Advisory Commission on Childhood Vaccines

March 8, 2018

105th Meeting

Members Present

Karlen E. (Beth) Luthy, D.N.P., Chair ('18)
H. Cody Meissner, MD, Vice Chair ('19)
Kathleen F. Gaffney, PhD, RN ('19)
John Howie, J.D., ('19)
Dino S. Sangiamo, J.D. ('19)
Tina Tan, MD, ('19)
Alexandra Stewart, J.D. ('18)
Martha Toomey ('18)

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

Narayan Nair, M.D., Director, DICP
Andrea Herzog, Principal Staff Liaison, ACCV

Welcome and Chair Report from Beth Luthy, Chair

Ms. Luthy called the meeting to order, welcomed the commission members, DICP staff, ex officio members, and guests on the teleconference call. A role call confirmed that all commission members were present, except for Alexandra Stewart, who was expected to join the meeting at a later time. Further introductions confirmed that Narayan Nair and Andrea Herzog (DICP staff), Andrea Davey (OGC), Catharine Reeves (DOJ), and ex officio members Valerie Marshall (FDA), and Tom Shimabukuro (ISO/CDC) were also present.

Public comments related to the agenda

Theresa Wrangham, representing the National Vaccine Information Center (NVIC), asked that some of her comments at the December 8, 2017 meeting of the ACCV be clarified. Specifically, with regard to the Institute of Medicine (IOM) study mentioned during the meeting, including comments from HRSA representatives, she said the record should include an explanation of how the IOM graded studies that were relied on to develop the report recommendations. The record should include a clarification of the causality and the quality of the science relied on. Ms. Wrangham stated that for most vaccine adverse events there is a lack of quality research or an absence of research. She suggested that there should be confirmation that the information presented by HRSA in this area was evaluated by the IOM, if it was reviewed.

Ms. Wrangham stated that during the December 2017 ACCV meeting she recommended that any individual from the public who presented the request for revision be allowed to present, on the record, a rationale for requesting the revision. Ms. Wrangham commented that this

recommendation was not accurately reflected in the minutes of the December meeting. However, she did commend the commission for inviting such public comment.

There were no other public comments about the agenda.

Nomination and vote for ACCV chair and vice chair

Ms. Luthy invited nominations for vice chair and for chair. She offered the first nomination for vice chair, Cody Meissner. There were no objections to the nomination and no other nominations were forthcoming. Ms. Luthy invited nominations for chair, and Ms. Toomey nominated Ms. Luthy. There were no objections and no other nominations were forthcoming. Ms. Toomey made a motion to accept Ms. Luthy's nomination. Each commissioner present was polled, and the vote was unanimous. Ms. Luthy called for a vote on the nomination of Dr. Meissner. Each commissioner present was polled, and the vote was unanimous.

Approval of the December 8, 2017 minutes

Ms. Luthy asked if staff was able to provide any guidance about the exceptions voiced by Ms. Wrangham, and Ms. Herzog suggested that it would require review of the minutes. She suggested deferring approval of the minutes until the next ACCV meeting so that the transcript and the audio recording of the meeting discussion could be reviewed.

Ms. Toomey stated that she had an issue related to the minutes. During the meeting she asked several times for information about the origin of the reports on which the commission based its recommendations, and the identity of the individual or agency funding the reports. She said she did not receive a response to the question during the meeting, and the minutes did not reflect her concern. Ms. Toomey commented that a specific question concerned the addition of tics to the Vaccine Injury Table (Table) and asked at the meeting about the report that concerned tics. She added that she felt there was insufficient research about tics and about PANDAS.

Ms. Luthy restated the concerns that should be reflected in the minutes. Ms. Toomey added that there was insufficient information about those two injuries and that the commission's understanding of the issue was incomplete. She felt the commission's treatment of the recommendation appeared to be dismissive. Ms. Luthy agreed that Ms. Toomey's point of view should be included in the minutes.

Dr. Meissner commented that Dr. Nair did a credible job in presenting the known facts about PANDAS, considering there is very little data in the literature about the condition. He felt the commission carefully followed the ACCV Guiding Principles. He added that the issue is not the existence of PANDAS, but that there is no evidence of an association between immunization and PANDAS.

Ms. Luthy stated that the December minutes should accurately reflect the comments of both Ms. Wrangham and Ms. Toomey. Therefore, the approval of the minutes should be deferred until proper review of the meeting proceedings is completed. There was consensus that approving the December 2017 ACCV meeting minutes should be tabled.

Report from the DICP, Dr. Narayan Nair, Director

Dr. Nair congratulated Ms. Luthy and Dr. Meissner on their selection to lead the ACCV as chair and vice chair. He briefly reviewed the highlights of his presentation and provided a brief discussion of the statistics related to claims filed since 2008. From 2008 to 2012, the average number of claims filed annually was 410. Since then the number has been steadily increasing; in Fiscal Year 2017, the number of claims filed with the DICP was 1,243. Through March 1, 2018 of the current fiscal year, 496 claims have been filed. Dr. Nair showed a chart of the comparison of the number of claims files versus the administrative funding for HRSA only. There was a steady year to year increase claims filed, but not corresponding increases in funding for HRSA.

Fiscal Year	Claims Filed	% increase	HRSA funding	% increase
2014	633	26%	$6.46 million	-.03
2015	803	27%	$7.50 million	16%
2016	1,120	39%	$7.50 million	no increase
2017	1,243	11%	$7.75 million	3%

Currently, there is a backlog of 539 claims that have medical records awaiting for review by DICP Medical Officers. 394 claims filed in 2017, and 145 claims filed to date in FY 2018. Total petitioners' awards have increased each year since 2014 and were about $252.3 million in 2017 and about $81.5 million to date in FY 2018. Total attorneys' fees and costs were $29.9 million in FY 2017 and $12.5 million to date in FY 2018.

In FY 2017, there were 877 claims adjudicated; 696 were deemed compensable and 181 were dismissed. To date in FY 2018, those numbers are 186 compensable and 86 dismissed. Of the compensable cases in FY 2017, 183 were concessions, 46 were the result of court decisions or proffers, and 467 were resolved by settlement between the parties involved. To date, in FY 2018, 248 cases have been adjudicated: 67 were resolved by concession, 22 by court decision, 97 by settlement and 62 were not compensable.

Finally, the balance in the Vaccine Injury Compensation Trust Fund was $3.7 billion on December 31, 2017. There was revenue of $59 million from excise taxes and $16 million from interest on the fund, for a total revenue of $75.6 million.

Significant activities of the DICP include a Notice of Proposed Rulemaking to implement maternal immunization provisions in the 21st Century Cures Act of 2016, specifically adding vaccines recommended for routine use in pregnant women as a category of covered on the Table, is currently under review. In the area of outreach, presentations have been made to the Biotechnology Innovation Organization and to the Johns Hopkins Bloomberg School of Public Health.

Dr. Nair concluded his presentation by providing contact information and Internet references to commission staff, the ACCV, DICP and HRSA.

During discussion, Dr. Nair clarified that the backlog of 539 claims from FY 2017 and FY 2018 was caused due to significant increases in claims filed and the inability to hire staff and contractors to conduct medical reviews of claims before they are adjudicated. There are two medical teams that review incoming claims, one for adults and one for children, and DICP also utilizes the services of outside contract reviewers to manage the case load. The backlog began in

2017, when claims outpaced the ability of staff to review them. Asked about the time to process a claim to final adjudication, Dr. Nair indicated that the average time is about two years.

There was a request to clarify the term "non-autism" case since the term suggests that there are also autism cases. Dr. Nair explained that about 15 years ago, a large number of claims were filed alleging autism was caused by vaccines. The U.S. Court of Federal Claims (Court) chose a fraction of those cases for review, which resulted in a determination that vaccines were not a factor and did not cause autism. Dr. Nair stated that the program has never compensated an individual based on a claim that autism was the primary injury. There have been individuals compensated who had diagnoses of autism in addition to other conditions.

Mr. Howie commented that the timeline from filing a claim to resolution for a civil case is much shorter than that of a vaccine injury compensation claim. In the latter instance, the attorneys are required to be able to present their case when the claim is filed, which is a major part of the legal argument. Mr. Howie asserted that the pre-litigation effort required to file a petition with the VICP is much greater than in a civil suit, which can be filed almost the same day as the alleged civil injury, after which the legal case is developed. If the backlog continues, or gets longer, the time to resolution will be lengthier.

Mr. Howie asked if a determination has been made as to how many reviewers will be needed to reverse or eliminate the backlog, whether new reviewers are being recruited, and whether the commission's previous recommendation to add staffing can be accomplished. Dr. Nair stated that the President's budget proposal includes additional funds for the program operations. Requests for additional funding in the program budget has been communicated to Congress, but if there is no increase or if the increase is inadequate the backlog will continue. Dr. Nair stated that his task is not to direct the commission with regard to any action, but to provide information that will help the commission in its deliberative process. He added that an increase in staffing in proportion to the increase in the caseload would alleviate the backlog.

There was a question about why there were 649 adjudicated claims dismissed in 2013 (63%), compared to 369 compensable claims, when typically compensable claims exceed dismissed claims. The following four years, dismissed cases fell to 20% of total claims, the more usual ratio. Dr. Nair responded that it was partially the result of increases in claims for SIRVA and influenza, but more because of dismissals resulting from the Court's ruling in the Omnibus Autism Proceeding. There was a discussion about the length of time that passes between filing a claim and final resolution and distribution of the first compensation payment, which could take more than 10 years. Ms. Toomey noted that in her son's case, the first compensation payment was made 14 years after filing the claim. She added that the government's attorney was very adversarial in eliciting her testimony. Ms. Reeves stated she was sorry that Mrs. Toomey had an unpleasant experience, but that DOJ attorneys always treat petitioners with respect.

It was observed that some of the delay might be because the medical records were not completely submitted at the time of the claim, requiring additional time to assemble and submit additional records. It could also be that the approach of the statute of limitations might push the plaintiff's attorney to file a claim with incomplete records. Another reason for the lengthened timeframe for adjudication of cases is the fact that attorneys must assemble the entire case before filing. In some compensation cases, the Court may direct that expert testimony be deferred until there is a determination of its relevance. In civil cases, some of that process can be accomplished while the case is proceeding.

Ms. Luthy closed the discussion and invited Ms. Reeves to make the Department of Justice presentation. Ms. Luthy noted that Ms. Stewart had joined the meeting.

Report from the Department of Justice (DOJ), Catharine Reeves, Deputy Director, Torts Branch

Ms. Reeves explained that the DOJ reporting period was different from the DICP reporting period, and begins on November 15 and ends on February 15. During the DOJ reporting period, 272 petitions were filed. The majority of cases were for adults, which is consistent with the same period last year. The number of petitions filed to date indicates that the number of petitions projected to be filed during FY 2018 will also be similar to last fiscal year. There were 181 cases adjudicated, 142 compensated and 39 not compensated/dismissed. Of those compensated, 56 were conceded by HHS and resolved by proffer, and 86 were resolved by settlement. Thirty-nine, all non-OAP, cases were not compensated/dismissed. Four petitions were voluntarily withdrawn.

No cases were decided at the U.S. Court of Appeals for the Federal Circuit (CAFC), but five were pending.

At the Court of Federal Claims (CFC), 12 cases were decided during the reporting period, evenly split between attorneys' fees and costs decisions and entitlement decisions, plus one case involving loss of future earnings, which is an element of damages. At the CFC, six motions for review filed by petitioners are pending: five involving entitlement and one involving attorneys' fees and costs. The other seven cases pending at the CFC involve motions for review filed by HHS (six for attorneys' fees and costs, one for entitlement, and one seeking interim damages).

Regarding oral arguments, two were heard on March 6, D'Tiole v. HHS (CAFC) and McCulloch v. HHS (CFC), and two are scheduled in 2018: Anderson v. HHS on April 5 (CAFC), and McIntosh v. HHS on March 22 (CFC).

Ms. Reeves showed the adjudicated settlements beginning with the case that took the longest to resolve (a Hodgkin's lymphoma case that took six years and seven months to resolve) and ending with the case that was most expeditiously resolved (a flu vaccine claim of SIRVA that took only seven months to resolve).

During discussion, Ms. Toomey commented that the proceedings seemed to be very adversarial, which caused some discomfort among the petitioners because they saw claims filed under the Program as citizens versus their own government. Ms. Reeves commented that even though the Program is designed to be less adversarial than customary civil procedure, the government is the defendant and not the drug manufacturers, as had been the practice before the Program's enactment. As such, the government is required to assess whether the claim is or is not valid, which may sometimes lead to an adversarial experience. But the Program is less adversarial and time-consuming than traditional civil litigation. There is no discovery, which can be a time-consuming process in civil litigation (that work is done before filing for Program claims), and the rules of evidence are less restrictive. The rules make it easier and faster to navigate the compensation claim process in the Program versus the traditional civil litigation process.

When asked how and whom to contact to promote congressional support without violating federal laws, Dr. Nair commented that federal employees cannot lobby Congress. The Program does inform congressional staff about Program affairs, if requested. There was also a question about whether the details of a settlement decision are publicly available. Ms. Reeves

stated that decisions adopting settlements are published, but the details of the process by which the settlement was reached are not. This is to protect the privacy of individuals, especially the injured parties. Ms. Reeves also noted that cases are settled for many different reasons. Dr. Nair added that decisions awarding compensation are not necessarily based on the scientific arguments. There are a number of reasons that compensation may be granted despite a lack of an airtight scientific rationale. There is also language in each case compensated through negotiated settlement that the Secretary does not concede that the vaccine in question caused the injury. Ms. Luthy ended the discussion and invited Dr. Shimabukuro to make his presentation.

Update on the Immunization Safety Office (ISO), Centers for Disease Control and Prevention (CDC) Vaccine Activities, Dr. Tom Shimabukuro, CDC

Dr. Shimabukuro stated that he would provide an update of the February 2018 meeting of the Advisory Committee on Immunization Practices (ACIP), and review selected recent publications. He informed the group that the information related to the meeting would be published on the ACIP web site.

At one session of the ACIP meeting there was a presentation on HEPLISAV- B (Dynavax Technologies Corporation), a recombinant, adjuvanted hepatitis B vaccine licensed in November 2017, and approved for use in adults 18 years of age and older, with 2 doses given intramuscularly one month apart. ACIP conducted a Grading of Recommendations, Assessment, Development and Evaluation (GRADE) for the vaccine. By vote at the meeting, HEPLISAV-B was recommended as a hepatitis B vaccine that can be administered in the age group for which it is indicated.

There was also a discussion about the use of hepatitis A vaccines for post-exposure prophylaxis and international travel. From that discussion, the following recommendations were approved by vote:

- Hepatitis A vaccines should be administered for post-exposure prophylaxis for all persons 12 months of age and older
- In addition to hepatitis A vaccine, immune globulin may be administered to persons over 40 years of age depending on the provider's risk assessment
- Hepatitis A vaccine should be administered to infants age 6-11 months traveling outside the United States when protection against hepatitis A is recommended

There was a presentation on Fluarix quadrivalent (GSK) efficacy in children 6-35 months of age, essentially an extension of the existing age recommendation for the vaccine. An influenza surveillance update was provided for the 2017- 2018 season. That season has been mainly an H3N2 season, although there has been a small increase in influenza B at the time of the ACIP presentation. Influenza-like illness has been the highest since 2009. Interim estimates of 2017-2018 seasonal influenza vaccine effectiveness against medically attended influenza from the U.S. Flu Vaccine Effectiveness Network was 36% at the time of the presentation. There will be a presentation at the June ACIP meeting that will update the final vaccine effectiveness number.

There was a presentation of the results of a randomized trial of a new H1N1 live attenuated influenza vaccine (LAIV) strain in U.S. children. The immunogenicity of that vaccine was similar to that observed prior to seasons when there were vaccine effectiveness problems with LAIV. Based on the data presented for LAIV, there was a vote that resulted in

recommending LAIV as an influenza vaccine for the 2018- 2019 season; immunization providers may choose to administer any licensed, age-appropriate, influenza vaccine (including LAIV, IIV, and RIV). LAIV is an option for influenza vaccination for persons for whom it is otherwise appropriate. A vote on whether to recommend a preference for inactivated influenza vaccine (IIV) over LAIV failed to achieve a majority. The recommendation was rejected.

There were two presentations on human papillomavirus (HPV) vaccines. Vaccine Adverse Event Reporting System (VAERS) monitoring of 9vHPV vaccine from December 2014 through December 2017. No new safety signals or unexpected patterns were observed. The safety profile of 9vHPV is consistent with data from pre-licensure trials and post-licensure data on 4vHPV. Vaccine Safety Datalink (VSD) Rapid Cycle Analysis data from October 2015 through October 2017 revealed signals that met the predefined statistical threshold for several adverse events after 9vHPV, including syncope and injection site reactions (which were anticipated); however signals for allergic reactions, pancreatitis, and appendicitis were not confirmed after further evaluation. The session also included a discussion of harmonization of HPV age recommendations for males and females, and trends in HPV-associated cancer. There were changes in cancer rates from 1999 through 2014: increased oropharyngeal and anal cancer among men and women, and increased vulvar cancer in women, and decreased cervical cancer. Penile and vaginal cancer did not change. Oropharyngeal cancer is the most common HPV-related cancer now, and it is increasing, particularly among males. The HPV vaccine should decrease the HPV-associated cancer burden, but because of the long time between HPV infection and the appearance of cancer, it may take decades to see the impact.

Finally, the Evidence-Based Recommendations Work Group proposed that an Evidence to Recommendation framework be adopted and used by ACIP to support decision-making. Other sessions at the ACIP meeting included presentations on anthrax, pneumococcal vaccines and other biologics for prevention and treatment of healthcare-associated infections, meningococcal disease, and Japanese encephalitis vaccine. Asked whether the HPV vaccine contributed to the decline in cervical cancer, Dr. Shimabukuro stated that there were certainly confounding factors, making it difficult to settle on a definitive connection to the vaccine.

Turning to recent publications, Dr. Shimabukuro mentioned the following:

- Moro et al, in Vaccine, 2018, 36(1) 50-54, assessed the safety of hepatitis B vaccination during pregnancy has not been well studied. This analysis of VAERS reports involving hepatitis B vaccination during pregnancy did not identify any new or unexpected safety concerns. The vaccine is not specifically recommended for pregnant women, so there is limited data on the safety of the vaccination. This paper did not identify any new risks. The hepatitis B vaccine is inactivated so there is no reason to believe it would be different from other inactivated vaccines.
- Loharikar, et al, in Vaccine. 2018;36(2): 299-305, found that anxiety-related adverse events following immunization (AEFI) clusters can be disruptive to vaccination programs, reducing public trust in immunizations and impacting vaccination coverage; response efforts to restore public confidence can be resource intensive. Health care providers should have training on recognition and clinical management of anxiety-related AEFI; public health authorities should have plans to prevent and effectively manage anxiety- related AEFI clusters. Prompt management of these occurrences can be even more important in an era of social media, in which information rapidly spreads.

- Hibbs et al, in Vaccine. 2018; 36(4): 553-558, looked at the safety of vaccines that have been stored in conditions outside the recommended temperatures (basically a study of medical errors) which can affect potency. There do not appear to be any serious risks involved. This review does not indicate any substantial direct health risk from administration of vaccines kept outside of recommended temperatures. However, there are potential costs and risks, including vaccine wastage, possible decreased protection, and patient and parent inconvenience related to revaccination. Maintaining high vigilance, proper staff training, regular equipment maintenance, and having adequate auxiliary power are important components of comprehensive vaccine cold chain management.
- McNeil MM and DeStefano F., in the Journal of Allergy Clinical Immunology, 2018;141(2):463-472, found that vaccine-associated hypersensitivity reactions are not infrequent; however, serious acute-onset, presumably IgE-mediated or IgG and complement- mediated anaphylactic or serious delayed-onset T cell-mediated systemic reactions are considered extremely rare. Hypersensitivity can occur because of either the active vaccine component (antigen) or one of the other components.
- Arana et al. looked at data from the Vaccine Adverse Event Reporting System (VAERS), 2009–2015, reported on post-licensure safety monitoring of quadrivalent human papillomavirus vaccine for unexpected safety concerns or reporting patterns of quadrivalent HPV vaccination (4vHPV) with clinically important adverse events. The safety profile of 4vHPV is consistent with data from pre-licensure trials and post-marketing safety data. The first VAERS review of this 4vHPV vaccine, Gardasil, looked at the first 2.5 years from licensure to 2009. This review looked at data through 2015 when the U.S. began transitioning to the 9-valent HPV vaccine. There were no new or unexpected safety concerns for the quadrivalent HPV vaccine. The paper was published in Vaccine in 2018.
- The last paper by Sukumaran et al on Infant Hospitalizations and Mortality after Maternal Vaccination was published in Pediatrics 2018. It focused on the first six months of life and mothers vaccinated with Tdap. There are limited studies of the long-term safety in infants for vaccines administered during pregnancy. In this VSD study, the authors found no association between vaccination during pregnancy and risk of infant hospitalization or death in the first 6 months of life. These findings support the safety of current recommendations for influenza and Tdap vaccination during pregnancy.

Dr. Shimabukuro ended his presentation.

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

CDR Marshall announced that in January 2018, the FDA approved a supplement to the Biologics License Application (BLA) for Influenza Vaccine (Fluarix® Quadrivalent) to extend the age range to include children 6 to 35 months of age. The vaccine was previously approved for persons three years of age and older. In January 2018, the FDA approved a supplement to the

Biologics License Application (BLA) for Influenza Vaccine (Fluzone) to include the 2018 Southern Hemisphere formulation.

On March 1, 2018, the FDA Vaccines and Related Products Advisory Committee selected the influenza vaccine strains for the 2018-2019 flu seasons for the Northern Hemisphere, which begins in the fall of 2018. The recommendations are based on worldwide surveillance data. The committee voted unanimously to include an A/Michigan/45/2015 (H1N1) 09-like virus. The panel voted unanimously to include an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus, which is a change from the 2017-2018 vaccine. The group voted by majority, to include a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage), which is a change from this season's vaccine. The committee also voted unanimously to include a B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage) as the second influenza B strain in the quadrivalent vaccine.

CDR Marshall concluded her report. There were no questions or comments from commission members.

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

Dr. Bok commented that the National Vaccine Advisory Committee (NVAC) included an update on implementation of HPV recommendations. In that presentation there was a discussion of the Assistant Secretary for Health mandate to establish a working group, which will produce a brief report by June 18, on recommendations to "strengthen the effectiveness of national, state and local efforts to improve HPV vaccination coverage rates." The second presentation was about the state of research on new vaccines and included a discussion on incentivizing vaccine development. An overview of Zika vaccine development by BARDA/ASPR revealed that there are many candidate vaccines in the research pipeline, from basic research to Phase II trials. During the NVAC meeting there was also a review of the next generation of influenza vaccines, which includes a significant number of new vaccines in Phase I and Phase II trials, part of which is the objective of developing a universal vaccine that will allow a single annual inoculation. The final NVAC session was an update on vaccine adjuvants that provided details on three new adjuvants licensed in 2017 -- AS01 (TLR4 ligand: MPL, and saponin: QS-21); MF59; and CpG ODN. That was followed by a discussion of disparities in adult immunization.

Finally, HHS announced the appointments of the new Secretary of Health and Human Services, Dr. Alex Azar, and the new Assistant Secretary for Health, ADM Brett Giroir.

Future agenda items

Ms. Luthy stated that since Dr. Mulach had not yet returned to the conference call, the next agenda item to be addressed would be future agenda items and new business. Ms. Luthy stated that three items had been mentioned during earlier discussions: final review and approval of the December meeting minutes; the current backlog and need to increase HRSA reviewers; and an update on the Commission vacancy, which would be filled by the parent or legal representative of a vaccine-injured child.

Dr. Nair commented on the vacancy, noting that his office had reached out to the Department of Justice for suggestions, and to John Howie for possible suggestions from the petitioner's bar. When asked about whether the vacancy could be filled by an individual with a vaccine injury, Dr. Nair commented that the charter requires two parents. Therefore, neither of

those slots could be filled by a vaccine-injured person. It is possible that a person with a qualifying vaccine injury (requires a court decision in favor of the claimant) could occupy the slot designated for a member of the public. There is information on the program web site (search web for ACCV) that explains how to apply for a position on the Commission, and the petitioner's bar might have information that could help. There was a suggestion that the process could be more proactive, in the sense of a recruitment effort. Mr. Howie stated that he had made the announcement to attorneys who are involved with the Vaccine Injured Petitioners Bar Association and to the American Association for Justice. Dr. Nair added that no parent had independently applied for membership on the commission.

Ms. Luthy invited other suggestions for future agenda items. Ms. Stewart suggested a clarification by Ms. Reeves of the resolution of claims related to HPV, Tdap and Hodgkin's lymphoma that was discussed during her presentation. She added that a discussion of future research on conditions such as PANDAS, could be enlightening and suggested the discussions could be added to the ex-officio presentations.

John Howie suggested that, when presentations are made regarding revisions to the Table, if the revision was proposed by a member of the public or other person, that the person making the proposal be invited to explain his or her rationale. He added that it might be helpful to establish a work group to review the items discussed thus far and finalize the parameters of the discussions for each.

There was a brief discussion about the best way to establish a work group that could review the several recommendations already submitted to the Secretary, with an eye to reformatting them and resubmitting, since there are newly appointed individuals in the Department to address those recommendations. Dr. Nair suggested that all the recommendations may not be appropriate to send to the Secretary and that each should be reviewed to determine the most appropriate recipient for any communication that is chosen.

Ms. Luthy summarized the discussion; the commission was in favor of establishing a work group to focus on process. There was consensus to schedule a conference call for those commission members interested in pursuing the establishment of the work group.

Ms. Luthy invited Dr. Mulach to make the NIH/NIAID presentation.

Update on the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH)

Dr. Mulach commented that, although there are vaccines for flu, there is always the possibility that a mutation could produce a strain that would threaten a pandemic. This year marks the 100th anniversary of the 1918 pandemic that caused many deaths worldwide. Dr. Mulach briefly discussed the NIAID strategic plan for the development of a universal influenza vaccine. CDC, BARDA, NIH and FDA and are making presentations on seasonal influenza and vaccine effectiveness to the House Energy and Commerce Subcommittee on Oversight and Investigations while ACCV is meeting.

Barney Graham and Nancy Sullivan published a paper, "Emerging Viral Diseases from a Vaccinology Perspective: Preparing for the Next Pandemic" in the journal Nature Immunology that discussed better preparation and more effective platforms for vaccines that will improve response time. In retrospect, the Zika epidemic just suddenly appeared two years ago, followed by a huge effort to understand the disease and develop vaccines. Nineteen papers appeared in the Journal of Infectious Diseases to explain the history, epidemiology, virology, immunology

and the unique characteristics and disease cycle of the mosquito that transmits the disease. Understanding the cycle provides an opportunity to develop ways to interrupt, slow or stop the spread of the disease.

There is a Zika DNA vaccine (VRC 705) going through clinical trials. A Part A non-placebo-controlled trial of 90 subjects began in March 2017, and a Part B placebo-controlled trial of up to 5,000 subjects launched in July 2017. In 2016, NIH launched a very large study to evaluate the entire range of health risks related to Zika virus infection in pregnant women and their babies. This study is co- sponsored by Fundacao Oswaldo Cruz-Fiocruz (Fiocruz), a national scientific research organization linked to the Brazilian Ministry of Health in Brazil. Currentlyalmost 6,000 mothers and 2,000 infants have been enrolled. The study is looking at the course of Zika infection, focusing on pregnancy outcomes, congenital anomalies, and other developmental problems.

Dr. Mulach described an NIH research initiative on health risks and resilience after hurricanes Irma and Maria. It supports time-sensitive research on risk and resilience factors related to short-and long-term health outcomes following Hurricanes Irma and Maria in Puerto Rico and the U.S. Virgin Islands. The research is expected to start in July 2018.

Finally, Dr. Mulach commented on the "All of Us Research Program" which was described at the December ACCV meeting. The program is an effort to gather data from a million or more individuals living in the United States to accelerate research and improve human health. The study will look at various lifestyles, environment and biology, to try to develop precision medicine and more personalized medicine. Ideas for research were solicited from participants and due by February 23, 2018. There will be a workshop at NIH in March 2018 to review the ideas submitted.

During discussion, Dr. Mulach was asked about research on reducing the threat of Zika infection by altering the genetics of the mosquito to prevent reproduction of mosquitoes that can carry the Zika virus. Dr. Mulach commented that the intent of this approach is to affect the disease risk but not the environment.

Ms. Luthy closed the ex-officio presentations part of the agenda.
Dr. Shimabukuro announced that he would be leaving the commission as an ex officio member and Mike McNeil would be taking over the responsibilities of reporting for the Immunization Safety Office. He expressed his appreciation for the diligent work of the HRSA staff who made the commission work so well during the past few years.

Public comment

1. Dr. Hooker – Parent/Private Citizen

Dr. Hooker stated that he was the parent of a vaccine-injured male. He said his son's claim was in the VICP claims process for 13 years, and when the claim was finally heard in 2016, it was dismissed based on the statute of limitations. He commented on the tics discussion from the previous ACCV meeting. He noted that thimerosal is still in multi-dose formulations of flu vaccine administered to infants, toddlers and pregnant women. The CDC response to the petition at the last meeting was scientifically inaccurate. A Thompson et al study in the New England Journal of Medicine (2007) and a 2012 study in the Journal of Pediatric Psychology, both showed a definitive and statistically significant relationship between thimerosal exposure and tics in boys. Dr. Hooker cited four other studies in peer-reviewed literature attesting to the relationship between thimerosal and tics, and the finding by the 2001 IOM Immunization Review

Committee, that a relationship between thimerosal and neurodevelopmental disorders is biologically plausible.

Dr. Hooker stated that he believed the petition should have been voted on or tabled for further review. Dr. Hooker suggested there should be a mechanism to facilitate more research by independent scientists to look at the link between thimerosal exposure and tics. Dr. Hooker expressed his concern about the negative adversarial process that parents face when pursuing a claim for an injury such as the one under discussion.

There was a question from a commission member about pursuing a discussion of Dr. Hooker's statement, and it was determined that such a discussion would have to occur at a time other than that provided on the agenda for public comment.

2. Theresa Wrangham – Executive Director, NVIC

Ms. Theresa Wrangham from NVIC, explained that the NVIC has followed the commission's work since its creation. The NVIC was co-founded by parents of children injured by the DPT vaccine 36 years ago. As the only federal commission concerned with vaccine-injured individuals, the ACCV is extremely important. There should be a discussion about how to reach out to Congress to provide the funding needed to close the research gaps that the IOM has repeatedly, over the last 20 years, identified. The lack of quality science to support causality results in obstacles to adding injuries to the Table. That, in turn, increases the level of adversarial proceedings that require parents to prove that the injuries to their children were caused by vaccine.

Ms. Wrangham observed that most of the recommendations to the Secretary of HHS go unanswered. It is also clear that, unlike many federal commissions, the ACCV does not publish reports. The NVAC issues very prompt reports which have resulted in parents not being able to opt out of vaccinations for their children. However, vaccine approval is fast-tracked. The IOM has stated that potential vaccine injuries cannot be determined until the vaccines are in use. The vaccine research mandate in the 1986 Act is not being addressed and it is creating the caseload discussed earlier in the meeting. Because injuries are slow to be placed on the Table, litigation on vaccine injuries increases. However, Guillain–Barré Syndrome (GBS) was added as an injury related to flu vaccine partly because of commission action.

NVIC has a standing request for more transparency in publishing information about injury awards. There is a way to do that without violating individual confidentiality. Ms. Wrangham stated that she would be pleased to serve on a work group looking into that issue.

Concerning membership on the commission, there is nothing in the law that requires that a parent be a successful petitioner in the VICP. Ms. Wrangham, who is also the parent of a vaccine-injured child, stated that a parent submitted her name for commission membership 18 months ago. She explained that she did not pursue membership because she was not aware of the process to be approved and she was never advised of her status.

The NVIC made a request that the commission revisit the recommendations made by the Altarum group and the Banyan group that observed there is no follow-up after an award to assess the opinions of those involved to see if the award recipients felt that the awards were adequate. Those groups stated that many are not aware of the process and many will not make it through the process, in part because of the statute of limitations.

Ms. Wrangham renewed the NVIC request that, like the NVAC, the ACCV issue informative reports that could be submitted to Congressional staff, rather than make repeated

recommendations to the Secretary, that are usually of no avail. She also felt that the commission should make room on its agenda for input from individuals, like those who file petitions for additions to the Table.

Ms. Luthy confirmed that there were no other callers who were interested in making a public comment. She stated that the e-mail about the new work group would be forthcoming. Dr. Nair stated he would investigate the question about qualifications for parental membership on the commission.

Adjournment

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