Advisory Commission on Childhood Vaccines

June 5, 2014
92nd Meeting

Members Present

David King, Chair ('14)
Charlene Douglas, Ph.D. ('14)
Kirsten Feemster ('14)
Edward Kraus, J.D. ('15)
Ann Linguiti Pron, DNP, CRNP, RN ('14)
Luisita dela Rosa, Ph.D. ('15)
Jason Smith, J.D. ('14)
Sylvia Fernandez Villareal, M.D. ('15)
Michelle Williams, J.D. ('14)

Division of Vaccine Injury Compensation (DVIC)

A. Melissa Houston, MD., Acting Director, DVIC
Andrea Herzog, Staff Liaison

Welcome, Report of the Chair and Approval of Minutes
Mr. David King, ACCV Chair

Mr. King called the meeting to order and, after introductions, noted that Commission members Mr. Krause and Dr. dela Rosa, would join the meeting later in the morning. He stated that the meeting was again being held via teleconference and not in person, which is less desirable in terms of effective discussion than an in-person meeting would be. He reiterated his conviction that the Commission should approach the issues to be discussed with an understanding that the Commission represents those who are injured by vaccines and decisions and recommendations should be made such that the interests of those injured parties are best protected.

Public Comment on Agenda

Mr. King invited public comment specifically related to the agenda.

Theresa Wrangham, Executive Director of the National Vaccine Information Center, spoke to two agenda items – the discussion of the Vaccine Injury Table (Table) and the review of Vaccine Information Statements (VISs). With regard to the Table, injury claims based on underlying conditions and genetic predispositions and susceptibilities should not be barred because it is not in consonance with the Institute of Medicine's (IOM) study report's comments on epidemiological study limitations. In individuals who may have such predispositions, if a vaccine triggers an event that might have otherwise occurred because of the predispositions, that

individual should not be barred from the benefits of the Vaccine Injury Compensation Program (VICP). That would be in harmony with the chair's statement that decisions should be made to protect the injured persons.

Ms. Wrangham commented that the vaccine information statements to be considered, again referring to the IOM report, take into account the report's reference to the many unknowns that exist in the research and in the state of the science as it is now understood. She also referred to the vaccine product insert that is often referred to in the VIS that contains a significant amount of information, much of which the consumer may not be aware of. Pertinent information in the inserts should be included in the VIS.

Approval of March 2014 ACCV Meeting Minutes

Noting no further comment from the public, Mr. King invited approval of the minutes of the December 2013 meeting. On motion duly made and seconded, the minutes were unanimously approved.

Report from DVIC, Dr. A. Melissa Houston, Acting Director, DVIC

Dr. Houston briefly reviewed the day's agenda, noting that the Commission would consider changes to the Vaccine Injury Table (including a petition to add diabetes mellitus as an injury for MMR), hear presentations from the Department of Justice and the ACCV Process Workgroup, review certain Vaccine Information Statements, and hear the regular reports from the ex officio representatives of the Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH) and National Vaccine Program Office (NVPO).

With regard to program statistics through May 6, 2014, Dr. Houston reported that with seven months' data, there were 311 petitions filed, which would extrapolate to about 533 for the fiscal year, a slight increase over the past year, perhaps because of the dramatic increase in influenza immunizations in adults. There were 246 adjudications handled by the Department of Justice, which projects to about 421 for the fiscal year. Although that is a slight decrease from the previous year, that could be the result of adding four new special masters and the concomitant additional time required for them to get up to speed in handling claims.

At this point, 18 minutes into the meeting, Dr. dela Rosa joined the meeting.

Dr. Houston continued with a report on adjudications, noting the types of adjudications to date and the estimated total in each category for the year:

Compensable	148	Projected for the fiscal year	253
Concessions	19	Projected for the fiscal year	32
Court decisions	17	Projected for the fiscal year	29
Non-compensable	64	Projected for the fiscal year	109

Finally, Dr. Houston noted that there had been awards in the amount of $128 million to petitioners, and $12.8 million to attorneys, which extrapolates to $219 million and $21 million respectively for the fiscal year. As of March 2014, the Trust Fund stands at about $3.4 billion, with a net income of $125.5 million (24% of which was derived from interest come on the corpus of the trust).

Dr. Houston described recent activities, including the second and final public hearing for the NPRM to add intussusception to the Table as an injury related to rotavirus vaccination. There were no public comments provided during the second hearing and the draft Final Rule to add the injury should be completed shortly. A Federal Register Notice was published on November 12, 2013 to add seasonal influenza vaccines to the Table, which would permit petitioners to file for all such vaccines not already covered by the program.

Dr. Houston noted that a Government Accountability Office (GAO) study of the VICP was initiated at the request of the U.S. House of Representatives Committee on Oversight and Government Reform. The GAO will look at the timelines for processing claims; changes in the Table and criteria for such changes; expenditures of funds from the Trust Fund; experiences of petitioners who file VICP claims; and efforts to publicize the VICP. The study began in March and the GAO has met with HRSA and DOJ representatives, had conversations with selected ACCV members and representatives of the Court. The study should be completed by August.

Turning to proposed changes to the Table, Dr. Houston explained that the trivalent flu vaccines were covered by the program in July, 2005 and all other flu vaccines (mainly the quadrivalent vaccines) were added in November 2013. The Department of Health and Human Services (HHS) Secretary has proposed changing the description of the category of vaccines from trivalent to seasonal. The Commission was asked to consider this recommendation and decide either to modify the category as recommended by the Secretary, or to not modify the category as recommended by the Secretary. Dr. Houston added that a pandemic vaccine would not be covered by the VICP, but injury claims for pandemic vaccines can be filed with a separate program, the Countermeasures Injury Compensation Program.

During discussion, Dr. Houston clarified that the Secretary's recommendation in effect combines the coverage provided under two sections in the Table, Category XIV and Category XVII, simplifying the Table. Asked if there was any argument in favor of rejecting the Secretary's recommendation, Drs. Houston and Shimabukuro both concurred that the recommendation was positive and there was no downside to endorsing the Secretary's recommendation. Dr. Houston also clarified that there are no injuries related to the flu vaccines on the Table, but that a proposal to add certain injuries was in the rulemaking stage. She reviewed the fairly lengthy process to complete the rulemaking process. She also reviewed the process by which a claim maybe filed for a flu-related vaccine injury.

Mr. King proposed that, when a recommendation is made to add a vaccine injury to the Table, that the DHHS should relax the process by which a petition is considered; that is, that the existing litigated causation in fact process be waived to expedite the final ruling for the claim. There was a recommendation that the issue be discussed at the end of the meeting under agenda item Future Agenda Items/New Business.

Dr. Houston continued her presentation of proposed changes, noting that the Secretary has recommended modifying Category IX Haemophilus influenza type b (HIB) polysaccharide vaccines to be categorized as simply Haemophilus influenza type b, to conform to the language in the Internal Revenue Code that imposes excise taxes on certain vaccines. It is a technical change that applies only to the nomenclature. As before, the Commission must recommend or not recommend approval of the Secretary's proposal.

Mr. .Kraus announced his presence at the meeting, noting that he had only been available for the discussion of the HIB vaccine change.

Dr. Houston continued the discussion, referring to the proposed clarifying language that would be added to the Qualifications and Aids to Interpretation. With regard to encephalopathy, a list of conditions is now included in the Table as examples of conditions that would be disallowed as an underlying systemic disease. The new wording proposed would eliminate some of the conditions that were deemed to be disallowable: An encephalopathy shall not be considered to be a condition set forth in the Table if it is shown that the encephalopathy was caused by an underlying condition or systemic disease shown to be unrelated to the vaccine *(change is underlined).* A list of conditions was included as examples, some of which were eliminated by the meaning of the new wording, which in effect reduced the number of exclusions (conditions) listed in the original wording.

Dr. Houston reiterated that the proposed change is based on scientific findings and not on suppositions that a vaccine might or might not trigger the onset of a condition. In addition, she clarified that the changes being discussed are changes to a previous change that was submitted to the ACCV for review at an earlier meeting. All of the changes are intended to make the criteria for filing claims less restrictive. She added that even if an underlying condition is specified as an exclusion, an individual would still be able to file a claim under the causation in fact provision.

Although the Commissioners attempted to conduct a discussion of the issues, because of difficulties in distributing all of the germane documents needed for proper consideration, there was consensus to consider the issue as an agenda item at a later meeting. The Commission agreed to take action on the first two issues discussed and, on motion duly made and seconded, the Commission unanimously approved the modification of Table Category XIV from "trivalent influenza vaccines" to "seasonal influenza vaccines;" and the modification of Table Category IX from "haemophilus influenza type b polysaccharide conjugate vaccines" to "haemophilus influenza type b vaccines."

Further discussion was deferred. Dr. Houston expressed appreciation for the commissioners' participation and provided the DVIC contact information.

Report from the Department of Justice, Vince Matanoski, Deputy Director, Torts Branch

Mr. Matanoski referenced the Department of Justice PowerPoint materials (DOJ PP), dated June 5, 2014, as part of his presentation. He commented that DOJ has also seen an increase in the number of cases filed versus the historical average since 2009, an increase of about 25%. There were

122 cases filed in the three-month reporting period, including 40 minors and 82 adults (DOJ PP at 2), which projects out to about 530 cases for the fiscal year. He advised that the increase in petitions filed should not be correlated to the number of vaccine injuries that may have occurred. Analysis of the filings shows that flu-related Guillain-Barré Syndrome (GBS) and shoulder injury related to vaccine administration (SIRVA) injuries are the main drivers in the increase. It appears that the increase will be sustained in the near future. Additional resources to process the claims will be needed to meet the increased case filing.

Mr. Matanoski noted that there were 120 adjudications in the three-month reporting period (DOJ PP at 3), versus 122 new claims filed, which is a good balance with little net increase in the number of pending petitions, but he observed that the proposed Table changes for SIRVA and flu could affect that balance as case filings increase. Mr. Matanoski noted a wide variety of petitioner's law firms filing petitions. During a discussion about the Table recommendations, Mr. Matanoski reiterated that some of the proposed Table changes are based on policy reasons and cast a wider net in terms of potential concessions. Discussing how cases that fall into the new Table criteria are treated pending the implementation of the recommendations, Mr. Matanoski offered that, as a practical matter, those cases become candidates for settlement early on in the process. Citing flu vaccine and GBS cases, Mr. Matanoski explained that the Court is already taking the proposed Table recommendations into account when the case is filed, and considers the strength of a petitioner's claim in terms of proposed damages. Mr. Matanoski pointed out that, of the more than 60 adjudicated claims in the current reporting period, half were for flu vaccine and GBS-related injuries (DOJ PP at 11-17). Although scientific evidence is the most important determinant of the outcome of a claim, the fact that the condition is on track to be added to the Table facilitates the settlement process, including the determination of damages. In fact, as the administrative process to add to the Table occurs in parallel with the judicial process of arriving at settlements, there is often very little dramatic impact when the condition is officially added to the Table.

Turning to appellate proceedings, Mr. Matanoski briefly reviewed a few cases. *Tembenis v. Sebelius* is pending before the U.S. Supreme Court (DOJ PP at 5). This was discussed at the last meeting. Briefly, the U.S. Court of Appeals for the Federal Circuit (CAFC) reversed the lower court and special master to find that the estate of a child who suffered an alleged vaccine related injury and death is not entitled to future damages based on expected lifetime earnings. Petitioners filed a *writ of certiorari* asking the Court to hear the issue. HHS filed a brief in opposition on May 21, 2014. The CAFC resolved two claims during the reporting period. In *Price v. HHS*, the CAFC affirmed *per curiam*, denying the motion for review because it was filed after the deadline (DOJ PP at 6). In *LaLonde v. HHS*, the CAFC in a 2-1 decision affirmed the dismissal of petitioner's case where petitioner suffered an episode of anaphylactic shock, but did not suffer six months sequelae. Respondent appealed two cases, *Paluck v. HHS* and *Dobrydnev v. HHS* (argued on June 4, 2014). Both appeals involved a question of deference by the U.S. Court of Federal Claims (CFC) of the special master's decision.

Turning to the CFC, Mr. Matanoski discussed *Tompkins v. HHS* (DJ PP at 8). The CFC affirmed the Special Master's dismissal of a petition alleging that the flu vaccine caused GBS based on evidence that there was a pre-existing respiratory infection shown to be the cause of petitioner's GBS. Mr. Matanoski mentioned this case because it was related to the earlier discussion about adding GBS to the Table where the case would be likely be defended even though GBS would be listed as a Table injury, if there was evidence that petitioner's GBS was due to a factor unrelated to the vaccine.

Responding to questions posed to Dr. Houston about how cases are being processed pending Table recommendations, Mr. Matanoski reiterated that the Court, petitioner's bar, and DOJ are sensitive to Table recommendations that are "in the works." Responding to Mr. King's question about whether or not science is being pushed too hard, Mr. Matanoski reiterated that claims are processed with the recognition that the Table may be more generous in terms of proving entitlement because the Table construct is based on policy considerations, as opposed to a petitioner having to prove cause-in-fact, which is based on science.

Petition to add diabetes mellitus as an injury for measles, mumps and rubella vaccine to the Vaccine Injury Table, Dr. Mary Rubin, Medical Officer, DVIC

Dr. Rubin stated that this petition was coming before the Commission because it was initiated by a public citizen and, by law, the Secretary must conduct a rulemaking proceeding on the terms of the petition or publish in the Federal Register an explanation for why such a proceeding was not conducted.

Dr. Rubin explained that diabetes mellitus is a common disease, often afflicting children. There are two forms. Type 1, an autoimmune disease, is most common in children and expresses itself by an insulin deficiency. Type 2 exhibits insulin resistance, an impairment in insulin secretion, is typically associated with hyperglycemia, and frequently affects obese individuals. The petition does not distinguish between the two types.

In the current scientific literature, which includes a 2012 Institute of Medicine study, there appears to be no causal relationship between measles-mumps-rubella (MMR) vaccine and Type 1 diabetes. There is also no apparent mechanistic evidence of any such relationship. Also in 2012, the Cochrane Collaboration assessed the administration of MMR vaccine in children to age 15 and found no likely association with Type 1 diabetes mellitus onset. Finally, also in 2012, Duderstadt et al., reviewed a cohort of military personnel in a retrospective study looking for initial diagnosis of Type 1 diabetes in the years 2002 through 2008 versus various vaccine exposures. The study found no increased risk in any vaccines studied, including MMR vaccine. Dr. Rubin noted that there were no studies of Type 2 diabetes. Dr. Rubin noted that she had provided a number of published studies to the Commission staff prior to the meeting, mainly related to diabetes in children.

Dr. Rubin invited discussion of the petition to add MMR-diabetes mellitus to the Table. Asked whether an individual with mumps may be more likely to become Type 1 diabetic, Dr. Rubin commented that there is no evidence that the live vaccine for mumps causes diabetes mellitus.

Mr. King confirmed that the individual who proposed the addition of diabetes mellitus to the Table was from the general public. Dr. Villareal observed that the Merck package insert includes a description of adverse events. Dr. Feemster added that the adverse events were listed in no rank order and included all adverse events that occurred during the drug trials. Mr. Kraus observed that there did not appear to be a rationale for adding the condition to the Table, and that there did not appear to be any basis for creating a presumption of causation of diabetes following MMR vaccination.

There was a motion, duly seconded, to recommend not adding diabetes mellitus to the Table. The motion was unanimously approved by the Commission.

Report from the Process Work Group, Dr. Luisita dela Rosa, ACCV Member

Dr. dela Rosa reported that the work group met by telephone on March 8 and focused discussion on two issues: consideration of the statistical table proposed by member of the public, Theresa Wrangham, on cases filed and adjudications; and a process by which the Commission could encourage action on recommendations submitted to the Secretary of HHS.

On the first topic, the work group looked at the differences in the table provided by Ms. Wrangham and the information published on the HRSA DVIC web site, which is updated monthly. The work group came to the following conclusions:

- Ms. Wrangham should be invited to a future Process Work Group meeting to discuss her proposal and related issues.
- In Ms. Wrangham's proposal, construction of the table requires detailed analysis of individual claims filed to determine facts related to the category "Not Compensable."
- All claim decisions are published on the CFC web site, including damages (but not attorney's fees), and various Internet search engines also provide access to case records. Cases decided by proffer or settlement are not usually described in detail.
- It appears that when a claimant attempts to engage an attorney to file a claim for which the statute of limitations has passed, the attorney is often reluctant to pursue the matter.

On the second topic, the work group agreed that the Secretary should respond to each recommendation submitted by the Commission, beyond the simple recognition that the recommendation was received. The work group recommends that the Commission discuss how to encourage action by the Secretary in at least making the recommendations public, especially those that would require legislative action for implementation.

The work group focused on extending the statute of limitations, a recommendation recently submitted to the Secretary. There was agreement that there are several circumstances that hinder timely submission of claims:

- There is an apparent lack of awareness of the program in spite of its being mentioned in the VISs.
- Health care providers often advise patients that a vaccine could not be a causative factor in an injury after vaccination.
- Attorneys may discourage claims by stating that a case has "no merit."
- Parents of vaccine-injured children may be so distracted by dealing with the injury that they become unaware of the passage of time.

Mr. King stated that the Commission had agreed to address the issue of the statute of limitations at the face-to-face meeting scheduled for September. At that time individuals from different interest groups will be invited to testify. He suggested that the work group consider that agenda item at their July work group meeting. Dr. dela Rosa agreed, but noted that it had been difficult to arrange meetings because of work group member scheduling conflicts. There was a suggestion that one individual on the work group, or a subgroup made up of the attorneys on the Commission, could act as coordinator of suggestions from the Commission members, which could be submitted by e-mail. Ms. Williams, Mr. Kraus and Mr. Smith agreed to be on the subgroup. Finally, Mr. King suggested that Ms. Herzog coordinate a July meeting of the work group, to which Ms. Wrangham could be invited.

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

Ms. Mulach reported on three NIAID activities, including a small study looking at immune response to tetanus-diphtheria-acellular pertussis (Tdap) vaccination in pregnant women, which showed safety and a positive immune response effect in women and newborns. A second intramural effort was undertaken to model human immune response to flu vaccine, and to predict the level of flu-specific antibodies after vaccination. The study might develop a potential framework for predicting an individual's responsiveness to vaccination.

The third activity, the Centers of Excellence for Influenza Research and Surveillance (CEIR) was begun about ten years ago. In addition to global surveillance in South America, Europe, Africa and the Far East, the program has a goal of developing a universal flu vaccine.

Finally, Ms. Mulach mentioned two planned meetings in June, one co-sponsored by NIAID and FDA on Common Barriers in Vaccine Research and Development; and a second under the NIAID Meeting Report umbrella looking at dengue fever and Staphylococcus aureus.

Review of Vaccine Information Statements, Mr. Skip Wolfe, CDC

The Commission first considered the VIS for Gardasil human papillomavirus vaccine (HPV). In the first section -- "Why get vaccinated?"—there was agreement that the vaccine should be described as preventing "many" types of cancer, which is more accurate than the phrase "Gardasil prevents cancer caused by HPV." There was also agreement to put the prevention of genital warts in both sexes under its own bullet. There was an observation that to emphasize that the infection comes from sexual contact, even though a correct statement, is often unsettling to parents of children of the age recommended for the vaccination – 11-12 years old. The final paragraph in Section 1 should begin, "Most people will become infected at some point in their life," and then mention the primary cause (sexual contact) later in the paragraph. Some parents may feel that their abstinent children would not need the vaccine.

Mr. Wolfe explained that Section 2 had been simplified by omitting the scheduling of HPV vaccinations and simply advising individuals that HPV vaccine is usually initially given at about age 11 or 12 and may be given up to age 26. There was a recommendation to add that the HPV series usually involves three doses, since without that information patients may not be aware of the number or finish the course.

Mr. Wolfe moved to Section 3, noting that, since individuals may not know they are allergic to yeast, that allergy was specifically mentioned in this VIS. He added that the word "severe" and "life threatening" may be redundant, and there was an observation that the parentheses could be removed. There was a brief discussion on the sentence "tell your doctor…" Should this read tell your doctor or health care provider? CDC is continuing to work on this language. Finally, although there was a comment that the last sentence about whether or not to accept vaccination if one has a mild or moderately severe illness is vague, there was agreement to leave it unchanged since the physician would be in the best position to advise the patient.

Under Section 4, Risks of a vaccine reaction, there was a comment about the missing warning about the most serious side effects, such as death, and Mr. Wolfe stated that the wording of that warning was under review, including legal counsel review, but that it would eventually be added.

Dr. Shimabukuro noted that the three statements in the section about serious side effects may be contradictory (serious side effects are very rare, serious problems have been associated with HPV, severe allergic reactions from a vaccine are very rare). He explained that if the statement was worded to indicate that no serious adverse reactions were causally associated with HPV vaccine, then the statement would be more accurate. However, adding a reference to Vaccine Adverse Event Reporting System (VAERS) might be inappropriate since any reaction can be reported to VAERS without any substantiation regarding causation.

Ultimately the Commission agreed that the following sentence should be removed from the VIS: No serious problems have been associated with HPV vaccine.

Mr. Wolfe noted that there had been no changes in Sections 5, 6 and 7, although in Section 6 wording about the statute of limitation will be added once that wording is finalized. Dr. Houston noted that there was a general statement in the VIS being reviewed that a time limit exists, and Mr. King suggested that the actual time limits of the statute should be included in the VIS. Mr. Wolfe commented that there is a line between providing enough information and too much information, such that individuals reading the VIS may be overwhelmed by the volume of information. Mr. King also suggested that the order of the VIS might be reversed, beginning with risks. After discussion, there was agreement that putting risks, including risk of death, at the beginning might first, unnecessarily intimidate patients, and second, might suggest that the risks are the most important consideration, rather than the benefits. There was also agreement that the natural chronology of the experience would be most appropriate – the reasons for the vaccine, contraindications, adverse reactions and responses to adverse reactions, and the final administrative information about the VICP and sources of information.

Mr. Wolfe turned to the VIS for Cervarix. With a few exceptions the text is the same for both Gardasil and Cervarix. A difference is that Cervarix is recommended only for women and the predominant risk is for cervical cancer. There is also no yeast in the Cervarix formulation so there is no mention of yeast effects in the VIS. Mr. Wolfe confirmed that the changes agreed on for Gardasil would also be made in the Cervarix VIS.

Finally, Mr. Wolfe described the VIS that covers multiple newborn vaccines. The structure of the VIS is similar to the individual VISs in that information about each of the six vaccines is covered in condensed form under the same major headings: (1) Why get vaccinated; (2) Some children should not get certain vaccines; (3) Risks of vaccine reactions; (4) Problems that could happen after any vaccination; (5) What if there is a serious reaction; (6) The VICP; and (7) Sources of additional information.

Asked why the consolidated VIS was developed, Dr. Wolfe explained that the single VIS replaces multiple forms that repeat most of the information, thereby reducing the time it takes for a parent to read and understand the content. The response from providers has been positive. There have been requests for a similar VIS for adolescents.

Mr. King noted that 15,000 individuals died before the universal vaccination program in the US and there was a brief discussion about the importance of the herd effect, which effectively eliminated fatalities. However, it was noted that publicizing herd immunity might cause people to bypass vaccination and lead to deterioration in herd immunity. There was agreement that the wording in the second paragraph following the description of rotavirus should not include the reference to "generations of parents who made sure their children were vaccinated," since it could be interpreted an indictment of parents who do not allow their children to be vaccinated, some or many of whom could have legitimate reasons.

Referring to the table of information describing the vaccines that are intended for newborns, doses in the series, ages and comments, Mr. Wolfe asked for consensus that the table was appropriate to the VIS. The Commission agreed that the information in the table would be helpful. Mr. Wolfe stated that the explanatory sentence following the table would serve to allow the provider to limit the vaccines to the six described.

There was a brief discussion about including some reference to the parents' role in deciding whether or not a child receives a vaccination, and the importance of the health care provider's recommendations. Under Section 2, *Some children should not get certain vaccines*, Mr. Wolfe agreed to review the list of specific conditions described under *"Talk to your doctor,"* to make sure that each is a true contraindication that would indicate that the child should not receive a vaccine.

Mr. Wolfe stated that the statute of limitation language would be added to this VIS, and Dr. Shimabukuro commented that the wording on the rare risk of death was being worked on and would be submitted for review when available. There was an observation that the incidence of death related to a vaccination is so rare that it would be impractical, if not impossible, to provide any statistical risk information. Mr. King suggested putting the reference to death risk in the VICP section, adding the simple statement that the reports are extremely rare without getting

involved with the statistics and causation. Dr. Shimabukuro suggested: In these rare instances the contribution of the vaccine to the condition can be difficult to determine. Mr. King commented that the wording was an improvement and should be considered for the VIS.

Update on the vaccine activities of the of the Center for Biologics, Evaluation and Research (CBER), FDA, LCDR Valerie Marshall, CBER, FDA

LCDR Marshall reported that in January 2014, the FDA approved three supplements to the biologics application for pneumococcal 13-valent conjugate vaccine, Prevnar13®, to include text in the US Prescribing Information (USPI) for the use of Prevnar 13® in HIV-infected adults 50 years of age and older, preterm infants less than 37 weeks of gestational age, and children and adolescents age 6 to less than 18 years of age with sickle cell disease.

In March 2014, the FDA approved a supplement to lower the age indication for Adacel (tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed) from 11 to 10 years of age.

In March and April 2014, the FDA granted breakthrough therapy designation, which is an expedited review program, respectively, to Pfizer's candidate type B meningococcal vaccine, and to Novartis' type B meningococcal vaccine.

In May 2014 the FDA approved a supplement to the Biologics License Application (BLA) for the rotavirus vaccine, live, oral, trade name Rotarix, to include a summary of post-marketing surveillance data suggestive of an increased risk of intussusception in the seven days following the administration of the second dose.

In May 2014, the FDA published an update to earlier FDA/CDC communications, which described increased VAERS reports of febrile seizures following vaccination with Fluzone during the 2010-2011 flu season. Results from an FDA Post-Licensure Rapid Immunization Safety Monitoring (PRISM) study demonstrated no statistically significant association between trivalent influenza vaccine (TIV) and febrile seizures in children during the 2010-2011 influenza season.

On June 4, 2014, the Science Board of the FDA discussed and made recommendations on the draft final report from CBER's Post-Marketing Safety Review Subcommittee.

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

Dr. Bok, a vaccine safety specialist at NVPO, reported that NVAC would meet in the week following the ACCV meeting, and would review and possibly approve recommendations to reduce patient and provider barriers to maternal vaccine administration. A number of public comments were received. A group B strep support group expressed concern that litigation in matters involving adverse vaccine outcomes might become barriers to health professionals in promoting maternal vaccine administration.

The American Academy of Pediatrics supported broadening the eligibility of the VICP to include infants injured in utero. It is important for VICP to define which fetal outcomes are related to vaccines. The Academy supported the NVAC report recommendation 5.

The National Vaccine Information Center expressed concern for the lack of credible research on vaccines for pregnant women. The NVIC is not in favor to providing legal protection under the VICP to vaccine manufacturers for liability for vaccine-related injury.

The final report from NVAC should be available after the meeting.

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

Dr. Shimabukuro previewed his presentation in which he would recap the February 2014 Advisory Committee on Immunization Practices (ACIP), and preview the upcoming June 2014 ACIP meeting, and look at several recent publications.

The Committee voted to accept the recommendations for the influenza vaccine formulation for the 2014-2015 flu season based on the same recommendations made for 2013-2014. The Committee also approved the updates for HPV – to consolidate recommendations for males and females; to consolidate bivalent and quadrivalent vaccine recommendations; to harmonize wording; and to add a section on history of sexual abuse or assault.

There was an interim vaccine safety update for live attenuated (LAIV) and inactivated (IIV) influenza vaccines (quadrivalent and trivalent), based on VAERS and Vaccine Safety Datalink (VSD) data through the end of last year in persons 18 years of age and younger, which revealed no safety concerns. Dr. Shimabukuro noted that the trivalent live attenuated vaccine had been replaced by quadrivalent vaccine for the 2013-2014 flu season. There was also a comparison analysis for LAIV and IIV in children aged two to eight which suggested a slightly higher efficacy for LAIV over IIV, but no significant differences in hospitalizations, flu-like illness or acute respiratory illness requiring medical attention. There was a slightly increased transient fever after LAIV versus IIV.

Dr. Shimabukuro reported on a presentation on Tdap in pregnancy based on VAERS that showed no new safety concerns for women who received Tdap (or their infants), but there were few reports on women who received repeated doses (CDC will continue to monitor reports with special focus on repeated vaccinations). There was also a presentation of VSD data that showed no increase in risk after Tdap vaccination of pregnant women for adverse birth outcomes, although there was a very slight increased risk of chorioamnionitis, a factor in increased risk of preterm birth that merits further study. However, there was no actual increased risk of preterm birth in the VSD data.

In the HPV session, epidemiologic data was discussed. With regard to cervical intraepithelial neoplasia grade 2 and 3 lesions: 50% were attributable to HPV 16/18 (which is in the HPV vaccine) and 25% were attributable to 5 additional types in investigational 9-valent vaccine. For cancers associated with HPV, about 62% were attributable to HPV 16/18 and about

11% were attributable to 5 additional types in 9-valent vaccine. Merck, manufacturer of the 9-valent version, made the presentation for that vaccine, which is under FDA review with licensure anticipated in 2015.

Dr. Shimabukuro previewed the agenda for the June 25-26, 2014 ACIP meeting. There will be two sessions, one an update on the 2013-2014 influenza season, and the other a vaccine safety session that will include reports on the PRISM system that evaluated the discovery of febrile seizures related to the 2010-2011 influenza season; and a VSD study of safety issues related to administration of multiple vaccines, also related to the 2010-2011 signal for febrile seizures.

Turning to publications, Dr. Shimabukuro mentioned the following:

- Hambidge et al, on timely versus delayed early childhood vaccinations ad seizures, showed that delaying MMR vaccine until the second year of life does increase the risk of febrile seizures, but Dr. Shimabukuro noted that the risk of febrile seizures in the first year of life it typically low, increasing in the second year.
- Haber et al, analysis of a post-licensure VAERS surveillance of trivalent live attenuated influenza vaccine in children 2-18, showed no new or unexpected adverse event patterns.
- Naleway et al, looking in two studies at the safety of influenza vaccine given during pregnancy showed no association between inactivated influenza vaccination and gestational diabetes, gestational hypertension, preeclampsia/eclampsia, or chorioamnionitis. The analysis should reassure women with regard to vaccination for influenza during pregnancy.
- Nordin et al, looked at maternal influenza vaccine and risks for preterm or small for gestational age birth. Receipt of trivalent inactivated influenza vaccine during pregnancy was not associated with increased or decreased risk of preterm or small for gestational age birth.

Public Comment

Ms. Wrangham expressed appreciation for the Commission's work on recommendations concerning the Table, noting however that the documents distributed at the meeting to Commission members were not available on the VICP web site. She requested that the Commission staff provide copies of those documents if possible.

Ms. Wrangham reiterated her remarks made at the outset of the meeting, that an individual who may have genetic predisposition or susceptibilities to a condition may not see the manifestation of those conditions unless triggered by an outside circumstance. A vaccine could be the trigger, and if that is demonstrated, that individual should be eligible for the protections of the VICP.

Ms. Wrangham commented that the statements made with regard to herd immunity were not completely accurate, and that the VISs must include a description of the three risks related to

vaccines – that the vaccines may fail to protect, that the vaccines may cause injury, that the vaccines may result in death. The VIS is less detailed than in the past and does not now fully explain these risks. Nor does the law require that parents read the VIS or that health care providers explain the contents of a VIS before administering a vaccine.

Ms. Wrangham stated that the first section of the VIS, "*Why get vaccinated*," is inappropriate. Since the VIS is an informational document, the data should be factual and not designed to encourage an individual to be vaccinated. The VIS should be more effective in explaining the importance of the time limits related to filing an injury claim. The gaps in research are not well understood by the general public, and explaining the known and unknown risks of a vaccine should be included in the VIS. A list of vaccine ingredients should be included to allow consumers to identify possible allergic components in a vaccine.

Ms. Wrangham stated that the ACCV should meet in person, as do the other important vaccine advisory committees.

Future Agenda Items/New Business

Mr. King recalled that recommendations to the Secretary should be supported by the other interested agencies. If the ACCV makes a recommendation about an issue that involves federal enforcement, that interested agencies should respond to the recommendation with a sense of cooperation – for example, if an ACCV recommendation is to add an injury to the Table, HHS and the Department of Justice should relax its position with regard to granting concessions for that injury and be more liberal in considering the petition. Dr. Villareal suggested that the Table be carefully reviewed at the September in-person meeting. Noting the problems encountered earlier in the meeting concerning the wording and formatting of the various versions of the Table language, Dr. Houston suggested that, before the next meeting, those issues should be fully reviewed and corrected so that the Commissioners will be dealing with the correct drafts.

Mr. King reiterated his concern that the new Commission members be added such that the entire Commission is not changed at a single time. It would adversely affect the continuity of the Commission's deliberations.

Adjournment

Mr. King called for a motion to adjourn. On motion duly made and seconded, the Commission approved adjournment.