Advisory Commission on Childhood Vaccines (ACCV)

Minutes

June 4, 2015

96th Meeting

Members Present

Kirsten Feemster, M.D., M.P.H., M.S.H.P. ('15)
Charlene Douglas, Ph.D. ('15)
Edward Kraus, J.D. ('15)
Ann Linguiti Pron, DNP, CRNP, RN ('15)
Luisita dela Rosa, Ph.D. ('15)
Jason Smith, J.D. ('14)
David King ('15)

Division of Injury Compensation Programs (DICP)

A. Melissa Houston, M.D., Director, DICP
Andrea Herzog, Staff Liaison

Welcome, Report of the Chair, Dr. Kristen Feemster, ACCV Chair

Dr. Feemster called the 96th meeting of the ACCV to order and, after roll call introductions, briefly reviewed the agenda. Dr. Feemster noted that Commission members Sylvia Villarreal and Michelle Williams would not be attending the meeting. She also noted that Dr. Shimabukuro submitted an updated presentation that was sent to Commission members before the meeting. The Department of Justice presentation would be made by Ms. Catharine Reeves (Mr. Vince Matanoski was not able to attend). In addition to the usual reports, the agenda included a welcome from Mr. James Macrae, the Acting Administrator of HRSA; and discussion of several action items from the last meeting – recommendations related to vaccine administration, including Shoulder Injury Related to Vaccine Administration (SIRVA), and a discussion of an increase in funding for the National Vaccine Injury Compensation Program to support a more efficient claims process.

Public Comment on Agenda Items

Dr. Feemster invited public comment on the agenda. Theresa Wrangham, National Vaccine Information Center, commented that the information on the ACCV and VICP web sites should be kept current, not only for ACCV members but for the public as well. She noted that the statistical information on awards was not up to date.

There were no other requests for comment

Approval of March 2015 minutes

Dr. Feemster invited approval of the March 2015 meeting minutes. On motion duly made by Mr. King and seconded by Mr. Smith, the minutes were unanimously approved.

Dr. Feemster invited the report from the Division of Injury Compensation Programs (DICP).

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

Dr. Houston welcomed those present on the teleconference and briefly reviewed the meeting agenda. The agenda includes an update from the Department of Justice (DOJ), a presentation on SIRVA, a review of Vaccine Information Statements, and finally updates from the ex officio members from the Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH) and the National Vaccine Program Office (NVPO). A previously scheduled report by the Adult Immunization Workgroup will be postponed until the next ACCV meeting. Dr. Houston added that data on the DICP web site is current, posted as of June 1, 2015. The statistics discussed at this meeting are current as of May 4, 2015.

Looking at petitions and adjudications, Dr. Houston stated, as of May 4, 2015, the Division had received 401 petitions and the projection, based on that number is about 700 petitions may be filed before the end of this fiscal year. The total adjudications for the current report period is 317, which projects to about 543 claims to be adjudicated in Fiscal Year (FY) 2015, more than the previous fiscal year. About 81% are anticipated to be compensated with 19% being dismissed. There have been awards of $146.5 million to petitioners, and about $12 million to petitioners' for attorney's fees and costs. It is anticipated that the totals for FY 2015 will be $250 million for petitioners' and $20 million for attorney's fees and costs. The Trust Fund stands at $3.5 billion as of March 31, 2015. Of the $127 million net income to the Trust Fund, $96 million came from tax revenue and $31 million from interest on the Trust Fund.

Dr. Houston stated that there were several activities since the last ACCV meeting. The VICP regulations, which include changes to the Vaccine Injury Table, are going through final review and clearance. The nominations for incoming ACCV commissioners have been approved and will be released when those nominees have submitted formal acceptance. The National Vaccine Advisory Committee (NVAC) will meet in Washington, DC, on June 9-10, 2015 and the Advisory Committee on Immunization Practices (ACIP) will meet in Atlanta on June 24-25, 2015.

Dr. Houston provided information for obtaining additional information on the web about the DICP and the ACCV. Dr. Houston invited discussion.

Mr. King asked about the status of nominations for new commission members and Dr. Houston indicated that three nominees have been approved. A second solicitation has been published in the Federal Register and responses are pending. She indicated that the new

members are expected to begin their terms in time for the September meeting. If that occurs, current commissioners whose terms have expired and have been extended would not participate in the September meeting. The retiring commissioners are Mr. King, Ms. Williams and Dr. Pron.

Discussion of Program Funding, Dr. Kristen Feemster, Chair

Dr. Feemster noted that this topic was discussed at the last meeting. It involves the allocation of funds to support the program and the possibility of increasing funding. She suggested that the initial discussion might look at next steps and the possibility of setting up a working group to develop a more detailed plan. Mr. King observed that it might be appropriate to wait until the three new commissioners are on board before making those decisions, since there are commissioners absent who might be interested in contributing comments. Dr. Feemster agreed, inviting consensus from those present to defer the discussion until the September meeting. There were no objections and Dr. Feemster stated that the discussion would be added to the September meeting agenda. The new commissioners, if any are on board at that time, would be appropriately briefed beforehand in order to participate in the discussion.

Report from the Department of Justice, Ms. Catharine Reeves Assistant Director, Torts Branch

Ms. Reeves explained that Vince Matanoski, who usually provides DOJ's report to the Commission, is on temporary military duty in the Democratic Republic of the Congo. Ms. Reeves referenced the Department of Justice Power Point materials (DOJ PP), as part of her presentation for the reporting period February 16, 2015 - May 15, 2015. During this reporting period, 178 petitions were filed. (DOJ PP at 2). This is 54 more petitions than the same period in FY 2014, and 24 more petitions than the immediate past reporting period (November 16, 2014 – February 15, 2015). Of the 178 petitions, 30 were filed on behalf of minors and 148 petitions were filed by adults. Ms. Reeves predicted that approximately 800 petitions will be filed for FY 2015. There were 163 adjudications, 21 more than the last reporting period (November 16, 2014 – February 15, 2015). (DOJ PP at 3). Of those, 136 were compensated, with 32 cases conceded by HHS resolved by a decision adopting a proffer. There were 104 cases resolved that were not conceded. Of those, 103 were settled followed by a decision adopting a stipulation, and one case was resolved by a decision adopting a proffer. There were 27 cases not compensated/dismissed. Of those, 23 were resolved by decisions dismissing claims. These were non-Omnibus Autism Proceeding (OAP) claims. There were 4 petitions dismissed from the OAP. (DOJ PP at 3). There were 8 petitions voluntarily withdrawn. (DOJ PP at 4).

Turning to appeals, three cases were decided by the Court of Appeals for the Federal Circuit (CAFC) (DOJ PP 5). Two appeals were filed by petitioners, *Simanski v. HHS* and *Griffin v. HHS*, and in both, the special masters' decisions were affirmed by the CAFC. In *Simanski*, the CAFC affirmed the special master's decision denying entitlement. As Ms. Reeves noted, *Simanksi* has been discussed at prior meetings, and has a lengthy procedural history. In *Griffin*, which involved a discrete legal issue about whether or not petitioner satisfied statutory requirements, the CAFC affirmed the special master's finding that a federal contractor working in Afghanistan was not eligible to receive compensation under the Act.

Griffin was decided *per curiam*, likely because the Court views the issue addressed in its decision as relatively non- controversial and therefore unlikely to come up again. In *Paluck v. HHS*, another case with a lengthy procedural history that has been discussed at prior ACCV meetings, the CAFC, on appeal by respondent, affirmed the decision by the Court of Federal Claims (CFC) that the special master was arbitrary and capricious in weighing evidence in the case; and, therefore, petitioner was entitled to compensation under the Act. Turning to pending CAFC appeals, petitioners filed two new ones. (DOJ PP at 6). In *Greenberg v. HHS*, petitioners appealed the CFC's affirmance of the special master's dismissal on entitlement and denial of a motion for reconsideration based on untimely filing. In *Moriarty v. HHS*, an OAP case that was stayed for seven years pending the outcome of the OAP, petitioners appealed the CFC's affirmance of the special master's decision dismissing petitioners' claim that their child's injuries were vaccine- related based on a different theory from that relied upon in the OAP litigation.

Turning to the CFC, Ms. Reeves reported that four cases were recently decided by the CFC. (DOJ PP at 7). In *Guerrero v. HHS*, a case involving attorneys' fees and costs, the CFC remanded the claim to the special master to re-evaluate his reduction of attorneys' fees and provide a more detailed explanation for his decision. In *Somosot v. HHS*, the CFC affirmed the special master's decision denying attorneys' fees and costs as the petition, filed untimely, lacked good faith and a reasonable basis. In *Contreras v. HHS*, this was discussed at the last ACCV
meeting, the CFC affirmed the original decision by the special master denying entitlement, after a second remand. In *Milik v. HHS*, the Chief Judge of the CFC affirmed the special master's decision denying entitlement based on evidence that the onset of petitioner's injury preceded vaccination and petitioner failed to prove significant aggravation of a preexisting condition under *Althen*.

There were five new motions for review filed at the CFC, all filed by petitioners. . (DOJ PP at 8). In *Nuttall v. HHS*, the special master denied petitioners' claim that the MMR vaccine caused a Table injury, finding respondent's expert more persuasive with regard to a diagnosis. In *McLeod-Hunt v. HHS*, the special master denied petitioner's claim that vaccines significantly aggravated a child's preexisting condition, finding respondent's expert more convincing in establishing that the injuries began too early to be vaccine-related. In *Mora v. HHS*, the special master denied petitioner's motion for relief from judgment, finding petitioner's counsel's negligence insufficient to demonstrate extraordinary circumstances sufficient to set aside the judgment. In *Hodge v. HHS*, the special master dismissed petitioner's claim as untimely, and determined that petitioner was not entitled to equitable tolling. In *Padmanabhan v. HHS*, the special master dismissed petitioner's case for lack of prosecution after petitioner ignored multiple court orders. Ms. Reeves noted that oral arguments were scheduled at the CAFC for *Stillwell v HHS*, on June 4, 2015, and *Crutchfield v. HHS*, on June 5, 2015. No arguments were scheduled in the CFC. (DOJ PP at 9).

Consistent with the DOJ's past practice of providing information about settlement timelines, Ms. Reeves discussed the compilation of adjudicated settlements reflected by decisions adopting stipulations. (DOJ PP at 10-20). This reporting period reflected 103 cases

resolved by stipulations. Ms. Reeves noted the Appendix containing the glossary of terms and flow charts for the appeals processes. (DOJ PP at 21-27).

Dr. Pron submitted a question via e-mail noting that within adjudicated settlements, a case involving a hepatitis B vaccine apparently took 15 years to settle. She asked about the reasons for the duration. Ms. Reeves responded that the case was filed on July 13, 1999 (at about the same time a large number of similar hepatitis B vaccine claims were filed); the claim eventually became part of the OAP, and was stayed at the petitioner's request until November 23, 2011. At that time, the petition was amended by the petitioner, processed in the usual course, and eventually a settlement was reached.

Dr. Feemster, noting the fact that the meeting was ahead of schedule, suggested that the SIRVA presentation be moved up on the agenda. Because of an unanticipated issue with construction noise at Parklawn, a recess was taken to move the conference call to a more suitable room. Upon reassembling for the call, an issue arose concerning assuring that a quorum was always present at the meeting, a quorum being required to conduct any ACCV meeting. After discussion, Ms. Herzog agreed to investigate whether or not the conference call contractor could maintain a running and continuously updated list of members on the phone, which would provide the assurance that a quorum was properly maintained. Dr. Feemster confirmed that a quorum was present so that the presentation on SIRVA could occur.

Feasibility of SIRVA Prevention, Dr. Terry Dalle-Tezze, Pediatrics Team Lead, DICP

Noting that SIRVA stands for Shoulder Injury Related to Vaccine Administration, Dr. Dalle-Tezze explained that the presentation would look at whether SIRVA could be prevented as an adverse event related to vaccination. In one study, two subjects who experienced shoulder injury within two days of injection were examined using ultrasound to map the anatomy of the shoulder and it was determined that the bursa which underlies the upper third of the deltoid muscle (into which the vaccine was injected using needles 1" to 1.5" in length) was vulnerable to damage. Therefore, the investigators recommended injection into the lower two-thirds of the deltoid muscle.

In a second study by Lippert et al in Pediatrics in 2008, in pediatric subjects, it was determined that using the recommended needle length for injection resulted in a risk of 11% to 61% needle penetration beyond the margins of the deltoid muscle, which could cause injury. In a third study in Britain in 1962, antigen (fibrin) was injected into joint space, with a likelihood that inflammation would occur.

Dr. Dalle-Tezze stated that at the time of the Bodor paper, clinicians at DICP noticed an increase in shoulder-related problems following vaccination, and a study led by Drs. Sarah Atanosoff, Thomas Ryan and Rosemary Johann–Liang, looked at 13 injury claims that occurred between 2006 and 2010, which resulted in significant shoulder pain and dysfunction. All 13 subjects, mostly females, filed program claims for shoulder pain, the onset of which occurred in less than 24 hours in 12 of the 13 subjects (in half of them the pain occurred immediately after injection). About half of the patients suggested that the injection location was too high on the arm. Symptoms included pain and decreased range of motion. The investigators confirmed that

the injury was confined to the vaccinated shoulder, and symptoms were consistent with a local inflammatory shoulder injury. Finally, the investigators agreed that the injection could unintentionally reach and injure musculoskeletal structures outside the deltoid muscle, and that the injection site should be confined to the lower two-thirds of the deltoid muscle, preferably administered to a patient in a seated position.

Dr. Dalle-Tezze stated that, based on this evidence and the findings of the DICP study, a recommendation was made to include SIRVA as an injury on the Vaccine Injury Table. He noted that, since 2011, 136 claims have been adjudicated for SIRVA, with settlements totaling $22.7 million. The proposed criteria for inclusion in the Vaccine Injury Table include: 1) No prior history of pain or dysfunction of the affected shoulder; 2) pain occurs within 48 hours of vaccination; 3) pain and reduced range of motion are limited to the shoulder in which the vaccine was injected; and 4) no other conditions or abnormality is present that could explain the symptoms.

In the past, Dr. Dalle-Tezze noted that vaccines were administered by trained medical personnel (physicians, nurses, nurse assistants, medical assistants) who were certified under state board criteria (although there has been no certification specifically for injecting vaccines or other medicines). The skill was acquired through normal school instruction and on-the-job training.

In the Healthy People 2010 report published in 2000, it was noted that the elderly and those in lower income situations were not being vaccinated at the desired 90% level set in the report. Reasons were related to patient attitudes and awareness, misunderstanding about risks of vaccines, and clinic-related issues such as inadequate staffing and service hours. In 1993 DHHS Secretary Donna Shalala challenged the American Pharmacists Association (APhA) to develop a program to train pharmacists to deliver vaccinations, and in 1996 the APhA called on pharmacists to take on one or more of three roles: advocate, facilitator, and immunizer. Answering that call, pharmacists initially focused on flu shots and pneumococcal immunizations. The program significantly expanded during the 2009 H1N1 flu pandemic.

Dr. Dalle-Tezze noted that today over 200,000 pharmacists in every state and U.S. territory are trained and licensed to provide vaccinations. Individual states set standards for that licensure. A gauge of the program's success can be seen in the 5% rate of vaccines given by pharmacists in 1999 versus the 18% administered by pharmacists in 2010-2011. In 2012 a survey showed that 20% of adults received vaccinations in pharmacies and 33% in doctors' offices. One effect of this program has been a notable increase in vaccinations given to the elderly (over 65 years of age). The CDC has issued guidelines regarding vaccine injection techniques that include the angle of injection into the deltoid muscle (90 degrees), and needle length depending on the age of the recipient. The American Academy of Pediatrics (AAP) and the APhA also published statements related to injection technique, with similar recommendations.

Dr. Dalle-Tezze suggested several recommendations to enhance the prevention of SIRVA:

- Universal certification for all vaccine administrators.

- Inclusion of SIRVA as a subject in all health care education programs (nursing, medical assistant, pharmacy).
- Alternative vaccination routes to avoid the problems related to deltoid muscle injection.

Dr. Dalle-Tezze discussed the pros and cons of each recommendation, noting that each has both positive and negative aspects. He mentioned that the CDC has a Vaccination Error Stakeholders Focus Group that includes partnerships with most major national health organizations. The Focus Group includes a SIRVA subgroup. Dr. Dalle-Tezze recommended updating all germane guidelines to include SIRVA, including needle size, position of administrator and recipient, and injection site. Finally, he suggested that DICP could work with nursing schools to develop guidelines, and join the CDC Vaccination Errors Stakeholders Focus Group as an active partner

Dr. Feemster expressed appreciation for a very thorough presentation. She invited discussion. Mr. King suggested that a brief comment might be included on vaccine information statements for vaccines that are injected into the shoulder area. It might even include a brief summary of the three guidelines – injection angle, standing/sitting position and needle length. Dr. Shimabukuro commented that, although a universal certification is an interesting idea, it may be difficult to justify a certification process only for injections and not for many other similar invasive procedures, such as inserting an IV line or a central line. Also, based on the passive reporting in the Vaccine Adverse Event Reporting System (VAERS), a valid risk level for a shoulder injection has not been determined, and it would be helpful to have a more valid evidence-based risk assessment. Mr. Kraus agreed that it would be helpful to have a more definitive quantitatively-based risk assessment of SIRVA injuries. Nonetheless he felt it was clear that SIRVA injuries are a part of the vaccination environment, and that many individuals may be unaware of the connection between their shoulder pain and a recent flu shot. He suggested that, since the issue is so complex, that a discussion of the SIRVA presentation be included on the agenda of the next ACCV meeting in September. Dr. Feemster agreed that it was an appropriate suggestion, and the agenda would include a discussion of SIRVA.

The Commission recessed for lunch.

Welcome Mr. James Macrae, Acting Administrator, HRSA

Mr. Macrae expressed how important the work of the ACCV was to HRSA in helping to identify what is working, what improvements can be made, and what actions would be appropriate. He felt advice on childhood vaccines was very important. He also solicited suggestions about what could be done to better support the ACCV, including one suggestion he had heard about trying to have more in-person meetings. He said there had been concrete accomplishments, including inclusion of information about the program in the vaccine injury statements, and useful proposals concerning improvements to the Vaccine Injury Table. Aware of the Commission's interest in how the recommendation process works, he stated that he would make every attempt to provide that kind of elucidation. He stated that he was aware of the recommendations made by the ACCV. An initial acknowledgment of the recommendations and the work done by the Commission is made, and then there are internal discussions with the

Secretary. He stated that the transition from Secretary Sebelius to Secretary Burwell may have caused some delays, but Secretary Burwell is interested in responding to the recommendations. The Secretary is very involved with maternal immunizations, although there have been no final actions taken to date.

Mr. McCrae commented that the Secretary is interested in focusing on the science related to the issues, and providing substantive data on the science is helpful. He invited questions or recommendation from the Commission. Mr. King reiterated his interest in the benefits of face-to-face meetings. He noted that the frequency of face-to-face meetings was more like once a year, or three virtual meetings to one face-to-face meeting. Mr. Kraus supported Mr. King's recommendation, noting that he was speaking for the Commission as a whole. He also expressed appreciation that the Secretary was apparently interested in responding to the Commission's concerns. Dr. Feemster expressed the Commission's appreciation for Mr. Macrae's appearance at the meeting and the positive comments that he made.

Review of Vaccine Information Statements (VIS), Mr. Skip Wolf CDC

Dr. Feemster stated that the review of VIS's would include meningococcal serotypes A, B, C, W and Y; and the MMR vaccine.

Mr. Smith recused himself from discussion regarding the meningococcal serotypes A, B, C, W and Y VIS. Dr. Pron stated that she would recuse herself from review of the MMR VIS. She added that she would be interested in discussing all intramuscular injections given in the arm. Dr. Feemster suggested that the Commission review each VIS and then, at the end of the discussion, turn to the previous discussion about the SIRVA injections issue.

VIS for Meningococcal Vaccine (Serogroups ACWY)

Mr. Wolfe stated that he would highlight the recommended changes to each VIS. He noted that the two meningococcal VISs had been harmonized as much as possible. In response to a question about the statement that serotypes A, B, C, W and Y might suggest that the vaccine does not cover serotype B, Mr. Wolfe agreed that the statement at the bottom of the paragraph (that B is covered under a separate VIS) would be moved into juxtaposition with the statement about A, B, C, W and Y.

In paragraph 2, Mr. Wolfe stated that the subject matter experts recommended revising the recommendation for immunizing lab personnel to read "microbiologists, who routinely work with isolates of N. meningitis," which would be the same for both VISs. Dr. Douglas commented that the phrase would be too technical for most readers of the VIS and that CDC should consider whether or not such language is counterproductive to the purpose of the document. Noting that the VIS is for individuals who are imminently anticipating vaccination, Mr. Wolfe suggested that he refer it back to the subject matter experts. Dr. Shimabukuro suggested reordering the list to place those who most commonly receive the vaccine at the top of the list and others, like lab personnel and military recruits, at the bottom.

In paragraph 3, Dr. Houston asked whether the use of generic language concerning allergens versus a more specific list had been discussed. Mr. Wolfe stated common allergen that apply to any vaccine are usually listed (e.g., egg, yeast) and that he would check to make sure the common allergens did not apply to this vaccine. Dr. Feemster asked about the use of MCV4 in pregnant women, and the statement that "it should be used only if clearly indicated" might be confusing. Mr. Wolfe responded that the wording was taken from the Advisory Commission on Immunization Practices (ACIP) recommendation and the drug labeling, and its use in pregnant women would probably be at the direction of a qualified health care provider. Mr. Wolfe asked for better wording for the term "working spleen" in the last sentence of the paragraph. Dr. Shimabukuro suggested "children with a damaged spleen or whose spleen has been removed."

In paragraph 4, Mr. Wolfe commented that the vaccine reactions are typical of most vaccinations. He also pointed out that the statistic concerning severe allergic reactions (such as anaphylaxis) was changed from "one in a million" to "about one in a million." That change would be made in all VISs.

Mr. Wolfe stated that the last three paragraphs were not changed.

VIS for Meningococcal Vaccine (Serogroup B)

Mr. Wolfe stated that the Serotype B VIS was very similar to the VIS for serotypes A, C, W and Y, and that all of the revisions made for the latter would be made in the serotype B VIS. He added that language, such as the words for a damaged or missing spleen, would be made in all applicable VISs. He noted that the addition of a schedule in paragraph 2 was made to avoid having to develop more than one VIS for the B serotype, since there is more than one generic vaccine available. He invited comments and there were no suggestions for further revisions.

VIS for MMR Vaccine (Measles, Mumps, Rubella)

Mr. Wolfe noted that this is the last review of an interim VIS before it becomes final. He invited discussion of paragraph 1. Ms. dela Rosa suggested that cerebral meningitis would be a more specific description for meningitis that affects the brain. Dr. Feemster commented that meningitis is generally considered by the medical community to be a general term for infection or inflammation of the central nervous system, which would include the brain and spinal column. Dr. Feemster noted that inflammation is more accurate than infection. Ms. dela Rosa also asked if seizures should be included under the bullet point for mumps. She added that her daughter had an intractable seizure disorder that arose from a mumps infection. Mr. Wolfe agreed to check with medical experts on that issue.

Dr. Shimabukuro suggested revising the mode of spreading the disease by using the words "coughing and sneezing" as being more specific and appropriately descriptive. Dr. Feemster agreed, noting that droplets can remain in the air. Dr. Shimabukuro suggested "measles can spread from person to person through coughing or sneezing and by direct contact."

Mr. Kraus asked for a brief explanation of the rationale for administering the three vaccines in one injection. Dr. Wolfe said that he would look into it, and that it would probably

fit best in paragraph 2. However, it was noted that there was more than one such combination vaccine. Dr. Shimabukuro suggested that a generic explanation might be appropriate since there are several combination vaccines (DTaP and others), where typically minimal risks involved, and the reasons for the combination is usually programmatic efficiency and reduction of needle sticks. Mr. Wolfe agreed, stating that if there are higher risks (as in MMR plus varicella), the risks can be covered in the VIS.

Asked about the last two sentences in paragraph 1 concerning the effect of reduced vaccination rates, there was agreement that incidents of infection would rise if vaccinations decreased. However, there was consensus that the word "but" should be deleted from the last sentence. There was also a suggestion that wording could be added to indicate the extent of the return of measles if vaccinations were reduced (e.g., to former levels before universal vaccinations).

Mr. Wolfe noted there were no comments on paragraphs 2 and 3. In paragraph 4, there was a brief discussion about severe problems following MMR vaccines and possible severe problems that might be related (deafness, neurological problems, brain damage), and the difficulty of establishing a link to the vaccine. Dr. Shimabukuro recommended wording previously proposed by Mr. Kraus – because these happen so rarely it is difficult to determine with certainty whether they were caused by the vaccine or not. Mr. Wolfe agreed to adapt that language to the VIS.

Mr. Wolfe noted that paragraphs 5, 6 and 7 were the same as other VISs. Dr. Feemster asked Mr. King to discuss the earlier comment about including some kind of information about SIRVA in any VIS that involves a shoulder injection. Mr. King commented that such information would enhance awareness of the risks related to shoulder injections that sometimes result in SIRVA. He suggested that it might reinforce to providers the importance of following guidelines when administering such injections. Mr. Wolfe responded with a concern that the focus of the VIS is about patient information and not providing education to providers. He was also concerned about whether a patient could comfortably instruct a doctor on how to administer an injection. Finally, he noted that provider guidelines are prepared for many VISs and all new VISs are available to providers on the same web site as the patient vaccine information sheets. Mr. Kraus agreed that the VIS might not be the best vehicle for educating providers and that provider guidance would be more appropriate. Ms. Smith agreed with that opinion.

Dr. Feemster invited further discussion and hearing none, moved onto the presentations by ex officio members.

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

ISO continues to work with the Food and Drug Administration (FDA) to prepare for implementation of manufacturer reporting to the Vaccine Adverse Event Reporting System (VAERS) using the E2B(R3) message standard. Implementation is scheduled for June 10, 2015.

ISO will present a 2014-15 end-of-season analysis of influenza vaccine safety at the June 2015 ACIP meeting on June 24, 2015. At the ACIP meeting there will also be a session on meningococcal vaccines, including a discussion of policy options for routine use of meningococcal group B (MenB) vaccines in adolescents, a GRADE presentation on evidence for use of MenB vaccine in adolescents and college students, considerations for routine use of MenB vaccines in adolescents, and a vote on proposed recommendations. The influenza session will include an influenza surveillance update, an influenza vaccine safety update, a high dose influenza vaccine update and a vote on proposed recommendations. The influenza A (H5N1) session will include an influenza A (H5N1) epidemiology update and a vote on proposed recommendations. The pertussis session there will include be a discussion on cocooning and diphtheria, tetanus and acellular pertussis (DTaP) vaccination, and acellular pertussis vaccine effectiveness among children in the setting of pertactin-deficient B. pertussis in Vermont, 2011-2013. The pneumococcal vaccines session will include a discussion on intervals between 13-valent pneumococcal conjugate (PCV13) and 23-valent pneumococcal polysaccharide (PPSV23) vaccines, and supporting evidence and rationale for change, and a vote on proposed recommendations. Finally in the herpes zoster session there will be an update on herpes zoster epidemiology and vaccine uptake, and a presentation of the results of GSK Phase 3 study of an investigational adjuvant-based zoster vaccine.

Dr. Shimabukuro mentioned several recent publications:

- Petrosky et al; Centers for Disease Control and Prevention (CDC). Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the advisory committee on immunization practices. MMWR Morb Mortal Wkly Rep. 2015 Mar 27;64(11):300-4.

- Iqbal et al. Relationship between Guillain-Barré syndrome, influenza-related hospitalizations, and influenza vaccine coverage. Vaccine. 2015 Apr 21;33(17):2045-9. The main findings were that pneumonia and influenza hospitalization rates were significantly correlated with hospitalization rates for Guillain-Barré syndrome, and vaccine coverage did not significantly affect the rates of Guillain-Barré syndrome hospitalization at the population level.

- McNamara et al. First Use of a Serogroup B Meningococcal Vaccine in the US in Response to a University Outbreak. Pediatrics. 2015 May;135(5):798-804. The main findings were that no serogroup B meningococcal disease cases occurred in persons who received 1 or more doses of 4CMenB vaccine, suggesting 4CMenB may have protected vaccinated individuals from disease. However, a case occurred in an unvaccinated close contact of a vaccinated university student demonstrating that carriage of serogroup B Neisseria meningitidis among vaccinated persons was not eliminated.

- Datwani et al. Chorioamnionitis following vaccination in the Vaccine Adverse Event Reporting System. Vaccine. 2015 May 11. [Epub ahead of print]. The main findings were that chorioamnionitis was found to be uncommonly reported, representing 1% of pregnancy reports to VAERS; a majority of reports had at least one risk factor for chorioamnionitis.

- Hibbs et al. Vaccination errors reported to the vaccine adverse event reporting system, United States, 2000–2013. Vaccine (2015), http://dx.doi.org/10.1016/j.vaccine.2015.05.006. The main findings were that vaccination error reports to VAERS have increased substantially from 2000-2013 and contributing factors might include changes in reporting practices, increasing complexity of the immunization schedule, availability of products with similar sounding names or acronyms, and increased attention to storage and temperature lapses.

- Miller et al. Deaths following vaccination: What does the evidence show? Vaccine. 2015 May 21. [Epub ahead of print]. This article reviewed the data on deaths following vaccination and reported that vaccines are rigorously tested and monitored and are among the safest medical products we use. Millions of vaccinations are administered to children and adults in the United States each year. Serious adverse reactions are uncommon and deaths caused by vaccines are very rare. Rare cases where a known or plausible theoretical risk of death following vaccination exists include anaphylaxis, vaccine-strain systemic infection after administration of live vaccines to severely immunocompromised persons, intussusception after rotavirus vaccine, Guillain-Barré syndrome after inactivated influenza vaccine, fall-related injuries associated with syncope after vaccination, yellow fever vaccine-associated viscerotropic disease or associated neurologic disease, serious complications from smallpox vaccine including eczema vaccinatum, progressive vaccinia, postvaccinal encephalitis, myocarditis, and dilated cardiomyopathy, and vaccine-associated paralytic poliomyelitis from oral poliovirus vaccine. The evidence for the safety and effectiveness of vaccines routinely given to children and adults in the Unites States is overwhelmingly favorable.

During discussion, Dr. Douglas asked about the age recommendations for children receiving HPV, suggesting that if the ACIP age is 11 it would be helpful to lower it further to 10 or even 9 to harmonize with DTaP immunizations. Dr. Feemster stated that the ACIP recommendation is age 12, but allows vaccination at age 9.

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

Ms. Schuster reported that a trial of the VSV-ZEBOV Ebola vaccine candidate has shown safety with strong antibody response in 40 study participants. The trial was conducted at NIH and the Walter Reed Army Institute of Research. The Phase I PREVAIL trial conducted in Liberia looked at the VSV-ZEBOV and cAd3-EBOZ Ebola vaccine candidates. The preliminary findings suggest vaccine safety in more than 600 subjects. The Phase II portion of the PREVAIL trial reached its enrollment target of 1,500 participants in May 2015.

Ms. Schuster noted that there is no commercially available human vaccine for West Nile virus. Investigators at Oregon Health and Science University have developed a peroxide-based platform that demonstrates the ability of hydrogen peroxide to inactivate the virus while maintaining key structures that trigger the immune system. A Phase I trial, supported by NIAID, is under way at Duke University.

As part of President Obama's Precision Medicine Initiative, there is a plan to establish a million-person cohort of individuals who will share biological, environment and lifestyle data. A group of experts has been convened to advance this study. The first preliminary report is planned for September 2015.

Finally, Ms. Schuster announced that the National Institute of Child Health and Human Development (NICHD) launched a Pinterest site containing information on NICHD research and educational resources. The web address is https://pinterest.com/NICHD_NIH.

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

LCDR Marshall reported that on March 24, 2015 the FDA approved the use of a single dose of Quadracel for children 4 through 6 years of age as the fifth and final vaccine in the DTaP series; and as a fourth and fifth dose in the inactivated poliovirus (IPV) series, in children who have received four doses of Pentacel and/or DAPTACEL vaccine. The vaccine is indicated for active immunization against diphtheria, tetanus, pertussis and poliomyelitis.

On April 30, the FDA approved a supplement for Fluzone, Fluzone High Dose, Fluzone Intradermal, and Fluzone Quadrivalent vaccines, to update the package insert to include efficacy data for children 6 to 24 months and for adults 18 to 49 years of age.

Earlier in April, FDA approved a BLA Supplement for human papillomavirus quadrivalent vaccine, recombinant (Gardasil), adding a new subsection, "Long-term follow-up studies" to the clinical studies section of the package insert.

LCDR Marshall mentioned two meetings, the Vaccines and Related Biological Products Advisory Committee (VRBPAC) met on May 12, 2015 to discuss the development and licensure of Ebola vaccines. On June 1-2, 2015 the FDA participated in a Respiratory Syncytial Virus (RSV) Vaccine Workshop. The purpose of the workshop was to identify obstacles to RSV vaccine development, discuss approaches to alleviating them, and identify gaps in research that could be addressed to enable vaccine development.

Finally, LCDR Marshall noted the continued activity among federal partners, the medical and scientific community, industry, and international organizations and regulators to assess investigational products and provide regulatory pathways that may expedite the development and availability of Ebola products.

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

Dr. Bok reported that the Cooperative Agreement on Research, Monitoring and Outcomes Definitions for Vaccine Safety had received eight applications from a solicitation published in April, 2015. After selection, two one-year awards of $250,000 each will be made.

The SMART Vaccines (Strategic Multi-Attribute Ranking Tool for Vaccines) is being moved to the NVPO. The new software will; provision the capabilities to transform the existing SMART Vaccines tool to a web-based platform that can be supported and sustained for public access; include iterative adaptation and refinement of the tool; expand and update of the data warehouse and standardized formats for data sharing; disseminate and use the tool supported by direct engagement and training of the public sector, academic, and private sector stakeholders and decision-makers associated with vaccine development, purchasing, and deployment/implementation programs; safety profile; and host the tool that is sustainable and provides global access to the tool by embedding it an infrastructure that utilizes existing resources for maintenance of standards and capabilities

Public Comment

Theresa Wrangham, Executive Director of the National Vaccine Information Center (NVIC), focused her comments on the need for greater transparency in sharing the data related to the VICP. She referenced a piece by Sharyl Attkisson, entitled "Government Wipes Recent Vaccine Data from Website," that indicated that the website has changed since February 2015. The current information was truncated to 2013. Ms. Wrangham expressed concern about what changed since February to cause the deletion of data. She noted that NVIC first raised the issue of transparency in 2012. She stated that the information should include what injuries were reported, the vaccines involved, in total and by year, and the number of cases dismissed because of the statute of limitations of the Act. During the September 2014 ACCV meeting the DICP indicated that the Division had appropriately and sufficiently informed the public. New information has been added to the data and statistics report, such as doses of vaccines distributed versus the number of compensation claims made. The report does not include reports to VAERS or discuss the contention that a majority of vaccine injuries are unreported.

Information to which the public should have access is not easy to obtain, requiring visits to a number of web sites to collect raw data and piece it together. The NVIC encourages the ACCV to consider recommendations to report information authorized by law and to provide a higher level of transparency. The NVIC also recommends that the ACCV meet face to face as do the other vaccine-related FACA committees. The NVIC commends the Commission for the SIRVA report, and endorses the proposal for a universal certification for those who administer injections.

With regard to the VIS discussion, Ms. Wrangham expressed concern when the phrase recommends use "when clearly necessary," when the vaccines have not been licensed for the purpose described (e.g., in pregnant women).

Ms. Wrangham expressed appreciation for being able to comment.

Dr. Feemster noted there were no additional public comment requests.

Future Agenda Items

Dr. Feemster noted two items for inclusion in the next meeting agenda: discussion of funding opportunities; and continuation of the SIRVA prevention discussion.

Drs. Houston and Feemster expressed appreciation to Mr. King, Dr. Pron and Ms. Williams for their dedicated service and for their willingness to extend their terms to accommodate the process for selecting replacement commissioners.

Adjournment

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