

Advisory Commission on Childhood Vaccines

March 8-9, 2012

Day One

Minutes

Members Present

David King, Chair
Charlene Douglas, Ph.D.
Kristen Feemster, M.D.
Edward Kraus, J.D.
Ann Linguiti Pron, MSN, CRNP, RN
Luisita dela Rosa, Ph.D.
Jason Smith, J.D.
Sylvia Fernandez Villareal, M.D.
Michelle Williams, JD

Division of Vaccine Injury Compensation

Geoffrey Evans, M.D., Director, DVIC
Andrea Herzog, Principal Staff Liaison

Welcome, Report of the Chair and Approval of Minutes David King, ACCV Chair

Mr. King called the meeting to order and, after introductions, called for approval of the minutes of the December 2011 ACCV meeting. There being no corrections, additions or deletions, on motion duly made and seconded, the minutes were unanimously approved. He invited Dr. Evans to present the Director's report to the Commission.

Report from the Division of Vaccine Injury Compensation, Geoffrey Evans, Director, DVIC

Dr. Evans welcomed all present and on the teleconference to the 82nd meeting of the Advisory Commission on Childhood Vaccines. Before briefly reviewing the agenda for the two-day meeting, he noted that this particular meeting was special in that it would consider recommendations to the Secretary of HHS for changes to the Vaccine Injury Table and Qualification and Aids to Interpretation (Aids). That has happened only a few times in the 24-year history of the program. It would eventually result in a notice of proposed rulemaking (NPRM), public comment, and eventually a final rule, putting the changes into effect.

Reporting on program statistics, Dr. Evans stated that numbers of petitions filed were 127 as of February 10th, indicating that the fiscal year total would be about 380. As has been the case in the past, about half are for influenza vaccine injuries, which is reasonable in light of the fact that over 150 million doses was distributed during the last flu season, far more than any other vaccine.

Adjudications continue to be dominated by settlements (over 80% of all claims to date in FY 2012). There were no concessions at the time of the report, although there were two concessions after the statistics were compiled. Part of the reason for that is that 65% of claims filed are for flu and HPV vaccines, neither of which have injuries listed in the Vaccine Injury Table.

In terms of awards, the total amount of awards for damages is lagging last year's record of \$234 million, and will probably be about \$170 million at the end of the fiscal year. In spite of this, the cash flow remains positive for the Vaccine Injury Compensation Trust Fund, which now has a balance of \$3.4 billion. The large number of influenza vaccine doses taxed is mainly responsible.

Regarding activities since the last Commission meeting, Dr. Evans and Dr. Douglas provided program updates at the February 7-8 National Vaccine Advisory Committee (NVAC) meeting, and Dr. Evans also provided an update at the February 22-23 Advisory Committee on Immunization Practices (ACIP) meeting in Atlanta.

During discussion, asked how the program had migrated from an Injury Table claims process to the present situation in which almost all claims require the petitioner to prove causation-in-fact, Dr. Evans explained that during the first 7-8 years of the program, DTP claims comprised 75% of filings, and many alleged conditions listed on the Table. Over time, nine more vaccines were added to the Table, almost all without injuries. In addition, changes to the Vaccine Injury Table for pertussis-containing vaccines (removal of seizures and shock-collapse), and licensure of DTaP (replacing DTP) and change from oral polio vaccine (OPV) to the Inactivated Polio Vaccine (IPV), all played a role in claims now mostly alleging off-Table conditions.

**Advisory Commission on Childhood Vaccines (ACCV) Meeting
Report from the Department of Justice
Mark W. Rogers, Acting Director,
Torts Branch, Civil Division, Department of Justice**

Mr. Rogers referenced the Power Point materials, entitled March 8, 2012 Department of Justice Power Point Presentation (DOJ PP), as part of his presentation.

Statistics

Mr. Rogers opened his presentation with a statistical summary for the reporting period of November 16, 2011, through February 15, 2012 (DOJ PP, pp. 2-4). He called the report a "three-month snapshot" of recent litigation in the Vaccine Program. In this reporting period, 67 new claims were filed, none of which were autism claims (DOJ PP, p. 2). Mr. Rogers remarked that this number is slightly less than usual, possibly due to the holiday period, but that the ratio of adult claims (45) to minor claims (22) was consistent with other reporting periods. Mr. Rogers then turned to a slide showing the number and types of petitions adjudicated in the last reporting period (DOJ PP, p. 3). The cases reported on this slide have gone to judgment, or the court has stamped it with "case over." Mr. Rogers highlighted a few statistics, commenting that the ratios found on this slide were also typical of past reporting periods. A total of 850 petitions were adjudicated, including autism petitions. There were 55 non-autism cases compensated, 3 of which were conceded by HHS and resolved with a proffer. Mr. Rogers briefly discussed the tracking of conceded cases, explaining that DOJ counts concessions at the time of judgment, whereas HHS counts them at the time of concession, which happens when they first review the case. DOJ's purpose in presenting this statistical report was to give a snapshot of recent ratios and trends in litigation, in a close to real-time fashion. Turning to the 3 conceded cases, Mr. Rogers noted that they were resolved by proffer on the damages. A proffer is the fastest, easiest path to compensation. It means that with a conceded case on entitlement, the parties agree to what the evidence showed on damages. Of the remaining 52 cases that were compensated but not conceded, 47 were resolved by settlement and 5 by proffer. There are two issues in a case that is not conceded by HHS: whether compensation should be paid at all, and, if so, how much. A settlement can encompass both of those two issues. Those are called litigative risk settlements and the vast majority of cases fall into that category, i.e., HHS has not conceded the case, but the parties discuss an amicable settlement incorporating whether entitlement is appropriate and amount of compensation. Some of the non-conceded cases are decided by a special master finding entitlement and then the parties settle damages. Proffers occur in cases where special master issues a decision for petitioner on entitlement and then the parties agree to what the evidence shows on damages. Proffers are the fastest path to compensation once entitlement has been decided. This reporting period,

795 cases were not compensated (DOJ PP, p. 3). Of those, 50 were non-autism and 745 were autism claims. In the autism cases, Mr. Rogers reported that petitioners' counsel, respondent, and the Office of Special Masters were working cooperatively to resolve the issue of attorneys' fees and costs for those cases using a "systems-based approach" that categorizes each case according to the amount of effort that was put into it by the attorneys. Dr. Douglas asked how the payment of attorneys' fees in the Vaccine Program differs from a traditional, contingency-based fee agreement. In a contingency-based fee system, an attorney is paid a certain percentage of the plaintiff's award. Mr. Rogers answered that in the Vaccine Program, the standard for an award of attorney's fees is statutory, and that the Vaccine Act calls for an award of a "reasonable" amount of attorneys' fees. Unique to the Program, petitioners' counsel are awarded reasonable attorneys' fees and costs whether they win or lose on entitlement, so long as there was a reasonable basis for the claim. The case law requires that attorneys keep contemporaneous records of their time and costs. A reasonable hourly rate is applied to that time. Mr. King asked how the hourly rate for petitioners' counsel was determined. Mr. Rogers said that Congress used the word "reasonable," which is good because the term is very flexible and adaptable, but bad because people can disagree on what constitutes "reasonable," and that can spawn litigation. There has been recent litigation about what is a reasonable rate for a particular attorney in a particular location, as well as how much an attorneys' rate should increase each year. However, Mr. Rogers emphasized that the vast majority of those issues are resolved through informal discussions with petitioners' counsel, respondent, and the Office of Special Masters. Mr. King asked if attorney fee litigation impacted the effectiveness of the Program. Mr. Rogers said that because the DOJ has a fixed budget and staff, increased time spent on fee litigation resulted in less time for other issues. Mr. Kraus added to Mr. Rogers's comments, stating that although it was concerning to see the increase in DOJ's resources used for fee litigation, it was even more troubling that fee litigation could be affecting the ability of the Office of Special Masters to timely and efficiently decide cases. Mr. King acknowledged that the issue of attorneys' fee litigation could not be resolved in the ACCV meeting, but asked if any solutions had been proposed to resolve the issue. Mr. Rogers stated that it was not appropriate for him to make suggested changes to the Vaccine Act, but to explain and apply the Act as it is currently written. Mr. King said the ACCV would address the issue at another time. Mr. Rogers completed the statistical summary by reporting that 3 non-autism petitioners had voluntarily withdrawn from the Program in the last reporting period (DOJ PP, p. 4).

Glossary of Terms and Overview of Petition Processing

Mr. Rogers presented three slides containing a glossary of commonly used terms in the Program (DOJ PP, pp. 5-7). These definitions are always included in DOJ's presentation, and are familiar to many members, so Mr. Rogers briefly explained a few appellate terms. "Affirmed" means the party that brought the appeal lost, and the decision below remains intact. "Reversed" means the party that brought the appeal won. "Vacated" means that the appellate court has thrown out the lower court's decision altogether. Sometimes the appellate court will "remand," meaning the case is sent to the lower court, or the appellate court will issue its own decision. Mr. Rogers then discussed the wire diagram that is also presented at each meeting, to illustrate the processing of a petition in the Program (DOJ PP, p. 8). The vast majority of compensated cases move through the settlement route (left side of chart) toward a final decision. These cases move through the program quickly. If a case is not conceded, and the Special Master decides that the petitioner is not entitled to an award of compensation, it goes to the yellow box. If the Special Master decides that the injury or death is vaccine-related, or "compensable," the case moves over to the "damages" box, and is typically resolved with a proffer, but could be decided by a damages hearing or settlement. Mr. Smith asked about the cases that are not conceded, but are resolved with a proffer, as mentioned in the statistics presented earlier. Mr. Rogers answered that in those cases, the Special Master determined the petitioner was entitled to compensation. If a Special Master decides that a case is entitled to compensation, i.e. compensable, the case moves to the "damages" box on the wire diagram. It is usually resolved by the parties outside of a court room through a settlement or a proffer, but the Special Master could convene a hearing on the amount of damages. Mr. Kraus asked if a published decision was available in those cases that are resolved by proffer, and what facts were made available to the public. Mr. Rogers said that proffers are sometimes made available, and that the petitioner has an avenue for requesting that it not be published. There has been some litigation on that issue.

Appeals

Mr. Rogers next turned to cases pending on appeal at the U.S. Court of Appeals for the Federal Circuit (CAFC) and U.S. Court of Federal Claims (CFC). (DOJ PP, p. 9-13). The first slide shows two cases that were recently decided, and were appeals brought by petitioner. Two cases were recently decided at the CAFC: *Caves v. HHS* (affirmed) and *Kennedy v. HHS* (dismissed). Both cases were appealed by petitioners. *Kennedy* was an unusual case. The case was dismissed many years ago, and petitioner tried to gain relief under a rule of the court that allows a judgment to be set aside under unusual circumstances. A judgment in a litigation context has many protections and is designed to be final. Ultimately, the CAFC decided there was not a sufficient showing to disturb the judgment of the CFC. Mr. Rogers then turned to cases recently decided at the CFC (DOJ PP, p. 11-12). The CFC is one step above the Office of Special Masters, and is the first level of review for Vaccine cases. Mr. Rogers reiterated that “affirmed” means the appeal was not successful, and the decision below remains intact. Ms. Williams asked if Mr. Rogers could provide a flow chart illustrating the levels of appeal in Vaccine cases. Mr. Rogers said that could be provided in the future. Dr. Shimabukuro asked for an explanation of the term “jurisdiction.” Mr. Rogers answered that “jurisdiction” literally means “the law to say.” It means whether the court had the authority to speak to the issue, or whether the case was properly before the court. Another comparable word is “authority.” Dr. Villareal asked if the appeals were predominantly pediatric or adult cases. Mr. Rogers answered that DOJ doesn’t track that, but he thought appeals would be roughly the same as the filing ratio, or a few more adult claims than child claims. Mr. Rogers then noted that DOJ PP, p. 12 identified cases currently pending before the CFC, pointing out that cases highlighted in yellow were new filings. (DOJ PP, p. 12). The cases of *Hammitt v. HHS* and *Stone v. HHS* were recently argued at the CAFC. (DOJ PP, p. 13).

Adjudicated Settlements

Mr. Rogers turned to claims that were recently resolved by settlement (DOJ PP, pp. 14-18). A past ACCV member asked DOJ to provide this list of settlements, and track the time between the filing of a petition and the filing of a stipulation of settlement. During this reporting period, there were 47 adjudicated settlements. The injuries on the list were those alleged in the initial petition. Sometimes that changes as the case progresses. Mr. Rogers discussed possible reasons for the outliers on the chart – cases that took 3 or more years to settle. These cases often require several years of development before they can be processed. This might include a petitioner searching for medical records or looking for an expert witness. If a case goes to trial, that normally adds at least a year to the proceedings. Similarly, cases that are resolved within one year or close to year reflect a case filed with everything working right and all parties, including the special master, involved as necessary to facilitate resolution.

Questions and Comments

Mr. King asked if certain special masters are more likely to settle cases. Mr. Rogers said DOJ doesn’t track those numbers. Mr. King commented that the data would be available through the decisions. Mr. Rogers was not inclined to draw any inferences from information such as this and be aware that DOJ has not seen a disparity in special masters’ approach to settlement sufficient to begin tracking that information.

Institute of Medicine Report Task Force on Updating the VIT Rosemary Johann-Johann-Liang, Chief Medical Officer DVIC

Dr. Johann-Liang provided a foundational discussion for the Commission’s consideration of revisions to the Vaccine Injury Table (VIT) and the Qualification and Aids to Interpretation (Aids), covering the Institute of Medicine (IOM) report on vaccines and related adverse events, and the work of a DVIC/CDC Task Force to prepare recommendations to the Secretary.

She began with a brief review of the IOM report on vaccines and vaccine-related adverse event, which was requested by HHS in anticipation of the revision. The last changes in the VIT were made in 1997, also following an IOM study. Since then nine vaccines have been added to the Table, although no related injuries were specified in the Table for those vaccines. Even though the vaccines were on the Table, causation-in-fact had to be shown. In September 2008, HHS finalized contract negotiations with IOM to convene an expert committee to review the available scientific literature on certain vaccines and adverse events. The list was built through the joint efforts of several HHS agencies, including FDA, CDC, and HRSA medical officers. Dr. Johann-Liang noted that autism, a condition that involves significant public interest, was included for review. However, since the IOM twice reviewed autism and vaccines, the request to the Committee was limited to reviewing the scientific literature available since 2009 and providing an update on information published since their autism report in 2004.

Initially four vaccines were selected, later expanded to eight when additional funds became available. The 15-person committee reviewed all the available medical and scientific literature, held several public meetings at which experts were invited to comment, and put a significant amount of information on an IOM web site inviting public comment. The HHS charge included a request that the Committee develop a framework that would allow an efficient review of each vaccine-adverse event combination considered. As with previous reports, their charge was to evaluate the literature and report their findings on vaccine causation. They were not asked to make any policy recommendations.

The vaccine and adverse events selected were based on claims history, and covered 92% of vaccine injuries handled by the program. Dr. Johann-Liang described the vaccines covered: hepatitis A and B, trivalent influenza, meningococcal, MMR (measles-mumps-rubella), tetanus-containing and varicella. Although the adverse events were compiled from program claims history, the Committee was also asked to look at some general issues, such as anaphylaxis and the effect of autoimmune conditions, and a recent issue related to physical injuries caused by the actual injection, regardless of the vaccine involved. There were 148 vaccine/adverse event combinations sent to the Committee. The Committee added 10 more for a total of 158.

Dr. Johann-Liang explained that the IOM review was not intended to establish any statistical basis for consideration of the vaccine/adverse event combinations, but to look at each individually and develop a conclusion based on a biological and mechanistic evaluation. The Committee's product for each vaccine/adverse event combination was an assessment of whether or not the vaccine caused the adverse event. Relying on the weight of the epidemiological evidence and the mechanistic evidence, the Committee developed a framework for each vaccine/adverse event combination consisting of four categories: the evidence convincingly supports a causal relationship; the evidence favors acceptance of a causal relationship; the evidence is inadequate to accept or reject a causal relationship; and the evidence favors rejection of a causal relationship.

Dr. Johann-Liang briefly described the IOM's "convincingly supports causation" category, which included adverse events related to varicella vaccine (disseminated varicella infection and vaccine strain viral reactivation), MMR vaccine (measles inclusion body encephalitis and febrile seizures), injection-related events (syncope and deltoid bursitis) and vaccines that might cause anaphylaxis (MMR, varicella, influenza, tetanus-containing, and meningococcal vaccines). In the "favors acceptance" category, Dr. Johann-Liang stated there were four, none of which are appropriate for consideration as revisions to the VIT. Although HHS was interested in demyelinating events, the IOM only placed them in the "inadequate to accept or reject" category.

Dr. Johann-Liang explained that when the report was received, and after initial review, a Task Force was set up to evaluate the report and to develop recommendations for Table revisions. The members came from DVIC, CDC's Immunization Safety Office (ISO), the HHS Office of General Counsel (OGC) and HRSA (medical officers). In Phase One, nine working groups within were set up to look at specific vaccine/adverse event combinations, and to review any newly published literature that may have occurred since the IOM ended its review. That was particularly germane to febrile seizures and asthma in the "inadequate to accept or reject" category, although in the end no revisions were recommended for vaccines in that category. The working groups recognized 21 vaccine/adverse events that would be more

intensely scrutinized in Phase Two, Dr. Johann-Liang commended Task Force members who dedicated a significant amount of time and effort to arriving at the proposals being presented to the ACCV

With regard to the overall process for changing the VIT, once the Commission makes a recommendation, the proposal undergoes review within the Department and eventual clearance by the Secretary for publication of Notice of Proposed Rulemaking (NPRM) in the Federal Register. A 180-day period of public comment follows, during which time there is the opportunity for a public hearing to take oral comments. There can be additional review by the ACCV, if it should so desire. The changes become effective 30 days after a final rule is published.

In terms of the Commission's review of the proposed revisions to the VIT and the Aids, Dr. Johann-Liang suggested three options. First, the Commission may concur with the recommendations and recommend moving forward (although Commission comments may be added to that recommendation). Second, the Commission may decide against moving forward with the proposed revision. Third, the Commission may prefer to defer recommendations, either to the second day of the meeting or a later meeting of the Commission. There was general agreement among ACCV members to follow this approach.

Updating the Vaccine Injury Table: Legal and Policy Considerations **Elizabeth Saindon, Attorney, DHHS OGC**

Ms. Saindon explained that entitlement to compensation under the presumption of causation provided by the Vaccine Injury Table requires that the injured party actually received the vaccine, suffered an injury listed on the Table, and experienced symptoms of the injury within the timeframe specified on the Table. Since there are very few injuries that currently meet those requirements, currently petitioners must rely on proof of causation by a preponderance of the evidence. In both cases, there must be residual effects of the injury – death, hospitalization and surgery, or a residual effect of the injury that lasts more than six months. The Qualifications and Aids to Interpretation (Aids) provide a more detailed explanation of entitlement.

The Secretary may make revisions to the Table and Aids, following regulatory procedure, and those changes may include addition/deletion of vaccines, addition/deletion of injuries related to a vaccine, or revision of the timeline for first symptom to appear. Any change affects only claims filed after the change is formalized. Regulatory requirements include the provision of the proposed changes to the ACCV for consideration and recommendation, and the Commission has at least 90 days to consider the proposed revisions. Although the Secretary *may* make changes to the Table, the Secretary *must* amend the Table within two years after the CDC recommends a vaccine for routine use in children. There is no such statutory requirement regarding adding injuries related to that vaccine, nor are there any statutory standards that guide the Secretary in changing the Table injuries.

Ms. Saindon noted that, in part in response to the lack of standards for changing the Table, an earlier Commission developed Guiding Principles, which may be useful to the current Commission (although not binding) in considering the present proposal. As a matter that might interest the Commission, Ms. Saindon stated that the task force looking at the IOM conclusions did refer to the Guiding Principles in their review process. One of the principles is that the Vaccine Injury Table should be scientifically and medically credible and that changes, whenever possible, should be made to the benefit of the petitioner. The Principles provide a detailed discussion of what "scientifically and medically credible" means, including the observation that an IOM study should be deemed credible. There is also a hierarchy of data sources, graded as to strength of credibility. In addition, the Principles emphasize that awards are meant by Congress to be compensate serious injury in a timely and generous way. Although Ms. Williams suggested that one of the principles should be consistency of criteria and awards, Ms. Saindon commented that the awards are the purview of the special masters, not DVIC. Ms. Saindon added that the task force included improving the presentation and readability of the Table in the revision process. The new Table should be more consistent and easier to understand and interpret.

After a brief discussion, there was agreement that the Commission should adopt the Guiding Principles in its consideration of the proposed revisions and a motion to that effect, duly made and seconded, was unanimously approved.

Proposed Table Change – Varicella Vaccine
Catherine Shaer, Medical Officer DVIC

In the first detailed discussion of proposed revisions to the Table, Dr. Shaer stated that the IOM report affirmed that there is convincing support varicella vaccine causes disseminated vaccine strain virus disease on the skin (chickenpox rash) and in other organs; and vaccine strain virus reactivation, which is appearance of the chickenpox rash months to years after vaccination, with or without concomitant infection in other organs (lungs, meninges, liver). However, in the literature reviewed the organs were affected only in immunocompromised individuals. In the spirit of the Guiding Principles, the task force did not recommend limiting infection to individuals with that condition.

Dr. Shaer noted that there was significant literature support for the proposal, most related to mechanistic data. One of the studies showed that VAERS reported 3,640 rash cases over about three years beginning in March 1995. Varicella virus was identified in 70 specimens – five not certain, 43 wild type (not related to the vaccine), and 22 vaccine-strain virus. Another report showed 259 reports of rash developing within 42 days of vaccination, seven were uncertain, 32 wild type and 5 vaccine-strain virus.

Dr. Shaer commented that varicella vaccine is currently on the Table with no associated injuries. The proposal is to add the disseminated varicella vaccine-strain viral disease without any time limitation if identified by conclusive lab testing, or within a time window of 7 to 42 days if lab testing is either not performed or inconclusive. A second injury under this listing would be an acute event (including death) related to the event, and a time interval would not apply. The proposed Aids would amplify the requirement, defining the illness as an illness that involves the skin beyond the dermatome, in which the immunization was given, and clear illness in an organ (not just mildly elevated lab levels). If an organ is involved with no virus identified in the organ, it must be clearly part of the discrete illness. If wild-type varicella virus, or any other non-vaccine-strain virus is identified, the associated viral disease will not qualify as a condition as set forth in the Table. If strain determination is not performed, or if the strain cannot be identified in the lab, the onset of illness must be within 7-42 days of vaccination. Dr. Shaer added that the justification for the latter provision is that it is in keeping with the program policy to be generous when the vaccine might have caused the injury, but proof is not available.

Dr. Shaer commented that the proposal to include vaccine-strain reactivation with no time limitation is more straightforward since demonstration of the vaccine-strain virus is required to establish the Table injury. The IOM specified that the brain and meninges could also be involved in vaccine-strain reactivation, usually in immune compromised individuals, but as with the prior injury, the proposal does not limit involvement to those two organ systems, and in this case does not require immunosuppression. To demonstrate the liberal interpretation of data with regard to the injury, there was a study in which 981 VAERS reports of herpes zoster were analyzed and only 28 could be linked to varicella virus, and of those only 8 to the varicella-strain virus. Herpes zoster (shingles) can emerge years or decades after the initial infection with varicella, whether acquired naturally or from the vaccine. Dr. Johann-Liang noted that that was an example of superimposing the Guiding Principles to make the Table more generous to the claimant.

The Aids states varicella vaccine-strain reactivation is the presence of a herpes zoster rash with or without concurrent disease in an organ other than the skin. Vaccine-strain varicella must be specifically identified in the skin or organ involved, and there is no timeframe since the vaccine-strain virus definitively links the condition to vaccination.

During discussion, asked about anaphylaxis. Dr. Shaer explained that the current discussion focuses on injuries specific to varicella vaccine administration. Anaphylaxis is related to several vaccines, to be discussed subsequently. Concerning the window of time for disseminated vaccine-strain viral disease, Dr. Johann-Liang explained that when vaccine-strain virus is identified, that is clear presumption that the vaccine was involved in the injury. However, there are many reports when the vaccine-strain cannot be proven, but the disease exists. In the literature there is evidence that exposure to varicella virus manifests itself as disease 14 to 16 days post-exposure. The Red Book indicates that it can be 10

to 28 days. In the spirit of the guiding Principles, and giving claimants the most generous window of opportunity to claim injury, the proposal expanded the timeframe to be 7 to 42 days post vaccination.

The Commission, on motion duly made and seconded, unanimously approved the proposed addition to the Vaccine Injury Table of disseminated vaccine-strain virus disease and vaccine-strain reactivation to the varicella listing that already exists.

Proposed Table Change – MMR Vaccine Mary Rubin, Medical Officer DVIC

The IOM concluded evidence convincingly supports a causal relationship between MMR (measles, mumps, rubella) vaccine and febrile seizures, transient arthralgia and measles inclusion body encephalitis (MIBE), Dr. Rubin presented the task force proposal for revisions in the Vaccine Injury Table. The vaccine itself is currently listed on the Vaccine Injury Table with five related adverse events, not including the three under consideration.

Febrile seizures occur mainly in infants and very young children, usually last less than a minute, and typically do not result in long-term adverse sequelae. Febrile seizures in infants and young children, usually under two years of age, are very common and most do not relate to any vaccine. Dr. Johann-Liang commented that febrile seizures occur at the rate of 3% to 4% in the general population of children (3,000-4,000 cases per 100,000), but in cases presumed to be attributable to vaccine occur at the rate of less than 34 per 100,000. There were a significant number of studies in the literature, most of which supported the premise that febrile seizures occur between 6 and 11 days after MMR inoculation (one paper set that time span at 8 to 14 days). Studies also support that febrile seizures after MMR vaccination hold no long term consequences. Patients who have febrile seizures after MMR vaccination had no higher risk of subsequent seizure, epilepsy or neurodevelopmental disability than other children with febrile seizures in the absence of vaccine administration. Dr. Rubin stated that, majority of children who have febrile seizures recover quickly and have no lasting effects. Rarely, febrile seizures can lead to serious injury or disability. The task force did not propose that febrile seizure be added to the Vaccine Injury Table. However, the Program will consider any such claims for febrile seizures leading to serious injury or death on a case-by-case basis.

Dr. Rubin described transient arthralgia, joint pain without swelling, adding that the IOM found evidence that convincingly supports a casual relationship with MMR vaccine. However, as with febrile seizures, the literature described no long-term adverse sequelae related to transient arthralgia and the task force did not propose adding the adverse event to the Vaccine injury Table.

Finally, Dr. Rubin stated that the IOM found that evidence convincingly supports a causal relationship between MMR vaccine and measles inclusion body encephalitis (MIBE). The condition “vaccine strain measles infection” is currently listed on the Vaccine Injury Table for immunodeficient individuals. Since MIBE is one type of measles-associated disease, the proposal involves revision of the current injury to include MIBE. MIBE is a rare, slowly developing encephalitis caused by a chronic infection with the measles virus. This disease is confined to immunodeficient patients. The task force is proposing changes to the time interval. The literature suggests signs of MIBE appear 4 to 9 months after inoculation. There was one case of vaccine strain measles infection with onset of symptoms in eight days. Another case report describes a patient with vaccine-associated measles pneumonitis with onset of symptoms 11 months after vaccination. The proposed changes to the time interval are as follows: a broad interval of up to 12 months, if strain determination is not done or if laboratory testing is inconclusive; if lab tests prove that vaccine-strain virus exists, no time frame is applicable. Dr. Rubin noted that the task force proposed significant expansion of the Aids for “vaccine strain measles disease in an immunodeficient recipient” to provide more detail as to the definition (involving skin and or other organs), testing, and exclusions (identification of wild-type measles virus or other non-vaccine strain virus).

During discussion there was concern that an individual might forego lab tests to avoid identification of an exclusionary virus. Dr. Johann-Liang commented that most such tests occur at the diagnostic and treatment stage, well ahead of concern about compensation. It was also noted that some

viruses are difficult to culture, and Ms. Saindon commented that failure of a test would allow a claim based on presumption of cause.

On motion duly made and seconded, the Commission unanimously approved the revisions to the Vaccine Injury Table related to MMR and vaccine-strain measles viral disease as discussed.

Proposed Table Change – Anaphylaxis (Multiple Vaccines)
Sarah Atansoff, Medical Officer DVIC

Discussing anaphylaxis, the first adverse event that was casually related to several vaccines, Dr. Atansoff commented that the IOM found evidence that convincingly supports a causal relationship between trivalent influenza vaccine, meningococcal vaccine, varicella vaccine, and human papillomavirus vaccine to the adverse event anaphylaxis. Citations from the literature reviewed by the IOM committee for flu vaccine were based mainly on mechanistic studies, and a few epidemiological analyses. All had onset shortly after administration, mostly occurring in less than an hour. The task force proposes to add anaphylaxis to the Table for these four vaccines, with an onset interval of 4 hours. Anaphylaxis occurring within four hours was already on the Table for tetanus-containing vaccines, vaccines containing pertussis bacteria, MMR and hepatitis A vaccines.

Dr. Atanasoff described minor changes in the Aids for anaphylaxis that simplifies the wording, deletes the descriptor “allergic,” since an anaphylactoid reaction is not technically an allergic reaction, and eliminates the description of autopsy results since there are no autopsy findings that would confirm anaphylaxis. Asked why anaphylaxis is not being added for other vaccines, Dr. Johann-Liang stated the IOM was not able to find studies that would support a conclusion that the adverse event was related to such as hepatitis A vaccine, for example. There was a brief discussion about long-term adverse effects and it was noted that usually an emergency procedure involves an airway restriction that may be treated in an ER, and no admission to the hospital is required. Failure to effectively treat may result in encephalitis, which is covered under the Vaccine Injury Table.

On motion duly made and seconded, the Commission unanimously approved the proposed addition of anaphylaxis to the Vaccine Injury Table under trivalent influenza vaccine, meningococcal vaccine, varicella vaccine, and human papillomavirus vaccine.

Proposed Table Change – Injection-Related (Multiple Vaccines)
Tom Ryan, Medical Officer DVIC

Dr. Ryan discussed the only two new adverse events. The IOM concluded that there was evidence that convincingly supports a causal relationship between any vaccine that is injected with a needle and deltoid bursitis, an injury caused by the injection itself and not the specific vaccine injected. The only vaccines for which this condition is not applicable are the influenza vaccine nasal spray and vaccines administered orally – oral polio vaccine (which is no longer administered in the U.S.) and the oral rotavirus vaccine. Dr. Ryan commented that the literature on this adverse event is limited, and the most definitive description of the injury is in papers by Atanasoff et al (Vaccine 2010 28(51):8049-52) and Bodor and Enoch (Vaccine 25-2007 pp 585-587). Bodor described two patients who developed shoulder pain and limited range of motion two days after an injection of a viral antigen, probably into the bursa or other synovial tissue under the deltoid muscle. Atanasoff reported on 13 VICP cases of post-vaccination shoulder injury which DVIC staff named SIRVA (Shoulder Injury Related to Vaccine Administration), 12 of which occurred within 24 hours of injection. The proposed Aids explains the adverse event as follows: SIRVA is caused by an injury to the musculoskeletal structures of the shoulder – ligaments, tendons, bursae – due to injection of vaccine antigen or trauma from the needle into and around the underlying bursa resulting in an inflammatory response. It is not a neurological injury. For purposes of the Vaccine Injury Table a claimant is presumed to have SIRVA if there is no prior history of shoulder pain in the affected shoulder, the onset of pain is within the specified timeframe (48 hours or less following vaccine injection), the pain and reduced range of motion are limited to the shoulder in which the vaccine is administered, and there is no other condition or abnormality which would explain the patient’s symptoms.

Dr. Ryan stated that the proposed addition to the Vaccine Injury Table would be called SIRVA, rather than the adverse event identified by the IOM, deltoid bursitis, and the onset of symptoms would have to occur within 48 hours of the injection. The IOM felt that the description of the adverse event by Atanasoff et al was consistent with deltoid bursitis. However, the DVIC program experience showed that the injury could include other conditions, such as tendonitis, impingement syndrome, frozen shoulder, adhesive capsulitis or aggravation of a pre-existing asymptomatic rotator cuff injury. Applying the Guiding Principles, the task force agreed to broaden the definition to insure that all such injuries were covered if they occurred within the 48-hour time limit. In fact, in the literature and from the DVIC experience, 93% of onset of pain occurred within 24 hours. Dr. Ryan added that shoulder injuries are very common in adults, so the limited time interval is important to assure the program that the injury is causally related to the injection. An individual who suffers the symptoms outside the timeframe may, of course, pursue a claim without relying on the Vaccine Injury Table. Dr. Johann-Liang commented that one reason for the timeframe decision was the very limited scientific information currently available on this injury. The task force felt that it was appropriate to add SIRVA to the Table now while acknowledging that further scientific and medical understanding of this injury might lead to revisions of either the symptoms or the timeframe in the future.

On motion duly made and seconded, the Commission approved the task force proposal to add SIRVA (Shoulder Injury Related to Vaccine Administration) as a new injury for every injectable vaccine.

Dr. Ryan moved on to the IOM finding that evidence convincingly supports a causal relationship between injected vaccines and syncope (fainting). The finding was based on analysis of 35 case reports that strongly indicated that syncope was related to the injection and not the vaccine administered. The symptoms before fainting were the same as those for vasovagal syncope – lightheadedness, pallor, sweating and nausea. The IOM stated that most episodes of syncope occurred within 15 minutes of vaccine injection suggesting vasovagal syncope as the mechanism.

Dr. Ryan proposed adding vasovagal syncope to every injectable vaccine in the Vaccine Injury Table if onset of symptoms occurs within one hour or less of vaccine injection. He commented that the wording in the Aids relied on the definition of vasovagal syncope – a loss of consciousness caused by a transient decrease in blood flow to the brain, normally restored to normal when the patient becomes prone as a result of the fainting. The condition is transient and usually benign, unless there is an injury as a result of falling or loss of consciousness. Dr. Ryan stated that loss of consciousness as a result of other causes would not be considered injection-related vasovagal syncope in the context of the Vaccine Injury Table (organic heart disease, cardiac arrhythmia, transient ischemic attacks, metabolic or neurological conditions, hyperventilation, and seizures).

During discussion, it was noted that, in the program's experience, females adolescents are most likely to faint, but other studies show that males are also susceptible. Concerns were expressed about prevention, and there have been efforts to educate those providing vaccines to administer the vaccine with both the patient and vaccine administrator in a sitting position, and to monitor the recipient for at least 15 minutes after the injection. Dr. Ryan suggested that procedure might also reduce the risk of SIRVA. It was also noted that, in the spirit of the Guiding Principles, an injured person is eligible for compensation even if he or she ignores the warnings to rest in a seated or reclining position for 15 minutes after the vaccination. Ms. Saindon added that both the vaccine manufacturers and the individuals who administer the vaccine are protected from liability by the Act.

On motion duly made and seconded, the Commission unanimously approved the proposed addition of vasovagal syncope to the Vaccine Injury Table under all injectable vaccines.

Proposed Changes to the Qualifications and Aids to Interpretation
Rosemary Johann-Liang, Chief Medical Officer DVIC
Stacy Stryer, Medical Office DVIC

Dr. Johann-Liang noted that review of the Aids by the task force revealed the need to update some of the medical and technical language, eliminate redundancies, reorganize the sections in a more logical sequence, and ensure the reading level was appropriate.

Specifically, Dr. Johann-Liang mentioned that in the current Table the phrase “Any acute complication or sequella, including death, of the illness, disability, injury, or condition listed,” was included under every vaccine for which any adverse event was also listed. To simplify the Table that phrase was deleted from the individual vaccines, and placed in a new subparagraph (b). Finally, to accommodate terms that are used more than once in the Aids, a glossary was added as subparagraph (d), which now includes definitions for chronic encephalopathy (moved from the encephalopathy section), injected (referring to intramuscular or subcutaneous vaccine injections), immunodeficient recipient (mentioned in MMR and polio vaccines), and three entries from the encephalopathy section – “significantly decreased level of consciousness,” seizure and sequella. Dr. Johann-Liang clarified that the newer jet injector procedure for some vaccinations was not included because it would not typically cause SIRVA.

Dr. Johann-Liang stated that the current 9 sections in the Aids were expanded to 13 to accommodate the new adverse events in the task force proposal: shoulder injury related to vaccine administration (SIRVA), disseminated varicella vaccine-strain virus disease, varicella vaccine-strain reactivation disease and vasovagal syncope. For clarity, a definition was added to the Aids discussion of chronic arthritis, although no revision for that condition is proposed. Similarly, again with no change proposed in the Table, the definition of thrombocytopenic purpura was expanded to make it compatible with medical diagnostic language instead of a lab test result definition.

During discussion, Mr. Kraus suggested that the examples of “identifiable defects” related to immunodeficient individuals was unnecessary. In response, Dr. Johann-Liang stated the task force wanted to provide concrete examples of two types of defects, one an inherited disorder and the other an acquired immune deficiency (HIV/AIDS). It emphasizes the need to verify the basis of immune deficiency for purposes of program compensation. Dr. Shimabukuro commented that the definition clearly notifies a claimant that medical record substantiation would be needed to pursue a claim based on immune deficiency. Dr. Johann-Liang added that staff would review the construction of the definition to see if it could be made more clear. Concerning other minor revisions, Dr. Johann-Liang pointed out that the paragraph on brachial neuritis was changed to make it harmonize with the new coverage for SIRVA, since the conditions are similar.

Dr. Stryer addressed encephalopathy and encephalitis and how the conditions relate to acellular pertussis-containing vaccines, noting that the IOM had concluded that evidence is inadequate to accept or reject a causal relationship between the vaccine and encephalopathy/encephalitis. Acellular pertussis was developed because of concerns about the whole cell pertussis vaccine, and the vaccine does have far fewer side effects. Although large-scale studies based on passive surveillance data failed to show an increased risk for acellular pertussis-containing vaccines, the task force did not propose any change to the Vaccine Injury Table (based on consideration of the Guiding Principles). The Task Force did propose amending the current Aids for encephalopathy and adding a definition for encephalitis, which is not in the Aids.

With regard to MMR vaccine, the IOM found little in the literature to support a causal relationship, either epidemiologically or mechanistically. Therefore the finding was that evidence was inadequate to accept or reject a causal relationship between MMR vaccine and encephalopathy or encephalitis. The task force decided that, in harmony with the Guiding Principles, the vaccine and the adverse events should remain in the Table, along with the new definition of encephalitis. The definition requires demonstration of an altered level of consciousness or other neurologic deficit; or a neurologic symptom that can be related to the central nervous system; and evidence of an inflammatory condition in the brain. The definition is new, but it is largely based on the existing definition of encephalopathy.

On motion duly made and seconded, the Commission unanimously approved the proposed changes to the Aids.

**Additional Task Force Deliberations Including GBS/Influenza Vaccine
Tom Shimabukuro, Medical Officer, Immunization Safety Office, CDC**

Dr. Shimabukuro discussed a number of IOM findings where evidence was insufficient to accept or reject a causal relationship between vaccination and the adverse event or the findings did not warrant

a Table change. The task force made no recommendations for revisions to the Table with regard to these vaccine-adverse event combinations. With regard to live attenuated influenza vaccine (LAIV), although there is evidence of increased wheezing episodes in very young children, there is no evidence of long-term sequelae. Children in the age group at risk for these wheezing episodes are not in the approved age group to receive LAIV. Although there is evidence that trivalent inactivated influenza vaccine (TIV) increases the risk for febrile seizures in young children, febrile seizures in and of themselves are transient events with no long-term sequelae, which is necessary to justify inclusion in the Table.

There are a number of studies on risk of Guillain-Barré syndrome (GBS) and 2009 influenza A (H1N1) monovalent vaccine (H1N1 vaccine) that are in progress or in press. GBS is a rare demyelinating disease that may be autoimmune in origin. Following the H1N1 influenza pandemic, the H1N1 antigen was included in the 2010-11 and 2011-12 TIV formulations. Since the H1N1 vaccine-GBS studies have not yet been published in the peer reviewed literature, the task force decided to defer a decision on GBS and TIV until the peer review and publication process is completed and the results of the studies are publicly available. As well, Dr. Johann-Liang commented that there is very little understanding of the possible mechanisms of action of influenza vaccine and GBS, and the epidemiological evidence is contradictory (although there is good evidence of risk of GBS associated with the 1976 swine influenza vaccine).

The IOM committee determined that there was no data available on the risk of anaphylaxis following hepatitis A vaccine. Therefore the IOM concluded that the evidence was insufficient to accept or reject a causal relationship between hepatitis A vaccine and anaphylaxis. There was also insufficient evidence for complex regional pain syndrome following vaccination, although the task force did look at data that was suggestive but not sufficient to support a causal relationship.

The information provided by Dr. Shimabukuro was informational and did not require a recommendation by the Commission.

Public Comment

Mr. King invited public comment. There were no requests to make a statement to the Commission.

(The meeting recessed at 4:30 p.m., to reconvene the following morning, March 9, at 9:00 a.m.)

Advisory Commission on Childhood Vaccines

March 8-9, 2012

Day Two

Minutes

Members Present

David King, Chair
Charlene Douglas, Ph.D.
Kristen Feemster, M.D.
Edward Kraus, J.D.
Ann Linguiti Pron, MSN, CRNP, RN
Luisita dela Rosa, Ph.D.
Jason Smith, J.D.
Sylvia Fernandez Villareal, M.D.
Michelle Williams, JD

Division of Vaccine Injury Compensation

Geoffrey Evans, M.D., Director, DVIC
Andrea Herzog, Staff Liaison

Welcome – Unfinished Business David King, ACCV Chair

Mr. King called the meeting to order and, after introductions, noted that there was no unfinished business from the day before. He invited Dr. Shimabukuro to provide an update on ISO activities since the last meeting.

Update from the Immunization Safety Office (ISO) Tom Shimabukuro, Medical Officer, Immunization Safety Office, CDC

Dr. Shimabukuro briefed the Commission on the February 2012 meeting of the Advisory Committee on Immunization Practices (ACIP), during which the following recommendation was approved: for adults aged 19 years and older who previously have not received a dose of Tdap, a single dose of Tdap should be given. The discussion before the vote included a review of the epidemiology of pertussis, the cost effectiveness of vaccinating older adults, and safety and immune response in older adults. The final implementation language is being drafted and will not be product specific (there are two licensed vaccines, only one of which is FDA approved for administration to older adults). The nonspecific wording allows health care providers flexibility with either vaccine in older adults.

Dr. Shimabukuro reported on the Institute of Medicine Committee on Assessment of Studies of Health Outcomes Related to the Recommended Childhood Immunization Schedule, which is looking at the feasibility of studying health outcomes of children who are vaccinated in accordance with the CDC recommendations, versus children who are not vaccinated or are vaccinated under an alternative schedule. The Committee, which has met twice, will address ethical issues, current scientific literature, stakeholder concerns, and identify potential research approaches, methodologies and study designs, including cost considerations. The report is expected to be completed by late 2012.

Finally, Dr. Shimabukuro reviewed several recently published papers. The first, by Shui et al. concluded that among US infants aged 4 to 34 weeks who received Rotateq, the risk of intussusception was not increased compared with infants who did not receive the rotavirus vaccine. Baxter et al, in a Vaccine Datalink study using a population of over 3 million, reported that during an 11-year period, risk of GBS recurrence was low. There were no cases of recurrent GBS after influenza vaccination and none within 6 weeks after any vaccine.

Stewart et al., in a study of laboratory workers who received anthrax vaccine (the vaccine is not available to the general public), reported no change from baseline in physical or mental scores in study subjects following Anthrax Vaccine Adsorbed (AVA). Study suggests no association between AVA and quality of life over 30 months. A study by Tse et al., discussed earlier in the Commission meeting, showed an increased risk of febrile seizures in children 6-59 months of age on the day of the vaccination and the day after vaccination with trivalent influenza vaccine (TIV) and 13-valent pneumococcal conjugate vaccine (PCV13) administered separately or simultaneously. The highest risk was in those children who received the vaccines simultaneously, with the risk peaking at 16 months of age. Finally, there was a paper by Broder et al. that focused on FDA-CDC policy around vaccine safety monitoring that discussed how signals are detected, assessed and publicly communicated. Expanding on the process, Dr. Shimabukuro briefly explained the basic concepts of proportional reporting analysis and data mining in the VAERS database.

During discussion, Dr. Evans noted that the VICP covers the use of licensed but not approved Tdap in older adults, also known as an off-label use. Off-label use would not affect an individual's injury claim under the VICP. There was also a question about the risk of febrile seizures that occurs when TIV and PCV13 are given simultaneously, and whether the ACIP would act to discourage that practice. Dr. Shimabukuro explained that ACIP had reviewed the data and concluded that changes in the recommendations were not warranted at this time.

Mr. Kraus commented on the IOM study and expressed concern that a parent's choice to comply with the ACIP recommendations, opt for an alternative vaccine schedule, or forego vaccines in their children is a sensitive issue and decisions are based on various considerations by the parents. He felt that the IOM committee could serve a positive purpose in encouraging studies on the issue. He felt that it would be important for public confidence in the vaccination program.

Update on the National Institute of Allergy and Infectious Diseases (NIAID) Jessica Bernstein, NIAID

Ms. Bernstein announced that the most recent Jordan Report was available on the NIAID web site. The Report, first published 30 years ago, was originally a discussion of the state of the science of vaccine research and development. Recently it has added perspectives on vaccine, including immunization and pregnancy, sex differences in immune response to vaccines, and an overview of personalized medicine. She also announced a new initiative by the NIH National Center for Advancing Translational Sciences (NCATS), which is focused on moving basic medical discoveries into clinical applications. One item of interest currently is the repurposing of drugs, finding new uses for existing drugs.

Ms. Bernstein briefly commented on NIAID's interest in vaccines, noting that the Institute has a significant portfolio of vaccine research. Information on that research is available at www.clinicaltrials.gov. There is also a very large inventory of videocasts and podcasts on a wide range of topics. The list of titles can be found at www.videocast.nih.gov.

During discussion, asked about the pediatric burden of hepatitis C, Ms. Bernstein commented that information on a newly initiated hepatitis C vaccine trial should be available on the NIH web site within days. About the very long list of vaccines in the NIAID research portfolio, Ms. Bernstein mentioned that the list is mainly basic research, and some of the studies are in early stages of research. Speculating

on possible future vaccines for the Vaccine Injury Table, Dr. Evans commented that there is currently interest in maternal vaccines (vaccination during pregnancy), including new vaccines for group B streptococcal infection, cytomegalovirus, and respiratory syncytial virus, any of which could be candidates for the program in the future. Asked whether a fetus would be covered for a vaccine administered to the mother, Dr. Evans commented that there had been several such claims, all of which failed to reach a conclusion, mainly based on legal questions about whether the fetus could actually be a recipient of a vaccine given to the mother. He added that there was interest in this issue in the medical community and some pharmaceutical companies.

**Update on the Center for Biologics, Evaluation and Research (CBER)
LT Valerie Marshall, FDA**

LT. Marshall reported that the FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) met on February 28-29 to consider the influenza strains that should be included in the 2012-2013 seasonal trivalent flu vaccine. The Committee recommended retaining the current A /California 7/2009, but replacing the other two strains with A Victoria/361/2011 and B/Wisconsin/1/2010. The Committee discussed a quadrivalent vaccine and agreed that, if it were to be approved, the B/Brisbane/60/2008 should be the fourth strain. The Committee also discussed regulatory pathways for licensure of pandemic influenza vaccines and reached consensus that safety and immunogenicity data should be accrued with the adjuvanted pandemic vaccine; and that it was reasonable to infer effectiveness of the pandemic vaccine from the efficacy of the seasonal vaccine made by the same manufacturer and same manufacturing process.

On February 29, the FDA approved the first quadrivalent influenza vaccine containing two influenza A strains and two influenza B strains. The vaccine would be licensed for use in individuals two years of age to 49 years of age. Finally, LT Marshall stated that, on January 10 and 11, the FDA held a workshop on the status of knowledge on human cytomegalovirus (HCMV) biology and epidemiology and the development of HCMV vaccines.

Dr. Evans observed that, under the law, only the trivalent influenza vaccine could be covered under the program, so that a revision to the tax language would be needed to include the new quadrivalent vaccine. LT Marshall commented that additional information about approved vaccines could be found at www.vaccines.gov.

**Update from the National Vaccine Program Office (NVPO)
Dan Salmon, Vaccine Safety Coordinator, National Vaccine Program Office**

Dr. Salmon focused his comments on the final report of the NVAC Vaccine Safety Risk Assessment Working Group (VSRAWG) to conduct rapid review of data accumulated from a number of surveillance programs monitoring the 2009 pandemic influenza A H1N1 vaccine program, the largest mass vaccination program in recent history. There were 60 million cases of H1N1 flu reported that year, 270,000 hospitalizations and 12,000 deaths. It was estimated that over 80 million people were vaccinated

VSRAWG was set up in 2009 with representatives of NVAC, ACIP, VRBPAC, DoD Defense Health Board, and NBSB, and included non-federal experts and a public representative. There was a rigorous conflict of interest review of each member. The Working Group met 20 times. The clinical trials reviewed involved over 3,000 subjects, and passive surveillance was through the Vaccine Adverse Event Reporting System (VAERS) and the Real-Time Immunization Safety Monitoring System (RTIMS). Other resources included the Post-licensing Rapid Immunization Safety Monitoring System (PRISM), data from the Indian Health Service, DoD and the Veterans Administration. Additional data support came from CDC's Emerging Infections Program, the CMS data base, and the Vaccines and Medications in Pregnancy Surveillance System (VAMPSS). Clinical assessment was provided by the CDC Clinical Immunization Safety Assessment Centers.

VSRWAG issued six reports, each reviewed, deliberated upon, and approved by NVAC. They were sent to the Assistant Secretary for Health, who distributed them to other federal agencies and international partners. The first four reports concluded that there were no adverse event signals with regard to the vaccine. The fifth report indicated a statistically significant signal for two adverse events – Bell's palsy and thrombocytopenia. The sixth report indicated a weak signal for a risk of Guillain Barre syndrome. The final report was reviewed at the last VSRWAG meeting however it is not a final report as the results from the surveillance systems have not yet been peer reviewed. The Working Group concluded that there was actually no risk of Bell's palsy; but confirmed that there was a very small increased risk of GBS (one to three additional cases per million doses of vaccine). It was noted that hypersensitivity reactions might be more likely with H1N1 than the seasonal flu vaccine. The NVAC discussed improving surveillance of pregnant women, continued methodological development of data mining procedures when signals are detected, and exploring ways to reduce vaccine administration errors.

During discussion Dr. Salmon commented that the federal ownership of the 2009 flu vaccine campaign, when all of the vaccine for that year was purchased by the federal government, was not planned for other years. Asked about availability of vaccine for the next flu season, Dr. Shimabukuro indicated that there should be no shortage.

Review of Vaccine Information Statements (VIS) Skip Wolfe, CDC

Mr. Wolfe invited discussion of comments submitted by outside reviewers concerning the sections in the various VIS about "what if there is a severe reaction?" The Commission had debated alternative statements at the last meeting – "get the person to a doctor or hospital immediately," and an alternative, "seek medical help right away." There was agreement that the language should be consistent across VIS versions and that it should be understandable to both parents and caregivers. Dr. Shimabukuro commented that getting a child to a doctor and calling 911 are very different, and Mr. Wolfe stated that it might be helpful to define "emergency," perhaps by examples. In any event, he said that the VIS needs one statement that would apply to a range of circumstances. He agreed to work on the wording for the Commission's consideration at the next meeting.

Moving to the measles, mumps, rubella (MMR) VIS, Mr. Wolfe commented that there were few significant changes. In Section 1, the words "arthritis (mostly in women)" would be moved to the beginning of the sentence so that readers would not think that rash and mild fever would also occur mostly in women. Dr. dela Rosa suggested adding pancreatitis under mumps, but Mr Wolfe pointed out that it was not part of the ACIP recommendation. It was noted that "death" was not included under rubella as it was under measles and mumps, and there was a comment that rubella is a much more benign disease.

Mr. Wolfe said there were no changes to Section 2, and a minor change to Section 3. He added that one provision was added (to advise the doctor if the individual had any other vaccinations within four weeks) because that was considered important information. In Section 3 there was a suggestion that the wording about whether or not to get a vaccination if mildly or moderately ill was discussed and there was a recommendation that the VIS suggest the parent obtain advice from the physician or other health care give who administer the vaccine. There was also an observation that parents receive the VIS at different times, which may not be timely in terms of the mild/moderate illness caveats. Mr. Wolfe agreed to revisit the wording of the section.

Mr. Wolfe noted changes to Section 4 were minor in nature; no substantive changes were recommended. Concerning the wording that getting the vaccine is safer than getting any of the three diseases (MMR), there was a recommendation to revise the wording to reflect the fact that the benefit of being vaccinated far outweigh the risks of not getting vaccinated. It was also suggested that clarifying the wording about rare events, such as serious allergic reactions, should be explained, perhaps with wording to the effect that some adverse events are so rare that it is difficult to ascertain whether or not the vaccine actually caused the reaction. Mr. Wolf explained that the adverse event time references are not

from the Table, but from the ACIP recommendations, which are often based on package inserts or clinical trial data. It was noted that the measure of risk may relate to number of doses or number of individuals vaccinated, depending on the data source. Finally, Mr. Wolfe stated that there were no changes to Sections 5, 6, and 7.

The last VIS reviewed was general advice to parents about “baby’s first vaccines.” Mr. Wolfe noted that, under Precautions, a warning about yeast when receiving PCV13 was added, as were admonitions to inform the vaccine provider of rotavirus if the child had severe combined immunodeficiency or had ever had intussusception, and for PCV 13, advise of any reaction to a vaccine containing diphtheria toxoid (e.g., DTaP), since diphtheria toxin is a carrier protein in the PCV13 conjugate vaccine. There was a formatting suggestion for clarification that, under the entire Precaution section, the vaccine be listed before the preexisting conditions. That is, start each paragraph: Talk to your doctor before getting a specific vaccine if your child has – then list the conditions. Under the section entitled “How Vaccines Work,” there was a suggestion to drop the words “without having to get sick first,” in favor of “without getting the disease first.”

There was a brief discussion about the “Routine Baby Vaccines” table and the reason for adding the column “Other Information.” Mr. Wolfe explained that the intent was to provide a place in the VIS for miscellaneous information that might not be easy to include elsewhere. There was a comment that the warning in the table that some children should not get pertussis vaccine was not backed up as a more detailed warning in the Precautions section. Mr. Wolfe agreed that the phrase could be removed without prejudice to the intent of the VIS, and to amplify the rationale would be more information than the parents should be required to consider since the physician would make that decision anyway. Mr. Kraus commented that the statement attributing reduction in disease burden to vaccines alone should be modified – the wording could be “thanks largely to vaccines.” He noted that other public health programs also contribute to reduction in disease. There was also a brief discussion about adding warnings about syncope, but it was noted that fainting rarely occurs in infants, and a general statement in all VIS documents about syncope was discouraged by the ACIP policy that statements must be evidence based, and most of the fainting studies focus on adolescents.

Public Comment

Mr. King invited public comment, and Theresa Wrangham, National Vaccine Information Center, made a statement about parents who choose to rely on alternative vaccine schedules or decide that their children should not be vaccinated at all. She stated that parents make those decisions relying on public information about safety, concern for the integrity of research, uncertainty about the efficacy of vaccines, personal and religious convictions, and concern about adverse reactions to vaccines. As an example, the CDC’s report to Congress on the HPV vaccine included the assertion that less than one percent of all cancers originate in the cervix; that HPV infection resolves without medical intervention in 91% of cases; and that it is an expensive vaccine that she felt was unnecessary. Secondly, she expressed the view that the influenza vaccine’s effectiveness is questionable, and that the labeling states that the risk of the vaccine to an unborn fetus of a woman who receives the vaccine is unknown. She expressed concern that the scientific literature was insufficient for the IOM to arrive at a risk evaluation in 85% of the adverse events reviewed.

Ms. Wrangham recommended that identifying individuals at risk of harm from vaccines should be a high research priority; that there should be higher regulatory standards for vaccine licensure; and that parents should be included in the vaccine policy making process. She added that the Commission should support marketing efforts to inform parents about the risks of vaccines as well as the benefits, and to more widely publicize the VICP.

Future Agenda Items

Mr. King invited suggestions for future agenda items. Mr. Kraus, referring to the comment made in the public comment segment of the meeting, suggested a future discussion about research on adverse events. Dr. Evans commented that the earlier IOM committees faced the same situation in about two-

thirds of the adverse events reviewed. The increase experienced in the current study is reflective of budgetary constraints, both in the funding of research and in the support of the surveillance programs. Dr. Evans noted that some favor using a portion of incoming Trust Fund revenues to enable more vaccine safety research by HHS agencies. The Commission has voiced its position on this at least twice, the first time being unanimously in support, while a more recent Commission reached consensus opposing use of Trust Fund monies for this purpose. Dr. Shimabukuro offered to make a presentation on the ISO's current research portfolio, perhaps at the next meeting. Dr. Evans suggested that Dr. Salmon could participate by bringing the perspective of the NVPO.

Mr. King appointed a small committee to develop the agenda for the next meeting,

Adjournment

Dr. Evans expressed appreciation for the extraordinary effort and contribution of the members of the task force that developed the recommendations for revisions to the Vaccine Injury Table that were considered and approved by the Commission. He particularly commended Dr. Rosemary Johann-Liang, whose scientific knowledge and ability to manage, allowed her to shepherd the project to its very successful conclusion. Dr. Johann-Liang added that the task force was an exceptionally productive team that had devoted a significant amount of their time to the project.

There being no other business, on motion duly made and seconded, the meeting was adjourned by consensus at 12:10 p.m.

David King, ACCV Chair

Geoffrey Evans, M.D.
Executive Secretary, ACCV

Date