Advisory Commission on Childhood Vaccines

March 6-7, 2014

91st Meeting

Meeting Day One – March 6, 2014

Members Present on March 6, 2014

David King, Chair ('14)
Charlene Douglas, Ph.D. ('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) (via telephone)

Division of Vaccine Injury Compensation

Vito Caserta, M.D., Acting Director, DVIC
Andrea Herzog, Staff Liaison
Andrea Davey, J.D., Legal Counsel

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, announced that Secretary Sebelius had responded to the Commission's request for comment on five recommendations submitted to the Secretary of the Department of Health and Human Service's (Secretary) office during the past year. She assured the Commissioners that each would receive careful review. The recommendations included the extension of the statute of limitations for filing injury and death claims; increasing benefit caps for pain and suffering and death; compensation for injuries sustained by a live-born infant whose mother received a vaccine while the infant was in utero; expanding coverage under the Vaccine Injury Compensation Program (VICP) to include vaccines that are recommended for routine administration in pregnant women but are not recommended for routine administration in children; and consideration of a health professional with expertise in obstetrics to serve as a member of the ACCV. A discussion will be scheduled as an agenda item in the future.

Mr. King commented that another item that should be considered for a future meeting is the succession plan for chair and vice-chair, since terms of office will certainly expire this year. He invited any member interested in serving in either capacity to indicate that interest.

Finally, Mr. King reminded the Commissioners of the purpose of the Vaccine Injury Compensation Program which is to support those who are injured as a result of receiving a

vaccine, and that the Commissioners should strive to put those individuals first in making recommendations and decisions with regard to the responsibilities of the Commission.

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 -- Report from the Division of Vaccine Injury Compensation, and the Report from the Process Workgroup. Ms. Wrangham commented that the intention to provide more meaningful information on the web site has not been successful, partly based on the premise that the privacy of injured individuals may be compromised. She maintained that the regulations define the information that should be protected as name, address and telephone number. She stated that the information desired concerned the epidemiology of the injury – the vaccine, the most prevalent specific adverse events. She mentioned that she had sent to the Commission a description of the information desired.

Approval of December 2013 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 the Division of Vaccine Injury Compensation, Dr. Vito Caserta, Acting Director, DVIC

Dr. Caserta briefly reviewed the day's agenda, noting that the Commission would hear a report from the Department of Justice (Vince Matanoski), and an update from the ACCV Process Workgroup, and review two Vaccine Information Statements. There will also be a presentation on pneumococcal polysaccharide (Pneumovax 23) vaccine, a vaccine recommended for adults. Finally there will be updates from ACCV ex officio member agencies -- FDA, CDC, NIH and NVPO.

With regard to statistics, Dr. Caserta reported that 174 claims had been filed in the first five months of FY 2014. Extrapolating to the end of the fiscal year the number would be 417, in line with previous years. Similarly, the number of adjudicated compensable non-autism cases stood at 73 cases, 80% of which were settled, and that number slightly lags the rate for the previous years. The awards for the fiscal year to date are $66 million plus $7.5 million for attorney's fees. If extrapolated the total would be slightly less than last year. The Vaccine Injury Compensation Trust Fund (Trust Fund) balance is about $3.5 billion, with income of $63 million.

Dr. Caserta noted that there was a public hearing on January 13th for the rotavirus Notice of Proposed Rulemaking. However, since there may not have been sufficient public notice, an additional public hearing will be held in the near future, after which the Department of Health and Human Services (HHS or Department) will review public comments and publish a final rule.

The Vaccine Injury Table Notice of Proposed Rulemaking is being finalized and should be ready for the clearance process within the next two months. Dr. Caserta noted that he would be retiring and that Dr. Avril Melissa Houston would be taking on the duties of Executive Secretary for the Commission.

Finally, Dr. Caserta noted that the National Vaccine Advisory Committee (NVAC) met on February 11-12 and the Advisory Committee on Immunization Practices (ACIP) met on February 26-27, and there will be reports on both later in the meeting. Dr. Caserta provided Program contact information to the Commission. He concluded his presentation and asked if any of the Commission members had questions.

He was asked about the timeline for approval of the Vaccine Injury Table Notice of Proposed Rulemaking. Dr. Caserta explained that HHS would share the initial draft internally with other HHS agencies (i.e., CDC, FDA, NIH, CMS), incorporate responses from those agencies, and complete a final HHS clearance. HHS will forward the final draft to the Office of Management and Budget (the Executive Office of the White House), which would send the draft to other Federal departments to obtain their comments, consolidate the comments from those departments, and the final version would then be published in the Federal Register. There would be a six-month public comment period and a public hearing, and then the HHS would finalize the rule and it would become effective when published in the Federal Register.

Mr. King asked about the best approach for realizing the Commission's goal to improve communications with the Secretary's office. Dr. Caserta suggested that a first step might be to identify the goals and objectives of the Secretary that, in terms of vaccines, comes under the aegis of the Office of the Assistant Secretary for Health (OASH). That office typically communicates with the National Vaccine Advisory Committee with regard to vaccine goals and objectives and it might be possible for ACCV to be included in that information loop.

Dr. Caserta suggested that the Commissioners should become familiar with the National Vaccine Plan and seek to develop a relationship with the NVAC and OASH to achieve that end. He added that staffing for ACCV is relatively limited, mainly to support the regular meetings that Ms. Herzog handles. To expand support for ACCV, such as developing the liaison with OASH and NVAC, might require additional staffing and requisite funding. Asked whether the Trust Fund could be such a source of funding, Dr. Caserta explained that the Trust Fund pays for compensable claims, the legal fees involved in those cases, some budget requirements related to the VICP for the Court, the Department of Justice and HHS. Ultimate budget decisions are made by the Office of Management and Budget.

Mr. King took exception to the practice of the NVAC to fund travel for all meetings, while the ACCV is not able to receive the same kind of meeting support. Dr. Caserta explained that the budget decisions are made by different departments, which may have different priorities and requirements. Mr. Kraus suggested that, rather than trying to resolve the issue at the meeting, it might be more appropriate if the Commission would draft a statement or recommendation describing its position with regard to the importance of face-to-face meetings, and the addition of sufficient staff support to provide the liaison with OASH and NVAC and to prepare appropriate reports as discussed earlier with regard to the National Vaccine Plan

priorities, the important issues related to the vaccine program as a whole, and how the ACCV plays a role in the process. Dr. Caserta endorsed that proposal. Dr. Pron added that the support might also serve to expedite the distribution of the meeting minutes to the Commissioners, and Ms. Herzog commented that she would work on expediting that process. Mr. King suggested, rather than a detailed set of minutes, perhaps a short summary of the main discussion points could be created immediately after the meeting.

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

Mr. Matanoski referenced the Department of Justice PowerPoint materials (DOJ PP), dated March 6, 2014, as part of his presentation. He commented that the DOJ's statistics reflect the period between ACCV meetings, whereas HHS reports statistics based on the fiscal year. As a result, there may be a slight difference in the numbers reported by Dr. Caserta and DOJ. During the three month reporting quarter, 128 cases were filed, which is a significant increase in the filing rate over similar historical periods (DOJ PP at 2), but a slight decrease from last quarter's numbers. The average annual filing rate for the preceding five years was approximately 400 cases; this year it is projected to be about 500, a 25% increase. Mr. Matanoski observed that the filing rate increased during the summer of 2013, and that higher filing rate continues. If the filing rate continues to increase, it may pose a challenge to the DOJ's ability to process cases as funding has not been increased. The rise in adult petitioner filings continues an upward trend. Of the 128 cases filed this quarter, 80% of the claims involved adult injuries compared with 75% for the two preceding reporting periods. In response to a question, Mr. Matanoski explained that a minor is considered anyone under the age of 18.

Mr. Matanoski reported that 113 cases were adjudicated since the last report, slightly down from last quarter, which may be attributable to fallout from the government shutdown. (DOJ PP at 3). While the number of adjudicated cases was slightly down from last quarter and less than the number of newly filed cases, Mr. Matanoski did not consider this to be a trend. He added that the Office of Special Masters now has a full complement of special masters, which may affect case adjudication levels.

Turning to appellate proceedings, petitioners filed a *writ of certiorari* in the U.S. Supreme Court in *Tembenis v. Sebelius*. (DOJ PP at 5), asking the Supreme Court to hear the case involving future damages available to the estate of a child who suffered an alleged vaccine related injury and death. The special master held that the child's estate could recover lost future damages based on the expected lifetime earnings of the child. The U.S. Court of Federal Claims (CFC) affirmed. On appeal by the government, the U.S. Court of Appeals for the Federal Circuit (CAFC) reversed, finding that the estate was limited to damages calculated up to the date of death. (DOJ PP at 5). Turning to the CAFC, in *Carson v. HHS*, the CAFC denied petitioners' request for a rehearing *en banc* after a three-judge panel dismissed the case as untimely. (DOJ PP at 6). In *Snyder/Harris v. HHS*, on appeal by respondent, the CAFC reversed the CFC and reinstated the special master's decision denying compensation in both cases finding that the genetic mutation, SCN1A caused the alleged injuries. This is consistent with other SCN1A cases affirming the special master's denials of compensation. There were two new cases filed by petitioners at the CAFC. (DOJ PP at 7). *Koehn v. HHS* was originally part of the Omnibus Autism Proceeding, and was dismissed by the special master. One year later, the petitioner, now *pro se*, moved for relief from judgment at the CFC claiming that the

vaccination date was erroneous. The CFC denied the appeal. *Price v. HHS*, involved a denial of entitlement.

Turning to the CFC, five cases were decided. Four of which involved entitlement and one involved jurisdiction. (DOJ PP at 8). Mr. Matanoski also discussed two new appeals filed by petitioners. (DOJ PP at 9). In *Contreras v. HHS*, petitioner appealed a decision on remand by the special master again denying compensation finding that the timing of onset of petitioner's injury was too soon for the type of injury alleged, and that the evidence did not support a short time frame. In *Chuisano v. HHS*, petitioner appealed the special master's denial of $45,000 in attorneys' fees sought by two different attorneys/firms because the claim lacked a reasonable basis. There was some discussion about the precedential value, if any, of this decision. Mr. King questioned whether a decision might prejudice an attorney's willingness to file claims. Mr. Matanoski observed that there has not been a decline in the number of filings or attorneys new to the Program filing cases. The statute requires that a petition be filed with complete evidentiary records, and that it is the responsibility of petitioner and his/her counsel to do that. In *Chuisano*, the special master focused on whether or not counsel should be compensated if the claim had no reasonable basis to begin with. The court typically looks at the circumstances at a given time in the case in determining whether there was a reasonable basis for the claim. A case filed without evidence because the statute of limitations was about to expire may be deemed to have a reasonable basis initially, but the Court may deem that reasonable basis would end if counsel continued to pursue a claim without developing evidence of causation, or if the claim was filed without evidence when no imminent deadline existed. Mr. Kraus added that the concern is attorney access, and very rarely do courts find that a case was filed without reasonable basis. Oral argument in *Flores v. HHS* took place on February 25, 2014 (DOJ PP at 10).

Turning to the slides entitled Adjudicated Settlements (DOJ PP at 11-14), Mr. Matanoski noted that 40 cases were settled during the current reporting period. Of those, it appeared that 33 were for adults and 7 for minors. Twenty-eight cases involved the flu vaccine or flu vaccine in combination with other vaccines. The average time to reach settlement for all cases in this quarter was two years, four months, up slightly from the past. Nevertheless, the overall percentages remained consistent. Of the 40 cases, 28% settled within one year, 63% within two years, and 80% within three years. The length of time to resolve the outlier cases went down to four years. Responding to questions about the overall time it takes to process cases, Mr. Matanoski explained that sometimes petitioners face challenges compiling medical records and obtaining expert reports. Mr. Kraus agreed that petitioners faced those challenges, and added that the Office of Special Masters had not been staffed to its full complement until recently. There was also discussion about the extent to which Court and DOJ resources may be strained if the upward filing trend continues. Mr. King asked that those issues continue to be monitored. Mr. Matanoski offered that some implemented efficiencies include a "fast-track" settlement process and shorter stipulation processing.

Finally, Mr. Matanoski noted a change in the DOJ presentation with the glossary of terms and diagrams illustrating case processing being moved to an Appendix at the end of the presentation. (DOJ PP at 15-21

Report from the Process Workgroup, Dr. Luisita dela Rosa, Chair

Dr. dela Rosa noted that the workgroup had only one opportunity to meet since the last meeting. She stated that the workgroup discussed the recommendations already submitted to the

Secretary. The first general area -- consideration of a third Commission membership category who could be a member of the general public who is a vaccine-injured adult (or his or her representative), a member of the medical community, perhaps from the maternal workgroup area; and an attorney who has experience with the vaccine injury compensation program. The second recommendation was to extend the statute of limitations for filing; and the third was to increase the cap on awards for death and pain and suffering.

Dr. dela Rosa reported that the workgroup agreed that one way to support the Secretary with regard to the membership recommendation would be to develop a list of potential candidates, perhaps by recommending three specific candidates in each of the three areas recommended. With regard to the other recommendations, the ACCV should invite comment from the Secretary on the feasibility of changing the statute of limitations and increasing the award cap. That feedback could help the Commission develop a strategy to achieve the objectives.

The Commission could also invite comment from other interested stakeholders, such as the Office of the Special Masters and vaccine manufacturers, as well as parents of vaccine-injured children, and others interested in the VICP. There was also a suggestion that parents be encouraged to take advantage of the opportunity to offer public comments during the regular ACCV meetings.

Dr. dela Rosa commented that there was discussion about data mining, and Mr. King commented that a proposed future science group would be concerned with data mining of reports of vaccine compensation settlements and awards. He noted that, as Ms. Wrangham mentioned in her public comment, there is some information available that could be sent to the Commission members for consideration at a future ACCV meeting. Mr. Kraus suggested that the information should be vetted by the Process Workgroup before the next meeting, perhaps inviting Ms. Wrangham to contribute her comments, and the Workgroup could develop the detailed agenda item for the next ACCV meeting.

Mr. King observed that some of the ideas and discussion that originated in the Process Workgroup would be appropriate for a more complete discussion at the Commission level. These ideas and issues could be articulated by testimony from stakeholders, including parents, special masters, attorneys, the DOJ, injured individuals, and the Commissioners, themselves. Dr. Douglas commented that recommendations to the Secretary may be promptly acknowledged as received, but before the recommendation actually reaches the Secretary it is processed through what can be a lengthy review process. Mr. Kraus suggested that the process does not preclude an occasional reminder that the Commission is interested in a response. Mr. King suggested that the reminder should consider a rationale for providing the response.

Concerning the Process Workgroup's recommendation to invite outside comment from stakeholders, Mr. King invited comments by the Commissioners. There was an observation that the Commission should have a mechanism to vet community input, and assess the value of testimony that the Commission had not heard in other ways, although that would require resources that might not be available to the Commission. For example, there was a suggestion that a presentation from the former Chief Special Master Golkiewicz might be enlightening in

terms of what the court must address. Since there is no clear national constituency for vaccine-injured individuals, there was also a suggestion that the Commission might benefit from hearing from Ms. Wrangham in her role asEexecutive Director of the National Vaccine Information Center, rather than a participant in the public comment section of the agenda. That would allow a more interactive discussion of the issues she might raise.

Jason Smith suggested there could be an agenda item for the June meeting that would address the statute of limitations in much greater depth than any earlier discussion, perhaps even inviting some testimony from appropriate advocates. An important question to address is why vaccine-injured people allow the deadline to pass? After consensus for the idea of the in-depth discussion was expressed by the members present, Mr. King asked how to implement the idea. Dr. Caserta suggested that a small group from the Commission develop a list of appropriate witnesses, after which staff could make the arrangements. Mr. Kraus suggested that the Process Workgroup might be the appropriate group to develop the witness list, adding that a face-to-face meeting might be more effective than a teleconference (in which case the target meeting would be in September).

Mr. King noted the consensus for the Process Workgroup to take on the responsibility for developing the proposal for the agenda item to be scheduled for the September meeting. He closed the discussion and invited public comment under the last agenda item for the day.

Public Comment

Ms. Theresa Wrangham, Executive Director of the National Vaccine Information Center, expressed appreciation for the Commission support of developing a spreadsheet of data related to settlement of vaccine injury claims. She also commented on the proposal to recommend to the Secretary an extension of the statute of limitations, mentioning her own experience of being unaware of the benefits of the VICP in part because of her family's absence from the country after her child was injured. She commented that people may be unaware of the program for various reasons, or may encounter discouragement in reporting injuries because a health professional suggests that the injury is not related to a vaccine. She also felt the research gaps identified in the IOM report may be responsible for physicians being unaware of some adverse events that are, in fact, caused by vaccines.

Adjournment

There being no further requests for public comment, Mr. King announced that the meeting would be recessed until 9:00 a.m. the following morning, March 7, 2014.

Meeting Day Two – March 7, 2014

Members Present on March 7, 2014

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

Division of Vaccine Injury Compensation

Vito Caserta, MD., Acting Director, DVIC
Andrea Herzog, Staff Liaison
Andrea Davey, JD, Legal Counsel

Federal Government Representatives

Steve Bende, M.D., NVPO, HHS
Theresa Finn, Office of Vaccines, FDA
Claire Schuster, NIAID, NIH
Tom Shimabukuro, M.D., Immunization Safety Office, CDC

Welcome and Introductions and Unfinished Business from Day One

Mr. King called the meeting to order and welcomed those present in person and on the phone. After introductions, he invited discussion of any item of business unfinished from the day before. Dr. Douglas asked for clarification on the extension requested for the statute of limitations, and Mr. Kraus confirmed that the recommendation to the Secretary was to extend the statute of limitation to at least six years, and preferably eight years. Ms. Herzog confirmed that the recommendation was for eight years, with no mention in the recommendation of an alternative six years.

Dr. Shimabukuro supported the recommendation made the day before by Dr. Caserta that the Commission obtain some supporting data that would indicate examples of individuals who missed the filing deadline and the reasons why they missed it, includingperhaps some data to indicate the extent to which individuals fail to file a claim in a timely way. Dr. Houston added that when any recommendation is put forward that both the positive and negative aspects, if any, be discussed, and in particular how the negative aspects could be ameliorated.

Dr. Pron commended the staff for preparing the table of statistics that is on the ACCV website under "Statistics Reports – February 3, 2014." It was referred to during the meeting on Day One as a "spreadsheet." Dr. Caserta added that, in cooperation with CDC, the statistics are updated monthly with regard to adverse events and annually with regard to doses distributed.

Dr. Villarreal commented that the terms of service for six of the current ACCV members would expire in 2014 and she requested a discussion about the succession and about which remaining members would fill required categorical positions. Mr. King agreed that the issue could be addressed during the "Future Agenda Items/New Business" agenda item at the end of the meeting.

Review of Vaccine Information Statements, Skip Wolfe, CDC

Mr. Wolfe announced that the Commission would review two VIS's, one for hepatitis A and one for hepatitis B. He commented that earlier in the year there was a meeting of the parents and professional consultants group (hereafter "consultants"), which reviewed VIS's unrelated to the two under consideration, but the consultants made some general observations that could be helpful to the Commission's review process. Those observations would be mentioned at the appropriate time during the discussion to follow.

Beginning with the hepatitis A VIS, under Section 1, Dr. Caserta suggested removing "dark urine" from "Hepatitis A can cause" because it could occur in the absence of jaundice. Mr. Wolfe commented that, concerning disease burden, the consultants felt that using actual numbers rather than percentages to describe reduction in disease burden was more effective. Barring providing both figures, there was agreement that, considering health literacy, numbers might be easier for the general population to understand. Particularly if the denominator was one – e.g., one person in 500. Mr. Wolfe commented that the CDC legal counsel, referring to a recent article in Pediatrics, suggested that the way risks are currently described may actually exacerbate public concern about adverse events. Although no alternative was suggested, Mr. Wolfe felt the issue could be considered in the future. Mr. Wolfe also stated that vaccine effectiveness is not explicitly addressed in the VIS, relying on the wording "vaccines *can* prevent," rather than stating that the vaccine is not 100% effective.

As a matter of process, Mr. Kraus asked about the original purpose of the VIS, and Dr. Caserta explained that the VIS is required by the National Childhood Vaccine Injury Act of 1986, as amended, (Act)to provide information to the public about the purpose of the Act, provide information about the risks and benefits of vaccines, and to provide an incentive for doctors to discuss vaccine issues since it was the feeling on the part of parents that doctors avoided the subject. Asked whether the VIS was intended to increase public acceptance of vaccines, Mr. Wolfe said that the purpose was rather to inform objectively about the benefits and risks and to provide information about the VICP. Dr. Pron noted that, for the physician informing a patient in a limited time frame, the VIS is useful as a supplemental information piece.

Mr. Wolfe commented that, by the nature of the format, the discussion of risks is longer than the discussion of benefits because of the need to discuss the numbers. Dr. Pron commented that the hepatitis A disease could affect an adult's ability to work. The risk section should be expanded to be more specific, perhaps mentioning specific occupations such as food handlers. Concerning the final notice about the VICP, Mr. King agreed with an earlier suggestion that the actual statute of limitation be specified on the VIS. Mr. Wolfe commented that the consultants

also made that suggestion. Dr. Caserta commented that the statute on death claims is different from injury claims, but Mr. Wolfe indicated that that issue could be resolved, perhaps with a general statement that there is a limited time to file.

In Section 2, Dr. Pron was concerned that the phrase "two doses are needed for lasting protection" could be confusing – lasting for years, a lifetime? Mr. Wolfe said that he would investigate the anticipated period of protection. Dr. Shimabukuro suggested that the wording be simplified to recommend two doses, rather than imply that one dose could be sufficient for protection. There was a brief discussion about high risk populations, such as Native Americans, although Mr. Wolfe pointed out that the risk in that population has been significantly reduced mainly because of vaccination programs. Dr. Villarreal suggested that adding the CDC web site link to travel recommendations under the heading "Others who should be vaccinated." Mr. Wolfe agreed that the reference should be added to Section 7, "How can I learn more?" Dr. Villarreal also suggested revision of the category "Men who have sex with men," to indicate unprotected sex.

In Section 3, about informing the health care provider, Dr. Pron suggested that the wording be expanded to include a health care provider other than the doctor. The doctor may not be available at the time. She emphasized that it is important to encourage communication. Mr. Wolfe commented that the change is a complicated issue since there are so many individuals who could be consulted – perhaps "health care provider" might suffice. Dr. Shimabukuro stated that health care professional would be more specific and exclude providers who are insurance companies and so on. Mr. Kraus suggested "tell your doctor (or the person giving the vaccine)."

Under Section 4, there was a discussion about placement in the VIS of the severe allergic reactions warning, and there was agreement to move the severe adverse reactions to the beginning of the section. Mr. Wolfe mentioned that the consultants had suggested dealing with unknown risks, but Dr. Shimabukuro commented that such a statement in the VIS could place the provider in the difficult position of trying to explain unknowns. Dr. Pron agreed that there are so many unknown risks, not only in vaccines but in foods, other medicines and so on, that trying to deal with unknowns could be a significantly complicating factor. Mr. Wolfe also commented that the term "death" is no longer used in VIS discussions, except in reference to disease outcome. Dr. Shimabukuro noted that there is almost no data on deaths from vaccines, which would impact the discussion of how to deal with death information in a VIS. Mr. Kraus suggested that if death is mentioned in a VIS it should be clearly explained that the risk is extremely low. Dr. Bende commented that, regardless of the remote possibility of a fatal outcome, the mere mention of the risk will have an effect on an individual's consideration about accepting a vaccination. Dr. Pron agreed, adding that a parent would probably be even less rational about a decision involving an infant. Mr. Wolfe also agreed, adding that if the decision is to include mention of death as a rare outcome, the wording must be very carefully crafted. He and Dr. Shimabukuro agreed to confer about the issue after the meeting.

Mr. Wolfe stated that the remaining sections are the same in all VIS's and have been extensively reviewed over the past years. Dr. Caserta suggested that the admonition to report severe allergic reactions should be generalized to apply to any adverse reaction. Dr.

Shimabukuro recommended depersonalizing the sentence about "they" Vaccine Adverse Event Reporting System (VAERS) do not give medical advice.

Hepatitis B VIS

Turning to Section 1 of the hepatitis B VIS, it was noted that data from 2009 appears to be dated. Mr. Wolfe felt it would be better to choose an average number that would apply to the last several years, and specify that the number applies to U.S. cases. There was also a suggestion that providing a statistic from the period before the vaccine became available would be helpful.

Dr. Villareal commented that most of the risks under paragraph 2 do not apply to children. She felt that the sentence stating that a baby whose mother is infected could be infected at birth is the most important warning for mothers. She commented that if there is no infection within a family there can be resistance to allowing vaccination in a child. There is also the issue of a person being positive but undetected, which would argue for a birth dose of the vaccine. Mr. Krause suggested that there should be a specific separate section for babies. Dr. Caserta observed that infection at birth is more likely to result in chronic hepatitis B, which has a higher risk for developing cancer.

There was a suggestion to include the CDC web site URL for travel vaccinations at some location in the VIS. Finally, sections 3 through 7 are standard in most VIS's. There was a suggestion that a timeframe would be useful in some of the adverse events, such as the caveat in the hepatitis A VIS that "If these problems occur they usually last 1 or 2 days."

Update on the Immunization Safety Office, CDC, Tom Shimabukuro, M.D.

Dr. Shimabukuro stated that he would provide an overview of the recent ACIP February 2014 meeting, an update on the serogroup B meningococcal vaccine programs that are ongoing, and review some selected publications. The influenza session included safety updates for live attenuated influenza vaccine (LAIV) and inactivated influenza vaccine (IIV) for children and individuals less than 18 years of age, and the safety of LAIV vs. IIV in healthy children (Grading of Recommendations Assessment, Development and Evaluation - GRADE). The presentations were provided to ACIP to inform discussions around a possible preferential recommendation for LAIV in young children. This season the new quadrivalent LAIV was used exclusively (in previous seasons it was a trivalent LAIV). Both IIV3 and IIV4 are being used this influenza season. The interim results indicate that the safety profiles of quadrivalent vaccines (both LAIV an IIV) are comparable to the trivalent formulations. In the GRADE analysis the safety data for LAIV vs. IIV were reassuring.

Data on Tdap vaccination in pregnant women in both VAERS and Vaccine Safety Datalink (VSD) data is reassuring. However, currently there is limited data on repeated Tdap in pregnant women. Dr. Shimabukuro stated that he would provide additional information in an update at the next ACCV meeting.

Dr. Shimabukuro commented on the outbreaks of serogroup b meningococcal disease at Princeton University and University of California (UC) at Santa Barbara. CDC is currently

working with these institutions, public health agencies and the FDA to coordinate vaccination programs with serogroup B meningococcal vaccine. The vaccine (Bexsero) is not licensed in the US and is being given under an Expanded Access to Investigational New Drug (IND) protocol approved by FDA. The vaccine is licensed in Europe and Australia. The vaccine is a two-dose regimen and the program was recently completed at Princeton and is under way at UC Santa Barbara.

Regarding recent publications of interest, Dr. Shimabukuro cited the Stockwell et al., study "Risk of Fever after Pediatric Trivalent Inactivated Influenza Vaccine and13-Valent Pneumococcal Conjugate Vaccine." JAMA Pediatr. 2014 Jan 6. [Epub ahead of print]. The authors found that simultaneous trivalent inactivated influenza vaccine (TIV) and 13-valent pneumococcal conjugate vaccine (PCV13) in young children was associated with higher transient increased fever risk than administration of either vaccine without the other product.

Moro et al., in the study "Reports to the Vaccine Adverse Event Reporting System after hepatitis A and hepatitis AB vaccines in pregnant women." Am J Obstet Gynecol. 2013 Dec 27. [Epub ahead of print], looked at reports to the Vaccine Adverse Event Reporting System after hepatitis A and hepatitis AB vaccines in pregnant women. In their review, they did not identify any concerning pattern of adverse events in pregnant women or their infants following maternal Hep A or Hep AB immunizations during pregnancy.

Vellozzi et al., in the review "Guillain-Barre Syndrome, Influenza, and Influenza Vaccination: The Epidemiologic Evidence." Clin Infect Dis. 2014 Feb 5. [Epub ahead of print], descried evidence of a small increased risk of Guillain-Barré syndrome (GBS) that has been observed following influenza vaccines but 10-fold less than that observed following the1976 swine-influenza vaccine. The authors note that the risk of GBS following influenza is much greater than the small risk following vaccination.

In a study by Hibbs et al., "Notes from the field: rotavirus vaccine administration errors - United States, 2006-2013." MMWR (Morbidity and Mortality Weekly Report). 2014 Jan 31;63(4):81, CDC identified 39 reports of rotavirus vaccine administration by injection in VAERS and 27 reports of eye splashes. Administration errors are largely preventable with proper education and training. During discussion, Dr. Villarreal noted that the product itself is delivered for use in a syringe, albeit one that should be used as a spray – but a needle could be attached for injection. She suggested that the manufacturer should be made aware of the errors, since they could have resulted from confusing packaging.

Lastly, a study by Vellozi et al., "Cumulative Risk of Guillain-Barré Syndrome Among Vaccinated and Unvaccinated Populations During the 2009 H1N1 Influenza Pandemic." Am J Public Health. 2014 Feb 13. [Epub ahead of print], found that cumulative GBS risk was less among the pH1N1vaccinated than the unvaccinated population, suggesting the benefit of vaccination as it relates to GBS. The observed potential protective effect on GBS attributed to vaccination warrants further study.

Update on National Institute of Allergy and Infectious Diseases (NIAID) Vaccine Activities, Ms. Claire Schuster, NIAID

Ms. Schuster cited two studies with regard to immune response to vaccines. In Haralembeiva et al, which assessed immune response to rubella vaccine, subjects of African descent demonstrated higher antibody response than individuals of European descent and/or Hispanic ethnicity. In Furman et al, a study examining the immune response of 53 women and 34 men to seasonal influenza vaccine, the women produced antibodies that more effectively neutralized influenza virus. In the men, testosterone appeared to suppress immune response by altering the expression of specific genes. This study helps explain differences in male and female responses to vaccines, but more research is needed.

In a recent issue of the publication Vaccine, the World Health Organization and NIAID put out a call to accelerate vaccine research for sexually transmitted infections, particularly in the areas of herpes simplex virus, chlamydia, gonorrhea, trichomoniasis and syphilis.

Ms. Schuster then provided links to several NIH web resources including the NIAID Showcase that provides information on HIV, malaria, dengue, RSV and universal flu vaccine; NIAID's Antibacterial Resistance Program: Current Status and Future Directions; and the Accelerating Medicine Partnership, a collaboration between NIH, industry and nonprofits, an effort to increase new diagnostics and therapies. Finally, Ms. Schuster mentioned the Global Vaccine and Immunization Research Forum (March 4-6) sponsored by NIAID, WHO and the Bill and Melinda Gates Foundation.

Update on the Center for Biologics Evaluation and Research (CBER) Vaccine Activities Theresa Finn, Ph.D., CBER

Dr. Finn commented that at the last meeting the Commission had heard about four vaccines approved for H1N1 influenza. These vaccines are manufactured by CSL Limited, MedImmune, Novartis and Sanofi Pasteur. On November 10 the FDA approved an additional H1N1 vaccine for use in adults 18 years of age and over. This vaccine is manufactured by IDBiomedical (distributed by GlaxoSmithKline), the manufacturing process is the same as the Flulaval manufacturing process. On the same date the FDA approved Afluria, a seasonal flu vaccine manufactured by CSL, for use in children 6 months of age through 17 years of age (it had previously been approved for use in persons 18 and over). This approval also expands use of the H1N1 vaccine manufactured by CSL for use in children 6 months of age and older. Another seasonal flu vaccine, Agriflu, manufactured by Novartis, was approved for use in adults on November 27. Finally, on October 19, FDA approved the seasonal influenza vaccine Fluarix for use in children three years of age and older (also previously approved for adult use).

Dr. Finn reported that FDA had approved Cervarix on October 16 for use in females 10 through 25 years of age. It is a HPV vaccine manufactured by GlaxoSmithKline for prevention of cervical cancer. On the same day the FDA approved Gardasil for use in males 9 through 26 years of age for the prevention of genital warts caused by HPV 6 and 11.

Dr. Finn reported that a number of other vaccines are currently under review, including a meningococcal conjugate vaccine for prevention of disease caused by *Neisseria meningitides,* and a seasonal influenza vaccine. She noted that the VRBPAC meeting in November had discussed and made recommendations on the safety and effectiveness of Prevnar 13, a pneumococcal conjugate vaccine for use in infants and FluBlok, a recombinant seasonal influenza vaccine made in insect cells and manufactured by Protein Sciences.

Update from the National Vaccine Program Office, Dr. Steve Bende, NVPO

Dr. Bende reported on the NVAC meeting in February. The annual report of the NVPO described the contributions of the federal partners to achieve the National Vaccine Plan, which is approaching its mid-course review, which NVPO will coordinate. During the meeting the CDC provided an update on state immunization programs and an analysis of funding in those programs. There was a presentation on the Institute of Medicine's Strategic Multi-Attribute Ranking Tool (SMART) that allows a ranking of vaccines to assist policy makers in prioritizing vaccines for development. IOM will release a report in November on its utility and future use based on current testing with potential users.

NIAID sponsored the Global Vaccine and Immunization Research Forum, a venue to track progress on the vaccine R&D agenda. BARDA also presented opportunities on the R&D continuum in terms of emergency preparedness based on threat assessments, and identifying areas in the "valley of death" where opportunities exist but where product development success is hampered by lack of funding and other limitations.

CDC provided a historical overview of supply management, including the pediatric stockpile that was established in 1983 to prevent interruptions in supply. The current management of the stockpile relies on vendor-managed inventories, but CDC remains the distributor for some vaccines. The stockpile has been successful for managing short-term shortages.

An ongoing issue is adult immunization, and the NVAC heard a presentation on adult immunization coverage data. The NVAC Standards for Adult Immunization Practices lay out a list of actions for organizations involved in adult immunization to insure that everyone is assessed for immunizations at every health care encounter. The NVAC discussed plans to implement the standards. NVPO discussed its intention to present a national adult immunization plan, including drafting the National Adult Immunization Plan expected in August.

NVPO announced it was collaborating with others within the OASHto administer a grant, Mobilization for Health: National Prevention Partnership Awards, to increase community awareness and action on community health services, including immunizations.

The Vaccine Hesitancy Working Group is developing metrics to measure vaccine attitudes, and assessing methods of communications to encourage such acceptance. The Maternal Immunization Working Group will release an early draft report of its activities within a week or so. There was a report from the President's Cancer Panel on human papillomavirus

vaccine, in which there was an assertion that increased acceptance of HPV vaccine could be a very important opportunity to prevent cancer. The recommendations in the report include reducing missed clinical opportunities; increase acceptance of HPV by parents, caregivers and adolescents; and maximize access to the vaccine. The NVAC Working Group also presented a report in its activities. Finally there was a session on vaccine storage and handling practices.

During discussion, Mr. Kraus requested a future briefing on the FDA PRISM surveillance program.

Public Comment

Ms. Wrangham, who introduced herself earlier in the meeting, stated that the National Vaccine Information Center (NVIC) supports the extension of the statute of limitations, but noted that the original intent of the Act would allow alternative recourse to pursue damages for vaccine injuries. The NVIC does not support the extension of the statute of limitation if the result is that the VICP becomes the sole recourse for damages. The NVIC recommends that the ACCV also recommend additional strategies to reduce the number of dismissals.

Ms. Wrangham noted that the VIS is shorter today and that information is limited and that the risk of death is not optional information and should appear on the VIS. Consumers should have complete information even if the information results in the consumer declining vaccination. The NVIC supports a recommendation that came from a parent consultation held by CDC that the VIS should be distributed well in advance of the vaccination, and not in the moments just prior to vaccination. There should also be information that there are other sources of vaccine safety information available.

The NVIC recommends that all VIS's introduce a different message than "Why get vaccinated?" That appears to be a policy statement. There must be an acknowledgment that vaccines do not always work. The risk statement should reflect the injuries in the Vaccine Injury Table. There should also be a clear description of the disease for which the vaccine is recommended.

Regarding the legal requirement to report adverse events to VAERS, it should be supplemented by information that helps individuals report adverse events beyond the minimum legal requirements. The VIS should identify the existence of the manufacturer's product insert, which should be mentioned in section 7. It should also clearly provide the information about how to file an injury claim and the length of time available to do so.

New Agenda Items/New Business

Mr. King noted that a discussion of replacement members was not appropriate since the Commission does not nominate or approve new Commission members. Dr. Caserta noted that the list of nominations has not been finalized, but there are several names being considered. Concerning the chair and vice chair, Mr. Kraus made a motion that the current leadership remain in place through the next two meetings. The motion was unanimously approved.

Adjournment

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