

*****AMENDED – Members voted during the June 2022 ACCV meeting to amend the December 2020 minutes to reflect that a vote was requested, and members were in favor, rather than stating that the members agreed, to Dr. Mawson speaking during a future ACCV Meeting.***

Advisory Commission on Childhood Vaccines (ACCV)

Teleconference and Adobe Connect

December 3, 2020

Members Present

John Howie, JD, Chair (2020)
Karen Kain, Vice Chair (2022)
Barbara Pahud, MD (2022)
William Spiegel, MD (2023)

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

Tamara Overby, Acting Director, DICP
Andrea Herzog, Principal Staff Liaison, ACCV

Welcome and Report of the Chair and Approval of the September 4, 2020 meeting Minutes, Mr. John Howie, Chair, ACCV

Mr. Howie welcomed participants to the meeting and announced that this is his last meeting, as his term expires December 2020. Mr. Howie did a roll call confirming the presence of a quorum. Next, he explained that the meeting would have several guest presentations about the National Vaccine Injury Compensation Program (VICP) Notice of Proposed Rulemaking (NPRM), proposing removal of Shoulder Injury Related to Vaccine Administration (SIRVA) and syncope from the Vaccine Injury Table (Table) and the usual updates from the DICP, the Department of Justice (DOJ) and the ACCV ex officio members.

Next, Mr. Howie invited public comment on the agenda.

Public Comments:

1. Ms. Theresa Wrangham, Executive Director of the National Vaccine Information Center (NVIC), asked if the information in the presentation by the Immunization Safety Office (ISO) is available to independent researchers, including citations and information about funding.
2. Mr. D. Hodges commented that he experienced SIRVA after receiving the pneumococcal polysaccharide vaccine, a vaccine not covered in the Table. He asked if a discussion of adding that vaccine to the Table could be included in the agenda at a future meeting.

There were no other requests to comment on the agenda.

On motion duly made and seconded, the ACCV unanimously approved the minutes of the September 4, 2020 meeting.

Report from the DICP, Ms. Tamara Overby, Acting Director, DICP

Ms. Overby briefly reviewed the day’s agenda items; which includes updates from the DICP, the DOJ and the ACCV Work Group, guest presentations about the VICP NPRM, an overview of the Countermeasures Injury Compensation Program (CICP), and reports from ACCV ex officio members representing the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the Office of Infectious Disease and HIV/AIDS Policy (OIDP).

Beginning with the DICP update, Ms. Overby reported that the 1,191 claims were filed in the VICP in FY 2020, slightly down from 2019. The claims filed included 1,084 for adults and 107 for children. During the first two months of FY 2021, 279 claims have been filed, which is slightly more than the same period last year. She added that administrative funding in 2020 was \$10.2 million, 11% higher than the previous year.

Ms. Overby stated that there are 1,021 petitions pending review. That backlog includes 968 claims for adults and 53 for children, of which 278 have not been activated by the pre-assignment review (PAR), which is a step in the process used by the U.S. Court of Federal Claims to screen claims to insure readiness for review. In FY 2020, petitioners’ awards amounted to about \$187 million and attorneys’ fees and costs were about \$31 million.

Adjudication Categories	Fiscal Year 2019	Fiscal Year 2020	Fiscal Year 2021
Compensable	641	706	79
Concession	237	265	27
Court Decision	45	47	6
Settlement	359	394	46
Not Compensable	181	198	24
Total	822	904	103

Ms. Overby reported that the balance of the Vaccine Injury Compensation Trust Fund (Trust Fund) was slightly more than \$4 billion as of September 2020. In FY 2020, the Trust Fund earned \$310 million in excise tax revenue about \$70 million interest income and approximately \$4.4 million in refunds.

Ms. Overby continued her presentation by reporting the following VICP statistics that may be of interest to the ACCV.

- 90% of petitions were filed for adults in the last 2 years.
- Over 54% of petitions filed in the last two FY allege shoulder injury related influenza vaccine administration (SIRVA).
- 73% of petitions filed in the last two FY allege an injury from the influenza vaccine.
- About 70% of petitions filed are compensated negotiated settlement since FY 2006 (but only 56% in FY 2019)
- There is nearly a 13-month wait for petitions to be reviewed by a HRSA physician.

Finally, Ms. Overby announced that ACCV is seeking nominations for all positions on

the commission. The positions on the ACCV include:

- Three members who are health professionals with expertise in the health care of children, the epidemiology, etiology, and prevention of childhood diseases, and the adverse reactions associated with vaccines, of whom at least two shall be pediatricians.
- Three members from the general public, of whom at least two shall be legal representatives of children who have suffered a vaccine-related injury or death.
- Three members who are attorneys, of whom at least one shall be an attorney whose specialty includes representation of persons who have suffered a vaccine-related injury or death and of whom one shall be an attorney whose specialty includes representation of vaccine manufacturers.

An ACCV member commented that since 2017, when SIRVA was added to the Table, petitioners' awards have decreased a total of about \$70 million annually, which appears to be inconsistent with the HHS position that SIRVA injuries are depleting the fund. Ms. Overby responded that there is no representative of HHS to explain the department's position.

Report from the DOJ, Ms. Catharine Reeves, Deputy Director, Torts Branch, DOJ

Ms. Reeves referenced the Department of Justice (DOJ) PowerPoint materials as part of her presentation for the three-month reporting period from August 16, 2020, through November 15, 2020. (DOJ PowerPoint (PP) at 2.) She noted that DOJ's reporting period is different from the HHS and CFC reporting periods. Ms. Reeves stated that during DOJ's reporting period, 411 petitions were filed, 37 (9%) of which were filed on behalf of minors and 374 (91%) of which were filed by adults. (DOJ PP at 2.)

Ms. Reeves stated that 219 petitions were adjudicated during this reporting period. (DOJ PP at 3.) One hundred and sixty-six of the adjudicated cases were compensated. (DOJ PP at 3.) Of the 166 compensated cases, 52 cases were conceded by the government, three of which had decisions awarding damages and 49 of which had decisions adopting proffers. One hundred and fourteen of the compensated cases were not conceded by the government, the majority of which (105 cases) involved settlements. Fifty-three cases were not compensated. (DOJ PP at 3.) Six petitions were voluntarily withdrawn. (DOJ PP at 4.)

Ms. Reeves discussed recently decided and pending cases in the U.S. Court of Appeals for the Federal Circuit (CAFC). (DOJ PP at 5-7.) She stated that during the reporting period, the CAFC affirmed two entitlement decisions appealed by petitioners, affirmed in part and remanded in part one entitlement decision appealed by a petitioner, vacated and remanded one attorney's fees and costs decision appealed by a petitioner, and denied a rehearing en banc of one entitlement decision appealed by respondent. (DOJ PP at 5.) She further noted that six appeals by petitioners were pending (five entitlement decisions and one attorney's fees and costs decision), and no appeals by respondent remain pending before the CAFC. (DOJ PP at 6-7.)

Ms. Reeves next discussed appeals at the Court of Federal Claims (CFC). (DOJ PP at 8-11.) She noted that the CFC affirmed seven decisions appealed by petitioners during this reporting period (six entitlement decisions and one attorney's fees and costs decision) and denied in part and remanded in part one attorney's fees and costs decision appealed by a petitioner. (DOJ PP at 8.) Ms. Reeves stated that there were ten appeals pending before the CFC filed by

petitioners, three of which were filed since the last reporting period (nine entitlement decisions and one redaction decision). (DOJ PP at 10-11.) She further stated that there were no appeals by respondent pending before the CFC. (DOJ PP at 12.)

Ms. Reeves noted that oral argument at the CAFC in *Orloski v. HHS* was scheduled for January 6, 2021, and oral argument at the CFC in *DeLozier v. HHS* was scheduled for December 9, 2020. (DOJ PP at 13.)

Ms. Reeves 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 14-23.) Ms. Reeves also provided the usual appendices, which include a glossary of terms and diagrams to help commissioners understand the appeals process.

Ms. Reeves concluded her report and invited questions from the commissioners. Mr. John Howie noted that, at the previous meeting, he inquired whether citations for appellate cases and decisions could be included in the DOJ ACCV presentation in the future and wished to reiterate this request. Ms. Reeves stated that all decisions by the CFC and the CAFC are published on the respective court's website, but DOJ would take the renewed request into consideration. She further noted that while oral arguments at the CFC are not public, oral arguments at the CAFC are recorded and available on the court's website.

ACCV Workgroup Updates

Mr. Howie explained that since there are only four commission members, activity of the workgroup has been limited. He stated his concern about the information on the Vaccine Information Sheet (VIS) perhaps not conveying the urgency that may apply to promptly filing a claim, since there are time limitations that might be misunderstood. He said the workgroup has been looking at revising the VIS language about the VICP filing deadlines and he presented proposed wording:

Current Language:

The National Vaccine Injury Compensation Program (VICP) is a federal program that was created to compensate people who may have been injured by certain vaccines. Visit the VICP website at www.hrsa.gov/vaccinecompensation or call 1-800-338-2382 to learn about the program and about filing a claim. There is a time limit to file a claim for compensation.

Proposed Language:

The National Vaccine Injury Compensation Program (VICP) is a federal program that was created to compensate people who may have been injured by certain vaccines. **Petitions regarding alleged injury or death due to vaccination have a time limit for filing which may be as short as 2 years from the date of vaccination.** Visit the VICP website at www.hrsa.gov/vaccinecompensation or call 1-800-338-2382 to learn about the program and about filing a claim.

Mr. Spiegel asked why the words "from the date of vaccination" were deleted from previous VIS language proposals. Ms. Overby explained that the statute specifies "from the date of first manifestation of a symptom." There was extensive discussion about the fact that a deadline depending on appearance of symptoms over an indefinite time could cause confusion about the actual filing deadline. Ultimately, the commission members agreed to vote on a recommendation for wording. Ms. Overby confirmed that the requisite public discussion had

occurred (as required by regulation) and that the vote would be appropriate. On motion duly made and seconded, the Commission unanimously approved the proposed wording that includes “from the date of vaccination.”

Guest Presentations and Discussions about the VICP NPRM

1. Ms. Theresa Wrangham, Executive Director, NVIC

Ms. Wrangham provided background regarding the establishment of the VICP, which was at the behest of Congress. The NVIC supported developing the language of the vaccine compensation legislation and provided support in garnering public endorsement of the program. Early on, the Institute of Medicine (IOM), now the National Academy of Medicine, invited NVIC to lend support to its programs. Other federal agencies have also requested NVIC’s input.

NVIC does not take a position for or against vaccines and vaccination programs. NVIC endorsed establishing a generous, no-fault and expeditious process for compensating vaccine-injured individuals. Originally the law was not intended to be a broad liability shield, although that occurred in 2011, as a result of the Supreme Court decision in *Bruesewitz v. Wyeth*, upholding a federal law that established protection for vaccine makers from lawsuits and provided compensation for certain vaccine injuries.

With regard to vaccine research, the Vaccine Act also mandated that there must be a commensurate investment in research. Ms. Wrangham explained that the NVIC supported the involvement of the IOM in vaccine research because of its reputation for impartial reports. Some of those reports revealed gaps in science and understanding of some vaccine injuries. The 2012 report looked at about 156 adverse event reports and deemed that in 85%, the IOM was not able to establish causality. The report also provided language in the case of SIRVA and syncope, noting that vaccines could not be ruled out as a cause of SIRVA. The IOM also stated that “evidence convincingly supports” causation, its strongest language concerning the issue, which resulted in the ACCV endorsing adding the injuries to the Table in January 2017.

Ms. Wrangham observed that the usual process, which would include presentations to the ACCV concerning the proposed Table changes, did not occur with this VICP NPRM. She noted that it has been about ten years since any new evidence about SIRVA and syncope has been provided to the ACCV, despite a significant number of papers published in PubMed that show a disproportionate number of incidents of syncope that occur with HPV vaccine, suggesting a possible involvement of the vaccine. There is also significant evidence of the involvement of the vaccine antigen in SIRVA, which does not usually occur with other vaccines and injection procedures.

Ms. Wrangham further commented that despite the VICP’s early success in responding to injury claims, by 2015, only 2% of petitions filed were for Table injuries, indicating that the process has become more adversarial. Ms. Wrangham noted that children are rarely compensated. She expressed the opinion that because it is more difficult to receive compensation, the original intent of the VICP, to err on the side of the petitioner, is not happening. Ms. Wrangham summarized her arguments against the VICP NPRM:

1. Public comments have supported retaining syncope and SIRVA on the Table.
2. Despite the increase in compensated claims, the balance of the VICP Trust fund continues to increase; suggesting that SIRVA and syncope are not having a negative impact on the VICP Trust Fund.

3. There is an administrative process (PAR) in place to avoid proceeding with frivolous claims.
4. Removing SIRVA and syncope from the Table means petitioners will need to pursue causation in fact claims, which will increase legal expenses.
5. Causation in fact claims will increase caseloads because claim will remain in the VICP process longer than necessary.

Ms. Wrangham concluded her presentation.

2. Ms. Christina Ciampolillo, President, Vaccine Petitioners Bar Association

Ms. Ciampolillo began her presentation with a chronological description of the process to add SIRVA and syncope to the Table, and now, to remove both injuries from the Table. She stated that HRSA presented a proposal to add SIRVA and syncope to the Table in December 2010, based on a paper from S. Atanasoff and a year later, HRSA submitted new Table language to the ACCV for their counsel. The ACCV and HRSA reviewed and revised the proposed Table language over the next few years. In July 2015, the Secretary of HHS (Secretary) published an NPRM in the Federal Register, proposing to add SIRVA and syncope to the Table. The final rule was published in the Federal Register in January 2017, and the injuries were officially added to the Table later that year.

Ms. Ciampolillo commented that the Secretary reversed the HHS position on SIRVA and syncope in March 2020, and the NPRM was published in the Federal Register four months later, in July 2020. There have been no recently published papers looking at providing evidence for or against removing SIRVA or syncope from the Table. Ms. Ciampolillo stated her opinion that the substance of the NPRM is flawed, and the timing of the change may damage public confidence in national vaccine policy. She added that if the NPRM were successful at removing the injuries from the Table, petitioners could still be pursue claims through the program; however, the costs and time involvement would significantly increase.

Ms. Ciampolillo ended her presentation.

3. Mr. Mike Milmoie, JD, Law Office of Leah Durant

By way of background, Mr. Milmoie mentioned that he had been with the DOJ for 30 years representing the federal government in vaccine litigation, until his retirement in 2017 and was an attorney for the DOJ in the first vaccine case in 1989. Noting his long dedication to making the VICP work as Congress intended and adding that he was invested in the program in that context, he expressed his opinion that the proposal to remove SIRVA and syncope from the Table is “illegal, contrary to science, and if successful, a disaster to national health policy.”

Mr. Milmoie explained that the main purpose of the ACCV is to provide advice and recommendations to the Secretary on implementing the VICP; this includes changes in the injuries and vaccines the program covers. In the history of the VICP, the Secretary has never effected changes to the Table without seeking the counsel and recommendations of the ACCV, until now. In May 2020, the ACCV considered the proposed change to the Table and unanimously opposed the proposal, submitting to the Secretary a complete explanation of the ACCV’s opposition. The Secretary, in turn, rejected the ACCV’s recommendation and moved

forward with the VICP NPRM. The Secretary has been silent in terms of offering any response to the ACCV's opposition and recommendations. Currently, many of the positions on the ACCV, normally filled by medical, public health, and legal experts, remain unfilled. Mr. Milmoie suggested that the indifference of Secretary to the ACCV's recommendations might be negatively affecting recruitment for those positions.

Finally, Mr. Milmoie stated that there is a provision in the NPRM to reverse the policy that automatically adds all vaccines recommended by the CDC for routine use in children, taking into account recommendations by the American Academy of Pediatrics, to the Table, including for any COVID-19 vaccines approved by FDA.

In the NPRM, the Secretary is proposing that the decision to add vaccines to the Table should be under his purview. Mr. Milmoie stated that this decision should not be determined by the Secretary alone and should be based on guidance from medical experts. Mr. Milmoie concluded his remarks.

Following Mr. Milmoie's presentation, there was a discussion among the ACCV members. During the discussion, members asked questions about emergency use of COVID-19 vaccines. Ms. Overby clarified that currently COVID-19 vaccines are covered under the CACP. To be covered under the VICP, the vaccine would have to be recommended for routine administration in children and/or pregnant women, and Congress must impose an excise tax on the vaccine, and then the Secretary must add it the Table.

4. Mark Bodor, M.D., Interventional Spine and Sport Medicine, Private Practice

Dr. Bodor briefly described the anatomy of the shoulder, pointing out the muscles that control arm movement, the deltoid muscle, the muscles of the rotator cuff, and the bursa that provides lubrication to the muscles. A vaccine injection should enter the deltoid muscle via a needle; however, the needle may injure the bursa or a bone if injected improperly, often by administering the shot too high or too deep on the shoulder. With over 300 million vaccinations a year, adverse reactions are expected. Those reactions can be transient or last for months or even years.

Dr. Bodor explained that research has revealed that if the vaccine is injected improperly it can be deposited in certain areas of the bursa. Specifically, two rotator cuff tendons are most often involved in cases of chronic pain caused by those vaccine deposits, the infraspinatus, and the teres minor. A procedure has been developed that removes the vaccine, and subsequently, the pain is resolved. Although a double blind, random controlled trial has not been conducted; eight patients have been successfully treated with this procedure. Dr. Bodor concluded with the comment that there are frequent treatments that involve injection in the shoulder of various compounds and medicines that do not result in SIRVA-like pain with the frequency of those that involve the two tendons mentioned.

5. Dr. Uma Srikumaran, MD, Associate Professor of Orthopaedic Surgery, Johns Hopkins Shoulder and Sports Medicine

Dr. Srikumaran commented that the VICP NPRM contends that SIRVA is caused by poor injection technique alone, rather than earlier proposals that SIRVA is caused by both injection technique and vaccine antigen. That statement was also in the IOM report, but Dr. Srikumaran expressed the opinion that vaccine antigen alone in or near the bursa could cause the SIRVA

response. A rapid onset of pain with limited range of motion following vaccination is consistent with a robust and prolonged immune response within already sensitized shoulder structures following injection of antigenic substance into the bursa or the area around the rotator cuff tendon. The NPRM also notes that medical literature supports the possibility that SIRVA may result from improper needle length or injection technique.

Dr. Srikumaran added that the issue is more accurately a risk versus benefit equation, similar to that of infection related to surgery. There are steps that surgeons take to reduce the risk of infection, but total elimination of infection is elusive. He noted that one report suggested that vaccine needle over-penetration that can lead to SIRVA could be prevented by refining the CDC's current injection guidelines. He argued that a more appropriate interpretation would be that proper technique could reduce the incidence of SIRVA. Increased training and education can certainly reduce the incidence, but that would not prevent it entirely. He added that absolute injection accuracy would require imaging guidance for every single injection, which would be administered by a physician with extensive imaging experience, a combination of technology and physician skill that is very difficult to achieve.

In conclusion, Dr. Srikumaran observed that research from all over the world is creating an increasing body of knowledge about shoulder-related injury following vaccination, looking at many aspects of the problem. He reiterated his recommendation that education and training, including the patient, could serve to reduce the instance of SIRVA. Patient understanding of the importance of injection location would be beneficial to the health care provider's efforts to reduce risk. In addition, it might be appropriate to consider using injection sites other than the shoulder, such as the thigh.

Discussion of Studies for Vaccinated vs. Unvaccinated Populations, Ms. Karen Kain, ACCV Member

Ms. Kain emphasized that the ACCV charter mandates the ACCV support efforts to ensure that vaccine products cause few, if any, adverse events. She noted that there are several surveillance programs that collect information on the frequency and severity of adverse reactions associated with childhood vaccines. When injury does occur, it is the responsibility of the program to compensate the children expeditiously and fairly. Ms. Kain stated that, "if you are pro vaccination, you must be pro compensation." Fairly and expeditiously compensating vaccine-injured petitioners requires availability of appropriate information on the science. Ms. Kain requested that the ACCV undertake a vaccinated versus un-vaccinated study (vax vs. un-vax study).

Ms. Kain continued, in 2019, the World Health Organization (WHO) declared vaccine hesitancy a major threat to global health. The risks related to the childhood vaccine schedule currently are unknown. The childhood vaccine schedules have never been studied despite a significant increase in the recommended vaccines since the 1983 schedule was developed, when children received ten vaccines. Today there are 16 vaccines on the childhood vaccine schedule. The effects of these vaccines is uncertain since vaccine adjuvants and preservatives have not been tested and the risks identified. A significant research question is whether vaccines play a role in neural disorders – learning disability, attention deficit, hyperactivity, and autism spectrum disorders.

The 2012 IOM report pointed out the lack of longitudinal comparative data between vaccinated and unvaccinated children, a fact conceded by the CDC. The IOM has consistently

noted the gaps in safety knowledge and in the science itself, and in the lack of comparative studies of vaccinated and unvaccinated children. Ms. Kain stated that there are a number of studies in the literature, prominent among them are studies by Dr. Bernard Moss. She suggested that the ACCV invite Dr. Moss to present data from his most recent published paper (November 2020, entitled “Multiple vaccinations and the enigma of vaccine injury), perhaps at the March 2021 meeting.

Ms. Kain concluded her remarks and **asked for a vote to invite Dr. Anthony Mawson to present. All members were in favor. However, Ms. Pahud expressed doubt and asked for an additional researcher(s), who works with VSD to be present on the call.** Ms. Overby added that she requested Dr. Jonathan Duffy, CDC, to share information about research that has been conducted in this area.

Update on the ISO, CDC, Dr. Jonathan Duffy

Dr. Duffy gave a presentation on “Studying the safety of the childhood immunization schedule in the Vaccine Safety Datalink.” Dr. Duffy commented that The National Vaccine Program Office asked the Institute of Medicine (IOM) to convene a committee of experts to identify feasible study designs to explore the safety of the U.S. childhood immunization schedule. The committee’s report, entitled ‘The Childhood Immunization Schedule and Safety: Stakeholder Concerns, Scientific Evidence, and Future Studies’ was published in 2013 and is freely available online. The charge to the IOM committee included two items. First, to review scientific findings and stakeholder concerns related to the safety of the recommended childhood immunization schedule. And second, to identify potential research approaches, methodologies, and study designs that could inform this question, considering strengths, weaknesses, as well as the ethical and financial feasibility of each approach. The report stated: “Even though the vast majority of parents adhere to the ACIP-recommended immunization schedule, some parents are concerned that the schedule may present unnecessary risks because of the timing and number of vaccinations.” The report identified the following four leading research questions of interest to select stakeholders.

1. How do child health outcomes compare between those who receive no vaccinations and those who receive the full currently recommended immunization schedule?
2. How do child health outcomes compare between those who receive the full currently recommended immunization schedule and those who omit specific vaccines?
3. For children who receive the currently recommended immunization schedule, do short- or long-term health outcomes differ for those who receive fewer immunizations per visit, or for those who receive their immunizations at later ages but still within the recommended ranges?
4. Do potentially susceptible subpopulations who may experience adverse health consequences in association with immunization with the currently recommended immunization schedule exist?

Guided by the IOM report’s findings, the CDC’s Immunization Safety Office commissioned VSD investigators to develop a White Paper to assess how the VSD could be used to study the safety of the childhood immunization schedule. That paper was completed and published in the journal *Vaccine* in February 2016. The white paper addressed three separate but

related content areas. The first content area is defining exposure in different schedules; identifying health outcomes to study in the context of the immunization schedule; and describing epidemiological and statistical methods. The second content area identified plausible health outcomes that could be studied in the context of the schedule as a whole, and studying longer-term outcomes, such as autoimmune diseases, asthma, and others. The third content area looked at the safety of the schedule. The white paper concluded that, although it will be possible to study the safety of the schedule, those studies will be complex and would have to address potential bias.

Dr. Duffy commented that the VSD had conducted some studies prior to publication of the IOM report, and since 2013 has published 13 studies related to the immunization schedule. Details on the studies can be found on the ISO web site. The IOM identified the CDC's VSD system as one of the best resources for research regarding the safety of the childhood immunization schedule. To date, the VSD has completed many studies related to the immunization schedule. Additional VSD studies of the immunization schedule are ongoing and planned to address the priorities outlined in the VSD White Paper. Dr. Duffy concluded his presentation.

Ms. Kain recommended adding a discussion to the March 2021 agenda concerning public confidence in the COVID-19 vaccine and the vaccine schedule. She suggested inviting Dr. Mawson to discuss his November study, adding that others had also published studies.

Update on the ISO Vaccine Activities

Dr. Duffy highlighted several recent publications:

1. Myers T, et al. Vaccine. 2020 Sep 11; 38(40):6291-6298. **Adverse events reported in the Vaccine Adverse Event Reporting System (VAERS) about Menactra, the first quadrivalent vaccine licensed in January 2005. Licensed for use in individuals age 9 through 55. During the study period 2005-2016.** VAERS received 13,075 adverse event reports following Menactra vaccination. Most reports (94%) were classified as non-serious (injection site redness and swelling, fever, headache, and dizziness). There were 36 reports of death, but researchers did not find any evidence to suggest the vaccine caused the deaths. This review did not reveal any new safety concerns.

2. Perez-Vilar S, et al. J Infect Dis. 2020 Nov 2; 543. **Guillain-Barré syndrome (GBS) following high-dose influenza vaccine administration in the United States, 2018–2019 season.** The Vaccine Safety Datalink (VSD) identified a statistical signal for an increased risk of GBS in days 1–42 following high-dose influenza vaccine (IIV3-HD) administration. The signal was rapidly evaluated using Medicare data by conducting early- and end-of-season analyses. The Medicare analyses, which administration of more than 7 million high-dose influenza vaccine injections, did not detect a statistically significant increased GBS risk.

3. Panagiotakopoulos L, et al. Obstet Gynecol. 2020 Nov 5. **Evaluating the Association of Stillbirths After Maternal Vaccination in the Vaccine Safety Datalink.** Research looked at vaccinations against flu and tetanus, diphtheria, and acellular pertussis (Tdap), which are recommended during each pregnancy. Researchers used the Vaccine Safety Datalink to evaluate whether vaccinations given during pregnancy were associated with stillbirth (fetal death occurring on or after 20 weeks gestation). The study compared 795 stillbirths (confirmed with medical record review) and 3,180 live birth controls between Sept. 30, 2015 and

Jan. 1, 2020. The findings showed that vaccination during pregnancy did not increase the risk of stillbirth, including recommended, non-recommended, and contraindicated vaccines.

4. Miller ER, et al. Vaccine. 2020. Nov 3; 38(47):7458-7463. **The Reporting Sensitivity of the Vaccine Adverse Event Reporting System (VAERS) for Anaphylaxis and for Guillain-Barré Syndrome.** Because underreporting is an important limitation common to passive surveillance systems, the number of adverse events that occur after vaccination and the percentage of those that are reported to the Vaccine Adverse Event Reporting System (VAERS) is unknown. Researchers analyzed pre-specified outcomes - anaphylaxis and Guillain-Barré syndrome (GBS) reported to VAERS. Sensitivity for capturing anaphylaxis after seven different vaccines ranged from 13-76%; sensitivity for capturing GBS after three different vaccines ranged from 12-64%. For anaphylaxis and GBS, VAERS sensitivity is comparable to previous estimates for detecting important AEs following vaccination.

Next, Dr. Duffy discussed the October 2020, ACIP meeting. In that meeting the pharmaceutical company, Seqiris, provided efficacy information for FLUCELVAX quadrivalent vaccine, a seasonal influenza vaccine for children age two to 17, which appeared to have a 54% efficacy. Influenza disease burden estimates for the 2019-2020 season are 38 million illnesses and 22,000 deaths. However, flu vaccine for the same season were estimated to have prevented 7.5 million infections, over 100,000 hospitalizations and 6,300 deaths.

There was a session on orthopoxvirus vaccines. The JYNNEOS vaccine is a live attenuated vaccine approved in 2019 for administration in adults to prevent smallpox and monkeypox. ACIP continues to review the vaccine for persons who are at risk for occupational exposure to orthopoxviruses, and to conduct Grading of Recommendations, Assessment, Development and Evaluation (GRADE).

There was also a session on a dengue virus vaccine, Dengvaxia, and ACIP is reviewing stakeholder acceptability, logistics, and feasibility for a potential phased approach to vaccination in Puerto Rico where dengue is endemic. ACIP plans to vote on this in 2021.

In the session on pneumococcal vaccines, two vaccines licensed in the U.S. were described – the 23-valent polysaccharide and the 13-valent conjugate vaccine. Two new PCV products are anticipated in 2021, including a possible vaccine for children that may be licensed by 2022.

Dr. Duffy gave brief updates on several other vaccines:

1. Cholera vaccine is recommended for adult travelers to areas where there is transmission risk, noting that ACIP will review pediatric data to determine a recommendation for children 2-17 years of age;
2. Shingrix, the herpes-zoster vaccine, for which there is a potential risk of Guillain-Barré syndrome (GBS);
3. Tick-borne encephalitis (TBE) vaccine for which there is a biologics license application that may be approved in 2021 for individuals visiting or living in TBE-endemic areas; and
4. Rabies vaccine, for which the ACIP is considering updates to pre-exposure dosing schedules and clinical guidance on risk groups.

Dr. Duffy discussed COVID-19 vaccines. There are four vaccines in Phase III trials in the U.S. Data from these trials will provide the information for a final decision and ACIP submits recommendations to the CDC director. COVID-19 was discussed at the October 2020 ACIP meeting, including the status of vaccine development, implementation plans and safety. The

ACIP reviewed post authorization/post licensure safety monitoring plans that will include VAERS, the VSD, and active participation by front line health care personnel, which includes V-Safe, a smart-phone based surveillance program for COVID-19 vaccine safety. Finally, the ACIP Vaccine Safety Technical (VaST) subgroup, composed of representatives of ACIP and NVAC, expert consultants and various interested federal agencies will review developments and offer recommendations to ACIP.

**Update on the National Institute of Allergy and Infectious Diseases (NIAID), NIH,
Ms. Claire Schuster**

Ms. Schuster reported that in March 2020, NIAID launched a Phase I clinical trial to evaluate the investigational mRNA-1273 vaccine co-developed by NIAID and Moderna, Inc., designed to prevent SARS CoV-2 infection. The trial included participants 18 years of age and older. The vaccine was well tolerated in the study population, including the older participants. A publication reporting on the use of vaccine among older adults noted that some experienced post-vaccination side effects including fever and fatigue, and overall the volunteers generated a strong immune response. Vaccine candidates being developed by Moderna and other companies are using several different platforms, including nucleic acid, viral vector, and protein subunit.

In April 2020, NIH announced Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership. ACTIV-1 is a Phase III clinical trial to evaluate three immune modulator drugs in hospitalized adults with COVID-19 (infliximab, abatacept, Cenicriviroc).

ACTIV-2 is an outpatient Phase II clinical trial to evaluate the safety and efficacy of potential new therapeutics for COVID-19. ACTIV-3 is an inpatient Phase III randomized, controlled trial that provides a “master protocol” to test multiple different kinds of monoclonal antibody treatments. The first agent tested in this trial was LY-CoV555 developed and manufactured by Eli Lilly and Company in collaboration with AbCellera Biologics. An independent Safety and Monitoring Board recommended that no further participants be randomized to receive this investigational monoclonal antibody because there appeared to be a low benefit to the treatment. ACTIV-4 is a “master protocol” to evaluate the safety and effectiveness of different types of blood thinners to treat patients with diagnosed COVID-19. Finally, in October NIAID launched ACTIV-5, the Big Effect Trial, a study to determine whether certain approved therapies in late-stage development show promise against COVID-19. The first drugs tested were risankizumab and lenzilumab, both in combination with remdesivir.

Ms. Schuster continued her presentation discussing acute flaccid myelitis (AFM), a respiratory enterovirus that predominantly affects children, that can cause muscle weakness and paralysis. There have been increases in cases in the U.S. every other year since 2014. In September, NIAID awarded a contract to the pharmaceutical company Intravacc to develop a vaccine to protect children against AFM.

Finally, Ms. Schuster noted that an NIAID-supported childhood pneumonia study has shown that a short-course 5-day antibiotic treatment is superior to the standard 10-day treatment in children up to 5 years of age.

Update on the Center for Biologics, Evaluation and Research, FDA, CDR Valerie Marshall

CDR Marshall reported that the Vaccines and Related Biological Products Advisory Committee (VRBPAC) would meet in open session on December 10, 2020 to discuss the request for emergency use authorization of a COVID-19 vaccine from Pfizer/BioNTech. VRBPAC will also meet on December 17, 2020 to discuss a COVID-19 vaccine developed by Moderna.

By way of background, on February 4, 2020, the Secretary of HHS determined that there was a public health emergency, the emergence of COVID-19 infection, which posed significant risk of affecting national security and/or the health and security of U.S. citizens. On March 27, 2020, the Secretary then declared that this situation justified the emergency use authorization (EUA) of available drugs to counter that risk. In August 2020, an EUA was issued for remdesivir to include treatment of all hospitalized adult and pediatric patients with suspected or laboratory-confirmed COVID-19, irrespective of their severity of disease.

Manufacturers may submit an EUA request for a vaccine to prevent COVID-19 that would be evaluated by FDA. Approval depends on adequate manufacturing information ensuring quality and consistency, and that the vaccine's benefits exceed the risk based on at least one Phase III clinical study that in a compelling manner demonstrates safety and efficacy. Once approved for an EUA, plans for continued monitoring must be submitted and would include surveillance by the existing programs (VAERS, VSD), CBER's Biologics Effectiveness and Safety Initiative, and analysis of Medicare claims.

Update on the OIDP, Dr. David Kim

Dr. Kim reported that the National Vaccine Advisory Committee (NVAC) makes recommendation to the Assistant Secretary for Health (ASH), ADM Brett Giroir, MD, about vaccine confidence and the maintenance of an infrastructure to distribute vaccines. NVAC is charged with providing support to the ASH about the approach and timing of developing the data required to improve the confidence in vaccinations and how to proceed with the vaccination program.

Dr. Kim turned to a discussion on the Vaccines National Strategic Plan 2021–2025 with five goals and objectives and strategies under each goal. The 2021–2025 plan updates the 2010 plan and has indicators to monitor progress. The plan considered NVAC recommendations and established an Interagency Vaccine Work Group to act as a steering committee. The plan is scheduled to be released by January 2021.

Finally, Dr. Kim mentioned the Vaccine Safety Report, last issued in 2014. Expected to be released in late spring 2021, this report is a systematic review of adverse events associated with vaccines routinely recommended for children and adults, including pregnant people, in the United States.

Overview of the CICP, Ms. Tamara Overby, Acting Director, DICP

Ms. Overby explained that the Public Readiness and Emergency Preparedness Act of 2005 (PREP Act) authorizes the CICP to compensate people who are seriously injured by covered countermeasures. CICP covered countermeasures are defined in PREP Act declarations issued by the Secretary and have been issued for medical countermeasures against the following:

COVID-19, Ebola, nerve agents and certain insecticides (organophosphorus and/or carbamate), Zika, pandemic influenza, anthrax, acute radiation syndrome, botulinum toxin and smallpox.

Persons eligible to file a claim include injured countermeasure recipients, legal or personal representative on behalf of an injured countermeasure recipient, survivors of deceased injured countermeasure recipients, and estates of deceased injured countermeasure recipients. Eligible requesters can expect compensation for reasonable unreimbursed medical expenses, lost employment income, and death benefits.

The CICP is administrative program, not judicial. CICP medical staff reviews the Request for Benefits Package, which includes medical records, to determine eligibility. If CICP determines a request is eligible for benefits, requesters may have to submit additional information to determine type and amount of compensation. If the CIP determines a request is ineligible, the requester may ask for a review by a qualified panel independent of the CICP, after which the Healthcare Systems Bureau Associate Administrator makes a decision about the case. The Associate Administrator's decision is final and there is no additional recourse.

As of October 1, 2020, 489 claims were filed, 446 were covered countermeasures and 43 claims were filed for products not covered by the CICP. Thirty-nine claims were ultimately eligible for compensation and 29 were compensated for a total of more than \$6 million. Ten claims did not receive compensation because the individuals involved did not have any compensable expenses or losses. Ms. Overby concluded her report.

Public Comment, Mr. John Howie, Chair ACCV

Mr. Howie invited public comment.

1. Mr. James Hodges added to his earlier public comment. He commented that further research on his part revealed that the CDC recommends pneumococcal polysaccharide for individuals aged two through 64 years of age with certain qualifying medical conditions. Therefore, the vaccine is routinely recommended for children. He said an individual at VAERS told him that his injury should be covered under the VICP. He suggested that all vaccines that cause injury related to vaccine administration be included on the Table. Ms. Overby suggested that he e-mail Ms. Annie Herzog for answers to his questions.

2. Ms. Theresa Wrangham, Executive Director, NVIC, commented that when the Vaccine Act was passed there was no adult vaccine schedule. Only routinely recommended vaccines for every child are covered under the Act. Commenting on the Secretary's NPRM proposal to remove the provision automatically adding any vaccines routinely recommended by the CDC for administration to children, if the NPRM goes to final rulemaking, the Secretary will still be required to add vaccines to the table that are routinely recommended for children no later than two years after the recommendation from the CDC. She cited US Code Section 300aa-14.

She commented that in addition to the Vaccine Act mandates, there should be a comparable investment in research to develop enough information to expedite VICP claims. She noted that the vaccine schedule is not regularly reviewed. Public trust issues were cited in the IOM report. For 40 years, NVIC has supported the establishment of an independent agency to monitor vaccine safety and research. If a vax-non-vax study is conducted, Ms. Wrangham stated that there would be significant conflicts of interest on the parts of all participants, and that the study should be done by an independent agency. She said there is no independent monitoring of the U.S. vaccine system. ACCV could make research recommendations that support the 1986

Vaccine Act mandate for research relying on independent monitoring work groups that could be formed under the ACIP and the NVAC.

With regard to the COVID-19 vaccines, the NVIC notes that, despite the interest in improving confidence in the vaccine, the engagement of the vaccine safety informed consent community had been excluded from promotion of vaccine confidence-building efforts, and in participation in the review of the 5-year plan. The plan focuses on vaccine innovation and development and does not support the human right of informed consent, which includes refusal of medical interventions. Finally, Ms. Wrangham expressed appreciation for Ms. Overby's presentation on the CICP.

Future Agenda Items

Mr. Howie noted that, with his retirement, the ACCV needs to elect a new Chair. Ms. Overby stated that the ACCV could defer selecting a Chair until more of the vacancies are filled. There was a discussion about the various possibilities, and an agreement to defer selection of a new Chair. On another subject, noting a significant decrease in sudden infant death syndrome events since the prior year, there was a suggestion to consider looking at the issue in 2021.

There being no further business, the meeting was adjourned.