Advisory Commission on Childhood Vaccines

September 5, 2013

88th Meeting

Teleconference Minutes

Members Present

David King, Chair
Charlene Douglas, Ph.D.
Kristen Feemster, M.D.
Edward Kraus, J.D.
Ann Linguiti Pron, MSN, CRNP, RN
Luisita dela Rosa
Jason Smith, J.D.
Michelle Williams, J.D.

Division of Vaccine Injury Compensation

Vito Caserta, MD., Acting Director, DVIC
Andrea Herzog, Staff Liaison
Amber Berrian, DVIC staff

Federal Government Representatives

Steve Bende, M.D., NVPO, DHHS
Valerie Marshall, Office of Vaccines, FDA
Vince Matanoksi, Office of the General Counsel, DOJ
Barbara Mulach, NIAID, NIH
Tom Shimabukuro, M.D., Immunization Safety Office, CDC

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

Noting a quorum present, Mr. King called the meeting to order and, after introductions, reminded the members of the charge to the Commission, to advise the Secretary of the Department of Health and Human Services (DHHS) particularly with regard to the Vaccine Compensation Act, which has the purpose of providing financial support for anyone injured by the vaccination process. He added that, at the end of the meeting when new business is discussed, one item will be how the Commission can be most effective in fulfilling its mission in the relatively new virtual meeting environment.

Public Comment on Agenda

Mr. King invited public comments regarding items on the day's agenda. James Lidier(?) commented that making the meeting materials available on the web site was helpful, particularly the ACCV work book, but requested that the materials be made available to the public at least the day before the meeting to allow time for review before the meeting begins. He added it would also be helpful to leave the materials on the web site after the meeting for future use.

Dawn Loughboro, parent of two vaccine-injured children, supported the addition of Guillain Barre syndrome (GBS) to the Vaccine Injury Table (table) (an agenda discussion scheduled for 11:20). She also stated the she would support the addition of Type 1 diabetes for Hib vaccine, regressive autism or thimerosol-related injury, both retroactive for 15 years; MMR encephalopathy leading to autism; and mitochondrial disorders to the table. Ms. Loughboro encouraged the conduct of a retrospective study of vaccinated versus unvaccinated children, innovation related to genetic and metabolic predictors prior to vaccination, and an active education program about VAERS, particularly for parents and pregnant women, and for pediatricians for whom there are few incentives to report adverse events to the VAERS. Finally, she encouraged holding "face-to-face" meetings.

Approval of June 2013 ACCV Meeting Minutes

There being no further requests to comment, Mr. King closed the public comment section of the agenda and invited approval of the June 2013 meeting minutes. Mr. King noted a discrepancy in wording on page 7 of the minutes, a reference to the Department of Justice being responsible for determining "legislative strategy." In fact, legislative strategy is determined by the Secretary of HHS. Mr. Matanoski, representing the Department of Justice, confirmed that the minutes should be corrected to read "litigative strategy."

There was a suggestion that the reference to "various data" in the Report of the Chair on page 1 was vague. After discussion there was agreement that the term referred to various types of information pertaining to specific cases and that the wording should be revised to read "various case data." Mr. King reiterated that, as was noted in the June minutes, no Commission member was willing to assume the responsibility of chairing the work group, making it impractical to consider the proposal further.

On motion duly made and seconded, the minutes were unanimously approved with the corrections discussed above.

Report from the Division of Vaccine Injury Compensation (DVIC), Dr. Vito Caserta, Acting Director, DVIC

Dr. Caserta briefly reviewed the day's agenda, noting that the Commission would consider the addition of GBS to the Vaccine Injury Table. Turning to the statistics since the last meeting, Dr. Caserta noted that 353 petitions had been filed to date, which indicates that the number of petitions filed this year will be similar to the number filed in the past several fiscal years (FY).

Compensable adjudications were 286, which is slightly higher than in the last two fiscal years. Continuing an upward trend, settlements represented 87% of adjudications (82% in fiscal year 2012 and 75% in fiscal year 2011). Finally, awards paid as of August 13 were $215 million and, with two pending awards of $48 million (which should be paid before the end of the fiscal year) and $40 million, the awards should hit an historic high.
Dr. Caserta announced that a new table had been added to the VICP web site, breaking out the adjudicated categories by vaccine for claims filed since calendar year 2006.

Dr. Caserta commented that the Trust Fund balance was $3.4 billion after net income in fiscal year 2013 through July 31 of about $161 million. Asked why OMB approval was required to meet the higher awards obligation, Dr. Caserta explained that, although there are more than sufficient funds in the Trust Fund, by regulation DVIC must request approval from the Secretary DHHS, who must request authorization from OMB to expend those funds. He added that rarely the level of funding may fall so low that there are very brief delays in issuing awards, usually only a few days. Although that actually occurred in the recent past because of the very high awards, petitioners are not affected since if payments must be delayed the delay is focused on attorney's fees. He reiterated that these issues are very short-lived, usually only a day or so.

In terms of significant activities, Dr. Caserta noted that the nomination deadline for new Commission members was extended 60 days because of a lack of qualified nominations in all of the categories required. He stated that the American Academy of Pediatrics had submitted a nomination for the provider category, but there were no others. Mr. King observed that the charter requires three attorneys on the Commission, one of whom must represent vaccine-injured individuals, one of whom must represent the vaccine manufacturers – but there is no specification of the third and no requirement for balance. He suggested that, as a matter of fairness and policy, the third attorney should represent vaccine-injured individuals. Ms. Williams expressed concern with that recommendation and suggested moving the discussion of the issue to the Process Work Group. Asked when the 60-day extension would end, Ms. Herzog explained that the clock would run from the day the announcement is published in the Federal Register, which should be within the next two weeks. The wording would be the same as the notice published on July 10, with a possible clarification of the term "qualified individual," a modification that would not affect any aspect of the announcement. Dr. Caserta added that, if the Commission is not able to fill slots being vacated by current Commission members, those members would be asked to extend their terms until a replacement could be confirmed. Ms. Pron requested that the Commission be informed when the announcement was published.

Asked to comment on increased efforts to recruit nominees, Amber Berrian explained that there would be an effort to publicize the requirement beyond the Federal Register by taking advantage of the HRSA web site and list serve.

Dr. Caserta announced that the rotavirus Notice of Proposed Rulemaking was published on July 24th, with public comments welcomed until January 21st, at which time there would be a public hearing on the matter. Under the heading Other Significant Activities, Kristen Feemster and Ann Jacobs made presentations at the June 11-12 National Vaccine Advisory Committee meeting, which were considered outstanding by the NVAC chair, and the Advisory Committee on Vaccine Practices met on June 19-20.

Finally, Dr. Caserta confirmed that Amber Berrian would be transitioning into the staff position that Annie Herzog had covered so capably. Annie would continue with DVIC in a supporting role until that transition was complete. He concluded his presentation with contact information.

During discussion, on a presumption that he would become the DVIC director, asked what he felt would be required to make the Commission most effective, Dr. Caserta suggested that he consider the question and formulate a complete response that he could present at the next Commission meeting.

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

Mr. Matanoski began his report with statistics, that 113 claims had been received between May 16 and August 15, all non-autism cases and mainly adults (86). The historical dip in filings in the summer months did not appear, which could portend a lightly higher rate of filings for the year than in the past. Adjudications of compensable cases were similar to past years – 9 conceded by DHHS through proffer; 79 not conceded, 77 of which were resolved through settlement. Because the Court had worked through most of the autism backlog, the number of non-compensated cases dropped dramatically, from 228 in the preceding reporting period to only 19 in the current reporting period.

Mr. Kraus commented that the distinction between autism and non-autism cases may no longer be applicable or appropriate as a descriptor since autism cases were so identified by being included in the Omnibus Autism Proceeding. Mr. Matanoski agreed, noting that the cases reported during this reporting period were not differentiated in that way. He also agreed that in the future the category of non-autism claims would not be germane and would not be included as such in the report to the Commission.

Ms. Pron commented on the low number of conceded cases, suggesting that the number might increase as the Injury Table is expanded. Mr. Matanoski agreed, pointing out that the number reported this time was nearly double the number reported at the last meeting, but still a very small number. He added that a significant number of claims filed do not allege a Table injury.

In the interest of time, Mr. Matanoski briefly referred to PowerPoints presented to the Commission at every meeting that included a glossary of terms and graphics that illustrated the flow of claims through the special master's process, and the appeals process. Commenting on specific cases, in Deribeaux v HHS, the medical issue involved a seizure that was apparently triggered by the vaccination. The seizure was actually a symptom of an underlying condition, Dravet's Syndrome that would not otherwise support a valid claim for vaccine injury since the syndrome was a pre-existing condition. The court has found in several previous cases that the vaccine may have triggered a symptom of Dravet's, but did not exacerbate the medical condition. On appeal to the Court of Federal Claims (CFC), the special master's decision was reversed, but the Court of Appeals in the Federal Circuit (CAFC) affirmed the original ruling disallowing the claim, affirming that the special master was in the best position to consider the evidence of the case.

In Paterek v. HHS, the CACF also ruled in favor of the special master, affirming that it was not appropriate for the appeals court judge to insert a finding of fact that overrode that of the special master, and that case was reversed and demanded to the CFC for reconsideration.

In a new appeal filed by the respondent, Dobrydnev v. HHS, the theme was similar – what level of deference should be accorded the fact finder, in this case the special master, who hears the direct testimony of the witnesses involved? That case should be heard within six months. There were five new claims filed by petitioners, and all regarding issues of fact, mainly questions about the determinations of the various special masters about medical issues concerning the injuries alleged.

Finally, Mr. Matanoski reviewed the profile of settlements since the last meeting update. There were 77 settlements in the three months, 60 for adult claims and 17 for children, about two-thirds of which were for flu injuries. During the last three months the percentage of settlements adjudicated within one, two and three years were similar to past reporting periods. Within one year 27% were settled, an additional 38% were settled before the end of the second year, and 18% settled in the third year, for a total of 80% in less than three years. In the most recent reporting period there was an interesting change – the number of cases was the same, 77, but 40% settled within the first year, 34% in the second year and 10% in the third year, for a total of 84% . Mr. Matanoski commented there one of the reasons might be that more cases are being filed with records attached at the time of filing or very shortly thereafter. Cases with records can usually be processed faster. Second, there is a Court initiative to fast track selected cases that appear to be good candidates for settlement. He added that the statistics would be followed closely to see if a trend might be developing.

During discussion, Mr. Kraus noted that about 28 cases involving alleged flu injuries listed Guillain Barre syndrome as the injury. Mr. Matanoski agreed, explaining that if Guillain Barre Syndrome is added to the Vaccine Injury Table it is probable that many of those claims would be conceded by HHS.

Mr. King reiterated his question to Dr. Caserta, inviting comment on how the Commission could be most effective in responding to its charge. Mr. Matanoski responded that becoming "most effective" might be unattainable, and that consideration to becoming "more effective" might be more feasible. He also expressed concern about providing advice to the Commission without significant contemplation. Dr. Caserta suggested that he and Mr. Matanoski confer and perhaps make a joint presentation. After a brief discussion of the alternatives, agreement was reached that the joint presentation would be appropriate, at least for the initial report. There was a suggestion that the Office of the Special Masters should participate in the process and Jocelyn McIntosh agreed to broach the subject with the Chief Special Master. Mr. Matanoski commented that any presentation by the Office of Special Masters would most appropriately be made separately from that of DVIC and the Department.

Adding GBS to the Vaccine Injury Table, Ahmed Calvo, M.D., Medical Officer, DVIC

Dr. Calvo stated that his purpose was to provide information about the proposed recommendation to add Guillain Barre Syndrome (GBS) to the Vaccine Injury Table, in anticipation of accepting advice from the Commission and obtaining Commission approval for the recommendation. He said that the changes proposed are based on established policy and that they apply specifically to GBS in relation to seasonal influenza vaccines

Describing GBS, Dr. Calvo said that GBS is a rare disorder caused by damage to the myelin sheath of the peripheral nervous system, which may result in paralysis, weakness and abnormal responses in the autonomic nervous system. People with GBS usually fully recover, although some may develop chronic symptoms that include respiratory distress caused by paralysis of parts of the breathing mechanism, and some of those may die of respiratory failure.

Dr. Calvo provided a physiologic explanation of the mechanism of action in GBS, explaining that the individual nerve cell develops a number of axons, which are protected by a myelin sheath, which is a multi-layer wrapping of Schwann cells. The wrappings are segmented by nodes at short intervals that provide a pathway for axon signals to move more rapidly from the nerve cell down the axon to the muscle the nerve controls. In effect the signal "skips" from node to node faster than would be the case if the signal had to traverse the entire length of each segment. If the myelin sheath is damaged, the signal to the muscle can be significantly slowed or even stopped. Although GBS is general seen as a single disorder, it is in fact several nerve-related disorders; hence the designation as a syndrome.

With regard to the vaccine involved, the H1N1 antigen has been included in each seasonal flu vaccine since 2010 and will be included in the formulation for the 2013-2014 flu season. In 2012 an Institute of Medicine report found that evidence in the scientific literature was insufficient to accept or reject a linkage between GBS and the vaccine, and the ACCV approved delay of consideration of a Table change until there was additional peer-reviewed evidence of the linkage. There were several studies thereafter, culminating in a meta-study published in March 2013 that showed a small increase in risk, an additional 1.6 cases per million vaccinations. The Agency for Healthcare Research and Quality (AHRQ) has a report (not yet published) that concludes that there is insufficient power in the studies to date to resolve the science issues related to risk of vaccine-related GBS. The report basically states that the strength of evidence that there is an increased risk is high, but post-licensure studies report mixed results with regard to the significance of that risk.

Although the scientific basis for adding GBS to the Vaccine Injury Table has not been resolved, the DVIC recommends the addition of GBS based on policy and the scientific data that has been published to date. The Table currently includes trivalent influenza vaccine and the recommendation would add seasonal influenza vaccine. Although not yet approved for inclusion in the Table, the following injuries have been approved by ACCV and are in the final Federal Register process of approval: anaphylaxis, shoulder injury related to vaccine administration (SIRVA) and vasovagal syncope. The recommendation would add Guillain-Barre syndrome with a symptoms time window of 3 to 42 days.

The National Childhood Vaccine Injury Act of 1986 authorizes the HHS Secretary to promulgate regulations that would result in a Table revision. Anyone may petition the Secretary to revise the

Table, and in all cases the ACCV must review the proposed revisions. The outcome of that review may be one of three determinations: ACCV concurs with the proposed revisions and recommends moving forward with or without comments; ACCV does not concur and recommends not moving forward; or ACCV recommends deferral of the recommendations pending further review at this or the next scheduled ACCV meeting.

In 2006, the ACCV developed "Guiding Principles" for recommending revisions to the Table: the recommendation should be scientifically and medically credible (there are criteria that define such credibility); and when such credibility is shown, either to recommend for or against a revision, the change should be made based on benefit to the petitioners. Dr. Calvo reminded the Commission that if there is conflict in judging credibility, ACCV members should lean towards adding or retaining the proposed injury.

Concluding his remarks, Dr. Calvo invited questions and/or discussion. Ms. Pron asked if there was precedent for a revision based solely on policy. Dr. Caserta affirmed that a finding in an early IOM report that there was evidence to support removing encephalopathy after DTP was not recommended by the ACCV based on policy. Later he noted that the Commission had approved the rotovirus vaccine as a policy action because, similar to this case, the hard epidemiologic evidence had not been developed (although it subsequently was published and supported the Commission's recommendation). Ms. Feemster asked if a briefing on the AHRQ report could be made to the ACCV and Dr. Caserta said he would look into the request. She also asked about the potential relationship of risk in the large monovalent studies and a similarity of risk in the seasonal vaccine. And Dr. Caserta commented that risk could not be extrapolated that way, and that in the large Vaccine Safety Datalink study in 2009 the risk of GBS was shown in the monovalent vaccine but not in the seasonal vaccine. Dr. Shimabukuro added that there was a more intense focus on GBS in the surveillance programs at that time, which could affect results.

Mr. Kraus commented that it would be inappropriate to discount the reports of GBS within a short period of time after vaccination. Just because an epidemiologic study fails to show a risk is not justification for a presumption that the vaccine does not cause the injury. He added that the fact that 90% of injury claims filed in that context are supported by the program. He recommended concurring with the proposed change to the Vaccine Injury Table and offered a motion to that effect. The motion was seconded by Dr. Williams. Mr. King invited discussion about the motion.

Dr. Shimabukuro commented on the three large 2009 studies that were characterized on Dr. Calvo's slides as "showing compelling evidence" for a rare, small increased risk of GBS after H1N1 flu vaccine. He noted that there were also two large studies which did not identify any such risk, and a finding by the PI of one of the VSD studies that, after considering preexisting infection, the GBS risk disappeared. He also expressed concern about the language in another slide that the "strength of the evidence and association is high between H1N1 and GBS, commenting that such a statement could be a matter of interpretation by various experts. He recommended toning the statements down with words like "weight of evidence supports" and avoiding terms like "compelling." He also noted that injuries related to flu vaccine are not covered by the DVIC, but by another federal program, the Countermeasures Injury Compensation Program

There was an extensive discussion concerning the issues involved, including the fact that the information about the vaccine risk was only received immediately before the meeting giving the members little time to consider the issues; the AHRQ report, although published for public comment, would not be available in final form until a later date; and the fact that the Commission can reconsider the issue and the decision made at any time during the complete revision process. Dr. Caserta observed that acting on the motion, rather than deferring consideration until the December meeting, would allow the Division to begin the clearance process, and if necessary at a later date the ACCV could change its position. Dr. King noted that the vote either way would not necessarily have a final impact on the ultimate objective of revising the Table.

Mr. King called for the vote and the final count was five in favor of the motion, three opposed to the motion. The motion carried. There was agreement that the opposing votes were based on the position that there was insufficient time to properly consider the issues.

Report from the Process Workgroup, Luisita dela Rosa, ACCV Member

Ms. Dela Rosa reported that the Process Workgroup had scheduled three meetings since the last ACCV meeting, but two were unavoidably cancelled and could not be rescheduled. The one meeting held on September 4 reviewed the progress of the Workgroup, which was established in June 2012. Three recommendations developed by the Commission were reviewed and affirmed: the addition to the Commission of a vaccine-injured adult (or his or her representative); the extension of the statute of limitations for filing a claim; and an increase in the cap for pain and suffering. The Workgroup agreed to continue to review the 2009 recommendations. There was also a brief discussion of the virtual format that has been adopted for the regular ACCV meetings.

Mr. King, noting that the virtual meeting format might be discussed later in the meeting, suggested that the Process Workgroup add a review of that meeting format to their own agenda, and Ms. dela Rosa agreed.

Report from the Maternal Immunization Workgroup,
Kristen Feemster, M.D., ACCV member

Dr. Feemster stated that the Workgroup had not formally met since the last ACCV meeting, but had nonetheless conferred in various ways to arrive at a final draft of the report and recommendations proposed previously. That report was presented to the Commission for review and approval at the June 7 meeting and relates to vaccines that pregnant women may receive that are not recommended for routine administration in children, which would therefore not be covered by the Program. There was a suggestion by National Vaccine Advisory Committee (NVAC) that the Commission might want to look at adult vaccines in general, beyond the narrow focus on pregnant women and vaccines recommended for children. The Commission might want to consider a new working group to address that issue. Mr. King observed that this would be an issue that could in some cases be outside the basic charge to the Commission.

Dr. Caserta noted that the broader recommendation involving adult vaccines was considered but that the final decision was to submit the more narrow recommendation because its approval would be more likely. He added that the Commission could still address the broader recommendation, noting that the only two vaccines not covered by the Program are the shingles vaccine and the polysaccharide pneumococcal vaccine, both of which are routinely recommended only for adults. Dr. Caserta emphasized that covering these adult-only vaccines would require a statutory change to the law. Congress, through OMB, would also have to consider the cost burden of adding adult vaccines to the Program. The Commission agreed that the issue should be discussed during the next commission meeting.

Vaccine Information Statements (VIS), Centers for Disease Control and Prevention (CDC), Skip Wolfe

Mr. Wolfe began with a proposed general statement about problems that could happen after any vaccine – syncope after any medical procedure of vaccination, severe shoulder pain and severe allergic reactions – all of which are possible with any vaccination. He proposed that this wording could be added universally to all VIS's. There were minor wording changes recommended. Dizziness, vision changes or ringing in the ears were clarified as being precursor symptoms of potential syncope; and the sentence about shoulder pain was revised to read "shoulder pain and loss of range of motion." The Commission approved the new wording and the insertion of the statement in any VIS related to an injectable vaccine.

Turning to the two VIS's pertaining to flu vaccines, Mr. Wolfe explained that both had been recently reviewed and published as interim information statements. The objective of the review is to move the document from an interim to a permanent status. Beginning with the inactivated vaccine, Mr. Wolfe stated that, except for a few recommendations made by the Commission at the last meeting that were incorporated in this version, the document is substantially unchanged from that review. In Section 2, Mr. Kraus suggested a minor change to the statement about thimerasol. He suggested that studies have not shown that thimerasol is harmful, be changed to studies have shown that thimerasol is not harmful. Mr. Smith commented that the paragraph about "high dose" vaccine for older people might be more appropriately placed in Section 2 immediately following the definitions of inactivated and live, attenuated vaccine. Dr. Caserta noted that the paragraph about vaccinating children under 8 should be clarified to indicate that the two doses should be given the first year they are vaccinated *for influenza*, not simply vaccinated.

There was a brief discussion about the bar code at the bottom of the last page of the VIS, which is placed there to allow providers to scan the information into a patient's electronic medical record. In the future it may also be able to allow patients to scan the VIS information.

Turning to the VIS for live, attenuated influenza vaccine, Mr. Wolfe stated that the only changes since the last review were made in sections 2, 3 and 4. Dr. Caserta took exception to the statement in section 2 that "the viruses in the vaccine have been weakened so they can't make you sick." The vaccine can certainly cause problems such as sinusitis. It was noted that there is a perception that flu vaccines can actually cause mild flu, so that some wording that explains that would be appropriate. Mr. King suggested explaining that the live vaccine could cause mild flu

symptoms but that the symptoms are evidence that the immune system is working properly. There was a suggestion to word the statement to the effect that "the weakened virus will not give you the flu." Mr. Wolfe agreed and indicated he would pass the objection on and work on a statement that would accurately reflect the advice of the Commission. He added that the statement in section 4, that the vaccine "does not cause flu" would also be revised.

(Ms. Michelle Williams left the meeting at 2:30 p.m.)

Update from the Immunization Safety Office (ISO),
Tom Shimabukuro, M.D., CDC

Dr. Shimabukuro began his report with a review of the June 2013 meeting of the Advisory Committee on Immunization Practices (ACIP), noting that the PowerPoint presentations and the video of the meeting are available on the web. There were several safety presentations, the first of which concerned the human papillomavirus (HPV) vaccine. The manufacturer, Merck, made a presentation about the Pregnancy Register maintained as required by Food and Drug Adminstration (FDA), and the data that pertained to exposure during pregnancy. Although the HPV vaccine, Gardasil is not recommended for pregnant women, there is inadvertent exposure when, for example, a woman receives the vaccine with no knowledge that she is pregnant. The Registry data from more than six years are reassuring with regard to safety, showing that spontaneous abortion, fetal deaths and congenital anomalies are no greater than background rates for those anomalies. The Registry, the largest vaccine pregnancy registry to date, will be discontinued because it has fulfilled its regulatory requirement of operating for five years.

Dr. Shimabukuro commented that there were five presentations on rotavirus vaccines and the risk of intussusception covering data from the Vaccine Safety Datalink (VSD) studies, a six-year assessment of data from the Vaccine Adverse Events Reporting System (VAERS), a Post-licensure Rapid Immunization Safety Monitoring System (PRISM) study, data from the Australian experience, and a general summary of intussusception risk and benefits of rotavirus vaccination in the U.S. The conclusions drawn from these presentations are that there is a small risk of intussusception following Rotateq or ROTARIX; the benefits of receiving the vaccine outweigh the small risk of intussusception; and the CDC continues to recommend rotavirus vaccines for all infants in the U.S.

The third major presentation concerned influenza, and end-of-season update on surveillance data on the 2012-2013 flu season. The presentation confirmed that there were no new safety concerns detected for either inactivated or live vaccines, the review of pregnancy data showed no unusual patterns, and no safety signals or increased risk was observed for febrile seizures in young children following inoculation with inactivated vaccine.

Dr. Shimabukuro announced the availability of four communications updates – one on the VAERS website that provides summary information about the 2013-2014 flu vaccine; another on the CDC web site that that deals with the risk of febrile seizure in children; a third on the CDC web site that provides general information on the 2013-2014 flu season; and the fourth on the CDC web site, a press release about HPV vaccine, emphasizing its underutilization among adults in the U.S..

Listing several publications of interest, Dr. Shimabukuro mentioned a paper by Dodd et al on the international collaboration to assess the risk of GBS following the 2009 H1N1 monovalent vaccines. That paper concluded that international collaboration to evaluate serious outcomes using a common protocol was feasible, and relying on pooled data there is evidence of an association between that vaccine and GBS. The paper also concluded that, given the rarity of the event, there is no evidence that international recommendations for continued use of influenza should be ignored.

Kharbanda et al described a large cohort of pregnant women who received inactivated flu vaccine, which did not increase risks for "medically attended adverse obstetric events." Iqbal et al showed that there were no adverse associations between antigens children received through vaccines in the first two years of life and neuropsychological outcomes in later childhood. Greene et al, as was mentioned earlier in the meeting, demonstrated that after adjusting for antecedent infections, there was no evidence of elevated GBS risk following influenza vaccines given in 2009-2010 (MIV) and 2010-2011 (TIV). However, the association between GBS and antecedent infections was strongly elevated.

Finally, concerning cause-of-death patterns in a an older vaccinated populations, McCarthy et al looking at a VSD study showed mortality rates were lowest in the days following vaccination, and the mortality rate was lower than in the general population, although the causes of death were similar in both.

Dr. Shimabukuro commented that the CDC looked at HPV vaccine coverage in adolescent girls and reported that despite the availability of safe and effective vaccines, and ample opportunities to obtain the vaccine in the health care setting, vaccination coverage among adolescent girls did not increase from 2011 to 2012.

Asked whether links to the papers discussed were available, Dr. Shimabukuro indicated that he would try to provide those links. There was a suggestion that the papers could be sent to the members in electronic format, if available.

Dr. Shimabukuro concluded his report and added that he would have to leave the meeting, but that Dr. Pedro Moro from his office would represent the CDC for the remainder of the meeting.

Update from the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH)
Ms. Barbara Mulach Ph.D.

Ms. Mulach stated that NIAID was working with other federal agencies to support efforts to develop an H7N9 influenza vaccine, should that strain become an issue. There will be clinical trials in the near future. Dr. Caserta interjected that H7N9 was covered by the Countermeasures Injury Compensation Program, because it is assumed to be a vaccine for a pandemic..

Ms. Mulach explained that there was a recent Phase I clinical trial of a newly developed malaria drug, PfSPZ manufactured by Sanaria, Inc., which showed some efficacy. In a small cohort

immunization against one strain of malaria was demonstrated. There will be additional studies in the near future.

Finally, NIH has been supporting studies of a vaccine developed by Bavarian Nordic to create immunity from smallpox. The vaccine, IMVANEX, has been approved for use in adults. It appears to cause fewer adverse events than earlier smallpox vaccines, and it is particularly appropriate for individuals with compromised immune systems.

In the area of genomics, a unique cell line, HeLa cells, came from a woman, Henrietta Lacks, who died of cervical cancer in 1951. Those cells have survived in research and for the first time NIH has contacted her family to discuss the privacy issues related to the use of those cells for research purposes. Ms. Mulach stated that she could provide more information if the Commission members were interested.

Also, NIH has established a new program with regard to expanding the understanding of newborn genomes, and three awards have been made for research projects in that arena. Finally, NIH has partnered with the Smithsonian Institution to support an exhibit on genome science -- Genome: Unlocking Life's Code, which opened recently. Hopefully it will expand awareness of genome science.

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

LT Marshall reported that in June and July the FDA approved strain chain supplements for the 2013-2014 formulations for Afluria, Flulaval, Fluarix, Flucelvax, Fluvirin and Fluzone. On June 7, the age window for Sanofi's Fluzone was expanded to infants 6 months of age and up. On August 1 the age recommendation for Mimbo, a meningococcal oligosaccharide, was expanded to 2 months to 23 months and up to 55 years) it had previously been 2 years to 10 years, and 11 years to 55 years. On August 16, for the supplement trivalent influenza vaccine made by GSK, the age was expanded to be from 3 years of age and up (previously 18 years and up). Finally, Flulaval, a quadrivalent flu vaccine, was approved for children 3 years of age and up.

Update from the National Vaccine Program Office (NVPO), Steve Bende, M.D.

Dr. Bende announced that the upcoming NVAC meeting has an important historical aspect in that it is the 25th anniversary of the advisory committee. The agenda will include an historical overview; a review of Healthy People 2020 (with a focus on adult immunization); a discussion of the Affordable Care Act (ACA), which includes a provision that providers must cover preventive health care services without requiring co-pay or co-insurance; and a look at immunization registries. With regard to immunizations, providers who offer vaccines will be asked to incorporate into routine clinical care an assessment of adult immunization status and to stock all vaccines recommended by ACIP for adults. Providers who do not normally make vaccines available will be asked to do so or to refer patients to other providers who are able to provide immunizations. Public health departments will be asked to maintain professional practice standards and to assess immunization program needs.

Next on the agenda will be a session on influenza, which will include a component on the importance of communicating information to health care professional and the public. There will be a session on viral hepatitis that will refer to the Healthy People 2020 goals of a doubling of individual awareness of hep A and B status (from 33% to 66%), a similar increase in awareness of hep C (from 40% to 6-%), a reduction in hepatitis infections by 25% and elimination of mother-to-child hep B transmission. There will also be a presentation on maternal and child health issues, including an update from the ACCV Maternal Immunization Workgroup.

The NVAC has a working group focused on the Healthy People 2020 goals related to HPV vaccine coverage, which is well below where it should be. Finally, the NVAC Global Working Group will present its recommendations for a vote at the meeting.

Dr. Bende noted that the AHRQ study discussed earlier in the meeting was commissioned by the NVPO. It is out in the public domain for comment and the final versions should be released sometime in October.

Public Comment

Mr. King invited public comment.

Dawn Loughboro, mother of two vaccine-injured children, questioned whether or not the ACCV has any legal authority to address adult-only vaccines, since they are not included in the basic legislation that established the VICP. Secondly, the ACCV should look at procedures that would be related to vaccines given to pregnant women that could affect the mother's unborn child. In addition, Ms. Loughboro was concerned about the statement in the Influenza VIS that was discussed earlier, that thimerasol in vaccines causes no harm. She stated that over 600 studies contradict that statement. Pregnant women should be informed of any risk related to thimerasol in vaccines.

Ms. Loughboro expressed concern that the Merck self-regulation of its HPV registry could present a conflict of interest, since there are no external controls for the registry. She also asked who would continue to manage the registry once Merck was no long involved. Finally, she commended the Commission for approving the recommendation to add GBS to the Vaccine Injury Table.

Theresa Wrangham, representing the National Vaccine Information Center, also commended the Commission for approving the addition of GBS to the Vaccine Injury Table, adding that the recommendation submitted to the Secretary should include a comment that the three votes in opposition related to a the timeliness of providing information to the Commissioners for consideration, and not to any other objection to the proposal.

Ms. Wrangham recommended an increased transparency in reporting information that should be available from the VICP. She noted that reporting doses distributed versus claims can be misleading, since the vaccine reactions reported to VAERS are not included in the report, nor is the fact that vaccine adverse events are underreported in general. There is also a lack of awareness of the VICP that detracts from its effectiveness. The report should include published

and unpublished awards. Although much the information is presented to the ACCV during its meeting, and is thereafter placed in the public domain, it is not reasonable to expect members of the public to compile consolidated information from various meeting documents and resources.

The revision process for the VIS's requires providing an opportunity for parent groups to participate in the process. At the last meeting NVIC volunteered to participate, but that fact was not included in the meeting minutes. NVIC requests that the minutes be amended to indicate that action. Concerning the VIS review, there should be a brief statement in every VIS about the lack of research related to many vaccine adverse events. And each VIS should be explicit about the vaccines covered by the VICP, and not use the general words "certain vaccines" are covered. Finally, Ms. Wrangham recommended that the ACCV provide information on the number of claims dismissed because of the statute of limitations, and consider ways to reduce that number.

In closing, Ms. Wrangham commended the Commission for putting historical information about recommendations to the Secretary on the VICP web site, noting that some of the recommendations have been made more than once at different times. Only one response from the Secretary was included, and it would be helpful to include all of the Secretary's responses, and each action taken by the Department with regard to each recommendation.

Mr. James Moody commended the DVIC staff for bringing the issue of GBS to the ACCV agenda. He also commended the chair for addressing issues related to research. A critical part of that research is developing baseline data on unvaccinated children. He requested that the ACCV specifically add that issue to its agenda.

Mr. Moody noted that the government apparently directed the IOM panel on adverse events to exclude consideration of the mercury risks. He commented that this was an issue that the ACCV should also add to its agenda.

There being no other requests, Mr. King declared the time for public comment closed.

Future Agenda Items

Mr. King commented that the effectiveness of the virtual meeting versus the face-to-face meeting was an issue discussed earlier, and referred to the Process Workgroup. Asked about the budget component of the issue, Dr. Caserta commented that, even though ACCV travel is paid through a mechanism that draws the funds from the Trust Fund, there is a government-wide policy that travel should be restricted to only the highest priorities. It is a matter of policy, not availability of funds. Mr. King expressed concern that all of the interpersonal events that occur at a face-to-face meeting are lost in the virtual environment, which detracts from the effectiveness of the Commission's mission. Dr. Caserta agreed, but noted that even presenting that kind of argument within the Department, the policy still prevents many of those types of meetings. The annual budget for DVIC's bureau was originally about $100,000 and was reduced to $25,000. He added that he had been able to reserve one face-to-face meeting per year.

Mr. King called for a comment from each Commission member present to develop a sense of the Commission. Dr. Douglas stated that, since she has had training is using virtual environments,

she is comfortable with the teleconference process. However, the remaining members of the Commission generally agreed that at least one in-person meeting per year would be preferable. The consensus of these six members was that the in-person meeting fosters a working relationship that cannot be built with phone-only discussions. The personal interaction during the meeting and during breaks is important to developing a sense of commitment and a cohesiveness that is necessary for conducting Commission business. Dr. Caserta committed to representing this position to the senior management of the bureau that makes decisions concerning travel. He added that one such meeting had been approved, which he intended to schedule when new Commission members were appointed.

Mr. King proposed creating a recommendation to the Secretary conveying the position of the Commission. Dr. Caserta conceded that the recommendation would promote the Commission's objectives, and it is likely that the Secretary would take the recommendation into consideration. On motion made by Mr. Kraus and seconded by Mr. Smith, the Commission unanimously empowered the Chair, David King, to draft a recommendation expressing the feelings of the Commission with regard to in person meetings.

Turning to new business, Mr. Kraus commented that the statement by Theresa Wrangham was correct that the Commission had discussed the importance of public input and collaboration in reviewing the VIS's. He recommended that staff investigate the situation and that Dr. Caserta investigate the CDC's position in the matter. Ms. Pron suggested that the topic be put on the agenda of the next meeting, particularly the issue of including adult vaccines in the program. There was a reminder that if the Commission wanted to recommend including adult vaccines the recommendation from the Commission would have to include a recommendation that the appropriate new legislation be considered.

There being no other business to discuss, Mr. King invited a motion to adjourn.

Adjournment

Whereupon, on motion made and seconded, there was unanimous approval to adjourn.