Advisory Commission on Childhood Vaccines

September 2-3, 2010

Day One

Minutes

Members Present
Charlene Gallagher, J.D., chair
Sherry K. Drew, J.D., Vice Chair
Tawny Buck (via teleconference)
Magdalena Castro-Lewis
Margaret Fisher. M.D.
Thomas Herr, M.D.
Sarah Hoiberg
Jeffrey M. Sconyers, J.D,
Tamara Tempfer, RN-C, MSN, PNP

Executive Secretary

Geoffrey Evans, M.D., Director, DVIC

Staff Liaison

Andrea Herzog, Principal Staff Liaison

Welcome, Report of the Chair and Approval of Minutes

Ms. Gallagher called the meeting to order and welcomed all in attendance in person and by teleconference to the 77th meeting of the ACCV. After calling for approval of the June 9-10 minutes, on motion duly made and seconded, the minutes of that meeting were unanimously approved. Noting that the minutes of the July teleconference meeting were distributed just before the meeting, and allowing for time to review those minutes, she invited approval. On motion duly made and seconded, the minutes of the July 29, 2010 teleconference meeting were unanimously approved.

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

After reviewing the agenda for the two-day meeting, Dr. Evans discussed the statistics since the beginning of the fiscal year to date. He noted that a large number of claims had been filed, over 400, most of which were not related to the Omnibus Autism Proceeding (387 versus 16). Those claims were also predominantly filed for adults who alleged injury, mainly as a result of receiving the influenza vaccine. In terms of adjudications, the number of adjudications is consistent with past years (355 through September 2) but with the unique event that the first claim filed under the Omnibus Autism Proceeding (OAP) was compensated. However, Dr. Evans emphasized that the compensation in that case was not based on a determination that the injury was caused by autism and that the Department of Health and Human Services has never concluded that any injury alleged in a claim was caused by autism. He added that the published statistics now make that distinction clear,through use of two footnotes under the compensated claims column under the OAP heading. He also noted that the special masters decision was not yet available but should be posted on the Court's web site in the near future. Ms. Buck commented that the footnote explaining that no claim for autism injury has ever been conceded by HHS appears to be in conflict with the description that this one case was compensated under the omnibus proceeding.

Dr. Evans continued discussing adjudications, noting that the categories assigned to adjudicated claims are consistent with past years. He explained that the HHS reports whether or not a claim is compensated or dismissed, and under compensated claims, distinguishes claims where entitlement to compensation is by HHS concession or Court decision, or much more frequently, compensated on the basis of a settlement. The Department of Justice utilizes additional categories (e.g., proffer, stipulation) to describe both the entitlement outcome, as well as the process to determine the amount of compensation.

Dr. Evans commented that awards this year are the highest in ten years, already at more than $150 million. Attorneys' fees are back on an upward trending track (at $9.5 million thus far), after a bolus of $15 million in 2009, in part because of interim payments in the autism proceeding. The trust fund stands at $3.2 billion and net receipts for the year should be around $100 million.

Turning to Division activities, Dr. Evans reported that Dr. Johann-Liang attended the Advisory Committee on Immunization Practices meeting in June, Ms. Herzog and Ms. Cook staffed the DVIC booth at the July Pediatric Nursing Annual Conference, distributing more than a hundred information kits (most questions from attendees related to flu vaccines). They also attended the July meeting of the American Academy of Family Physicians and distributed over 150 information kits. Similarly, the interest there was mainly flu and meningococcal vaccines. Asked about awareness of the VICP, Ms. Cook reported that most visitors to the booth indicated little knowledge of the program. Dr. Evans commented that a survey of membership by the Academy of Pediatrics showed that more than two-thirds of the respondents were aware of the VICP. He added that inquiries via e-mail and telephone to the DVIC have focused on how to file a claim (nearly 70% of inquiries), followed by questions related to medical advice and to the various vaccines, most of which were concerns about flu and meningococcal vaccines.

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

Power Point Presentation Summary

Mr. Rogers, Department of Justice (DOJ) referenced the Power Point materials, entitled September 2, 2010, Department of Justice Power Point Presentation (DOJ PP), as part of his presentation.

Personnel

Mr. Rogers reported that his office had added one attorney, Justine Daigneault, who was previously a paralegal in the office.

Statistics

Mr. Rogers reported that overall, autism filings are decreasing, most cases filed are adult cases, and that upwards of 400 non-autism cases are filed each year. Mr. Rogers explained that every case filed in the Vaccine Injury Compensation Program (VICP) is assigned to a Special Master who is in charge of the case from beginning to end, and always issues a decision, no matter the outcome. DOJ reports statistics by the type of decision that the Special Master issued. Mr. Rogers explained the process of DOJ and HHS working together to ensure a judgment is ready to be compensated, and reminded the ACCV that DOJ and HHS see the judgment at different stages in this process, so statistics between the agencies may vary.

In the last reporting period (May 25 to August 2), there were 98 claims filed. (DOJ PP, p. 3). Three were autism claims and 95 were non-autism claims. (DOJ PP, p. 3). During that same period, 178 cases were adjudicated. (DOJ PP, p. 4). There were 53 cases compensated, 3 of which were conceded by HHS, and 50 which were not conceded. (DOJ PP, p. 4). Mr. Rogers noted that in all cases of compensation, DOJ finalizes the judgment, obtains the petitioner's formal acceptance (which can take up to 90 days), obtains a final approval by the petitioner's attorney, and when all is in order, submits the judgment to HHS for payment. Part of the judgment can include identification of the legal vehicle by which payment will be made to a minor child, which typically involves petitioner obtaining a court-ordered guardianship.

Guardianship requirements are governed by individual states, and that process can take several months for petitioner to complete.

Distinguishing among the types of resolutions, Mr. Rogers noted that of the 3 conceded cases, 2 were determined by a proffer in which there was agreement on the evidence that shows damages. (DOJ PP, p. 4). Normally, this means that both parties used a single life care planner, and the Special Master incorporated the life care plan into the decision. One case was resolved by a decision adopting a stipulation. This usually involves two life care planners (one for the petitioner and one for respondent) to work out a final life care plan. Mr. Rogers noted that no cases were resolved by a decision awarding damages. In that instance, damages would have been decided by a Special Master because the parties and life care planners could not agree. In sum, DOJ does not send a judgment to HHS until all steps are completed and the judgment is ready for payment. DOJ statistics, however, are drawn from judgments as soon as they are entered by the court and therefore provide a snapshot of the Program closer to "real time."

Responding to Dr. Herr's question about stipulations, Mr. Rogers clarified that a stipulation and settlement are the same thing – a compromise agreement between two competing positions, whereas in a proffer, there is only one position demonstrated by the evidence. The best example is when there is only one life care planner and only one life care plan.

Responding to Ms. Buck's question about whether the proffered judgments are posted on the Court's web site, Mr. Rogers stated that it is up to the Court - some are posted and some are not.

Mr. Rogers explained that of the 50 cases not conceded by HHS, (DOJ PP, p. 4), some of these cases were settled in a "litigative risk settlement." In these cases, there was no decision by the Special Master deciding whether the case is vaccine-related or not. If a case is not conceded by HHS, and not settled by litigative risk [which resolves entitlement and damages], then it is resolved by the Court. (DOJ PP, p. 8, "wire diagram"). After hearing the case, the Special Master may decide that vaccine causation has been shown, and the case moves to damages processing. (DOJ PP, p. 8). At this point, the case can be settled, proffered, or have the Special Master decide the damages. If the Special Master dismisses the case, it may be appealed. (DOJ PP, p. 8).

As Mr. Rogers explained, the 42 decisions adopting stipulations for non-conceded cases, along with the 8 decisions adopting proffers equals 50 case resolutions on non-conceded cases. (DOJ PP, p. 4). Mr. Rogers reiterated that proffers always reflect a decision on damages amounts, not entitlement.

Next, Mr. Rogers turned to the category of non-compensated, dismissed cases, of which there were 125. (DOJ PP, p. 4). There were 31 non-autism cases and 94 autism cases that the Court determined were not vaccine-related and dismissed. (DOJ PP, p. 4). There were 3 voluntarily withdrawn cases, 1 non-autism and 2 autism. (DOJ PP, p. 5). Responding to Mr. Sconyers' question about the activation of autism cases, Mr. Rogers explained that autism cases were being activated on a schedule by the Court, and that most, but not all, of the dismissed cases had already been activated.

Mr. Rogers reviewed the wire diagram that depicted the path each claim may take from initial filing to final disposition. (DOJ PP, p. 8). Reiterating, Mr. Rogers explained that most cases go down the left side of the diagram. (DOJ PP, p. 8). Once a petition is filed, HHS reviews it. If HHS does not concede the case, and the case is settled in a litigative risk settlement, the case reaches the red box for a final decision awarding compensation. (DOJ PP, p. 8). In this reporting period, there were 3 conceded cases, moving down the right columns of the wire diagram to damages. (DOJ PP, p. 8). Those 3 cases could have been resolved by a hearing on damages, settlement, or a proffer, to reach the green box awarding a final decision of compensation. (DOJ PP, p. 8).

Decisions that are not compensable move to the yellow box. (DOJ PP, p. 8). Most of the cases are processed through the left side of the wire diagram - not conceded but compensated cases as litigative risk settlements [final decision in red box.] Reiterating, Mr. Rogers emphasized that if the case is not

conceded, but the Special Master decides that petitioner should be compensated, the case moves over to the damages side of the wire diagram. The case is either settled on damages, a proffer is reached (or hearing on damages convened) before it moves to the green box for a final decision (award of compensation). (DOJ PP, p. 8).

Autism

Mr. Rogers noted that the Cedillo decision (Theory One) was recently affirmed by the U.S. Court of Appeals for the Federal Circuit (CAFC). (DOJ PP, p. 9). It involved broad issues of causation, the role of Daubert, and good science in the courtroom. The petitioners may accept that affirmance by doing nothing, request a rehearing of the decision, or seek certiorari to the Supreme Court. When asked by Mr. Sconyers about details of the case, Mr. Rogers said he could not comment until after it was clear whether rehearing or certiorari would be sought, and referred those interested to read the briefs on the Court's web site. Mr. Rogers reported that there had been no significant change in the status of the Theory Two autism cases. (DOJ PP, p. 10). The appeal window for those cases is over and the decisions are considered final.

Appeals

Mr. Rogers briefly reviewed the status of cases on appeal at the CAFC and the U.S. Court of Federal Claims (CFC). Two new appeals are now pending before the CAFC: Davis, a statute of limitations case which may be affected by Cloer; and Hall, an hourly rate of attorney's fees case. (DOJ PP, p. 11). Three cases were recently decided at the CAFC: Cedillo, Shaw, and Cloer. Mr. Rogers previously discussed the Cedillo decision during the autism update. In Shaw, the CAFC determined that there is jurisdiction to hear an appeal of an interim fee decision. Mr. Rogers noted that DOJ requested rehearing en banc (rehearing by the full Court of the panel's decision) in Cloer, but stated that such a petition is rarely granted.

Two new appeals have been filed in the CFC (Rickett and Simanski), both based on the Special Masters' decisions that petitioners failed to prove causation. (DOJ PP, p. 13).

Stipulations

Finally, Mr. Rogers presented a list of adjudicated stipulations from the last reporting period. (DOJ PP, pp. 16-20). The list included the vaccine, alleged injury, and time elapsed from petition filing to stipulation filing. (DOJ PP, pp. 16-20). Processing time varied from five months to over ten years. Mr. Rogers observed that most cases processed within one to one and a half years were likely resolved by litigative risk settlements. Mr. Rogers explained a number of reasons why a case might take years to be settled. Petitioners often request extra time to locate medical records, identify an expert witness, or sideline the case while the science related to the alleged vaccine injury develops. Mr. Rogers noted that the Special Masters regularly monitor the petitioners' efforts and progress during these delays in proceedings.

Responding to Mr. Sconyers' question about the type of case, outside of an omnibus group, that has taken the longest to process, Mr. Rogers referenced cases involving rubella and arthritis that took years, as did Hepatitis B cases. He commented that the 10-year Hepatitis B case on the list (DOJ PP, p. 18) likely was in the omnibus group. Responding to Dr. Fisher, Mr. Rogers acknowledged that Guillain-Barre Syndrome is not a Table injury, and that the vast majority of the stipulations reflected in the Power Point most likely did not result from concessions.
During discussion, Ms. Buck expressed appreciation for DOJ's efforts to increase the level of information and transparency in the presentation to the ACCV. In so doing, however, she also expressed the opinion that the process seems unnecessarily complex and that a more straightforward process should be considered. She commented that the process should be simpler - a claim filed, public decision issued listing the vaccine, injury and liability, compensation, if any, and a rationale. Thanking Mr. Rogers for providing the information requested, Ms. Buck reiterated her concern about the complexity of the process.

Mr. Rogers responded that one aspect of the complexity is the congressional requirement that each case be compensated on its merits, rather than specifying a standard outcome. Because there is discretion, there will be differences of opinion and litigation. A second consideration is the cause-in-fact standard, which the CAFC recently reiterated in Cedillo is a heavy burden. Also, there are no evidentiary rules that apply to VICP cases, which alleviates laying a foundation for evidence but petitioners still need to provide an expert, which takes time.

Ms. Gallagher thanked Mr. Rogers for DOJ's clarifications.

Communications and Outreach Workgroup Report
Sarah Hoiberg, ACCV Member

Ms. Hoiberg reported that there had been conference calls with Banyan concerning the progress being made on the outreach program recommendations. They are currently working on Phase Three of their original work plan. Banyan agrees that the primary focus of the outreach effort will be on healthcare workers, although because of the increase in claims based on alleged influenza injuries, adults will also be an important audience. Ms. Hoiberg noted that Banyan would make a presentation at the October 28th meeting of the ACCV. She recommended a break after the presentation to allow members to collect thoughts in anticipation of a discussion of the presentation. Asked about when the draft report for that presentation would be available, Ms. Cook commented that she would try to get clearance from HRSA so that the report would be available shortly before the meeting for review by the Commission.

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

Dr. Salmon discussed the activities of the NVAC Vaccine Safety Working Group, established several years ago to review the CDC Immunization Safety Office's research agenda, for which a report has been released. A second task was begun in July 2009, looking at vaccine safety very broadly and to develop a white paper with recommendations on enhancement of the national safety system especially with regard to opportunities afforded by advances in science and information technology. The chairmanship of the Working Group is shared by Marie McCormick, Andrew Pavia and Tawny Buck, and the Working Group is composed of members of the public who serve on the four main HHS vaccine advisory committees (ACCV, NVAC, VRBPAC and ACIP), as well as others with expertise in immunology, neurology, pediatrics, ob-gyn, genetic epidemiology, biostatistics and others.

The Working Group held a public information gathering meeting in July 2009. The Working Group has broken into five main subgroups to consider structure and governance, epidemiology and surveillance, and biological mechanisms, stakeholder engagement and implementation. Based on a RAND report, there was agreement that NVAC should begin considering implementation early in the development of the recommendations. Since that first meeting, the Working Group has held a significant number of briefings, hearing from experts within the federal government as well as private individual experts, international vaccine experts, and others on a wide range of topics. The Working Group has also conducted a small stakeholder meeting to solicit discussion about the report.

The Working Group will discuss the first draft of the report at the NVAC September 15th meeting to begin to receive input from NVAC members. The report is in draft form, but it has substantial content including three broad areas of recommendations and action steps to support the recommendations. Dr. Salmon mentioned the three areas in general terms – internal leadership oversight and coordination within the federal entities involved in vaccine safety; enhanced use of available tools related to vaccine safety science; and expanded science and epidemiology surveillance to better understand biological mechanisms and causality assessment to promote greater knowledge about risk, especially in subpopulations.

A larger stakeholder meeting is planned for the fall for additional feedback. The goal is to present the final report at the February NVAC meeting for final deliberation and, hopefully, a vote of approval. During discussion, Dr. Gidudu stated that the Working Groups initial report on the ISO research agenda was considered very helpful in finalizing the agenda, which is currently going through final clearance.

Update on the Immunization Safety Office Vaccine Activities
Dr. Jane Gidudu, ISO, CDC

Dr. Gidudu reported on the appearance of adverse events related to an inactivated trivalent vaccine (Fluvax and Fluvax Junior manufactured by CSL) administered during the 2010 influenza season in Australia (which precedes the flu season in the US because of the reversal of seasons in the Southern Hemisphere). The adverse event, fever and febrile seizures, occurred with an increased frequency in children aged six months to four years, and increased incidence of fever occurred in children five to eight years of age. An antigenically equivalent vaccine for the Northern Hemisphere, Afluria (also manufactured by CSL), approved by FDA for children 6 months and older, includes a warning that fever and febrile seizures are associated with the vaccine. In August the ACIP recommended against administering the vaccine in children aged six months to eight years.

Dr. Gruber interjected that Afluria was approved by the FDA for individuals 18 and up in 2007, then licensed for infants 6 months and over in November 2009. Although the Afluria vaccine would have comprised about 10-12 million doses in the US market, the 0.25 milliliter dose for children was not marketed by CSL in this country. Therefore the number of CSL doses is much smaller. Asked about whether the CSL vaccines contained adjuvants, Dr. Gruber stated that there are no adjuvants added to any influenza vaccine in the U.S. Concerning the biological mechanism that may be involved in the CSL vaccines, even though Fluvax is not licensed in this country the company has provided animal test data related to endotoxins and pyrogenicity, and there was no significant evidence of fever. She added that initial uptake of the vaccine in Australia was low, but increased as a result of immunization campaigns and immunization programs, which is when the increased incidence of fever appeared. Finally, Dr. Gruber explained that CDC had conducted extensive audits of the CSL manufacturing process for Afluria, including receiving reports from the company that no manufacturing changes had occurred in the last 18 months.

Dr. Gidudu commented that the CSL vaccine is the only vaccine associated with increased risk of fever and febrile seizures, but that the CDC, FDA and other federal agencies will monitor all vaccines for such risks, mainly through VAERS and the VSD. The criteria for monitoring seasonal flu vaccines are the same as for other vaccines, except that there are additional criteria since the formulation changes every year. The surveillance includes a focus on the occurrence of Gullain Barre syndrome following vaccination with seasonal flu vaccine.

Turning to vaccines for measles, mumps, rubella and varicella, Dr. Gidudu commented that the VSD reported a twofold increase in risk for febrile seizures when the combination MMRV was administered versus giving children the MMR vaccine plus separate varicella vaccine). The number of children in the sample was substantial (about 83,000 received MMRV; about 376,000 received MMR plus varicella. In that specific group of children aged 12 to 23 months, between 2000 and 2008, there was a clear increase of febrile seizure – the risk was 4.3 additional events among the children who received the MMRV vaccine. That translates to one additional febrile seizure for every 2,300 doses of MMRV administered.

Dr. Gidudu described a retrospective study to assess the association between acellular pertussis vaccine (DTP) and the risk of febrile seizures. The study looked at data between 1997 and 2006 and no increased incidence of seizures was identified after vaccination with diphtheria, tetanus and acellular pertussis (DTaP) in children 6 weeks to 23 months of age.

Finally, Dr. Gidudu briefly discussed the risk of narcolepsy after administration of Pandemrix, an H1N1 vaccine used in Scandinavia. The vaccine is not licensed in the U.S. The Finland National Institute for Health and Welfare recommended cessation of use of Pandemrix when an increased incidence of narcolepsy in children was observed. Although the risk has not been observed in the U.S. related to any vaccine, the CDC is aware of the issue and is monitoring the risk through VAERS and VSD. Neither surveillance system has seen any indication of the risk in the U.S. Dr. Fisher commented that she was a

member of the Brighton Collaboration, which has proposed a significant study to look at the narcolepsy risk, even though Pandemrix is different from any vaccine used in the U.S.

Update on the National Institute of Allergy and Infectious Diseases. NIH Vaccine Activities
Dr. Bernstein, NIAID, NIH

Ms. Bernstein described a new program to establish six U.S.-based research centers to develop human immune phenotypes for specific subpopulations – newborns, young children, the elderly, individuals on immunosuppressant therapy, and individuals with underlying immune disorders. The program is funded under the Recovery Act.

Ms. Bernstein then described a newly formed autism informatics consortium supported by Autism Speaks, the Simons Foundation, the Interactive Autism Network, and the National Database for Autism Research, which is part of NIH. The objective of the consortium is to harmonize the major autism informatics platforms.

Update on the Center for Biologics, Evaluation and Research (CBER) Vaccine Activities
Dr. Marion Gruber, CBER, FDA

Dr. Gruber reported that since the last ACCV meeting there have been no new vaccine approvals. She noted that there are seven U.S. licensed influenza vaccines – FluMist (Medimmune), Fluzone and Fluzone High Dose (Sanofi Pasteur), FluLaval (ID Biomedical), Fluarix (GSK), Agriflu and Fluvirin (Novartis), and Afluria (CSL).

Commenting on the 2010 seasonal flu vaccine, Dr. Gruber noted that it contains three strains -- type A H1N1 strain (the strain that caused the 2009 pandemic), an H3N2 type, a strain that was included in the 2009-2010 seasonal vaccine, and a type B strain. This year both the seasonal and last years' pandemic H1N1 flu viruses are covered by the single trivalent vaccine.

As previously discussed, there are two flu seasons globally, one in the Southern Hemisphere, one in the Northern Hemisphere, both separated chronologically. Some vaccine manufacturers provide vaccines for both hemispheres, for example, CSL which manufactures Fluvax for the Southern Hemisphere and Afluria, for the Northern Hemisphere. The latter is licensed in the U.S. As also previously discussed, an increased incidence of fever and febrile seizures has been identified in children less than 5 years of age administered Fluvax during the 2010 Southern hemisphere influenza season , but not with other Southern Hemisphere vaccines. There is no data yet for Afluria, made by CSL, and different from Fluvax. As a precautionary measure, the FDA has required additional label warnings for Afluria to inform health care providers about the febrile reactions observed with Fluvax. CSL has announced that it will only market its 0.5 ml single dose syringe in the U.S., which is not meant for children less than 3 years of age. The FDA has also required that CSL provide additional information, including an Afluria study in Australian children five to eight years of age to measure any fever or febrile seizure events. Dr. Gruber indicated that once all the data has been reviewed the indications for use of Afluria may or may not change. Asked about informing parents, Dr. Gruber stated that the package insert, the patient package information document, will contain information to inform parents of the issues related to Afluria. Also, FDA has posted relevant question and answers regarding Afluria and Fluvax on its website.

Asked about the ACIP universal recommendation for everyone over six months of age to be inoculated for influenza, Dr. Gruber commented that the latest numbers available suggest that the seven licensed vaccine manufacturer may be able to cover about 160 million doses, clearly not enough for every eligible U.S. resident.

Dr. Gruber mentioned the presentation at the last ACCV meeting discussing the presence of porcine circovirus in U.S. licensed rotavirus vaccines. As discussed then, the FDA has called a special meeting of VRBPAC to discuss the findings and to look at novel and highly sensitive techniques for identifying adventitious agents in vaccines, the kind of technology that was required to make the initial discovery. The FDA also contacted all manufacturers to provide information of any plans they have to use these new technologies for adventitious agents testing, including but not limited to porcine circovirus. Testing

vaccine using new technologies requires validation and standardization thereof. FDA has also been working with the main manufacturers, Merck and GSK, to update package inserts to include a discussion of the presence of porcine circovirus in their vaccines.

During discussion, asked about bacterial vaccines, Dr. Gruber explained that most of the US licensed vaccine manufacturers do manufacture bacterial and viral vaccines and FDA is working with them to address the issue. Asked about whether influenza vaccines being distributed for the 2010/11 influenza season in walk-in facilities, like pharmacies, are the new or old influenza vaccine formulations, Dr. Gruber explained that the expiration date of influenza vaccines is intentionally set to expire end of June of each year so that last year's influenza vaccine cannot be administered as the new flu season begins in the fall.

Public Comment

Ms. Gallagher announced the opportunity for members of the public to comment during the proceeding.

Catherine Frompovich, representing herself, commented on recent cases of parents being accused of child abuse when their infant children suffered brain trauma with or without hemorrhage, brain swelling or cardiorespiratory events shortly after being vaccinated. The parents may be accused of shaken baby syndrome, Munchhausen by proxy, non-accidental injury and physical abuse, and may even be charged with a crime. She cited an Iowa case in which a child was removed from parental custody after the child suffered traumatic brain injury after simultaneous administration of Pentacel, Prevnar and Rotateq. Ultimately the court ruled that the parents were not responsible for the injury.

Ms. Frompovich urged the Commission to support efforts to inform the medical profession about this issue, and to encourage identification of offending agent toxins and adjuvants in vaccines.

Laraine Abbey, representing herself, commented that consequences of vaccinations may be affecting the totality of a child's health. There are claims that vaccine studies are flawed, and short-term studies may fail to reveal long-term consequences. Ms. Abbey expressed concern about the presence of aluminum in vaccines, an issue that should be studied.

Ms. Abbey pointed to what she considered a violation of personal liberty, the mandate that many school districts require vaccinations before enrollment in school or vaccination before employment. She expressed the concern that mandating administration of inadequately tested vaccines is especially egregious.

Ms. Abbey offered five recommendations. First, discontinue mandates and begin informed consent for all vaccinations. Second, consolidate all toxicity data on all vaccine components separately. Third, encourage a reduced vaccination schedule until the safety issues can be clarified. Fourth, limit or eliminate vaccinations in families with a prior history of vaccine reactions or autoimmune disease. Fifth, revisit the legislation that protects manufacturers from liability in cases of vaccine injury.

Dr. Harold Buttram commented that when he was a young boy in the 1930s, he recalled there was very little illness, no allergies and no child was on chronic medications. He suggested the dramatic change in all three, and that the degradation in the health of young people may well be related to the increased presence of vaccines in their lives.

Dr. Buttram described a European study, published in the New England Journal of Medicine in 1984, in which 11 healthy adults received tetanus booster shots, after which blood tests revealed a dramatic drop in T-helper lymphocytes, some to the levels of active AIDS patients. He suggested that the study should be repeated.

James Moody, representing SafeMinds, commented on the increasing uncertainty concerning vaccine safety on the part of the general public. He cited the increased level of applications for exemption from vaccination in California, as much as 51% in a San Diego school. He noted that reports from the DVIC

and DOJ indicate that as much as 90% of adjudications are litigated risk settlements, the details of which are not reported in any public way, which leads to a loss of transparency, and hampers a petitioner's ability to construct a meaningful vaccine injury claim. This information is not available to the public, nor are data details available from surveillance programs like the VSD.

Mr. Moody also expressed concern that there should be research on vaccine safety that takes into account a population of children who are not vaccinated, to determine whether or not there is a difference in the kinds of conditions that occur after vaccination vis-a-vis no vaccination. The unvaccinated children could provide a baseline for that purpose.

He urged the ACCV to develop recommendations to the Secretary for both the transparency of court records and the growing gaps in science exemplified by the lack of data on unvaccinated children.

Ms. Gallagher extended a final invitation for public comment and, hearing none, ordered a recess until the following day.

(The meeting recessed at 5:30 p.m., to reconvene the following morning, March 5, at 9:00 a.m.)

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Day Two

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Executive Secretary

Geoffrey Evans, M.D., Director, DVIC

Staff Liaison

Andrea Herzog, Principal Staff Liaison

Welcome, Ms. Charlene Gallagher, Chair.

Ms. Gallagher called the meeting to order and introduced the first presentation by Drs. Johann-Liang and Atanasoff

DVIC Clinical Case Update
Dr. Rosemary Johann-Liang, Chief Medical Officer, DVIC
Dr. Sarah Atanasoff, Medical Officer, DVIC

Dr. Johann-Liang stated that, to protect individual privacy, her updates are based on grouping of cases rather than individual cases. As previously discussed, claims are nearing 400, mainly non-autism cases. The number of medical reviews, which is the first step in the claims process, stands at 601, of which 176 are activated autism claims that were put on hold during the Omnibus Autism Proceeding. The newly filed cases are divided roughly between adults (two-thirds) and children (one-third), with very few autism claims.

The vaccines being alleged in the claims are influenza (39%), human papillomavirus (17%), tetanus (9%), and other vaccines, each of which represents about 3%-4% of claims, including rotavirus, hepatitis B, meningococcal, varicella and MMRV/MMR. Twenty percent of the claims allege injury from two or more vaccines. Asked about the exceptionally high number of claims related to influenza and whether there was some correlation to safety, Dr. Johann-Liang commented that one might infer some rate of injury by comparing the claims to the total number of vaccine doses distributed. Thus, the high numbers of claims most likely is a reflection of the large utilization of the vaccine. Although there is no source of information as to the actual number of doses administered, the distribution number might be helpful. Ms. Hoiberg expressed concern about the handling and administration of the influenza vaccine that is given out at so many non-medical locations (schools, pharmacies, retail outlets). The required procedures for shipment, handling and storage may be compromised. Dr. Johann-Liang suggested that most individuals who administer vaccines are medically trained (pharmacists, nurses, etc.) and that those procedures are

probably done properly, but did agree that the proper procedures surrounding the administration of vaccines is important to educate and monitor particularly during this time of changing locations and changing populations. She noted also that children usually have a detailed vaccine record that can be easily produced by a parent from the pediatrician's office records. Adults on the other hand present a problem in obtaining that kind of information. Since the majority of claims being submitted to the Program are now in adults, lack of proof of vaccination in the records continues to be a challenge.

Dr, Johann-Liang discussed the types of adverse events that are currently represented in the records reviewed by the medical analysis team during the last quarter (June – August 2010). Guillain Barre syndrome, a demyelinating disorder, accounts for 35% of injuries alleged, with other demyelinating disorders adding another 8%. Shoulder and arm injuries account for 8% of claims, immune and autoimmune reactions account for 7%, and encephalopathies (including seizures) 6% in the cases reviewed. Death is named in 5% of claims, psychiatric disorders in 5%, and a the rest at25% is a catch-all category that includes disorders of the intestinal tract, blood, heart and lungs, etc. Dr. Johann-Liang described in general terms the pathology of the various adverse events.

It was noted that the medical review takes into consideration what is claimed as the injury, but in many cases the review reveals the actual injuries are different from those claimed. Ms. Gallagher recalled in the early cases involving influenza vaccine that in some claims alleged Guillain Barre when the actual condition proved to be multiple sclerosis. There was also a comment that a claim might allege Guillain Barre, but the medical records show onset far too soon after vaccination to be related to the vaccine. Dr. Johann-Liang suggested that for a future meeting she might be able to prepare an analysis of conflicting diagnostic claims without compromising individual privacy.

Dr. Johann-Liang commented that the increase in claims related to arm and shoulder injury prompted an analysis of claims in a group format (case series study) to describe the demographic, clinical and laboratory characteristics of the group. The injuries were called SIRVA, Shoulder Injuries Related to Vaccine Administration. Dr. Atanasoff made a brief presentation, noting at the outset that the results of the summer research had been the development of a paper that was submitted for a peer-reviewed publication.

Dr. Atanasoff explained that 13 claims between 2006 and 2010 related to shoulder injuries which may have been due to vaccination administration were identified in the DVIC database. The age range of the individuals was from 26 to 83; the geographic location in the U.S. where the injection took place was not considered. The database search parameters included arm pain, shoulder pain, shoulder dysfunction, frozen shoulder, adhesive capsulitis, shoulder bursitis, and brachial neuritis (a neurological injury). Brachial neuritis was included in the initial search because claimed injuries are often not the correct diagnoses, and they wanted to identify non-neurological shoulder injuries that may have been incorrectly filed as "brachial neuritis" Other injection sites in the body were not considered since evidence did not develop as did the evidence of the shoulder injury.

The results of the search showed that 85% of the claims were from women, 62% from obese individuals (none from individuals who described themselves as underweight), and the majority of claims were for influenza vaccine. About 70% of the individuals had received a prior vaccination of the same type, and it was assumed that in those tetanus cases where prior vaccination could not be confirmed, the adults had had a prior tetanus vaccination. None reported a prior history of shoulder pain and 93% had onset of pain within 24 hours of vaccination (54% claimed immediate onset of pain). Forty-three percent expressed concern that the inoculation was improperly given (e.g., location in arm too high, or needle hit something hard). Physical symptoms were similar – decreased range of motion, pain on range of motion, no symptoms related to the injection site (e.g., swelling or redness) and reflexes, when tested, were typically normal. Various tests had been performed, including nerve conductance tests, MRIs (which revealed some abnormal findings). Therapy included steroid injections; a third of the individuals had surgical interventions, half of whom required a second surgical procedure. Symptoms persisted in all patients for at least six months, and in some patients symptoms lasted for years.

Dr. Atanasoff commented that the literature revealed several studies in children of over- or under-penetration of needles related to body mass (the target is the deltoid muscle), one of which suggested that the risk of over-penetration in children ranged from 11% to 61%. There was also consideration of the

possibility that injecting an antigen into the synovial space, or the joint itself, might result in a prolonged inflammatory response that would not normally occur in other muscle tissue, particularly if the person had previous exposure to the vaccine antigen.

In the final analysis the objective was to identify commonalities that could be used to identify the particular injury in the future – and in the cases analyzed there was lack of prior shoulder injury, exposure to a vaccine which had been administered previously, relatively rapid onset of shoulder pain, symptoms limited to the shoulder, symptoms consistent with immune mediated inflammatory response, and painful limitation of range of motion of the shoulder.

There was also agreement that the specific vaccine was not an issue, although previous exposure to the vaccine was. Second, needle length may not always be an issue, since injury to an underweight person, which might be expected, did not occur in the cases reviewed. Lastly, improper vaccination techniques leading to antigen entering an inappropriate area of the arm or shoulder might be an issue, in some cases.

Dr. Atanasoff suggested consideration be given to avoiding the upper third of the deltoid muscle during vaccination to ensure that the vaccine is injected into the deltoid. That both the patient and the individual administering the injection should be in the same position, preferably seated, to avoid both the tendency to aim the needle in a downward path, and to reduce the risk of injury in the event of a syncope episode. Finally, in older patients, consideration should be given to proper needle length, and in some instances, use of an alternate injection site might be more appropriate.

During discussion, Dr. Fisher commented that, considering the wide variety of vaccination locations (retail outlets, pharmacies, schools, etc.) and the similar wide variety of technicians performing the injections, that an education effort would be appropriate, that would include information related to the discussion about shoulder injury.

Asked about the future of the paper that was written, Dr. Johann-Liang noted that the study was not a randomized trial, analysis of a significantly large database, or an extensive surveillance, and that the paper, once peer reviewed (which will provide feedback that could serve to improve the paper) may be useful as an educational tool. Once published, the goal would be to disseminate it as extensively as possible to the medical community. Mr. Sconyers suggested that the material, even though not yet peer reviewed and published, could be shared at the upcoming NVAC and ACIP meetings.

Dr. Johann-Liang concluded the discussion by noting several other projects (studies analyzing claims in a group format) in progress. First, 71 HPV claims are under detailed review and a presentation of the results is planned for a future ACCV meeting. Preliminarily, it is clear that syncope is an important consideration since the recipients are typically adolescent females. Another study, which is being completed to be in part prepare for the updating of the Vaccine Injury Table, as a supplement to the Institute of Medicine's current comprehensive review of the literature, , is on the Program's experience with anaphylaxis claims. Fifty-three cases have been identified from the Program's database alleging anaphylaxis or anaphylactic shock during the last ten years and these cases are currently being analyzed in detail. Among other things, this analysis will help to assess whether the four-hour interval as noted in the current Vaccine Injury Table after vaccination is appropriate. Finally, an update on meningococcal cases is also under way and will be presented to ACCV in 2011.

H1N1 Vaccine Safety Update
Dr. Marie McCormick

Dr. McCormick explained that the H1N1 Vaccine Risk Assessment Working Group was established in the summer of 2009 to conduct rapid reviews of available safety monitoring data as it became available. There are regular reports to the NVAC. The members, who met extremely tight conflict of interest restrictions, were selected based on a range of expertise. They looked at data from 12 different surveillance systems, as well as data from NIH-sponsored clinical trials which assessed different dosage levels, adjuvants, and other variables. They received input from VAERS, which provided comparisons of

the rate of adverse events related to H1N1 versus the seasonal flu vaccine, comparisons of other live vaccines versus live H1N1, and other killed vaccines versus killed H1N1. The Working Group also received full information on all deaths following H1N12 vaccination. In addition, the Working Group reviewed the results of rapid cycle analysis conducted in five surveillance systems. This process involves a continuing comparison of a preselected set of diagnoses from electronic health record systems for those receiving H1N1 vaccine and seasonal flue with preset levels to trigger further analyses.

As of the end of April 2010 there were 105 million doses of H1N1 inactivated vaccine and 21 million doses of live attenuated H1N1 vaccine that had been distributed. Four surveillance systems are tracking three adverse events – Guillain Barre, thrombocytopenia and Bell's palsy – to determine if a signal occurred that would suggest a higher rate of adverse event than would be anticipated by chance alone. In most cases additional effort is required to insure accuracy of the result (e.g., if thrombocytopenia occurs there must be confirmation from the medical records that it occurred or worsened after the vaccination and was not a preexisting condition). The current projection is that the monitoring systems will complete data collection by late October and that the data can be analyzed in time to submit a report to NVAC by February 2011.

During discussion, Dr. McCormick confirmed that a system was specifically set up to monitor pregnant women, but that the data will probably not be available in the same timeframe as the other data discussed since the study will follow the women's babies for a period of time after birth. However, two of the rapid-cycle systems do have comparisons for pregnant women who receive H1N1 vaccine with those receiving seasonal influenza (VSD and PRISM) for miscarriage, still birth and preeclampsia/eclampsia without any signals for an increase in adverse events with H1N1 vaccine.

Future Agenda Items

Ms. Gallagher invited volunteers for the agenda committee for the next meeting on October 28th. Mr. Sconyers, Ms. Hoiberg, and Dr. Fisher agreed to serve. Ms. Hoiberg mentioned that Banyan would make a presentation of progress to date, which might take an hour, and she suggested that the discussion following the presentation be scheduled following a break of about 30 minutes after the Banyan presentation. Ms. Gallagher suggested scheduling the Banyan presentation just before lunch, breaking for lunch, and discussing the presentation after returning from lunch.

It was noted that there would not be a presentation by Dr. Johann-Liang since she would be attending the ACIP meeting in Atlanta on the 28th. Ms. Gallagher invited members to submit suggestions for agenda items by e-mail after the meeting, adding that if necessary, a teleconference could be arranged to discuss any issues that require especially timely consideration.

Public Comment

Ms. Gallagher invited comments from the public participants at the meeting or on the teleconference.

Eileen Dannemann, representing the National Coalition of Organized Women (NCOW), reported that her organization had identified 248 cases of vaccine-related miscarriages – 178 derived from VAERS reports, 70 from other sources. Although there were seven overlapping reports to VAERS and other sources, the number were sufficient to complete a capture-recapture statistical analysis of data from two or more sources. That analysis indicated that there were probably 1,588 miscarriages related to the 2009 H1N1 vaccine (the confidence interval put the range from 946 to 3,587 events). In addition, one study claimed that 56 maternal death reported to VAERS after H1N1 vaccination were never confirmed as deaths specifically caused by the H1N1 vaccine.

Ms. Dannemann claimed that the CDC-sponsored campaign to vaccinate pregnant women resulted in physicians coercing their pregnant patients to be vaccinated. She stated that NCOW recommends that the ACIP cease recommending flu shots for pregnant women, amending the recommendation such that pregnant women are vaccinated only if clearly needed. The NCOW further recommends that potential recipients of the N1N1 vaccine be informed of the VAERS reports, and of the composition of the H1N1 vaccine including the fact that it may contain thimerosol.

Theresa Wrangham, representing the National Vaccine Information Center (NVIC), expressed concern about the increasing public concern about vaccine safety and the increasing number of vaccine injury claims related to influenza vaccines. She also expressed concern that the 2010-2011 vaccine incorporates the 2009-2010 H1N1 pandemic vaccine as part of the trivalent seasonal flu vaccine, noting that data from this season's trivalent vaccine should be thoroughly evaluated. That concern is exacerbated, she said, by the convulsions in children related to vaccines that have been reported in Australia earlier this year.

NVIC is concerned that pregnant women are a target for this year's influenza vaccine even though the vaccines have not been studied in pregnant women. Finally, NVIC encourages ACCV to recommend that settlements arrived at through the litigated risk process be made fully public in a way that protects the individual claimants privacy rights but that allows a greater understanding by the public of the injuries related to vaccines.

James Moody, representing SafeMinds, described two studies related to thimerosol. The first, published in Neurochemical Research, concerned a study in neonatal rats given thimerosol. Those rats experienced changes in brain opioid receptors, which relates to one theory of causation of autism. Analogous changes in the human brain may result in profound neurological, physiological and behavioral consequences and may impact certain developmental disorders. The second study, published in Neurological Experiments, reviewed 58 papers looking at the epidemiology of thimerosol and autism, concluding that in 43 of the papers the authors identified a link between autism and heavy metal toxicity.

Mr. Moody noted that in 1999 the CDC, FDA, AAP and AAF called for industry to remove thimerosol from vaccines as soon as possible. Ten years later thimerosol is still in some vaccines. He recommended that ACCV take a strong stand for the immediate removal of thimerosol from all vaccines, requesting that the topic be considered for inclusion in the agenda of the next meeting.

Adjournment

There being no other business, on motion duly made and seconded, the meeting was adjourned by consensus at 10:47 a.m.

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Charlene Gallagher, ACCV Chair Sherry K. Drew, ACCV Vice-Chair

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Geoffrey Evans, M.D. Date
Executive Secretary, ACCV