Advisory Commission on Childhood Vaccines (ACCV)
Adobe Connect Webinar and Telephone Conference meeting
September 6, 2018

Members Present

Karlen E. (Beth) Luthy, D.N.P., ('18), Chair
Kathleen F. Gaffney, PhD, RN ('19)
John Howie, J.D., ('19)
Tina Tan, MD, ('19)
Alexandra Stewart, J.D., ('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 Report of the Chair, Beth Luthy, ACCV

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 the presence of a quorum.

Public Comment on Agenda Items, Ms. Beth Luthy, Chair

The invitation to submit comments on agenda items was announced by the conference operator and there was one request to speak:

(1) Theresa Wrangham, Executive Director of the National Vaccine Information Center (NVIC) requested that the Process Work Group look at ways to enhance the program's interaction with the public. Ms. Wrangham discussed petitions to add injuries to the Vaccine Injury Table (the Table) and noted that they may be submitted to the ACCV by anyone. Currently HRSA responds to petitions with a PowerPoint presentation of about 20 minutes, and then responds to questions from the ACCV commissioners. However, the parties who submit petitions have no opportunity for a similar response. The NVIC recommends that members of the public who submit petitions be allowed that opportunity to make a presentation to the Commission. NVIC believes this could improve the quality of the information provided to the Commission for its consideration of the petition. Ms. Wrangham requested that this request be considered as an item for the Work Group to discuss. She added that there is nothing in the legislation to prohibit such a change in process.

Ms. Wrangham also commented that since the ACCV is part of the review process for Vaccine Information Statements (VIS), the NVIC encourages the ACCV to support expanding information in the VIS, such as including vaccine ingredients related to

allergies, encouraging the review the vaccine manufacturer's product insert that is available on the Food and Drug Administration (FDA) website, and including informed consent which was in the VIS prior to the 1995 amendments to the legislation. Ms. Wrangham stated that the regulations limit the VIS to a single page, printed on both sides. More complete information would support the public's ability to make informed vaccine decisions, although it might require permitting more than one page printed both sides.

There were no additional requests to speak.

Approval of June 2018 Minutes, Ms. Beth Luthy, Chair

Ms. Luthy invited approval of the June 15, 2018 ACCV meeting minutes. On motion duly made and seconded, the minutes of the June 2018 ACCV meeting were unanimously approved.

ACCV Work Group Update, John Howie, Member.

Mr. Howie reported that the work group was established to address some of the issues with the program for ACCV consideration. Three meetings have occurred and a mission statement was developed, as well as identification of tasks for the work group to address. The work group has agreed to submit to the full ACCV an updated recommendation to allocate more resources to Department of Justice (DOJ), Department of Health and Human Services (HHS) and the U.S. Court of Federal Claims (Court) which have roles in administering the National Vaccine Injury Compensation Program (VICP).

The work group will look at the process currently in place to present proposals for Table changes. The work group would also like to find ways to increase interaction with the community, and is working on a list of actions to accomplish that objective.

Ms. Luthy invited comments or questions. She added that the draft of the recommendation will be made available to the Commission for review and discussion. When the recommendation is finalized and approved by a vote, the letter will be sent to the Secretary. The public may request a copy by sending an e-mail to Ms. Herzog (aherzog@hrsa.gov). There was no additional discussion.

Report from the Division of Injury Compensation Programs, Dr. Narayan Nair, Director, DICP

Dr. Nair outlined the meeting agenda beginning with an update on the VICP, followed by a report from the Department of Justice, brief reports from ex officio members (FDA, Centers for Disease Control and Prevention [CDC], National Institutes of Health [NIH], and National Vaccine Program Office [NVPO]), VIS reviews for MenACWY and DTaP, and a discussion of ACCV Work Group activities (presented earlier in the meeting).

Dr. Nair presented the current VICP statistics. Regarding petitions filed, Dr. Nair noted the average number of petitions filed for FY 2008 through FY 2012 was 410. The fiscal year for the agency is October 1 through September 30 of the following year. There have been steady increases each year through FY 2017, with the petitions to date in FY 2018 at 1,090 claims. Dr.

Nair presented a five-year snapshot of claims versus administrative funding which went from $6.48 million to $7.75 million between 2013 and 2017. That funding increased in FY 2018, to $9.2 million. Those amounts do not include for funding for DOJ or the Court.

With regard to the backlog of DICP cases, Dr. Nair explained that there was no backlog for FY 2017; all claims with proper medical records have been assigned for that year. In FY 2018 there are currently 612 claims with medical records awaiting review assignment. Petitioners' awards in FY 2017 amounted to $252.2 million and attorney's fees and costs were $29.9 million. In FY 2018, to date, those amounts are $170.6 million and $26.8 million respectively. In FY 2017, 879 VICP cases were adjudicated; of those cases, 696 were compensated and 183 were dismissed. In FY 2018, to date, 573 cases have been adjudicated; 417 cases were found to be compensable and 156 were dismissed.

Dr. Nair reported additional statistics where the adjudication number are slightly different because a different database was used. According to that data there have been 554 adjudications to date in FY 2018; 423 of those cases deemed compensable and 131 of these cases were dismissed. The compensable cases include 155 that were resolved by concession, 56 that were resolved by Court decisions, and 212 were resolved by settlements between the parties.

Dr. Nair reported that the balance in the Vaccine Injury Compensation Trust Fund was nearly $3.8 billion. Excise tax contributed $193.5 million; and interest on the fund contributed $56.5 million, totalling $250 million in income to date in 2018.

Finally, Dr. Nair commented on significant activities, one of which is the ongoing implementation of maternal immunization provisions. On April 4, 2018, a Notice of Proposed Rulemaking that would add the category of vaccines for pregnant women to the Vaccine Injury Table was published in the *Federal Register*. The public may comment before October 1, 2018, and a public hearing is scheduled for September 17, 2018, at which time the public may provide testimony. Dr. Nair also reported that the VICP continues to engage in outreach activities. T here was a presentation to the Adult Vaccine Immunization Coalition. More information about the meeting, presentations and minutes can be found at: http://www.hrsa.gov/advisorycommittees/childhoodvaccines/index.html.

During discussion, in response to a commissioner's question, Dr. Nair clarified that there are 642 that have not undergone final review, for various reasons such as petitions filed without medical records. Cases, once assigned to a reviewer, are generally completed within about 90 days.

Report from the Department of Justice, Ms. Heather L. Pearlman, Assistant Director, Torts Branch

Ms. Pearlman noted that the reporting period for the Department of Justice (DOJ) is different from that of the Division of Injury Compensation Programs. Ms. Pearlman referenced the DOJ PowerPoint materials as part of her presentation for the three-month period from May 16, 2018 through August 15, 2018. (DOJ PowerPoint (PP) at 2.) During this reporting period, 294 petitions were filed. (DOJ PP at 2.) Of those 294 petitions, 17 were filed on behalf of minors and 277 were filed by adults. (DOJ PP at 2.)

Ms. Pearlman noted that 198 petitions were adjudicated during this reporting period. (DOJ PP at 3.) One hundred thirty-nine cases were compensated, the majority of which were

resolved by proffer. (DOJ PP at 3.) Fifty-nine cases were not compensated. (DOJ PP at 3.) Seven petitions were voluntarily withdrawn. (DOJ PP at 4.)

Ms. Pearlman discussed recently decided and pending cases in the U.S. Court of Appeals for the Federal Circuit (CAFC), including Depena v. HHS and Oliver v. HHS, the latter of which was decided after this reporting period ended. (DOJ PP at 5, 6.) In Depena, the CAFC affirmed the U.S. Court of Federal Claims' (CFC) determination that the special master appropriately denied compensation in a case in which the petitioners alleged that the measles, mumps, and rubella (MMR) vaccine caused their minor son to develop pneumonia. In Oliver, the CAFC affirmed the CFC's conclusion that the Chief Special Master did not err in dismissing a petition in which the petitioners alleged that their child developed Dravet Syndrome as a result of various childhood vaccines. Four appeals regarding entitlement (Olson v. HHS, McCollum v. HHS, Rogero v. HHS, and Gaiter v. HHS) and one appeal regarding attorneys' fees and costs (R.K. v. HHS) remain pending in the CAFC. (DOJ PP at 6.)

Ms. Pearlman next discussed appeals at the CFC and noted that six appeals by petitioners and five appeals by HHS were decided by the CFC during this reporting period. (DOJ PP at 7, 8.) Five of those 11 appeals involved entitlement and six involved attorneys' fees and costs. Ms. Pearlman briefly discussed Boatmon v. HHS, a case in which the CFC overturned a special master's determination that vaccines can cause Sudden Infant Death Syndrome (SIDS) and dismissed the petition. Ms. Luthy inquired as to the cases appealed by HHS involving attorneys' fees and costs. Ms. Pearlman explained that, in those cases, the appeals related to the amount of fees and costs awarded to petitioners by the special masters. Eleven cases remain pending at the CFC. (DOJ PP at 9.)

Ms. Pearlman noted that no oral arguments are scheduled at the CACF or the CFC at this time. (DOJ PP at 10.)

Finally, Ms. Pearlman provided a list of cases that were settled during the reporting period, which are listed in the DOJ PowerPoint presentation in order of the time they took to resolve. (DOJ PP at 11-17.) Ms. Pearlman noted that most of these settled cases alleged Guillain-Barré Syndrome (GBS) and Shoulder Injury Related to Vaccine Administration (SIRVA) injuries. Ms. Pearlman further noted that only five of these settled cases took more than three years to resolve.

Review of Vaccine Information Statements (VIS), Skip Wolfe and Suzanne Johnson-DeLeon, CDC.

Mr. Wolfe announced that there were two Vaccine Information Statements to review, one on meningococcal ACWY vaccine and the other on DTaP vaccine. The ACCV is responsible for review of VIS and subsequent revisions.

Meningococcal ACWY

The MenACWY vaccine prevents meningococcal infection which is effective against serogroups A, C, W and Y. These are the serogroups most commonly responsible for infection. The infection is caused by a bacteria called *Neisseria meningitidis*. A previous vaccine, MPSV4, is no longer available. This revision mainly deletes all references to that vaccine. The VIS contained the same information for the MPSV4 vaccine.

Ms. Johnson-DeLeon commented that one addition to the VIS was under Section 3, "Some people should not get this vaccine". In addition to routine vaccination for adolescents, MenACWY vaccine is also recommended for certain groups of people, namely, people with HIV. There was also a revision to the VIS encouraging women who are pregnant or breast-feeding to be vaccinated if they are at increased risk.

It was noted that in Section 3, last paragraph, the phrase "your doctor can advise you." After discussion of this language, there was a recommendation to maintain provider neutral language to include health care providers other than doctors. Mr. Wolfe acknowledged that this issue was longstanding and generally "health care provider" is used unless there is a specific reason to prefer the word "doctor." He added that switching to a consistent use of health care provider in the entire VIS, as well as others, would be considered.

Ms. Johnson-DeLeon commented that this particular VIS review was intended to fast track approval to delete any references to MPSV4. She said that future submissions for review should reflect the recommendation of the ACCV to use health care provider exclusively. She noted that the next VIS to be reviewed, for DTaP vaccine, has eliminated the word doctor in favor of health care provider.

DTaP (Diphtheria, Tetanus, Pertussis) Vaccine

Mr. Wolfe stated that this VIS had been completely updated because new DTaP recommendations were recently approved by Advisory Committee on Immunization Practices (ACIP). The changes are not extensive, and are mainly format changes. Mr. Wolfe noted that only children up to age 7 receive this vaccine. Other vaccines that include diphtheria and tetanus vaccines are covered under separate VISs. He added that to strengthen the rationale for administration to children, the risks of the diseases was added to Section 1. When asked by a commissioner if it would be helpful to add a sentence about the fact that some school systems require the vaccine for admission to the school, Mr. Wolfe suggested that such a statement might be irrelevant since the parents receive the VISs after they've already consented to have their children vaccinated. Ms. Johnson-DeLeon added that the requirement is typically a state level issue, not a federal issue.

Mr. Wolfe moved to Section 2, which addresses the vaccination schedule, and includes one new note; the DTaP vaccine may be given alone or in combination with other vaccines. There were no comments on Section 2.

In Section 3 there were no substantive changes. The wording was changed to emphasize that parents should consult the child's health care provider if he or she has the conditions described. This section deals mainly with precautions and underlines the importance of informing the health care provider in the event of an adverse event. Mr. Wolfe asked for comments about the last bullet under "Tell your health care provider" that states that if a child had severe pain or swelling after a previous DTaP or DT vaccination. Mr. Wolfe explained that the last bullet specifically refers to Arthus reaction, which has a variety of symptoms, including rare instances of necrosis, which would be challenging to fully explain in the VIS. This type of reaction may not be clearly recalled by the parent if it occurred. It is uncommon and localized when it occurs. There was agreement among commissioners that the present wording was sufficient.

Section 4 of the DTaP VIS discusses risks of a vaccine reaction. Mr. Wolfe explained that a section (also Section 4 in the previous VIS) was deleted because it explained that this

vaccine is not licensed for children over 7 years of age and that there are other vaccines (Tdap and TD) available for adults. It was determined that this earlier section was not relevant. The last bullet of this section in the proposed DTaP VIS under review uses the term "lowered consciousness," which refers to the technical conditions of hypotonic, hyporesponsive episodes, which was considered too technical for a VIS. He asked if that term was acceptable. The commissioners agreed that a parent should be able to understand the term.

Mr. Wolfe continued with section 5 of the VIS. The language in Section 5, concerning problems that arise after leaving the clinic, conforms to the format currently being used in all new and revised VISs. Further, Sections 5, 6 and 7 are standard language used in all VIS.

There was a question related to informed consent, specifically, about the possibility that the VIS may be used in some areas as a consent document. Mr. Wolfe explained there is a legal definition of informed consent and that there is no federal requirement for informed consent for vaccines. If there is a state requirement and if the VIS meets the standards for that state, it may be used as an informed consent document. However, informed consent is not the purpose of a VIS; a VIS is for information purposes to meet the requirements of the National Childhood Vaccine Injury Act. Mr. Wolfe concluded his discussion.

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

Dr. McNeil explained that he would give an update on June 21-22, 2018 ACIP meeting, and present a brief discussion about selected publications. The influenza session at the ACIP meeting summarized the 2017-2018 flu season findings. The 2017-2018 season was a severe season dominated by Influenza A (H3N2) virus. The efficacy of the vaccine was moderate. The vaccine reduced outpatient visits for influenza-associated acute respiratory illness by 40% in persons 6 months of age and older. Among adults, vaccine efficacy estimates were similar for outpatients and inpatients, reducing influenza-associated hospitalization by 22%.

ACIP Meeting Updates

Dr. McNeil discussed an FDA presentation about a Centers for Medicare & Medicaid Services (CMS) study that showed that cell-cultured and high-dose vaccines were marginally more effective than egg-based standard dose quadrivalent vaccines for hospital outcomes among U.S. persons over 65 years of age during this season. The ISO determined that Vaccine Adverse Event Reporting System (VAERS) monitoring detected no safety concerns for vaccines given during the 2017-2018 flu season, and in a separate monitoring process, FDA detected no signal for GBS. Finally, the Vaccine Safety Datalink (VSD) conducts rapid cycle analysis (RCA), which confirmed no RCA signals for pre-specified outcomes of acute disseminated encephalomyelitis (ADEM), anaphylaxis, Bell's palsy, encephalitis, GBS, seizures, or transverse myelitis.

Dr. McNeil described two studies undertaken and continuing by CDC's Clinical Immunization Safety Assessment (CISA) project. One of which assessed the safety and immunogenicity of Fluad versus Fluzone High-Dose in older adults for two flu seasons (2017 through 2019). The other study is an ongoing randomized clinical trial looking at fever incidence in children 12-16 months of age who received simultaneous vs. sequential vaccination.

The subjects were given either simultaneous (PCV13, DTaP, and IIV4) or sequential (PCV13 & DTaP, then IIV4 2 weeks later).

The safety presentation included an update of the Systematic Observational Method for Narcolepsy and Influenza Immunization Assessment (SOMNIA), an international study conducted at 14 sites. The study looked at adjuvanted 2009 pandemic influenza vaccines, Arepanrix and Pandemrix, which did not show an increased risk of narcolepsy vaccines.

At the ACIP meeting, there was a presentation by Seqirus, a manufacturer of a quadrivalent influenza vaccine (aQIV), which conducted a randomized clinical trial in children comparing aQIV with Fluzone TIV/QIV. The Seqirus vaccine showed higher rates of local and systemic reactogenicity. Most reactions began day 1 through 3, were moderate, lasted 2-3 days, and resulted in higher incidence of fever but no increase in febrile convulsions. The vaccine showed superior efficacy and immunogenicity, but in the US is it recommended only for those 65 and older. Recommendations for the 2018-2019 flu season included some changes:

- LAIV4 was again recommended after a two-year hiatus because of poor efficacy;
- Two new strains in the trivalent vaccine;
- Afluria Quadrivalent age range was changed from over 18 to over 5 years; and
- Fluarix Quadrivalent age range to infants older than six month (previously greater than 3 years).

The ACIP session on human papillomavirus vaccine (HPV) revealed that a Biologic License Application (BLA) was submitted to the FDA in April to extend the age indication for 9vHPV to age 45 years for males and females. Some countries have already approved that age range. One trial in females aged 24-48 years showed high statistically significant efficacy against persistent infection.

In October, ACIP recommended the use of a third dose of the measles-mumps-rubella (MMR) vaccine during mumps outbreaks, which have increased since 2012. The mumps work group is updating guidance on third dose implementation.

With regard to recombinant zoster vaccine, the uptake has been rapid with nearly 7,000 reports sent to VAERS. The VSD reports 37,303 doses administered by six VSD monitoring sites as of May 31, 2018. Also, there have been over 130,000 doses administered in the VSD monitoring sites, which will be conducting rapid cycle analysis. Information on short- and long-term outcomes/adverse reactions is available. A Morbidity and Mortality Weekly Report (MMWR) article published in May 2018, described some administration errors that may have been the result of confusion between the new Shingrix vaccine and the old live Zostafax. The Shingrix vaccine is administered intramuscularly, the Zostavax was one dose administered subcutaneously. More detailed information will be published in MMWR before the next ACIP meeting in October 2018.

ACIP recommended pneumococcal vaccine (PCV13) in 2014. VAERS reporting through the end of 2017 revealed no safety signals and a VSD study did not support an increased rate of adverse events following PCV13 administration versus PPSV23 (which contains capsulated polysaccharide antigens). Studies cited at the ACIP meeting strongly suggest a direct impact of PCV13 on pneumococcal-community acquired pneumonia.

Recent Publications

Dr. McNeil briefly discussed the following recent publications:

1. Haber P, Amin M, Ng C, Weintraub E, McNeil MM. **Reports of lower respiratory tract infections following dose 1 of RotaTeq and Rotarix vaccines to the Vaccine Adverse Event Reporting System (VAERS), 2008-2016.** Hum Vaccin Immunother. 2018 Jul 11:1-5.

SUMMARY: A 2018 manufacturer post-licensure safety study identified a possible association between Rotarix (RV1) rotavirus vaccine and lower respiratory tract infections (LRTI) in infants within 0-6 days following receipt of RV1 dose 1. We reviewed reports to the VAERS of LRTI occurring 0-6 days and 0-29 days post vaccination following RotaTeq (RV5) or Rotarix (RV1) vaccinations in conjunction with either Prevnar (PCV7) or Prevnar 13 (PCV13), in infants aged 6 to 15 weeks. There was no significant difference in LRTI reports to VAERS in the 0-6 days and 0-29 days following receipt of either RV5 or RV1 given with either pneumococcal vaccine
Available at https://www.ncbi.nlm.nih.gov/pubmed/29993327

2. Kharbanda EO, Vazquez-Benitez G, Lipkind HS, Sheth SS, Zhu J, Naleway AL, Klein NP, Hechter R, Daley MF, Donahue JG, Jackson ML, Kawai AT, Sukumaran L, Nordin JD. **Risk of Spontaneous Abortion After Inadvertent Human Papillomavirus Vaccination in Pregnancy.** Obstet Gynecol. 2018 Jul; 132(1):35-44.

CONCLUSIONS: Inadvertent 4vHPV exposure during or peripregnancy was not significantly associated with an increased risk of spontaneous abortion.
Available at https://www.ncbi.nlm.nih.gov/pubmed/29889760

3. Su J, Ng C, Lewis PW, Cano MV. **Adverse events after vaccination among HIV-positive persons, 1990-2016.** PLOS One, Published: June 19, 2018

CONCLUSIONS: We identified no unexpected or unusual patterns of AEs among HIV positive persons. These data reinforce current vaccine recommendations for this risk group. However, healthcare providers should know their HIV-positive patients' immune status because immunocompromising conditions can potentially increase the risk of rare, but severe, AEs following vaccination with live virus vaccines.
Available at http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0199229

4. Moro PL, Perez-Vilar S, Lewis P, Bryant-Genevier M, Kamiya H, Cano M. **Safety surveillance of diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccines.** Pediatrics. 2018 Jun 4.

CONCLUSIONS: No new or unexpected adverse events detected. Observed disproportionate reporting for some non-serious vaccination errors calls for better education of vaccine providers on the specific indications for each of the DTaP vaccines.
Available at https://www.ncbi.nlm.nih.gov/pubmed/29866795

5. Jackson ML, Yu O, Nelson JC, Nordin JD, Tartof SY, Klein NP, Donahue JG, Irving SA, Glanz JM, McNeil MM, Jackson LA. **Safety of repeated doses of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine in adults and adolescents.** Pharmacoepidemiol Drug Saf.2018 Jun 3.

SUMMARY: We evaluated the safety of repeated doses of tetanus-containing vaccine in 68,915 non-pregnant adolescents and adults in the VSD population who had received an initial dose of Tdap. Compared with 7,521 subjects who received a subsequent dose of tetanus toxoid, reduced diphtheria (Td) vaccine, the 61,394 subjects who received a subsequent dose of Tdap did not have significantly elevated risk of medical visits for seizure, cranial nerve disorders, limb swelling, pain in limb, cellulitis, paralytic syndromes, or encephalopathy/encephalitis/meningitis. These results suggest that repeated Tdap vaccination has acceptable safety relative to Tdap vaccination followed by Td vaccination.
Available at https://www.ncbi.nlm.nih.gov/pubmed/29862604

6. Shimabukuro TT, Miller ER, Strikas RA, Hibbs BF, Dooling K, Goud R, Cano MV. **Notes from the Field: Vaccine administration errors involving recombinant zoster vaccine—United States, 2017-2018.** MMWR Morb Mortal Wkly Rep. 2018 May 25; 67(20):585-586.

SUMMARY: Early monitoring indicates that vaccine providers might confuse administration procedures and storage requirements of the older ZVL and the newer RZV. Failure to reconstitute the vaccine and administration of only one component of RZV also appears to be occurring, similar to errors observed for other vaccines that require mixing. Whereas RZV administered through the appropriate intramuscular route is associated with high rates of local and systemic reactions, erroneous subcutaneous injection can increase the likelihood of these episodes. Some errors could potentially affect vaccine effectiveness. To prevent RZV administration errors, vaccine providers should be aware of prescribing information, storage requirements, preparation guidelines, and ACIP recommendations for herpes zoster vaccines.
Available at
https://www.cdc.gov/mmwr/volumes/67/wr/mm6720a4.htm?s_cid=mm6720a4_w

During discussion following Dr. McNeil's presentation, Ms. Luthy asked about the wording "unexpected adverse events" and what adverse events would be unexpected? Dr. McNeil responded that short-term systemic injection site reactions would be considered expected, which would typically be listed in the VIS. The package insert also lists extensive adverse events that may be rare, which makes it difficult to assign causality to the vaccine.

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 began by discussing current NIAID research related to influenza virus. Ms. Schuster described virus-like particles (VLPs), which are protein-based structures that mimic viruses and bind to antibodies. Because VLPs are not infectious, they could serve as vaccine platforms for many viral diseases, including influenza. A team of NIAID researchers developed

a 3-D model based on the 1918 H1N1 pandemic influenza virus VLPs. A better understanding of these VLPs could help researchers find effective seasonal and universal influenza vaccines. The research could also benefit a range of other VLP vaccine projects, including for HIV, Ebola and SARS coronavirus.

As discussed at previous ACCV meetings, in February 2018, NIAID launched a strategic plan for developing a universal influenza vaccine and is actively supporting projects that are working toward development of a universal influenza vaccine that would provide durable protection against various flu strains.

NIAID announced several new funding opportunities to stimulate research community interest in vaccine research. Two such announcements occurred in July 2018 to support research aligned with focus areas from NIAID's universal influenza vaccine strategic plan, including transmission, natural history, pathogenesis, characterization of influenza immunity and correlates of protection, as well as rational design of universal vaccines. Also, in July 2018, NIAID began soliciting proposals for a new program, the Collaborative Influenza Vaccine Information Centers (CIVICs), which has the goal of improving seasonal influenza vaccines and developing universal influenza vaccines, and will include human challenge studies, in which researchers expose a person to an influenza virus under carefully controlled conditions to better characterize the course of disease and evaluate new treatments and vaccines.. Participants will be closely monitored and cared for during these studies.

NIH and CDC have jointly supported program announcements on vaccine safety research since 2008. The latest announcements were released in July 2018. The research would focus on physiological and immunological responses to vaccines and components; how genetic variations affect the responses; risk factors and biological markers; statistical methodologies; genomic technologies and systems biology; and vaccine combinations and vaccine schedules. Since 2009, NIH has funded 24 awards under these announcements.

NIH has formed the Trans-NIH Pediatric Research Consortium to coordinate pediatric research across its 27 institutes and centers, with total support of over $4 billion in FY 2017. The consortium seeks to harmonize research activities, explore research gaps and opportunities and establish priorities.

Finally, in August 2018, NIAID announced that a first human trial of an experimental live attenuated Zika virus vaccine developed by NIAID scientists has begun at the Johns Hopkins Center for Immunization Research and at the Vaccine Testing Center at the University of Vermont. The trial will enroll 28 non-pregnant adults 18 to 50, and the Phase I Clinical trial will assess the experimental vaccine's safety and generation of an immune response. Ms. Schuster concluded her comments.

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

CDR Marshall reported that the FDA approved supplements for the BLA for seasonal influenza vaccines to include the 2018-2019 United States formulation and associated labeling revisions.

CDR Marshall also discussed that over the last several years, there's been growing scientific and public interest in the role of microorganisms in the maintenance of overall health and prevention and treatment of disease. To this end, the FDA will convene a workshop, co-hosted with NIH, on September 17, 2018, to exchange information with the scientific community

about the clinical, manufacturing, and regulatory considerations associated with live microbiome-based products, when administered to prevent, treat, or cure a disease or condition in humans.

Update from the National Vaccine Program Office, (NVPO), Ann Aikin, NVPO

Ms. Aikin announced that the National Vaccine Advisory Committee (NVAC) recently released a report entitled "Strengthening the Effectiveness of National, State, and Local Efforts to Improve HPV Vaccination Coverage in the United States" that focuses on four key areas:

- Additional national partners that may be interested in supporting that area of research;
- Coalitions at the state and local level;
- Ways to engage integrated health care delivery networks; and
- Ways to address provider needs in rural areas.

The report is available on the NVPO website. Future 2018 NVAC meetings are scheduled for September 12-13 at the Hubert Humphrey Building; and in 2019, February 5 (Virtual meeting); June 4-5 (In person); September 17-18 (In person).

Ms. Aikin announced that the 21st Century Cures Act required NVPO to submit a report to Congress on encouraging vaccine innovation. Main points in the report include the fact that the vaccine enterprise is well-established and has been successful in bringing new and improved vaccines to the market (over 120 vaccine candidates were under development when the report was written). The prevailing business model that prioritizes vaccine candidates is for large markets, but some of the markets may be smaller than anticipated for the vaccines that will be developed. There is a consideration that a substantial investment will be needed to address some of the complex needs of the remaining targets. There is uncertainty about public health priorities and the estimated public demand for some of the vaccine candidates, which affects the return on investment on the development of the candidates. The report is available on the NVPO website.

Ms. Aikin described the "Your Best Shot" video series, which is educational rather than promotional, and focuses on the importance of vaccines across the lifespan. Three vaccines are highlighted – shingles, pneumococcal disease and whooping cough. The videos are available online at: https://www.vaccines.gov/resources/videos_and_tools/index.html

Finally, a major content audit and refresh was completed on www.vaccines.gov, an award-winning website developed in 2011 to provide trusted and consumer-friendly information about vaccines and vaccine-preventable diseases.

Public Comment

Ms. Luthy invited comments from anyone on the teleconference call. There was only one comment from Ms. Theresa Wrangham.

Ms. Wrangham commented that NVIC has worked with ACCV and NVAC, has successfully sponsored members on both committees, coordinated vaccine safety workshops with the IOM, and has presented parent perspectives to the IOM in their reporting process. However, in recent years NVIC appears to have been excluded from some stakeholder processes. This is of concern to NVIC, given its historic standing and involvement in processes relating to vaccine injury and death, and the fact that NVIC worked with congress to pass the 1986 Act

establishing the VICP. The NVIC welcomes and requests the inclusion in the stakeholder processes related to the ACCV and what is put before the commission for their consideration. Ms. Wrangham noted that the NVIC represents the interests of those who have vaccine safety concerns and those who are injured or die as a result of adverse events following the use of vaccines.

Ms. Wrangham said that as the Process Work Group considers recommendations, NVIC requests that the Commission continue to review the 2009 Altarum and Banyan reports, and the 2014 GAO VICP report and consider their findings and recommendations relating to the need for a mechanism to gauge ongoing petitioner satisfaction within the VICP, and adequacy of the VICP awards. Ms. Wrangham recalled that in the December 2016 ACCV meeting and the DOJ's report that a successful VICP petitioner deemed their injury award inadequate. Currently there is no measure of adequacy of awards, particularly from the standpoint of the petitioner.

Ms. Wrangham noted that NVIC works in consultation with CDC, not in collaboration, with regard to VIS revisions. NVIC supports the provider-neutral language in the VIS. It worked with congress to include informed consent protections in the 1986 Act that led to the VIS, which prior to vaccination provides information on diseases and the risks and benefits of vaccines. Many of those protections were removed from the law in 1995 to simplify the VIS, which reduced transparency and information needed to make educated vaccine decisions. NVIC encourages ACCV to review those changes in the law. There is no regulatory impediment to reinstating previously-required information. The purpose of the VIS is to provide information prior to vaccination. Ms. Wrangham felt the first section, "Why get vaccinated," is a marketing statement, rather than information about vaccine risks and benefits or information about the disease. She said that NVIC supports more neutral language in the VIS. Prior to the change in 1995 more information was available on the VIS.

Ms. Wrangham continued, with regard to pregnant women mentioned in the VIS, it would be helpful to explain which vaccines are licensed for use in this population. With regard to mention of the VICP in the VIS, consumers would benefit from a statement therein that contains more specificity on the statute of limitations. The Altarum and Banyan reports stated that consumers want more detail, not less, where vaccine injuries are concerned. NVIC encourages the commission to review those reports and determine whether they would apply to VIS content and revisions.

Finally, NVIC notes that there are significant gaps in vaccine safety research, mentioned in the IOM reports. NVIC requests information on what efforts are under way to close these gaps. The concern is that vaccines are being created and mandated more quickly than research that would assure the public that they are safe and clarify the risks related to the.

Future Agenda Items/New Business, Ms. Beth Luthy, Chair

Ms. Luthy ascertained by voice affirmation that only four commission members were on the telephone conference, which is insufficient for a quorum. Therefore, all relevant votes, specifically the letter of recommendation to the Secretary, would have to be deferred until the December 2018 meeting.

Regarding future agenda items, the Commission discussed the decision to continue the current active Process Work Group or to establish a new work group to address petition issues, like impending statute of limitations that might shortstop a case and remove the VICP's obligation to pay attorney's fees and costs. Another example is the possible reticence of an

attorney to accept a complicated claim in preference to a simpler, more straightforward claim, which could be prejudicial to an injured party. There was consensus that the Process Work Group should continue to handle such issues.

Ms. Luthy referred to Ms. Wrangham's comments regarding consent and the VIS and suggested that a presentation to educate and clarify the issue would be helpful. Dr. Nair reminded the commission that consent is not a federal requirement or issue, but one that is required by some states. That issue could still be placed on the agenda for clarification. Ms. Stewart suggested assigning the issue to the Process Work Group for review before putting it on the agenda.

Mr. Howie also referred to a comment by Ms. Wrangham about how the public is permitted to make presentations about Table revisions. There was consensus that the issue was valid, but that it should be referred to the Process Work Group.

Adjournment

Ms. Luthy expressed appreciation to those on the call for their participation. There being no further business, the meeting was adjourned.