there is a concomitant seasonal fluctuation in clams filed for

vaccine injuries. There was also a notable increase in shoulder injuries related to vaccine administration (SIRVA).

With regard to total cases adjudicated, even though there were 337 claims filed, only 150 petitions were adjudicated, which indicates an increasing backlog. That issue will be discussed under a separate agenda item. A total of 116 cases were compensated, 34 cases conceded by HHS (nearly all by proffer), and 82 cases not conceded by HHS, all by settlement. Thirty-four were not compensated and seven claims were voluntarily withdrawn.

Mr. Matanoski discussed a number of cases now going through the appeals process

Appeals by Petitioner in the U.S. Court of Appeals for the Federal Circuit:

- A decision was handed down in Hirmiz v. HHS that the alleged injury occurred before the vaccination. That decision was affirmed by the U.S. Court of Appeals for the Federal Circuit (CAFC).
- In Mora v. HHS, one of five newly filed appeals, the petition was dismissed at the request of the petitioner in order to pursue a civil action. The claim was ineligible for that process under current regulations. The claimant then tried to return to the original claim process but was ineligible there as well.
- D'Angiolini v. HHS, involved a claim of ASIA (autoimmune syndrome induced by adjuvant), but the U.S. Court of Federal Claims (CFC) ruled against the petitioner after hearing evidence that ASIA was not the cause of the injury.
- In Nutall v. HHS, the CFC affirmed the Special Master's decision that that the claimant failed to demonstrate that he had suffered an injury, specifically encephalitis.
- Padmanabhan v. HHS and Greenberg v HHS were both *pro se* cases in which the claimant represented himself, without engaging an attorney. Padmanabhan alleged that the child suffered from an underlying mitochondrial disease that was significantly aggravated by the vaccination. The claimant failed to submit court ordered medical information and ultimately failed to pursue the case for action and the special master dismissed the case for failure to prosecute. In Greenberg the issue related to the fact that the injury occurred after three years, past the statute of limitations for filing, as well as a ruling that, even if the claim had been timely filed, the claimant failed to prove causation. Review of that decision is pending at the CFC.

Appeals by Petitioner in the U.S. CFC:

Five cases were decided, three involving entitlement and two related to attorneys' fees and costs.

- In Hodge v. HHS, regarding timely filing of the claim, the CFC remanded the case to the special master to review whether the claimant had the mental capacity to properly file the claim in a timely manner. It is pending with the special master.
- Greenberg v. HHS was discussed above.
- In Waterman v. HHS, the claim involved a vaccination containing several vaccines and the issues of the claim revolve around proof of cause of death. The

CACF affirmed that there were insufficient facts to support the allegation in that case.

- In Scharfenberger v. HHS, the special master reduced the original award from $100,000 to about $80,000. An appeal to restore the original amount failed and the special master's decision was affirmed.
- In Guerrero v. HHS, the appeal was originally affirmed for the award handed down at the special master level, then reversed by the CFC so that the special master could review the circumstances (a small amount was added to the award).

Five new appeals pending in the CF C:

- In Graham v. HHS, the petitioner's attorneys filed a claim before fully developing the case and the claim was dismissed when it was clear the vaccine was not involved. Although attorneys are entitled to fees and costs whether the case is won or lost, in this case the special master deemed that there was no reasonable basis for filing the claim and the claim for fees and costs was rejected.
- In Bloch v. HHS, the special master determined that there was no evidence produced by the petitioner to show that the injury was aggravated by the vaccine, so the claim was dismissed.
- In Tomberlin v. HHS, the appeal was filed to cause a review of a decision, but the decision was actually an intermediate ruling on a particular damages issue. The question before the court is whether or not the ruling constitutes a final decision.
- Kenzora v HHS involved a settlement agreed on by the petitioner and respondent without requiring a finding that the vaccine in question actually caused the alleged injury. An award was made and the petitioner, deciding the award was not sufficient, petitioned the court to vacate the judgement in order to renegotiate the award. The special master denied the request, leading to this appeal.
- In R.K. v. HHS, the child involved suffered from a preexisting mitochondrial illness, which the petitioner believed was exacerbated by the vaccine such that the child suffered a subsequent neurological injury. After a lengthy hearing lasting more than a week, the special master found there was insufficient evidence to support the claim, resulting in this appeal.

Finally, Mr. Matanoski stated that one oral argument is scheduled in the CAFC on December 8 – Moriarity v. HHS.

Adjudicated settlements

Mr. Matanoski summarized the history of adjudicated settlements. Eighty-three cases were resolved by settlement in the period beginning August 16, 2015 through November 15, 2015. There were 72 adult cases and 11 cases involving minors. Flu vaccine was included in the alleged vaccines causing injury in 63 claims. The average time to process the claims was one year and ten months; the median processing time was 10 months. The percentage of cases resolved within one year was 43%; 75% within two years; and 85% within three years. Within the last few years the time to resolve cases has decreased, but in this time period that trend has ended, a cause for concern. Of course, Mr. Matanoski added that one instance is not sufficient to make conclusions about the future.

With regard to conceded cases, there were 33 such cases in this period, and the average processing time was 10 months, the median was eight months. Noting that this was an excellent result, Mr. Matanoski concluded his report.

Presentation on Impact of Increased Claims Filed, Dr. A. Melissa Houston, Director DICP, and Mr. Vince Matanoski, DOJ

Dr. Houston introduced the discussion of the impact of the increasing number of claims being filed under the VICP. She noted that HRSA administers the program, reviews claims as they are filed, reviews medical and scientific literature as it applies to the types of claims made under the program, and determines if the claims meet the medical criteria for compensation. Finally, HRSA submits a preliminary recommendation on behalf of the Secretary of HHS to the Department of Justice. Once a claim has been adjudicated, HHS provides the logistical service of payments to petitioners and to their attorneys for fees and costs.

Historically, after a relatively stable rate of annual claims from 2002 through 2008, the number of claims began to increase at an exponential rate, climbing from an average of about 200 claims a year to 804 claims in fiscal year 2015. However, in the last three years HRSA VICP staffing levels responsible for processing those claims has remained stable (17 FTEs in 2013, and 18 FTEs in 2014 and 2015). Various strategies have eased the pressure on the staff, including the use of technology (in writing and distributing checks, for example), and a vacancy announcement was posted in late 2015 to recruit additional staff.

Mr. Matanoski commented on the situation at the DOJ where attorneys and paralegals work with HRSA medical officers, petitioners, expert witnesses, and others to develop the cases and reach an equitable outcome. The process involves conferences and hearings, a significant time requirement. Mr. Matanoski explained that the process is budget limited and that budget has remained flat since 2009. It was originally designed to accommodate about 400 claims per year, a number that increased to over 800 in FY 2015.

Noting that Omnibus Autism Proceeding cases were significantly reduced by March 2012, Mr. Matanoski also explained that a backlog of unresolved cases began to build by September of 2013. That backlog has grown to about 500 cases, which means that an unacceptable number of individuals are having to wait a longer time for resolution. There is also an added maintenance cost to a large backlog. There is an internal requirement for reports to update management about the delays, reports that take time to prepare, and there is an increased need to respond to petitioners' attorneys, who request clarification for the delays.

The resolution to the challenge is to increase the resources devoted to each case, which flies in the face of budget limitations, or to decrease the resources needed to resolve the cases, which speaks to making the process more efficient (e.g., relying on greater support from paralegals). It is also possible to increase support by "borrowing" attorneys from other federal offices, even to work on a part-time basis. Streamlining the way cases are processed is another way to reduce costs, such as defining cases that have similar medical issues, such that a single case can serve as a model to reduce the resources required to process other similar cases.

Looking ahead, the environment is changing. There are more adult claims now than before. Pertussis-related claims, common years ago, are being displaced by flu injury claims, and the complex neurological injuries, although still part of the claims profile, are giving way to more defined injuries like SIRVA. These changes may enable the development of more standard paradigms for awards and the determination of attorneys' fees. These kinds of changes could improve efficiencies that would reduce total costs.

Dr. Feemster expressed appreciation for the presentations and invited questions or comments. Ms. Toomey asked who is championing the effort on behalf of HRSA or ACCV for greater financial support for the program. She conceded that ACCV could not lobby for the cause and Ms. Douglas suggested identifying organizations, such as nonprofits, interested in the issues. Contacting those groups as a private citizen is one opportunity. Dr. Feemster suggested that there may be little understanding of the challenges related to the vaccine injury compensation program. Ms. Toomey asked if there were statistics about how many individuals may have died while waiting for results from a vaccine injury claim. Mr. Matanoski stated that those numbers were not well defined, but a consideration is the fact that flu-related vaccine injuries affect older adults more than children and those individuals may experience a higher rate of very negative outcomes.

Dr. Feemster asked if there were internal impediments to developing solutions for improving processing time for straightforward cases, such as SIRVA, versus the more complex neurological cases. Mr. Matanoski commented that SIRVA claims, in general, impose far fewer challenges and there should be few internal impediments to developing more efficient processes to resolve those cases within DOJ. But moving toward the paradigm model, including resolution of a model for attorneys' fees and costs, would require coordination among the players – DOJ, HRSA, petitioners and the CFC – which implies that the process would take time and funding to put together, even though it should have a positive outcome. Ms. Toomey commented that her impression of the process with her son was that the situation was adversarial, but that her participation in the ACCV discussion has demonstrated that the various players do seem to be interested in reaching a positive outcome, which she considered encouraging. Mr. Kraus agreed that there is a positive aspect to the discussion, but that the vaccine program was based on providing a litigation approach to achieving the best outcome for clients, which may not always be the most efficient route to ultimate resolution.

Mr. Matanoski concluded his comments by noting that, although the objective includes improving efficiency in attaining resolution, the focus of the process must always be on the interests of the individual involved, and not the aggregate of a 500 case backlog. He added a concern that, although there is an effort to identify simpler cases that can be fast tracked to resolution, that focus cannot or should not work to the detriment of the more complicated cases that, by their nature, take more time and resources to resolve. Two considerations related to the speed a case moves through the system are the petitioner's diligence in responding to requests for information, and the fact that, if the case must go to trial, it must also get in line to be heard, which can induce some delays.

Asked about whether it would be practical to have specialists on staff, both medical and legal, to address specific issues, such as SIRVA, both Dr. Houston and Mr. Matanoski said that the number of cases that must be addressed would make it impractical to reserve review of a specific injury to one or two staff members, although Mr. Matanoski commented that they had set up teams that were expert in certain issues (such as ASIA or complex award solutions).

Discussion of Petition to Add Food Allergies to the Vaccine Injury Table, Dr. Narayan Nair, Chief Medical Officer, DICP

Dr. Feemster explained that this agenda item was the result of a request from a member of the public to add food allergies to the Vaccine Injury Table (Table).

Dr. Nair stated that his office had received an e-mail from a citizen requesting that food allergies be added to the Table based on the contention that food proteins present in vaccines may be able to cause the development of food allergies in the vaccinated individual on September 19, 2015. Dr. Nair briefly described the process by which an injury or a vaccine/vaccine component can be added to the Table, which includes a petition by a private citizen. Dr. Nair described the nature of food allergies, including the possibility of anaphylaxis.

The first exposure to a food allergen may or may not produce allergic symptoms, but the exposure can cause sensitization. Re-exposure can result in more specific symptoms, including hives, itching, nausea, vomiting, swelling of the mouth and throat and low blood pressure. Although rare, the most serious reaction was anaphylaxis.

The ACCV has established guiding principles for recommending changes to the Table. The first is that the proposal should be scientifically and medically credible, and the second, when such a proposal indicates a change, that change should be made for the benefit of petitioners. The request from the private citizen cited two studies, the 2012 Institute of Medicine (IOM) Report, "Adverse Effect of Vaccines: Evidence and Causality" and a 2002 paper by V. Pool et al, "Prevalence of anti-gelatin IgE antibodies in people with anaphylaxis after MMR vaccine in the United States".

The IOM report reviewed 8 of the 12 vaccines covered by the VICP and provided 158 causality conclusions. It did not specifically evaluate evidence regarding a causal association between vaccination and food allergies. Therefore, the IOM did not recommend the addition of food allergies as an adverse event to the Table. The Pool study was a case controlled study relying on Vaccine Adverse Reporting System (VAERS) reports, comparing individuals who had anaphylaxis after vaccination. Fifty-seven individuals were identified as having anaphylaxis, 22 underwent IgE testing, and, although there was an indication that the gelatin in vaccines could cause anaphylaxis, the authors of the paper did not contend that the gelatin actually caused food allergies. The primary purpose of VAERS is not to develop causality conclusions.

Dr. Nair added that his office did an extensive literature search without finding any evidence of vaccines as a factor in causing food allergies. In the literature there are a number of papers related to food allergies, but there were no references to vaccines as a factor in causing food allergies. The National Institute of Allergy and Infectious Disease (NIAID) conducted an

expert panel to develop guidelines for diagnosing and managing food allergies, and vaccines were not mentioned as causative or even related to food allergies.

Dr. Nair articulated the recommendation options available to the ACCV: 1) add food allergies to the Table, or 2) do not add food allergies to the Table.

Dr. Feemster invited discussion. She noted that the Commission could choose either of the options, or propose alternative options. Ms. Stewart suggested a third option, to recommend additional study. If the government is not interested in sponsoring a study on causality, it might be appropriate for the ACCV to make such a recommendation. Dr. Houston conceded that the third option was viable, but she added that it should be considered apart from the two options presented. That is, the Commission should address the petition, which specifically asks for the addition of food allergies to the Table. The vote, either yes or no, should be based on currently available information.

Ms. Toomey noted that some families are reluctant to allow vaccination of their children because they are concerned about what is in the vaccine. Mr. Kraus commented that, based on the presentation, there is insufficient information to vote for either adding or not adding food allergies to the Table. He noted that if the second option prevails, an individual retains the right to file a claim under the VICP and show causation as with any other claim not supported on the Table. If the Commission must vote on the options immediately, he recommended Option rejecting addition of food allergies to the Table, but that perhaps under new business the Commission should look into the relationship between vaccines and food allergies.

Dr. Feemster suggested that the action should be to vote on the two options. Then the question of additional study could be addressed. Dr. Douglas commented that the serious adverse event of anaphylaxis is a rare event and it is difficult to design a study with sufficient power to make definitive conclusions. Dr. Feemster noted that the study presented looked at a different outcome – it is a different question as to whether receipt of a vaccine leads to food allergies versus developing anaphylaxis after vaccination. She suggested that the petition is based on developing food allergies after vaccination as the rationale for adding food allergies to the Table. Ms. dela Rosa commented that, if anaphylaxis a germane injury, it is already on the Table.

Concerning developing a third option that would include further study, Dr. Houston suggested that sufficient information to make that decision may not be available. She suggested that before making a recommendation for further study a more substantive rationale for further study should be developed as part of the recommendation.

On motion duly made and seconded, the Commission unanimously approved Option 2, not to add food allergies to the Table.

Report from the Adult Immunization Workgroup, Dr. Sylvia Villarreal, ACCV Member

Dr. Villarreal reported that, at the December 2013 ACCV meeting, Dr. Steve Bende stated that an important area in immunization is among adults. He said that the NVPO supported

the objectives of the adult immunization plan. In March 2014 he announced that the NVPO intended to release the National Adult Vaccination Plan later in the year. In December 2014 the ACCV discussed whether recommended adult immunizations should be considered for inclusion in the National Vaccine Injury Program, and a working group was established to look at the issue.

The working group met monthly via teleconference from January to October 2015 to discuss issues related to vaccines recommended for adults only. The Workgroup asked the DICP to provide claims data for Zoster (Zostavax) vaccine, and the pneumococcal 23 vaccine (PPSV 23) vaccines. Because these vaccines are not routinely recommended for children and are not covered by the VICP, if claims are received for these vaccines, they are categorized as unqualified vaccines in the DICP information system. Therefore, these is not any specific data about claims filed for these two vaccines.

It is the conclusion of the workgroup that because of data limitations, claims limitations, and possible unintended consequences of allowing amendments to the National Childhood Vaccine Injury Act of 1986, neither vaccine should be recommended for coverage under the VICP. The rationale is that the risks to the program of any legislative change would outweigh any perceived benefit of modifying the legislation.

The workgroup strongly recommended that the Commission remain open to further discussion regarding amendments to the VICP in that new vaccines might be developed that would qualify for coverage. That could include vaccines routinely recommended for pregnant women solely for the benefit of a live born child. The workgroup also recommended a continued follow-up to the recommendations submitted to the Secretary regarding maternal immunizations.

Dr. Feemster expressed appreciation for the report. She invited comment. Dr. Douglas asked if there was a parallel advisory commission in HHS for adult vaccines. Dr. Feemster commented that the ACIP makes recommendations for both adults and children. Ms. Stewart commented that the adult vaccines under discussion were recently recommended and she felt there was a presumption that they would be included in the VICP. If not included, she asked if individuals alleging injury would have to seek redress by pursuing a tort lawsuit. Mr. Kraus clarified that the adults would not have recourse through the VICP, and would have to seek redress in the civil court system.

Mr. Smith commented that he had provided information to Biotechnology Industry Organization (BIO), a trade organization representing pharmaceutical manufacturers, about the deliberations of the Workgroup. BIO had responded that they felt the recommendations were acceptable, considering the risks that could be exposed if the original legislation was open to revision. There would be no way to limit legislative revisions to the specific recommendations that might be made by ACCV. All of the vaccine legislation would be open for review and revision, and special interest groups might be able to significantly change the Act. Mr. Smith added that earlier recommendations that might require legislative change (statute of limitations, limits on awards, etc.) were less vulnerable to unanticipated outcomes that could negatively impact the provisions of the program.

Asked about whether a recommendation should be formalized, Dr. Villarreal stated that the workgroup did not recommend any specific action. Dr. Houston added that the rationale for an adult vaccine commission, the National Vaccine Advisory Committee (NVAC) and ACIP makes recommendations for both children and adults. Dr. Feemster, noting that a vote on the report was not required, declared the discussion closed.

Review of Vaccine Information Statements (VIS), Skip Wolfe and Suzanne Johnson-DeLeon, CDC.

Mr. Wolfe noted that the Commission would complete the final review of the vaccine information statements (VIS) for hepatitis A and hepatitis B. He added that this final review followed several previous reviews when substantive changes were made. Therefore he did not anticipate significant revisions. He stated that the content of both VIS's has been vetted by the subject matter experts and reviewed by the FDA. Dr. Feemster announced that she would recuse herself from the discussion.

Hepatitis B

Mr. Wolfe stated that FDA commented on Section 2, entitled "Why get vaccinated," that one drug company recommended a different schedule than other manufacturers as described in the first paragraph. He explained that no change in the wording would be made because the slightly different schedule was not relevant to the patient. Keeping the wording simple avoids having to reissue the VIS if a minor change is made. FDA also observed that the manufacturers recommend completing the series by six months of age if the series begins at birth, so that wording will be revised to reflect that schedule.

Finally, in that section, the FDA noted that the last sentence was not supported by research. However, Mr. Wolfe commented that there is a CDC recommendation that, with very few exceptions, all vaccines may be given simultaneously. Mr. Kraus suggested that the wording be changed to "currently there is no evidence that there are additional safety concerns caused by giving the hepatitis B vaccine at the same time as other vaccines."

In Section 3, FDA suggested mentioning latex when discussing allergic reactions.

In Sections 4 through 7, FDA had no comments.

Mr. Wolfe asked if risk should be quantified (e.g., one out of X people experience a risk event), or whether stating the fact that a risk exists is sufficient. He stated that the CDC's inclination is to make the latter the policy. He noted that additional risk information could be included in the provider guide. Mr. Krause felt that the quantified risk information might be helpful to the reader. Mr. Wolfe commented that since the quantified risk is usually included in the provider guide, a sentence advising the patient to ask his/her provider about specific risk numbers should suffice.

There was a brief discussion about the instance when a provider does not distribute the VIS as required, especially in non-medical environments (such as pharmacies like CVS). It was noted that this failure had nothing to do with wording in the VIS.

Hepatitis A

The change in the hepatitis B VIS was also made in the Hepatitis A VIS – the wording in the last sentence in Section 2 changed to "currently there is no evidence that there are additional safety concerns caused by giving the hepatitis B vaccine at the same time as other vaccines."

Update on the Immunization Safety Office (ISO), CDC Vaccine Activities, Dr. Mike McNeil

Dr. McNeil explained that the one-day ACIP meeting held in October included a number of workgroup reports. The first, on meningococcal B vaccine, a permissive recommendation (allowing individual clinical decision-making), indicated that the vaccine may be administered to individuals aged 16 to 23 to provide short-term protection against meningococcal B disease. There is no recommendation for routine use since there is limited data and a low prevalence of disease.

The workgroup on influenza vaccine reported there was limited activity to date in the US, and that the currently circulating viruses are similar to those included in the 2015-2016 vaccines. A manufacturer made a presentation on cost effectiveness of high dose versus standard dose Fluzone, which revealed that high dose, even at three times the cost, is more cost effective than standard dose because of reductions in cardiovascular complications. Novartis discussed its new product, Fluad, an adjuvanted trivalent flu vaccine that contains squalene, surfactants and citrate. The vaccine has an enhanced immune response and a safety profile similar to other flu vaccines.

The presentation on human papillomavirus (HPV) vaccine indicated that coverage has increased (although it is still low) to 34% of girls and 21% of boys. Parents believe the vaccine is not needed for boys (not officially recommended) and possibly risky for girls (safety concerns). The CDC has sponsored a public campaign to increase coverage. Dr. McNeil stated that his office provided an update on HPV vaccine safety that showed no elevated risk of venous thromboembolism (VTE), fetal loss, spontaneous abortion or congenital abnormalities. There have been, however, recent safety concerns including primary ovarian insufficiency, complex regional pain syndrome, and postural orthostatic tachycardia syndrome.

Dr. McNeil concluded with four brief workgroup reports: Japanese encephalitis vaccine; a combination vaccine (pediatric hexavalent vaccine containing DTaP, IPV, Hib and Hep B); a new cholera vaccine (anticipated to be licensed in the US in 2016); and Ebola vaccine administered to 5,550 health care workers as of October 18, 2015 with no serious adverse events.

Dr. McNeil discussed several publications:

- Sukumaran et al, a study among women who received Tdap during pregnancy showed no increased risk of adverse events or adverse birth outcomes for those with previous recent tetanus-containing vaccinations. JAMA Oct 2015

- McNeil et al, looked at data from the Vaccine Safety Data Link (VSD), and found anaphylaxis after any vaccine was very rare, two or less cases per million doses in children and adults. Journal of Allergy Clinical Immunology Sep 2015
- Sukumaran et al, study showed that concomitant administration of Tdap and flu vaccines during pregnancy did not result in an increased risk of adverse events or negative birth outcomes compared with sequential vaccination. Journal of Obstetrics and Gynecology, Nov 2015
- Moro et al, reviewed components of the CDC's public health response to ACIP's recommendation to study and monitor the safety of Tdap vaccines in pregnant women. Human Vaccines and Immunotherapeutics Dec 2015
- Two studies evaluated the risk of venous thromboembolism (VTE) after HPV4. Naleway et al, showed among individuals 9 to 26 risk was not elevated following HPV4 exposure. Yih et al, showed no evidence of increased risk of VTE in females 9 to 26 years of age. Vaccine Jan 2016

During discussion Dr. Villarreal asked if CDC had seen any adverse events from either HPV4 or HPV9 in a subpopulation of Native Americans. A parent in her clinic had indicated reports that sudden death syndrome had occurred after HPV vaccinations. Dr. McNeil responded that the Vaccine Safety Datalink (VSD) which follows more than 9 million people, should have good information of that kind of adverse events, and there is no association of that adverse event with childhood and adolescent vaccines. However, the Native American populations may not be well represented in the VSD.

Dr. Feemster asked about coverage of meningococcal B vaccine. Dr. Houston responded that meningococcal vaccines, as a group, are covered by the program, so the meningococcal B vaccine would be covered.

Update on the National Institute of Allergy and Infectious Diseases (NIAID), NIH Vaccine Activities, Dr. Barbara Mulach

Dr. Mulach reported progress on the development of a vaccine for respiratory syncytial virus (RSV), which is the leading cause of lower respiratory tract infections in infants and young children. A candidate vaccine developed by NIAID, Johns Hopkins Bloomberg School of Health and Medimmune has proven safe in an early Phase I clinical trial. When compared with results from the previous leading live-attenuated RSV vaccine candidate, the experimental vaccine appears to elicit a stronger protective immune response.

NIH-supported researchers conducted a chickenpox vaccine dosing study of 432 HIV-infected children and 221 HIV-exposed but uninfected children. The study showed that children who received two doses versus one dose had a stronger antibody response that lasted a longer period of time. The study also showed that there was greater effect if the first dose was given at least three months after initiating anti-HIV treatment.

Dr. Mulach noted that several candidate Ebola vaccines were being tested. One promising candidate combines the Ad26.ZEBOV vector (based on the AdVac platform

developed by Crucell Holland B.V., one of the Janssen Pharmaceutical Companies of Johnson & Johnson) with a modified vaccinia virus Ankara (MVA)-vectored vaccine (MVA-BN Filo) developed by Bavarian Nordic. There were Phase I trials in the UK,US and Africa. In July 2015, a Phase II trial was initiated in the United Kingdom and France. In October 2015, a safety and immunogenicity study of the vaccine regimen commenced in Sierra Leone, the first study of this regimen in an endemic country.

NIAID is involved in malaria vaccine research. Forty percent of the world's population lives in areas where exposure to malaria infection is a significant risk. Thus far the most advanced malaria vaccine in terms of research is RTS,S vaccine, which has shown a 30%-50% efficacy in protecting children for about a year. One research question now is why it is only partially protective. Relying on genomic sequencing technology, it was discovered that there is variability in the surface protein that the vaccine targets, which may drive the efficacy of the vaccine. In another study, changes in the shape of this protein provided a basis for further research into how to make a more effective malaria vaccine.

The Commission may recall a briefing on a Phase I trial of a chikungunya vaccine. That trial of 25 subjects saw a robust immunity that encouraged development of a Phase II trial. That trial is underway in the Caribbean and is designed to enroll 400 subjects at six sites. In 2015, more than 600,000 cases of Chikungunya were reported in the Americas.

Finally, Dr. Mulach discussed the Precision Medicine Initiative, which will involve a research cohort of over a million subjects. There is more information on the web at www.nih.gov/precision medicine.

During discussion, Ms. Toomey, speaking from St. John in the Virgin Islands, commented that chikungunya is a serious problem there. An early response was to attempt mosquito control by spraying with methyl bromide. The chemical has a serious toxic effect in humans, which has affected all of the members of one family, who suffered severe neurological damage because of the pesticide.

Update on the Center for Biologics, Evaluation and Research (CBER), FDA Vaccine Activities, LCDR Valerie Marshall

LCDR Marshall reported that on November 24, 2015, the FDA approved Fluad, the first seasonal influenza vaccine containing an adjuvant. The vaccine is approved for the prevention of seasonal influenza in persons 65 years of age and older.

LCDR Marshall commented that in November 2015, a supplement to the biologics license application for Anthrax Vaccine Adsorbed (Biothrax) was approved to include post-exposure prophylaxis (PEP) of disease resulting from suspected or confirmed *Bacillus anthracis* exposure when combined with the recommended course of antimicrobial therapy in individuals 18 through 65 years of age.

In September 2015, FDA approved a supplement to the biologics license application for the hepatitis B vaccine (Energix-B) to include safety and immunogenicity data for adults with

type 2 diabetes mellitus in the Energix-B package insert prescribing information. The ACIP recommended vaccinating all adults with diabetes against hepatitis B. However, the efficacy of the vaccine had not been well defined, so the manufacturer initiated a study to assess the immunogenicity and safety of the vaccine in adults with or without type 2 diabetes. Protection rates were similar in both groups.

In November 2015, the Vaccine and Related Biological Products Advisory Committee (VRBPAC) met to discuss considerations for evaluation of the safety and effectiveness of vaccines administered to pregnant women to protect the infant.

LCDR Marshall gave an update on recent FDA publications related to vaccines.

Researchers within the FDA's Office of Vaccines Research and Review developed a baboon model of pertussis. They used the baboon model to compare immunity from whole-cell vaccines from three different manufacturers that are approved outside the United States. Investigators found that compared to clearance rates with no vaccine and with an acellular pertussis vaccine, immunization with any of the three whole-cell vaccines significantly accelerated the clearance of B. pertussis following challenge.

PsA-TT (MenAfriVac) is a conjugated polysaccharide vaccine developed to eliminate group A meningococcal disease in Africa. Vaccination of African study participants with 1 dose of PsA-TT led to the production of anti-A polysaccharide antibodies and increased serum bactericidal activity measured using rabbit complement (rSBA).

Update from the NVPO Vaccine Activities, Dr. Karin Bok

Dr. Bok reported that NVPO is conducting a mid-course review of the 2010 National Vaccine Plan following five years of implementation. NVPO sent a survey to non-federal stakeholders between October 9 and November 9 and received 38 responses from a broad range of stakeholders including consumers. NVPO will continue to engage both federal and nonfederal stakeholders in the analysis process. NVPO is currently drafting the NVPO Vaccine Confidence Strategy document and a cooperative agreement to support the project. NVPO expects that the request will be published at the beginning of 2016. The early data from an NVPO-funded study of first-time mothers was published in November in the American Journal of Preventive Medicine. This study looked at vaccination-related intentions, knowledge, and confidence among 200 expectant mothers during their second trimester of pregnancy.

Finally, the National Adult Immunization Plan (similar to the National Vaccine Plan but focused on adults) is expected to launch in January 2016. The plan has four goals; strengthen the adult immunization infrastructure; improve access to adult vaccines; increase community demand for adult immunizations; and to foster innovation in adult vaccine development and vaccination-related technologies.

In response to the earlier question about whether there was a commission dedicated to adult vaccines, Dr. Bok stated that there is an Adult Immunization Task Force. NVAC will also issue adult immunization standards. Asked about whether there could be an ACCV-type

commission for adults within the adult immunization plan, Dr. Bok stated that the ACIP and NVAC serve that function. The plan does not propose a new commission. Dr. Feemster suggested it would be helpful for the ACCV to work with those entities.

Dr. Feemster expressed appreciation for the presentations.

Public Comment

Comments by Janet Cakir, parent of a child alleged to have been injured by a vaccine.

Janet Cakir commented that the ACCV sent recommendations to the Secretary of HHS in December 2013 concerning extending the statute of limitations. Secretary Sebelius confirmed receipt of the recommendations, but subsequently resigned before taking action. Secretary Burwell succeeded her in the position, but there has likewise been no action since she took office. The Senate committee responsible for health matters is also unaware of the recommendations and stated that there have been no communications with DHHS about the recommendation. Secretary Burwell's staff is unaware of the recommendations. An official in DHHS (Andrew Morris, policy analyst) confirmed that there is no intention to act on the recommendation. He said he was unaware of the recommendations. He added that it was not his responsibility to sponsor legislation. Ms. Cakir stated that the recommendation to extend the statute of limitations should be resubmitted to the Secretary, who can send a letter to the appropriate committees in the House and Senate articulating actions needed for DHHS programs.

Ms. Cakir explained that developmental milestones that would suggest a vaccine-related injury may take years to appear. Often vaccine injury is the last consideration, placing parents in a timeline well past the statute of limitations. She stated the opinion that parents will accept vaccination if there is a reasonable safety net to cover possible vaccine injury. She added that a reiteration of the original recommendation should be sent to the Secretary and it should include the fact that the appearance of injury in the very young can take a longer time than presently considered.

Ms. Cakir stated that the ACCV is the only advocate for American children and the recommendation to the Secretary should be to open the legislation to revision. To avoid the obstacle of legislative revision, HHS could add inflammation to the Vaccine Injury Table. She requested a discussion of the presentation before terminating her time on the agenda.

Dr. Feemster thanked Ms. Cakir for her comments and assured her that the points she made would be discussed as new business.

Comments by Theresa Wrangham, Executive Director of the National Vaccine Information Center (NVIC)

Ms. Wrangham commented that the materials posted on the web do not fully reflect the presentations, and there are instances when the presentation made at the meeting have been revised and do not reflect the content of the revised remarks in the presentation. Referring to an example presented of a petitioner who appealed the judgment award, NVIC points to the 2009

Altarum Report that surveyed VICP satisfaction. It emphasized inadequacy of settlement as a significant issue. Ms. Wrangham posed several questions: Why is there not an ongoing VICP survey process? Are settlements adequate to meet the need of those injured? Is there consistency in the award amounts? What progress has been made since the Altarum, Banyan and GAO reports to assess satisfaction with VICP?

Ms. Wrangham stated the opinion that the VICP process has become more adversarial for petitioners over the years. It is well known that there are risks associated with vaccines, and vaccines should not be exempt from informed consent. Non-medical vaccine exemptions are under attack. NVIC requests that actual presentations made at ACCV meeting, annotating what materials was actually presented, be published online. Conduct a review of the findings of the 2009 Altarum Report, 2010 Banyan Report and 2014 GAO report of the VICP, and issue a report including an analysis of what is needed to improve satisfaction and awareness of the VICP, including an analysis of the impact to the VICP of vaccine safety deficits reported by the IOM, and how closing research gaps would improve the process.

A process should be created to inform the public when a scientific presentation is made by the government related to a public request for additions to the Vaccine Injury Table, and an equal opportunity for the public entity making the request to present information to the Commission.

The ACCV should affirm the fact that vaccines carries the risk for injury and death, and because of that the ACCV supports the right of every parent to make decisions about vaccination without prejudice.

Future Agenda Items

Dr. Feemster invited discussion of future agenda items and new business. Since there was a public comment about the recommendations to the Secretary, she asked for comment about whether the recommendation should be re-submitted. Mr. Kraus commented that the Commission should ascertain where the recommendations already made stand. He suggested adding an agenda item for the next meeting to clarify the status of the statute of limitations recommendation.

Dr. Feemster suggested that the Commission revisit the issue of increasing resources for handling the increased caseload. Mr. Kraus agreed that an agenda item should be included in the next meeting to consider a recommendation to increase the budget for that purpose. Dr. Houston interjected that such action is a congressional prerogative and such a recommendation must be submitted to the Secretary.

Dr. Feemster recalled an issue that related to the addition of food allergy to the Vaccine Injury Table, and Mr. Kraus commented that if commissioners were interested it could be added as a discussion item. Dr. Feemster concluded that there was no interest in adding the food allergy issue to the agenda of the next meeting.

Mr. Kraus suggested that the Commission consider the importance of complying with the provision of information to the public, posted on the web by the time of the meeting. Ms. Herzog assured the Commission that every effort is made to provide all relevant information by the time the meeting begins.

Finally, there was a request that additional information be provided concerning the details of SIRVA claims (e.g., where the injections take place, the training of the vaccine administrators) and Dr. McNeil stated that he would pass that request on to Dr. Shimabukuro.

Adjournment

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