Advisory Commission on Childhood Vaccines

December 8-9, 2011

Day One

Minutes

Members Present

Sherry K. Drew, J.D., Chair
Charlene Douglas, Ph.D.
Kristen Feemster, M.D.
Thomas Herr, M.D.
Sarah Hoiberg
David King
Ann Linguiti Pron, MSN, CRNP, RN
Jason Smith, J.D.
Michelle Williams, J.D.

Executive Secretary

Geoffrey Evans, M.D., Director, DVIC

Staff Liaison

Andrea Herzog, Principal Staff Liaison

Agenda Item: Welcome, Report of the Chair and Approval of Minutes

Ms. Drew called the 81st meeting of the Advisory Commission on Childhood Vaccines to order, welcomed the commissioners and others present and on the phone. She welcomed two new Commission members present for the meeting, Mr. Ed Kraus, an attorney for vaccine-injured individuals, and Ms. Luisita dela Rosa, a parent of a vaccine-injured child. She noted that Dr. Sylvia Villarreal, a pediatrician at the Taos Clinic for Children and Youth, was a third new member who would be attending meetings in the future.

Ms. Drew called for approval of the minutes of the September 1-2, 2011 meeting and, on motion duly made and seconded, those minutes were unanimously approved. Dr. Herr interjected that, although not related to the minutes, per se, he felt that the Commission should consider the issue of vaccine labeling that may not indicate clearly the presence of latex. It was suggested that the issue be added to a future agenda for discussion.

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

After reviewing the meeting agenda, Dr. Evans discussed the activity of the program for the fiscal year to date. He noted that only non-autism claims had been filed to date, half of them influenza vaccine-related. Since the Omnibus Autism Proceeding is no longer accepting claims, there have been no claims filed in the autism category. On the adjudication side there has been significant activity in the Omnibus Autism Proceeding, mostly related to cases being dismissed and efforts by the Department of Justice and the petitioners' bar to work out attorneys' fees and related costs. Another aspect of adjudications reveals that 75% of compensable claims were resolved through settlements in FY 2011. Of the remaining 25%, unlike past history, the majority were referred for a court decision, while Department of Health and Human Services concessions declined accordingly.

Dr. Evans commented that the awards in FY 2011 were $228 million (petitioners and attorneys fees), a record for the life of the program. Those outlays were more than offset by significantly increased Trust Fund income as a result of the over 140 million influenza vaccine doses that were distributed. The Trust Fund netted over $100 million.

In terms of activities, Dr. Evans reported that he attended the annual meeting of the American Academy of Pediatrics in Boston on October 15-18; an excellent workshop on October 19th on vaccine ethics and legal issues sponsored by the University of Pennsylvania Center for Bioethics; and the regular meeting of the Advisory Committee on Immunization Practices (ACIP) on October 25-26 in Atlanta. At that meeting ACIP approved Gardasil, the human papillomavirus vaccine, for permissive use in boys.

Finally, Dr. Evans provided contact information for those interested in contacting the DVIC about any issues related to the program.

Report from the Department of Justice
Mark W. Rogers, J.D.
Acting Director, Torts Branch, Civil Division, Department of Justice

Power Point Presentation Summary

Mr. Rogers referenced the Power Point materials, entitled December 8, 2011 Department of Justice Power Point Presentation (DOJ PP), as part of his presentation.

Personnel

Mr. Rogers began his presentation by greeting the ACCV and welcoming the new members. Mr. Rogers first reported a personnel update, explaining that a new Director of the Constitutional and Specialized Torts Branch will be hired early next year. Until then, Mr. Rogers is currently serving as Acting Director, and Vincent Matanoski is serving as Acting Deputy Director. Mr. Matanoski had previously given the DOJ presentation at the past two ACCV meetings. Mr. Rogers reported that his office recently hired two new attorneys: Tara Kilfoyle and Gordon Shemin. The office is also planning to hire two paralegals.

Statistics

Mr. Rogers turned to a statistics summary for the reporting period of August 16, 2011, through November 15, 2011 (DOJ PP, pp. 2-4). Mr. Rogers emphasized that the reporting period was a "three-month snapshot" of recent activity in the program. He contrasted DOJ's statistics with HHS's statistics, which are reported by fiscal year and provide a more comprehensive summary.

In this reporting period, DOJ recorded 121 new petitions filed (DOJ PP, p. 2). Only one newly filed case was an autism petition. Of the 121 new petitions, 33 were filed on behalf of minors, and 87 were adult claims. Mr. Rogers noted that this was consistent with an overall trend of more adult claims than minor claims being filed in the Program.

Mr. Rogers then turned to a slide illustrating the number and types of petitions adjudicated in the last reporting period (DOJ PP, p. 3), and highlighted a few statistics. A total of 920 petitions were adjudicated. There were 61 compensated cases, one of which was conceded by HHS. The remaining 60 compensated cases were resolved through either a proffer or stipulation. The majority of the non-compensated cases were autism dismissals. There were 14 cases that were voluntarily withdrawn, and exited the Program without a judgment (DOJ PP, p. 4). Mr. Rogers reminded the ACCV that statistics from this three-month reporting period were not necessarily indicative of overall trends, but instead represented a recent snapshot of activity in the Program.

Glossary of Terms and Overview of Petition Processing

Mr. Rogers presented several 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, but Mr. Rogers explained a few key terms for the benefit of the newer members. A petition is "adjudicated" after the court enters final judgment. This means the case has ended and closed. A "compensable" case is one where a petitioner is left with an award. A case is "conceded by HHS" if HHS has reviewed the claim and concluded that the injury or death was vaccine-related. Very few cases are conceded, as the statistics illustrate.

A "decision" is issued when the parties cannot agree, and the Special Master has to decide the case. A "settlement" is an alternate to litigation. It involves a discussion between the parties about the merits of a case. A settlement results in a "handshake" between the parties, and an award to petitioner. Mr. Rogers explained that a "proffer" is very much like a settlement, but the distinction is important internally to DOJ. In a settlement, one party believes the award should be high, the other thinks it should be low, and after negotiations, they agree on a middle point. Neither party gets everything they want. In contrast, in a proffer situation, the parties actually agree that a particular award is supported by the evidence in the case. Mr. Rogers acknowledged that because both settlements and proffers are amicable agreements between the two parties, it may be difficult to discern the differences between the two. However, settlements have to be approved by certain authorities within DOJ, so it is important for DOJ to distinguish settlements and proffers when reporting statistics.

Ms. Hoiberg asked if the term "stipulation" was synonymous with "settlement." Mr. Rogers said that it was, and stated that DOJ would make an effort to clarify this in future power point presentations.

Mr. Rogers then explained several terms related to appeals. After a Special Master issues a decision, if one party is unhappy with the outcome, they can appeal to the Court of Federal Claims (CFC). If the appellate court "affirms" the case, they agree with the Special Master's decision. That means the party that brought the appeal lost. A case is "reversed" on appeal if the judge does not agree with the Special Master's decision and reverses it. Usually a reversal is accompanied with an explanation and a new decision in the case. Sometimes the appellate judge will "remand" a case, which means the judge sends it back to the Special Master with instructions to fix some problems with the decision. Mr. Rogers explained a remand as a "do-over." A case is "vacated" when the appellate court completely eliminates the lower court's decision, and sends it back for a new decision. While a remand may be used to fix some minor parts of the decision, a vacation of the decision means the decision is gone completely.

Mr. Rogers then presented a flow chart that illustrated the processing of a petition in the Program (DOJ PP, p. 8). Most compensated cases move through the settlement route toward a final decision (pink box). 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, the case moves over to the "damages" box.

Once a case is in the "damages" box, it is usually resolved by the parties outside of a court room through a settlement or a proffer. Very few damages cases are decided by a Special Master.

Appeals

Mr. Rogers then discussed recent appellate activity in the program at the U.S. Court of Appeals for the Federal Circuit (CAFC) and the U.S. Court of Federal Claims (CFC) (DOJ PP, pp. 9-13). First, Mr. Rogers mentioned that although it was not documented on the slides, Cloer v. HHS is still pending. There is still time for petitioners in that case to seek *certiorari*, or appeal to the Supreme Court. The petitioners asked for an extension until January 2nd for that appeal. The Cloer case was discussed at the last ACCV meeting, but Mr. Rogers provided a brief review. Cloer was decided by the CAFC en banc, meaning all of the judges heard the argument, rather than the usual panel of three judges. The decision

held that the Vaccine Act statute of limitations, or deadline for filing a petition for compensation in the Program, runs from the date of the first sign or symptom of manifestation of onset of the vaccine injury, for 36 months. The decision also ruled that the doctrine of equitable tolling applies. This means that the running of the deadline might be delayed for reasons that merit equitable tolling.

Mr. Rogers next discussed two recent decisions from the CAFC, Rickett and Lombardi (DOJ PP, p. 9). In both of these cases, the Special Master ruled that the injury was not vaccine related. Petitioners appealed to the CFC, which affirmed the Special Masters' decisions. Petitioners then appealed to the CAFC, which agreed with the CFC.

Respondent appealed two cases to the CAFC: Rotoli-Knight and Porter. In both of these cases, the Special Master held that the injury was not vaccine related. The CFC reversed that decision, finding that the Special Master had applied an improper standard. HHS appealed to the CAFC, and the CAFC found that the Special Master had applied the correct standard, and his decision should have been affirmed.

Several new appeals are pending before the CAFC (DOJ PP, p. 10). Hibbard and Locane involve basic entitlement decisions. Griglock involves a statute of limitations issue. In that case, the petitioner received a vaccine, allegedly suffered an injury, and then died. The petition was filed more than three years after the vaccine injury, so that statute of limitations had expired, but the petition was filed within two years of the death, so that statute of limitations had not expired. The Special Master dismissed the injury claim and proceeded with the death claim. Griglock is an example of the types of jurisdictional and statutory issues that are being resolved on appeal.

One appeal, Heinzelman, was filed by Respondent. Briefs have not yet been filed in this case.

Mr. Rogers then turned to cases recently decided at the CFC (DOJ PP, p. 11). The CFC is one step above the Office of Special Masters, and is the first level of appeal. Mr. Rogers referenced slide 11, which provides the outcome of the case and the issue in question, as well as identifies which party appealed the case. He then pointed to the cases that were currently pending before the CFC (DOJ PP, p. 12). There were three new appeals since the last meeting, all filed by petitioners: Viscontini, Phillips-Deloatch, and Goetz. Goetz involves the issue of finality of judgment. The case was dismissed for exceeding the statute of limitations, and petitioners want to re-argue the case in light of the recent Cloer decision.

There are no oral arguments scheduled before the CAFC. Goetz is schedule for oral argument before the CFC on December 15th (DOJ PP, p. 13).

Adjudicated Stipulations

Mr. Rogers turned to claims that were recently resolved by stipulation of settlement. (DOJ PP, pp. 14-19). During this reporting period there were 52 cases adjudicated by stipulation. Mr. Rogers presented a chart showing the amount of time required in each case from the petition filing to the filing of the stipulation of settlement.

Mr. Rogers suggested that if a case was well-documented, with no litigation involved, it can move quickly toward settlement. Settlements take longer when petitioners request additional time to document their case, find an expert, and/or complete the medical record. These cases can stall for years before a settlement is processed.

Questions and Comments

Ms. Drew asked if the stipulation chart included cases resolved by a proffer. Mr. Rogers stated that these slides only showed cases resolved with stipulations of settlement, not a proffer. Mr. Rogers explained that these slides were initially provided at the ACCV's request, because there was some concern that DOJ was taking too long to get internal approval for these settlements. DOJ does not need that same internal approval for a proffer – a proffer can be filed the next day if the attorneys shake hands. A

settlement, however, has to go through appropriate internal channels at DOJ, and will therefore require more time to process than a proffer.

Mr. Rogers emphasized that the alleged injury column on the Adjudicated Stipulations chart is only "alleged." That information is pulled from the initial petition. Through the course of litigation, the alleged injury sometimes morphs into something else as additional medical records are collected. Dr. Herr clarified that the alleged injury was not necessarily the final diagnosis for settlement, and Mr. Rogers agreed that it is not. He commented that the reason for settlement may be something completely different from what is listed on the chart.

Ms. Drew thanked Mr. Rogers for his presentation, and commented that the information was valuable to ACCV members.

Report from the 2011 Judicial Conference – Ms. Sherry Drew

Ms. Drew explained that the Court of Federal Claims Bar Association, supported by the Court, sponsors the Judicial Conference. In alternate years it is held in Washington, DC and the following year in another city in the U.S. Ms. Drew said that she attended the 2011 conference, which was held in Berkeley, California. The conference addresses a broad range of appeals areas, including vaccine injury-related appeals, and that specialty conducts its own program sessions in conjunction with other specialty areas of appeals. Ms. Drew stated that this year the program was quite extensive dealing with a number of issues, including ethics and peer-reviewed science. She added that the Vaccine Petitioners Bar (separate from the Bar Association of the Court of Federal Claims), was given a slot on the agenda during the vaccine injury segment of the program. She noted that the sessions on the first day were recorded and were available on the Court of Claims' web site; but the recordings for the second day failed and are not available.

Review of Vaccine Information Statements

The Commission reviewed three Vaccine Information Statements (VIS) for tetanus and diphtheria (Td) or tetanus, diphtheria and pertussis (Tdap), hepatitis B and polio vaccines. Beginning with Td and Tdap, Dr. Feemster commented that the VIS mentions reactions in adolescents but not in infants, where there is a higher degree of morbidity. It was noted that both are recommended for children over 7, but that younger children may have received DTaP. Concerning the effects of pertussis discussed in the VIS, Dr. Herr mentioned that the term "disturbed sleep" is not specific or clear. It might be better described by specific symptoms – coughing, difficulty breathing, vomiting.

There was a comment that the VIS stated that Tdap should be taken only once, but some may receive the vaccine more than once (e.g., after an injury), and some may not be aware that they received the vaccine earlier because of faulty memory or incomplete medical records, especially true for adults. Dr. Feemster commented that everyone over 11 should have one Tdap vaccination, but there was no significant risk to receiving Tdap more than once. Mr. Wolfe agreed that a statement in the VIS to that effect might be appropriate to allay fears anyone might have because of the "one time" statement. In addition, since there is a ten-year interval between Td boosters, it should be noted that there is no harm in having the booster at intervals less than ten years, especially if an injury suggests a tetanus vaccine.

There was a brief discussion about the recommendation to avoid vaccination if one is severely or moderately ill, although there is no restriction if one is mildly ill. It was felt that defining those terms was not easy, but Dr. Herr suggested that such a decision should be made by the physician rather than the parent. It may be that the risks of not receiving the vaccine would outweigh the risks of receiving the vaccine when mildly or even moderately ill. Mr. Wolfe agreed that it was a clinical judgment as to how ill a child might be. Ms. Hamborsky added that circumstances would affect such decisions as well; for example, an office patient might be able to defer the vaccination and return at a later date, but in the ER or urgent care setting such follow-up might be impractical.

There was a suggestion that in paragraph 5, under "Mild Problems," the VIS includes statistics on adolescent and adults separately for some problems, but does not provide that separation for other

problems. In addition, it was noted that, for the category of chills, body aches and so on, the descriptor "uncommon" is unclear – is it lack of data or a known very low number? There was also concern that the frequently quoted "less than one in a million" events might be a guess or statistic based on data, and that should be clarified. There was a discussion of the term "severe allergic reaction," when the specific reaction, anaphylaxis, is not mentioned at all. Mr. Wolfe felt that the term might be too technical for some and, in any event, that was an adverse event for which the criteria were specifically defined by ACIP.

Finally, moving to the final section, paragraph 7, Mr. Wolfe stated that no changes were anticipated since that section had been thoroughly reviewed and edited previously.

Turning to hepatitis B vaccine, Mr. Wolf stated that no significant changes were made since the Commission last reviewed the VIS. The statistics in the first paragraph had been updated because of new data available. Ms. Pron suggested that the sentence referring to the combination of hepatitis B vaccine with other vaccines be moved to the second paragraph, where it is discussed in more detail. Mr. King reiterated a recommendation he had made at an earlier meeting that a move toward more consistency among the various VIS would be appropriate, in wording, in content and in format. Mr. Wolfe agreed in principle, but added that some vaccines require a variation from a standard format.

Dr. Herr commented that he provided all germane VIS to parents before vaccinations were begun, to give them a chance to read and digest the information, Others indicated a similar experience. Mr. Wolfe commented that there is little data about how individuals treat the information, and whether the format or distribution method makes any difference.

A discussion at an earlier meeting was raised as to whether advice to ask only "your doctor" was appropriate, or whether the list should be expanded to include others – nurses, pharmacists, nurse practitioners, physician assistants. Mr. Wolfe explained that focus groups and other consultants had emphatically agreed that only the word "doctor" should be used in the context of asking questions related to vaccines, such as a dosing schedule. He added that if a doctor were not available he was confident that the individual would ask another expert, such as a nurse. He also felt that, since alternative dosing schedules are not common, the entire sentence concerning "other dosing schedules" could be omitted.

Dr. Feemster commented that the dosing schedule for adolescents was not included, and that adding a recommendation for the three-dose regimen for anyone not previously vaccinated as an infant would be appropriate. Ms. Hamborsky said that the list of risks under paragraph 3, Who Should Get Hepatitis B Vaccine and When, was developed by ACIP and probably could not be amended easily. But there was a catch-all provision that invited anyone who desired immunization to get the vaccine.

Moving to paragraph 4, Who Should NOT Get Hepatitis B Vaccine, Ms. Hoiberg expressed concern that a recommendation to tell the doctor about severe allergies is not realistic for infants who receive vaccines at birth. Mr. Wolfe agreed, stating that until a child is exposed to a potential allergen (any untried food or medication) there is no way to know what allergies might exist. He added that at one time a parent could choose to delay vaccination until two months of age, which would provide a better cushion to reveal that an allergy exists.

The review of the polio VIS was very brief. Mr. Wolfe stated that no significant changes had been made except that a manufacturer had requested the addition of a statement that a child might receive an additional dose of IPV, above the four prescribed by ACIP, if the child was given Pedarix or Pentacel. There have been no reports that the additional fifth dose causes any ill effects. In addition, the reference to OPV was deleted from the VIS since that vaccine is no longer available.

No significant changes were recommended by the Commission members.

Public Comment

Ms. Drew invited public comment.

Mr. James Moody, representing the National Autism Association, expressed concern that the federal government agency sponsoring the IOM study of vaccine adverse events had requested that the IOM not include studies related to mercury in vaccines. He felt that was inappropriate in light of the fact

that the IOM's initial literature search revealed a significant number of research articles about mercury in vaccines and the possible link to autism. He stated that there was a large amount of information on the epidemiology of mercury and there is ongoing research that appears to implicate mercury as a factor in the development of autism. He expressed the belief that this omission from the study deprived petitioners, their counsel and the Special Masters from having access to the analysis that the IOM review might have included in its final report.

In light of this, Mr. Moody asked that the ACCV recommend a moratorium on further dismissals of autism cases until the IOM can be directed to complete a review of the scientific literature with regard to mercury as a possible contributory factor to the development of autism, and amend its final report to include that analysis.

Noting that there were no other individuals interested in making a public comment, Ms. Drew recessed the meeting until the following day.

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

Advisory Commission on Childhood Vaccines

December 8-9, 2011

Day Two

Minutes

Members Present

Sherry K. Drew, JD, Chair
Charlene Douglas, Ph.D.
Kristen Feemster, M.D.
Thomas Herr, MD
Sarah Hoiberg
David King
Ann Linguiti Pron, MSN, CRNP, RN
Jason Smith, J.D.
Michelle Williams, JD

Executive Secretary

Geoffrey Evans, M.D., Director, DVIC

Staff Liaison

Andrea Herzog, Principal Staff Liaison

Welcome, Ms. Sherry Drew, Chair

Ms. Drew called the meeting to order and invited comments on any unfinished business from the first day of the meeting. There being none, Ms. Drew invited Dr. Johann-Liang to lead the first presentation and discussion.

DVIC Clinical Update
Dr. Rosemary Johann-Liang

Overview of the IOM Report on Vaccines and Adverse Events – Dr. Rosemary Johann-Liang

Dr. Johann-Liang announced that, because of time constraints, the usual quarterly update on medical review and analysis activities within her office would be deferred until the next ACCV meeting. This presentation would focus on the IOM report on adverse events and the latest developments in the area of rotavirus vaccine. She added that at the last ACCV meeting Dr. Clayton, the chair of the IOM committee, provided a full review of the final committee report. That report is making its way into print, but because of extensive review procedures at the Institute of Medicine, it will not be published until the spring of 2012. However, ACCV members will be given a pre-publication report, which is subject to whatever changes emerge from the review process.

For the benefit of new members who may not have attended the past meeting, Dr. Johann-Liang provided a brief summary of the IOM review process, stating that the step to establish a contract with the IOM began in the fall of 2008, after which details of the study were worked out between the IOM and

HRSA in April 2009. The objective was to obtain from the IOM an independent assessment of the latest science related to a specific number of vaccines and specific adverse events. Funding was available to look at four vaccines – influenza, varicella, meningococcal and human papillomavirus. Fortunately, after the initial contract was executed, ARRA funding allowed the addition of four more vaccines – hepatitis A and B, MMR (measles/mumps/rubella) and tetanus-containing (Tdap, T, Td and DTaP). These eight vaccines are named in 92% of VCIP claims.

Dr. Johann-Liang explained that DVIC chose the vaccines, and developed a list of adverse events that the IOM would review. The IOM was allowed freedom to add to the adverse events list, which finally included 158 vaccine-adverse event combinations. This information was posted on the IOM web site for public review and comment. The IOM committee looked at epidemiological evidence at four levels (high, moderate, limited and insufficient), and mechanistic evidence, also at four levels (strong, intermediate, weak and lacking). The committee also looked at causality evidence, taking both epidemiology and mechanism of action into consideration. The final conclusions based on causality evidence were also in four categories – convincingly supports, favors acceptance, inadequate to accept or reject, and favors rejection.

Once the report was completed and preliminary findings released to HRSA, a task force was established to review the findings. The task force includes HRSA reviewers; the Immunization Safety Office, CDC: the Office of General Counsel; and DVIC. The tack force has nine working groups, one for each vaccine, and one to review injection and administration adverse events, a narrow research area that the IOM committee included in its report.

Dr. Johann-Liang commented that the IOM was not charged with looking at rotavirus vaccines, but some recent post-marketing surveillance data prompted DVIC to establish a rotavirus working group to look at a possible vaccine-related side effect, intussusception. A draft of a proposal to add rotavirus vaccines to the Injury Table was prepared, and was included in the Commission members meeting documents. As medical background, Dr. Johann-Liang explained that rotavirus infection is nearly universal in children up to five years of age. Mortality, not an issue in the U.S., is a problem in developing countries. However, morbidity is an issue in the U.S. because dehydrating diarrhea can be a serious problem in infants and young children.

Dr. Johann-Liang explained that intussusception occurs when a section of the bowel folds back on the preceding section of bowel, reducing blood flow, inducing swelling (edema), which can then progress to an obstruction, that if not caught early, can lead to surgical intervention. Naturally occurring intussusception is uncommon in the United States, affecting only about 1,400 children each year. It usually affects infants from two to six months old, peaking at that latter age, although less frequent events can occur in older children. An early diagnostic process, a barium enema, can also be a treatment modality by reversing (reducing) the intussusception.

Intussusception – Proposal to Add to Injury Table as an Adverse Event Related to Rotavirus – Anna Jacobs, Office of the General Counsel, and Mary Rubin, Medical Officer, DVIC

Ms. Jacobs explained the Vaccine Injury Table. The Table lists the vaccines covered by the VICP and the specific adverse events that are associated with the vaccine. If the claimant can prove that he or she received a vaccine listed on the Table, and sustained a listed injury within the time frame specified on the Table, then the claimant does not need to prove causation—rather, causation is presumed.

The Vaccine Act provides a way for the Table to be changed in a reasonably timely way, since it was acknowledged that the science related to the vaccine injury might change. Through the regulatory process, the Secretary of DHHS may add or delete vaccines from the Table; and may add, delete, or modify the adverse events and/or time limitations specified for any vaccine. This is done by publishing a Notice of Proposed Rulemaking (NPRM) in the Federal Register, allowing a public comment period of180 days and an opportunity for anyone to testify at a public hearing, and publishing a final rule in the Federal Register.

Ms. Jacobs explained the role of the ACCV. According to the Vaccine Act, the Secretary must provide the ACCV with a copy of the proposed Table revision, and give the ACCV the opportunity to comment for 90 days before the proposal is published in the Federal Register in an NPRM. Ms. Jacobs described principles that the ACCV may use in developing their comments and recommendations for a proposed revision. In 2006, the ACCV developed a set of guiding principles that were based on the premise that the Injury Table should be scientifically and medically credible, and that changes should, in most cases, benefit the claimants. The guiding principles suggest that the ACCV should consider the methodological limitations of the studies, any biases or other confounding factors that might affect the results, and keep the policies of the program in mind – that Congress intended that individuals with valid vaccine injuries should be properly compensated in a timely way.

Ms. Jacobs turned to the issue at hand, the addition of the injury of intussusception to the Injury Table, and described the history of rotavirus on the Vaccine Injury Table. In August 1998, the FDA licensed the RotaShield vaccine—a live, oral, rhesus-based rotavirus vaccine—that was recommended by the CDC for routine use in children. In accordance with the Vaccine Act, in October 1998, the Secretary added the general category of rotavirus vaccines to the Injury Table, with no condition specified. Almost immediately, the Vaccine Adverse Events Surveillance System (VAERS) began receiving adverse events reports of intussusception, and shortly thereafter the CDC recommended suspension of administration of RotaShield. By October 1999, the manufacturer withdrew the Rotashield vaccine from the market. The ACIP subsequently recognized an increased risk of intussusception within 14 days of administration, and withdrew its recommendation for routine use in children. Following this, in 2002, the Secretary modified the Vaccine Injury Table to add a second, more specific rotavirus category– live, oral rhesus-based rotavirus vaccine—with the injury of intussusception, and a specified time frame of 30 days after vaccination. By October 2008, because of the statute of limitations on filing a claim, it was determined that any potential claim would be time-barred and could not be filed. For this reason, the Secretary removed from the Table the specific category of live, oral, rhesus-based rotavirus vaccines and the injury of intussusception. However, the Injury Table continued to list the general category of rotavirus vaccines with no condition specified.

Dr. Johann-Liang explained that there were now two rotavirus vaccines available, Rotarix, used mainly outside the U.S., and RotaTeq, for which adverse event data is not yet fully developed. Dr. Rubin described a major, ongoing study of Rotateq and Rotarix, part of FDA's Post-licensure Rapid Immunization Safety Monitoring (PRISM), that began in 2004, which will eventually include a study population of 1 million infants. Final data will be available in 2012. Even so, the ACCV will consider the addition of vaccines containing rotavirus that specify the injury of intussusception, with a time period of 0 to 21 days post-inoculation. Dr. Rubin added that to support the basic criteria in the Injury Table, Qualifications and Aids to Interpretation (QAI) are developed to provide more specificity to the Table entry. In the case of rotavirus vaccines, the QAI states that adverse events may occur after the first or second dose, but that the third dose of Rotateq appears to be protective. In addition, naturally-occurring intussusception (not caused by vaccines) has been associated with infectious disease (viral diseases, bacterial enteritis, enteric parasitic diseases), conditions causing what are known as "lead points," such as intestinal masses and cystic structures, anatomic abnormalities and underlying conditions or systemic diseases (e.g., inflammatory bowel disease, inflammation, edema, cystic fibrosis and celiac disease).

Dr. Johann-Liang presented the limited claims data available at the end of FY 2011 – 15 Rotateq claims, 11 males and 4 females, ages 8 to 31 weeks; five after the first dose, five after the second dose and five after the third dose. Twelve had surgical procedures to treat the condition, and about half of the children had the confounding issues listed in the QAI. In summary, Dr. Johann-Liang stated that there appeared to be a very slight risk of intussusception caused by the two second generation rotavirus vaccines (there is more data on Rotarix mainly from Australia and Mexico) after the first dose and usually within seven days of administration. The data indicate a possible increased risk of one additional case per 100,000. The CDC and ACIP continue to recommend the vaccines based on the fact that the benefits far exceed the risks.

For the record, Dr. Johann-Liang stated that the ACCV members had received a copy of the proposed regulation and the statute pertaining to changes in the Injury Table. She add that there are four options – concur with the proposed regulation and proceed with review of the NPRM and a recommendation to the Secretary; not concur with the proposed regulation; defer action until the ACCV has time to further review the proposed regulations and associated data; agree to postpone consideration until the PRISM study is complete and that data is available for review.

Discussion of Proposed Addition of Intussusception to the Injury Table and Proposed Language to the Qualifications and Aids to Interpretation

Aware that only Rotateq is currently used in the U.S., Dr. Herr asked whether the Vaccine for Children (VFC) program anticipated any shortages or increased purchases of Rotarix, which appears to have a slightly higher risk than Rotateq. Dr. Johann-Liang stated that CDC does not foresee shortages of the vaccine and, although it is not known whether the VFC will change its purchasing, there is a possibility that the manufacturer of Rotarix may develop a more competitive marketing strategy in the U.S. She added that there is no data to indicate that Rotarix has a greater or lesser risk than Rotateq. Ms. Hoiberg expressed concern about the QAI exemptions, and Dr. Johann-Liang commented that, even if the exemptions prevent presumption of injury under the Table, the claimant can still pursue causation in fact. Concerning the evidence that the third dose of Rotateq is protective, Dr. Johann-Liang stated that it would not be reasonable to allow presumption of injury in that circumstance. Mr. King expressed concern about acting prematurely on, among other things, the exemption of the third dose of Rotateq, when data is limited and the ACCV has not had an opportunity to thoroughly review the available information. Ms. Drew also expressed concern about the exemptions in the QAI regarding infectious diseases – she wondered if ailments like the common cold, which could be viral, would prevent presumption of injury. Dr. Rubin explained that the QAI was quite specific about the infectious diseases that would constitute an exemption, diseases that have been shown to contribute to intussusception.

Asked about other studies, Dr. Johann-Liang said there was a completed VSD study involving up to a million subjects that is being prepared for publication. Informally, because it has not been published, Dr. John Smith, CDC indicated that there was no increased risk for Rotateq, which was the vaccine used in the study.

There was an extensive discussion about whether supporting the first option, to concur with the proposed regulation, would prevent further consideration of change in the future. Dr. Evans explained that, even if the ACCV approved the proposed changes to the Table and Aids, there would be the opportunity for additional input during the rulemaking process. First, it will take time to finalize the NPRM, then once published in the Federal Register, the ACCV has the option to review the Secretary's proposal during the six-month period of public comment. Mr. King asked if the proposal could be amended based on the discussion and then approved. Dr. Evans commented that there would not be time to develop changes in the proposal text during the meeting, but that the discussion points made during the meeting would be available and could accompany the ACCV's approval letter to the Secretary in the form of recommendations.

Asked if deferring the decision until the next meeting would have a significant effect on the timeline to change the Injury Table, Dr. Johann-Liang stated that the timeline is not within the control of DVIC. She added that the ACCV's plate will be full in the future dealing with the review of the IOM report, and that a timely approval of the rotavirus vaccine Table change would be helpful to that process. After discussion, the Commission crafted a motion that would accommodate both the basic approval of the proposed regulation and the Commission's concerns about the QAI provisions. The Secretary should proceed with the recommendations for a change to the Table, with the understanding that comments have been made concerning wording of the Qualifications and Aids to Interpretation and with the anticipation that the Secretary will review that wording and consider the suggestions and comments made by the Commission. The motion, duly seconded, was unanimously approved.

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

Dr. Shimabukuro noted that a clinical trial was underway to look at immune response in adults with Adacel as a ten-year booster vaccination. Reviewing the recent ACIP meeting, he noted that there was an extensive discussion of Gardasil that included a review of pre-licensure studies, VAERS data for both males and females, data from the Vaccine Safety Datalink (VSD), and two studies additional studies – the Nordic long-term follow-up study and the long-term study of Gardasil in adolescents. No new adverse event concerns or clinical patters were identified in the VAERS review of Gardasil. In the VSD rapid cycle analysis of Gardasil in females, a non-statistically significant increased relative risk of venous thromboembolism was detected and further evaluation of that adverse event is ongoing. Long-term follow-up of adolescents who have received Gardasil have not identified any safety concerns. ACIP voted to recommend routine vaccination of males aged 11-12 years. The series may be started as early as 9 years of age. Males 13 to 21 who have not been vaccinated should receive a catch-up vaccination and there was no recommendation for routine use in males aged 22-26 years.

Dr. Shimabukuro described a VSD study of febrile seizures in young children after receiving the 2010-11 trivalent inactivated influenza vaccine (TIV). In this study there was an increased risk of febrile seizures on the day of and the day following vaccination in children 6 to 59 months of age. The risk was highest in children aged 16 months and in those children that received TIV and pneumococcal conjugate 13-valent vaccine concomitantly. Most had received other vaccines as well in combination with TIV. After evaluating the data, the CDC concluded that there should be no change in the current childhood immunization recommendations.

With regard to the Institute of Medicine report generated HRSA-CDC Task Force; Dr. Shimabukuro stated that there are 16 ISO staff working with HRSA staff on various working groups to develop proposals to update the Table. He commented on two publications, one by Duderstat et al., that concluded that that there was no increased risk of type 1 diabetes in the vaccines studied (anthrax, smallpox, typhoid, hepatitis B, MMR and yellow fever) and one by Mullooly et al., that described a VSD study that showed no evidence of wheezing lower respiratory disease after routine vaccination of premature infants. A third study by Huang, et al., indicated that physicians are generally unaware of the recommended post-vaccination observation for syncope, and even among those who are aware compliance is poor.

Update from the National Vaccine Program Office (NVPO)
Dr. Dan Salmon, NVPO

Dr. Salmon announced that the next NVAC meeting agenda for the February 7-8 meeting included in its agenda discussion of the Adult Immunization Working Group, the Health Care Personnel Influenza Vaccine Subgroup, discussion of vaccine financing and the usual updates from the agencies. There should be a report from the Vaccine Safety Risk Assessment Working Group, set up to monitor H1N1 safety data from various surveillance groups. The Working Group has finished a final report that will be considered at the February NVAC meeting.

Update on the National Institute of Allergy and Infection Disease, NIAID, NIH
Barbara Mulach

Dr. Mulach announced that the program announcement for Research to Advance Vaccine Safety, expected to end in September, had been extended through January. That program will support research into the understanding of vaccine safety.

Update on the Center for Biologics Evaluation and Research, Food and Drug Administration, Valerie Marshall, CBER, FDA

Ms. Marshall announced that Dr. Marion Gruber, who had previously reported to the ACCV on CBER activities, was appointed Acting Director of the Office of Vaccines Research and Review. Since the last ACCV meeting, no new biologic applications had been approved, but several vaccines are currently under review – a meningococcal vaccine to prevent the illness in infants two to sixteen months of age, a vaccine to prevent pneumococcal disease in adults 50 years of age and older, and an influenza vaccine containing four strains. The Vaccine and Related Biological Products Advisory Committee met on November 16, 2011 to discuss and make recommendations on the safety and immunogenicity of a pneumococcal 13-valent conjugate vaccine in adults aged 50 years and older using an accelerated approval regulatory pathway.

On September 16, 2011, a workshop sponsored by FDA and NIH (NIAID), looked at key issues related to the development and evaluation of next generation smallpox vaccines. The workshop included presentations on the human response to smallpox vaccines and development of animal models for demonstration of effectiveness of next-generation smallpox vaccines.

Nomination/Election of New Chair

Ms. Drew invited nominations for chair and vice chair for the next term of the ACCV. Mr. King was nominated and elected by acclamation to be the next ACCV chairperson. Dr. Feemster and Ms. Williams were nominated to be vice chair and, after a secret ballot, Ms. Williams was selected.

Public Comment

There were no requests from the public to comment during this part of the agenda.

Future Agenda Items

Ms. Drew invited suggestions for future agenda items, noting that Dr. Herr had requested that labeling of latex components in vaccine packaging and delivery systems be included on a future agenda. There was also a request, pursuant to the discussion about rotavirus vaccines and the Table, to review the most recent revision of the rotavirus VIS. Mr. King suggested an update on the Future Science Group. Ms. Drew invited volunteers for the agenda committee, noting that she and the newly elected chair and vice chair would be on the committee automatically. Dr. Feemster and Ms. Pron also volunteered to participate.

Adjournment

Dr. Evans expressed appreciation for the service of the members who would be leaving. Dr. Herr and Ms. Hoiberg both expressed appreciation for having had the opportunity to be a part of the ACCV, and to benefit from the learning experience that service afforded.

There being no other business, on motion duly made and seconded, the meeting was adjourned by consensus at 11:45 a.m.

_____
Sherry K. Drew, ACCV Chair

_____ _____
Geoffrey Evans, M.D. Date

Executive Secretary, ACCV