Advisory Commission on Childhood Vaccines

September 17, 2009

Day One

Minutes

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

Executive Secretary

Geoffrey S. Evans, M.D., Director, DVIC

Staff Liaison

Andrea Herzog, Principal Staff Liaison

Welcome, Report of the Chair and Approval of Minutes

Ms. Castro-Lewis called the meeting to order and after introductions, announced that Commission member Tawny Buck had been appointed to the National Vaccine Advisory Committee (NVAC). Ms Buck had joined Dr. Evans at the NVAC meeting, which was mainly concerned with the H1N1 issue.

On motion duly made and seconded, the minutes of the June 4-5, 2009 meeting were unanimously approved.

Report from the Division of Vaccine Injury Compensation
Geoffrey Evans, M.D., Director

Dr. Evans welcomed Commission members, staff and guests to the 73rd quarterly meeting of the Commission. After reviewing the agenda for the two-day meeting, he announced personnel changes since the ACCV last met. Andrea Herzog has joined the Policy Analysis Branch as Principal Staff Liaison to the Commission, and Drs. Barbara Shoback and Marco Melo have joined the Medical Analysis Branch. Both are trained in adult medicine.

Turning to the statistics, Dr. Evans noted that non-autism cases have exceeded the average of the last seven years, totaling over 260 as this fiscal year nears its end. The 2007 exception of 242 filings was the result of expiration of the 2-year filing deadline for influenza vaccine claims dating back 8 years, a deadline that exists whenever a new vaccine is added to the VICP. Just over 40% of claims filed in FY09 were for influenza vaccines, and more than half were filed on behalf of adults, a trend that will likely continue. Although autism filings increased in 2007-2008, apparently as a result of the test case hearings, there is a downward trend this fiscal year. Less than half as many autism claims have been filed versus the previous fiscal year.

Concerning non-autism adjudications, as of September 14, 2009, of the 147 claims in 2009, 106 were compensable and 41 were dismissed. In response to a Commission request, a breakdown of compensable claims was given for three categories of outcome: HHS concession, court decision and litigative risk settlement. Of the 106 compensable cases, 9 were concessions, 9 were court decisions and 88 were settlements. The percentage of compensable claims was 49% in FY07, 64% in FY08 and 72% in FY09, with a few weeks still remaining in the fiscal year.

With regard to awards and attorneys' fees, awards totaling $72 million were slightly lower than last year due to a decrease in the average individual award. Attorneys' fee, however, are significantly higher, about $12.5 million, versus $8 million in 2008 and much lower than total fees in prior years. One key difference is the Court's awarding interim attorneys' fees in the Omnibus Autism Proceeding. The balance in the Trust Fund is just over $3 billion. In 2009 it is anticipated that receipts will be about $275 million against outlays of less than $100 million, resulting in a net contribution to the trust fund of about $185 million for the year.

Dr. Evans outlined DVIC activities since the last meeting. Along with members of the Commission, Dr. Evans stated that he attended the Advisory Committee on Immunization Practices on June 24-26, which included an extra day's session to discuss the novel H1N1 vaccine. A special 1-day session of the ACIP was held July 29 to vote on priority groups to receive the H1N1 influenza vaccine. On July 23rd, Dr. Caserta attended FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting, which discussed the pending licensure of several vaccine products.

There were two outreach efforts which DVIC staff attended with the VICP booth; the National Association of County and City Health Officials conference in Orlando on July 29-31, and the National Association of Community Health Centers meeting in Chicago on August 23-24. A number of brochures were distributed. The main interest was the H1N1 flu vaccine and whether it would be covered under the VICP. On June 24 and August 26, Dr. Rosemary Johann-Liang attended the second and third scientific workshops held by the Institute of Medicine Committee on Vaccines and Adverse Events. Finally, Dr. Evans noted that Ms. Castro-Lewis joined him and Ms. Buck in attending the NVAC meeting on September 15-16. A key agenda topic was discussion of H1N1 planning.

During discussion, Dr. Evans stated that the Department was reviewing nominations for Commissioners to replace those leaving (including Dr. Sconyers, Ms. Buck and Ms. Tempfer). Hopefully all three will be able to attend Commission meetings until the nominations are approved. He added that legal counsel had determined that it was acceptable for Ms. Buck to serve simultaneously on the ACCV and the NVAC. Asked about additional nominations, Dr. Evans stated that there are candidates currently under review, but that additional nominations in the appropriate Commission categories would be welcome. Asked about the increase in non-autism filings in 2009, Dr. Evans suggested that it was likely the result of the very large volume of

influenza vaccines administered annually along with the increased publicity for the program that accompanied the autism hearings. Finally Ms. Hoiberg reiterated a previously stated concern that the response from the Secretary's office, mainly being a basic recognition that the recommendation was received, was less than satisfying for the Commission.

Report from the Department of Justice, September 17, 2009, ACCV Meeting
Mark W. Rogers, J.D.
Deputy Director, Torts Branch, Civil Division, U.S. Department of Justice

Personnel

Since the last meeting, the office lost four paralegals. Two recently joined, however, the office is currently down two paralegals.

Power Point Presentation Summary

Mr. Rogers referenced the Power Point materials, entitled September 17, 2009, Department of Justice Power Point Presentation (DOJ PP), as part of his presentation.

Statistics

Mr. Rogers presented statistics from the litigation standpoint, as opposed to the Department of Health & Human Services (HHS). DOJ uses the date of the last meeting as the reference point for its statistics. Since then, 103 claims were filed. Of those, 15 were autism petitions (down from 24 for the last reporting period) and 88 were non-autism petitions. (DOJ PP, p. 3). The non-autism filings represented a slight uptick from last time and the breakdown between adult and child cases slightly favors adult cases, also slightly up from the last period. (DOJ PP, p. 3). In that same time period there were 183 adjudications. Of those, 21 were compensable (the method of disposition was by settlement, not a special aster's decision), and 162 were not compensable. (DOJ PP, p. 4). Of the 21 found compensable, none were conceded by HHS, and 17 were settled by proffer. A proffer means that both parties jointly produce a recommended award to the special master, who issues a decision consistent with the proffer. Judgment enters rather quickly. Of the 162 non-compensable claims, which is much higher than the 33 reported for the last period, 139 represented voluntary dismissals following the decision in autism on Theory One. The non-autism cases represented 23 of the dismissals, which is consistent with the last reporting period. (DOJ PP, p. 4).

Mr. Rogers identified the Glossary of Terms, which will remain in DOJ's presentation. (DOJ PP, pp. 5-6). As in previous meetings, Mr. Rogers used a flow-chart to illustrate the processing of cases once a petition is filed in the Program. (DOJ PP, p. 7). He emphasized that the most of the case processing is occurring on the left side of the chart meaning that the majority of cases are not conceded by HHS; rather, they are resolved through the settlement process. A petitioner can also seek compensation through a hearing. Ms. Drew asked whether an award of compensation represents a decision by a special master or when the check arrives. Mr. Rogers stated that he's referencing the decision, which includes settlements.

Autism

Mr. Rogers reported that the U.S. Court of Federal Claims (CFC) affirmed all three autism test cases for Theory One, (whether thimerosal containing vaccines combined with the MMR vaccine to cause autism spectrum disorders), in Hazelhurst v. HHS, Cedillo v. HHS, and Snyder v. HHS. (DOJ PP, p. 8). Hazelhurst was affirmed on July 24, 2009. Cedillo was affirmed on August 6, 2009, and Snyder was affirmed on August 11, 2009. The clock has started for whether or not petitioners will appeal to the U.S. Court of Appeals for the Federal Circuit (Federal Circuit). Regarding Theory Two (whether thimerosal containing vaccines alone can cause autism), post-hearing briefing is complete so those cases, Mead v. HHS, King v. HHS, and Dwyer v. HHS, are pending before the three Special Masters for decision. (DOJ PP, p. 9).

Appeals

In the Federal Circuit, there are four new appeals. (DOJ PP, p. 10). New cases are

highlighted in yellow for ease of reference. All cases at the Federal Circuit were filed by petitioners. One case, Shaw v. HHS, involves interim fees and costs. Hocraffer v. HHS and Doe 11 v. HHS, involved burden of proof cases where petitioner did not prevail before the special master but petitioners believe that the special master imposed a more rigorous legal standard inconsistent with Federal Circuit law. Wilkerson v. HHS, involved a statute of limitations issue. At the CFC level, 14 new cases were filed and 11 were decided. All appeals were filed by petitioners. (DOJ PP, p. 11-13). A substantial number of appeals involve attorneys' fees and costs.

Ms. Castro-Lewis sought clarification about the burden of proof standard and appeals. Mr. Rogers explained that in a given case, petitioners present evidence and a scientific expert. HHS presents its experts. The special master considers all of the evidence, which may include articles and expert testimony, and issues a decision. In these cases on appeal, a special master found that petitioners' expert was unconvincing for the reasons described in the decisions, and denied compensation. Invariably, a special master concludes his/her decision by stating that based on the evidence produced, petitioners have failed to carry their burden of proof that the vaccine caused the injury. On appeal, petitioners claim that the special master erred by not applying Federal Circuit law, i.e., the special master should have given more weight to a particular medical article or was unfair in characterizing an expert's testimony.

Comment

Ms. Buck asked if DOJ's litigation fees and costs were publically available. Litigation fees are not available for an individual case, but the ACCV is welcome to information concerning DOJ's budget, which is available under the Freedom of Information Act. As far as how DOJ allocates its budget in litigation –which attorney worked on any particular case and for how long, however, Mr. Rogers did not consider that information publically available. That type of information shows DOJ litigative strategy and would be considered privileged. DOJ's total budget would likely be available. Ms. Buck asked whether payments made to petitioners are publically available. Mr. Rogers explained that unless the award is in a published decision, payments to petitioners, whether interim or final payments, are not available to the public unless the petitioner specifically provides permission to release the information. Most of the cases that are settled or concluded by proffer are unpublished and are not available except with the consent of petitioners.

Ms. Buck observed that attorneys' fees and costs seem to be appealed frequently, and questioned how petitioners' fees and costs compare with DOJ. Acknowledging the point, Mr. Rogers noted that the total of petitioners' attorneys' fees and costs for any given period could be compared with DOJ's budget using the same fiscal time period. DOJ uses the fiscal year for operational expenses. Responding to Dr. Fisher's questions about the type of fee issues on appeal, Mr. Rogers noted that the litigation involves certain categories of fees, including attorneys' hourly rates and inadequate amounts. Within the provided materials from HHS, Mr. Rogers noted that for FY09, petitioners' attorneys' fees in compensable cases was $4.8 Million. For dismissed cases, it was $7.7 Million. The total for both compensable and dismissed cases is approximately $12.5 Million dollars. DOJ's budget for FY 09 is $7.7 Million in comparison. The $12.5 Million paid to petitioners' counsel is paid from the Trust Fund and represents FY09, with the caveat that FY09 is not quite complete so payments to petitioners' counsel may increase before the fiscal year ends. DOJ pays some of the its expert fees along with HHS. Ms. Buck appreciated the information. Mr. Rogers clarified

that interim fee payments are included in the HHS document. Dr. Herr commented upon the differences between comparing DOJ's operational expenses and case related expenses for petitioners.

Ms. Hoiberg expressed concern that while the DOJ attorneys received regular paychecks, the petitioner's attorneys must wait until final settlement to collect their fees, a situation she deemed unfair. She added that the hardship on families was even greater, often delaying treatment and other care for injured children. Mr. Rogers explained that payment of DOJ attorneys assigned to the Vaccine Program is governed by same provisions that apply to all DOJ attorneys. How petitioners' attorneys are paid is covered by the Vaccine Act. Presently, the standard for petitioners' attorneys' compensation is "reasonable," which in Mr. Rogers' view, requires a litigative process to determine what is "reasonable" in individual cases. The special masters are charged with making a final determination regarding reasonable fee amounts for petitioners' counsel. For example, the Commission could recommend changes to the Vaccine Act to include recommending that a certain hourly rate or that a schedule be developed and applied for determining all petitioners' attorneys fees. Such an approach would reduce the need for litigation.

Ms. Buck asked about interim fees in the context of payments to families given the lengthy process involving life care plans and valuing future expenses. Such a payment would require a legislative change. Mr. Rogers recalled legislative proposals five or six years ago that sought to provide interim medical costs. Ms. Buck asked about awarding interim payments for pain and suffering and even lost wages. Ms. Hoiberg commented that pain and suffering amounts should be awarded once they are agreed upon to reduce delay for the family. She expressed concern over the delay in receiving awards. Ms. Castro-Lewis cast the question in terms of whether the ACCV can recommend legislative changes, to which Dr. Evans replied, yes. Mr. Rogers elaborated that the Federal Circuit determined that interim attorneys' fees were available under the Act after litigation. Another legal determination for an interim award of the items being discussed, or a statutory change would be required.

Mr. Sconyers noted that in the Commission's letter to the Secretary, they expressly recommended that interim payment of attorneys' fees and costs be written into the statute rather than rely upon the Federal Circuit decision given that a panel decision could be reversed, changed or clarified by a later panel. Dr. Fisher expressed interest in proposing a recommendation that when a case is settled or decided, a payment or portion of the award be made not only to the attorneys but also to the petitioners. Dr. Evans offered institutional history noting that in the nineties, a recommendation for interim medical payments had been made to Secretary Shalala and some legislation had been drafted but was never enacted. He added that the Commission advises the Secretary and that a legislative proposal is drafted within the Department. Ms. Gallagher asked about consulting with the HHS attorney regarding the provisions of the Vaccine Act, related decisions, and legal implications of any recommendations. Ms. Buck commented that the RAND Corporation Report for the NVAC provided guidance to the NVAC about writing recommendations that could actually be implemented. Ms. Buck agreed with Ms. Gallagher that they need to write viable recommendations, adding that it might be appropriate to request a copy of the RAND Report from the NVAC. Ms. Castro-Lewis requested that a briefing of the Report should be added to the agenda for the next meeting. Ms. Saindon noted that the statute would need to be amended in order to permit for more than one payment to petitioners. Dr. Evans reiterated that ten

years ago there was no argument over the spirit or language in the proposal, the difficulty lies in getting legislative packages approved. Mr. Sconyers moved to create a work group to prepare a recommendation letter for approval by the Commission at the next meeting on this issue. Those expressing interest in serving on the workgroup were Ms. Hoiberg, Ms. Drew, and Dr. Fisher. Ms. Gallagher expressed her interest and sought Ms. Saindon's involvement given her knowledge of the Act.

Final DOJ Power Point Slides

Mr. Rogers returned to the recently decided cases from the CFC noting that the most significant cases were the three autism decisions. (DOJ PP, p. 12-13). The case Shaw v. HHS, involved attorneys' fees and costs. (DOJ PP, p. 13). In response to Dr. Fisher, Mr. Rogers explained that the hepatitis B cases of Hager v. HHS, Porter v. HHS, and Rotoli v. HHS, are companion cases that were remanded for further proceedings on damages following a special master's decision that the claims were not vaccine-related. In the two other companion claims (Myers v. HHS and Torbett v. HHS), Judge Firestone affirmed the special master's dismissal. These claims all involved the same vaccine, same basic fact patterns and injuries. (DOJ PP, p. 12).

Returning to the autism slide on Theory Two, Mr. Sconyers commented that over one year between the conclusion of the hearing and the filing of petitioner's post-hearing brief was long. He encouraged the parties to litigation to expedite the cases because petitioners need a resolution. Acknowledging the point, Mr. Rogers understood that petitioners' counsel agreed to the briefing schedule, but recognized that there is a premium in the Act to move the cases expeditiously.

Discussion of Burden of Proof
Betsy Grey, Arizona State University and Clifford Shoemaker, Esq.

Ms. Drew commented that one of the greatest challenges in the hearing process is the issue of burden of proof of causation. She introduced Dr. Betsy Grey and Mr. Clifford Shoemaker, who commented on that issue and the overall hearing process.

Dr. Grey explained that, although her area of academic focus is civil tort law, she has remained aware of the vaccine claims process and offered to provide a comparison of the two in order to highlight the challenges that the special masters, and both the plaintiffs' and respondents attorney's face in pursuing resolution of claims filed under the VICP. In effect, it is an evolutionary process that involves trying to develop innovative solutions to problems posed by a law that is not as specific as might be desired, with solutions developed by the special masters that may or may not be accepted by the appellate courts.

In a traditional tort proceeding involving injury the plaintiff must provide sufficient evidence at a preliminary hearing to reasonably convince a jury that, first, the cause of injury can be rationally supported and, second, that there is reasonable evidence to show that the defendant could have caused that injury. The plaintiff must prove both. The defendant will present evidence to the contrary in an attempt to refute the plaintiff's argument. In civil proceedings this burden of persuasion requires the presentation of a preponderance of evidence, which is defined as more than fifty percent, which the jury or other decision maker can rely on to rule in favor of the plaintiff.

In tort cases the plaintiff must rely heavily on scientific evidence, the presentation of animal studies, epidemiological studies, clinical trials, etc., with the objective of demonstrating a strong link between a toxic exposure and an adverse effect. Then the plaintiff must show a direct effect resulting in the injury, and the defendant will pursue other possible causes -- lifestyle, age, health, gender, and other environmental factors. Scientific testimony must be shown to be valid, accomplished thorough a process resulting from a 1993 Supreme Court case involving a plaintiff named *Daubert*. After that case the expertise of the individual testifying on scientific matters was much more stringently assessed and evidence was subject to peer review standards.

Dr. Grey turned to the VICP procedure, noting that it could have been based on the tort model requiring rigid scientific evidence, or it could have been based on a model related to policy-based decisions. She briefly described the components of the VICP, which are well understood by the Commission. She noted the contrast to the tort process, that in vaccine injury proceedings the special master is the sole decision maker, who must decide on the balance of the evidence as presented by both sides. In a tort case, if the evidence appears to be exactly equal, the ruling is usually against the plaintiff. In vaccine injury cases, when that occurs, the ruling is in favor of the petitioner.

Although the rules are different in vaccine injury cases, as in tort cases the petitioner must show that the vaccine could reasonably cause the injury to anyone, and then that the injury to the petitioner was a result of the administration of the vaccine. The first step was facilitated by the legislation that established an injury table describing the specific injuries that were presumed to be related to vaccines. The petitioner then could establish a presumption of injury causation if the injury was on the injury table, and that would obviate the onus of establishing a prima facie case (as in tort litigation) that would require an extensive presentation of evidence.

If the petitioner cannot establish a cause of injury based on the injury table, or if the respondent successfully refutes the petitioner's claim that the injury is covered under the injury table, then the petitioner may develop a "cause-in-fact" case, but then evidence must be presented to substantiate that claim. The legislation gives little guidance for this process and the special master may consider a vast array of medical and scientific evidence that may be presented by either side in the case.

Although the original legislation anticipated a predominant use of the injury table for establishing claims, changes made to that table over time have dramatically increased the number of off-table claims. Since there is almost no guidance for that type of claim, the special masters have struggled with the issue of sufficiency of evidence to make decisions and how much to rely on the civil tort procedures in deciding causation. Over the years certain cases have played a role in the evolution of the requirements for establishing causation. In 1993, the Federal Circuit established the first guideline -- show a medical theory of causation, show a logical sequence of events supporting the notion that the vaccine was the direct cause of the injury, based on a reputable medical/scientific explanation.

This kind of guidance leaned toward the tort process with the result that cause-in-fact (non-table) cases became lengthier and more expensive. In response, Chief Special Master Gary Golkiewicz developed guidance to help petitioners understand the requirements of a preponderance of evidence test of causation: medical plausibility confirmed by published studies in the medical/scientific community; proof of injury also

supported by scientific evidence; proof of a temporal relationship between vaccination and onset of injury; and proof of elimination of other causes of the injury. As a result of several appeals, the Federal Circuit ruled that a petitioner need not present such scientific/medical evidence, but could rely on "reputable medical or scientific explanation." That is, medical opinion alone, not published studies, would be sufficient.

Three cases defined the current requirements. In *Althen* v. HHS, the petitioner must provide three bases for showing causation -- a medical theory of causation, a logical sequence of cause and effect, and a temporal relationship between vaccination and injury. In *Capizzano* v. HHS, the Federal Circuit affirmed that treating physicians should be considered reliable in providing evidence of causation (a departure from the stringent Daubert requirements). There was also a decision that "close calls regarding causation are resolved in favor of injured claimants." The third case, *Pafford* v. HHS basically reaffirmed the rulings.

These cases also describe a process by which the petitioner may establish a prima facie case -- "rule in" a vaccine as a cause by meeting the *Althen* criteria, or "rule out" other obvious potential causes. The respondent may attack the petitioner's prima facie case or prove an alternative cause.

Dr. Grey concluded that the evolution of evidentiary requirements in vaccine injury cases has been from a tort-based approach to a policy-based approach to cases. The rigid peer-reviewed scientific evidence is not required, and reputable medical opinion is acceptable. However, because of the limited timeframe for filing claims, this means that petitioners may have to enter the process long before scientific evidence to support their claims is available

Mr. Shoemaker recalled that in the late seventies, as a result of the first swine flu immunization on a large scale, it was discovered that those who received the vaccine had a ten-fold increased risk of Gullain-Barré syndrome, a serious illness, and that data was developed from an epidemiological study of those vaccinated at that time. That kind of scientific data is not available for most vaccines today.

Recalling Dr. Grey's presentation, he noted that in a tort case the jury would be composed of individuals who typically had no prior knowledge of the issue under consideration, unlike the current situation in which the special masters hear so many cases and so many expert witnesses that they become very well informed to the point where they are as qualified as many attorneys who specialize in such medical cases. However, each special master is not bound by the decisions of any other special master, and there is not yet a way to establish reliance on precedent decisions, such that decisions can be inconsistent, and there is a requirement to try each case as if it was de novo. Mr. Shoemaker expressed the opinion that a policy should be considered to require that when a decision is made by a special master that a vaccine causes a specific injury subsequent petitioners should be able to rely on that decision as a basis for causation.

Mr. Shoemaker mentioned other ways to establish causation -- the occurrence of adverse events on re-challenge (multiple vaccinations with the same vaccine), animal studies, biomarkers (e.g., testing an infected child to ascertain whether the infection derived from a specific strain present in the original vaccine). He added that epidemiology is not the only scientific evidence that could establish causation, and he

expressed concern that there was little motivation to launch studies to prove vaccines cause damage. Vaccines are popular and in fact do reduce disease and death. And the adverse events caused by vaccines can also be caused by a number of other things.

Mr. Shoemaker suggested a potential epidemiological study of pregnant women and children who will soon be vaccinated with flu vaccines, some of which will contain mercury and some of which will not.

Turning to the Vaccine Injury Table, Mr. Shoemaker noted that initially 90% of filings relied on the injuries on the table; now, after the 1995 changes, 90% of filings are off-table injuries. In 1997, although hepatitis B was added to the table, the extant burden of proof requirement made it nearly impossible to obtain a positive ruling. Now after keeping cases alive for a number of years, the recent changes described by Dr. Grey have made it possible to effectively represent injured individuals. A similar impediment to effective representation of injury cases is the three-year statute of limitations. In many cases there is just not enough time for the science to be developed to the point that it can be added to the evidence. In 2001, the American Academy of Pediatrics made a presentation and recommendations to the ACCV that petitioners be allowed to file but delay proceedings for that reason. Mr. Shoemaker suggested it was a valid recommendation, citing the number of years it took to prove that Agent Orange was a carcinogen and that Gulf War syndrome was a legitimate injury. In criminal law a defendant is entitled to a speedy trial; but that defendant can also opt for a slower trial process. The same should be true of vaccine injury claims. Finally, Mr. Shoemaker endorsed the Federal Circuit's influence on facilitating the claim process.

Mr. Shoemaker commended the establishment of the VICP, but added that it should be a program that is able to take the risk of overcompensating and a program that is designed to be expeditious and in some way eliminate the four stages of litigation -- establishing causation, dealing with experts, working out damages and establishing fees. It should be simpler and more streamlined than that. The program should be sensitive to the realities that most cannot afford extensive research, expert witnesses, and attorneys being unsure of whether or not they will ultimately be paid fairly for their services. He made the point that, although the Program pays for extensive research through Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD), petitioners' attorneys are not allowed access to that data for their own analysis. And independent studies undertaken by petitioners'' attorneys are not eligible for reimbursement under the program.

Citing *Andreu* v. HHS, Mr. Shoemaker noted that a petitioner's attorney may not challenge the competency, credibility or content of the testimony of a medical expert witness. Only a testifier of fact may be challenged, which can discourage a petitioner's attorney from calling non-expert witnesses. There is also a problem related to the inadmissibility of written records by treating physicians, considered by the court to be related to patient-doctor confidentiality.

During discussion, asked about the way close calls are resolved, Dr. Evans stated that the policy is reflected in the increased reliance on litigated settlements that has become the principal way cases are managed. The Program seeks to balance its defense of the Secretary's decisions by including policy and the medical evidence in the process, although in many cases the medical evidence is not conclusive in linking causation with

the injury. On another matter, Ms. Buck expressed concern that a conflict of interest exists when HRSA funds a study by the Institute of Medicine.

Mr. Shoemaker pointed out the negative effect of protracted litigation and adversary environment in the current claims process with regard to the public's confidence in the VICP. He added that the VICP has a lower burden of proof requirement, which translates into a reticence on the part of attorneys to pursue civil litigation if a claim fails. A civil tort procedure would focus on the negative aspects of the vaccination program to the possible detriment of public participation. He suggested that it would be better to almost automatically compensate any injury that is linked temporally to a vaccination even if there is doubt as to the specific causation. Ms. Hoiberg agreed that a prompt non-adversarial settlement would benefit the overall mission of the VICP.

To clarify any misunderstanding of a comment made by Mr. Shoemaker, Dr. Evans stated that the trust fund has never paid for VSD research.

Update on the Immunization Safety Office and CDC Vaccine Activities
Jane Gidudu, M.D., MPG, ISO, CDC

Dr. Gidudu explained that the mission of the Immunization Safety Office is to conduct research on vaccine safety; to identify vaccine-related adverse events mainly through surveillance programs; and to assess vaccine risk factors. With the imminent release of the novel H1N1 vaccine, the ISO will be a key player (among a number of other federal and state entities) in the effort to identify adverse events early on. It is anticipated that the side effects of H1N1 will be similar to other flu vaccines, which have shown a very low serious adverse event rate. The surveillance will be timely and adverse events will be promptly identified and analyzed with regard to their effect on public health. One goal will be to determine if H1N1 vaccine increases the risk of Gullain Barré syndrome (GBS) as has been the case in other vaccines.

The surveillance process will rely on the usual programs, including the Vaccine Adverse Events Reporting System (VAERS), Clinical Immunization Safety Assessment (CISA) and the Vaccine Safety Datalink (VSD), which is a cooperative program between CDC and eight managed care organizations involving over 9 million participants. The surveillance process will be enhanced by including the Real Time Immunization Monitoring System (RFTIMS), a collaboration between CDC and the Johns Hopkins School of Public Health focusing on certain subpopulations, the Defense Medical Surveillance System (1.5 million military personnel), and information from GBS active case findings and input from certain large health plans. There will be enhancements to the existing communications system. In anticipation of a greater number of reports there will be more staff to handle those reports. There is also a new collaboration between CDC and FDA relying on post-licensure reports and data. Dr. Gidudu explained that CISA was collaboration among CDC and six leading academic centers to provide a resource of expert clinical evaluation of serious or difficult adverse events related to the H1N1 vaccination program.

Finally, Dr. Gidudu mentioned the report, Postlicensure Safety Surveillance for Quadrivalent HPV Recombinant Vaccine, the first published comprehensive analysis of adverse events from more than 23 million human papillomavirus vaccinations in the US reported to the Vaccine Adverse Events Reporting System (VAERS) between June 2006

through Dec 31, 2008. This was published by Slade B and others in JAMA “The adverse events reported were mainly mild (syncope, local skin reactions, dizziness, nausea, headache) but included 772 (6%) more serious adverse reactions, including vanous thromboembolic events which were common in women using oestrogen containing birth control measures. It is however important to note that VAERS reports do not establish causal relationship between the vaccine and the adverse event. Additional studies are needed to verify this.

Update on the Institute of Allergy and Infectious Diseases Vaccine Activities
Barbara Mulach, Ph.D, NIAID, NIH

Dr. Mulach discussed NIH clinical trials on H1N1 vaccine, conducted in collaboration with two manufacturers (Sanofi Pasteur and Australia-based CSL), adding that the manufacturers are also conducting trials independently. The trials were based on healthy adults and later trials focused on the elderly, children 6 to 17 months in age, and pregnant women. Children and pregnant women receive thimerosal-free vaccine. Preliminary data has indicated safety and efficacy at the 15 microgram dose.

Dr. Mulach stated that only interim results are available from the clinical trials. Information about the adult trials is posted on the NIH web site and data from the pediatric trials would be posted when available.

Asked about whether doctors will inform vaccines of the type of vaccine being administered, Dr. Gruber indicated there was no such legal requirement, but that the pertinent vaccine information sheet would include that information and would be available to all recipients of vaccines.

Update on the Center for Biologics, Evaluation and Research
Marion Gruber, Ph.D., CBER, FDA

Before her formal presentation, in response to a question about the dosage and formulation of influenza vaccine against the pandemic H1N1 influenza virus , Dr. Gruber (FDA) explained that manufacturers would produce single-dose, thimerosal-free sigle-dose vaccine vials as well as multi-dose vaccine vials. In accordance with federal law the multi-dose formulation must contain apreservative. The manufacturers currently do not have the capacity to produce the vaccine in only the single-dose formulation. Also, vaccine formulated in multi-dose vials requires less refrigeration space, a logistic consideration by some health care providers. Current estimates project thatabout half of the pandemic H1N1 2009 influenza vaccine distributed at the beginning of the flu season will be multi-dose, thimerosal-preservative containing vaccine Dr Gruber added that the initially available 45 million doses of pandemic H1N1 influenza vaccine are not sufficient for the entire population, which is why vaccine distribution should be administered topregnant women, caregivers for children under 6 months of age , healthcare providers and emergency medical personnel first. Dr. Gruber mentioned that there will be an intense, real-time safety surveillance associated with the distribution of the pandemic H1N1 2009 vaccine.

In providing her update, Dr. Gruber stated that the FDA approved the pandemic H1N1 vaccines on September 15, 2009. These are a monovalent vaccines (unlike the trivalent seasonal flu vaccine) that will be manufactured by four commercial companies -

- Novartis, Sanofi Pasteur, Medimmune and CSL. Each manufacturer will produce a pandemic H1N1 vaccine approved for the very sameage groups that the variousseasonal flu vaccines manufactured by the respective companies are indicated for. None of the pandemic H1N1 influenza vaccines contain an adjuvant. Currently ongoingclinical trials have indicated that a singledose of 15 micrograms is safe and effective in healthy adults, and that data regarding the pediatric dosageshould become available shortly.

Dr. Gruber mentioned that FDA has several other applications pending, including those for vaccines to protect against HPV, Neisseria meningitides and pneumococcal disease. One of these products, an HPV vaccine, Cervarix, was discussed at the FDA advisory committee, VRBPAC, in September . It approved, it would be indicated forfemales 10 to 25 years of age to prevent cervical cancer.

During discussion, asked about the pediatric dosage, Dr. Gruber stated that the children's dose for seasonal flu, depending on the age of the child, is half of the adult dose, and the pandemic H1N1 2009 vaccine dosage recommended for childrenwould likely depend on results from currently ongoing clinical trials. Asked about whether H1N1 might be included in next year's seasonal flu formulation, Dr. Gruber stated that this is a likely scenario. She added that this determination would be made by the WHO and also FDA's VRBPAC usually in February. Commenting on whether H1N1 can be administered at the same time as the seasonal flu vaccine, Dr. Gruber stated that the studies have not been completed to determine that. Ms. Buck noted that the speed with which the H1N1 was brought to fruition has not allowed the time to collect much safety data. She hoped that physicians would be sensitive to the information needs of pregnant women and parents concerning that lack of data.

Finally on another topic, Mr. Sconyers requested that the Commission send a formal request to the Secretary to adopt a policy that is consistent with the Althen and Capizzano decisions and that resolves close calls regarding causation in favor of injured claimants. There was agreement that the issue should be considered by a work group, and Mr. Sconyers agreed to chair the work group.

Public Comment

Ms. Castro-Lewis invited public comment.

Mr. Shoemaker, a speaker during the day's proceedings, noted that allowing 25 microgram of mercury in a vaccine dose would work out to an infant or child weighing 550 pounds, based on the EPA's safe dose of 0.1 microgram per kilogram of body weight per day. He indicated that it emphasized the importance of thimerosal-free vaccines for pregnant women and children. Secondly, he asked whether there was any requirement to provide thimerosal-free vaccines to women in the military.

Mr. James Moody, representing Safe Lives, commented that there would be no safety data available for pregnant women and parents to consider in face of the alarmist announcements concerning the H1N1 pandemic. He urged that the Commission immediately adopt a resolution to forward to the Secretary to require that thimerosal-free vaccine be available for all pregnant women and children who are entitled to receive the vaccine. .

The meeting recessed at 5:30 p.m., to reconvene the following morning, September 18, at 9:00 a.m.

Advisory Commission on Childhood Vaccines

September 18, 2009

Day Two

Minutes

Members Present
Magdalena Castro-Lewis, Chair
Sherry K. Drew, J.D., Vice Chair
Margaret Fisher. M.D.
Charlene Gallagher, J.D.
Thomas Herr, MD
Sarah Hoiberg
Elizabeth Saindon
Jeffrey M. Sconyers, J.D,
Tamara Tempfer, RN-C, MSN, PNP

Executive Secretary

Geoffrey S. Evans, M.D., Director, DVIC

Staff Liaison

Andrea Herzog, Principal Staff Liaison

Welcome and Unfinished Business from Day One
Magdalena Castro-Lewis, ACCV Chair

Ms. Castro-Lewis called the meeting to order and invited comments with regard to the previous day's meeting content. Ms. Gallagher noted that during the public comment segment of the meeting Mr. Shoemaker made a statement concerning EPA reference doses. Part of that statement suggests clarification. First, ethylmercury released from thimerosal-containing vaccines is metabolized more rapidly than methylmercury, which may be found in fish, for example. Therefore it is of less concern from a safety standpoint. Second, the reference dose (RfD) of mercury established by EPA of 0.1 micrograms per kilogram body weight per day was ten times less than the amount that was determined by EPA to be safe in humans. Those tests were also based on methylmercury. Finally, measurement of mercury consumption is based on a cumulative process, and not any measurement in a single day. Ms. Gallagher stated that she would submit a paper explaining the issues related to the RfD for mercury for inclusion in the next Commission's meeting materials.

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

Dr. Salmon provided a brief update on the National Vaccine Plan, which he said would revise the 1994 version of the Plan. The primary objective is to develop a strategic framework at the national level for vaccine activities during the next ten years. There are five goals: one, to develop new, improved vaccines; two, to enhance the safety and efficacy of vaccines and to improve vaccination practices; three, to promote informed vaccine decision making and policy development; four, to ensure a reliable, stable supply of recommended vaccines and to achieve more effective use of present vaccines in preventing disease, disability and death; and five, to prevent disease on a global basis through effective vaccination programs.

A draft plan has been prepared and the Institute of Medicine will review the plan to develop a set of recommendations related to priorities. Having already held information-gathering workshops, the IOM anticipates submitting a report by the end of November 2009. The Rand Corporation is also interviewing stakeholders and should be ready to submit a report on those interviews by the end of November.

There has been an extensive public comment period during which more than 500 comments were received from advocacy groups, industry (including vaccine manufacturers and insurance companies), foreign governments and other international agencies (such as WHO), and individuals. NVPO set up interagency working groups to look at each goal. The working groups included representative from CDC, NVPO, FDA, HRSA, USAID, NIH and others. The comments were sent to those working groups, which will consider them in light of several criteria -- feasibility, consonance with the strategic plan, and fit with regard to the overall objectives of the Plan (non-redundancy). Every comment was considered and either accepted (with or without modification) or rejected as either incompatible with the Plan or informational but not suggesting specifics that would apply to the Plan. Since most of the reports and recommendations will be available at the end of November, by the end of December the NVPO hopes to develop a process by which the National Vaccine Plan can be completed.

Dr. Salmon turned to the NVAC Safety Working Group, which has completed review of the CDC Immunization Safety Office's research agenda and has moved on to looking at the national vaccine safety system and developing a white paper addressing infrastructure requirements for that vaccine safety system. The Working Group leadership is shared by Andy Pavia, Tawny Buck (a member of ACCV) and Marie McCormick. An information gathering meeting was held on July 15th, and the sessions included policy alternatives for a robust vaccine safety system, overcoming gaps in vaccine safety, ideal vaccine safety systems, lessons learned from other safety systems (e.g., NHSTA, the NTSB, the Chemical Safety Board, etc.). Working with all of this information, one possible recommendation of the Working Group is a re-direction of funds to the Vaccine Data Safety Link and to the Clinical Immunization Safety Assessment Network.

Looking toward the future, the Working group has set up a number of subgroups to look at structure and governance, epidemiology of adverse events, basic and applied science in genomics, risk factors for adverse events, and the ultimate white paper that will be the final product of the Working Group. In fact the white paper might be a series of papers on specific issues such that all of the reports can come together as a consolidated white paper by September 2010.

ACCV Outreach Workgroup Report

Sarah Hoiberg, ACCV Commissioner

Ms. Hoiberg announced that contract specifications for continuing the outreach program are being developed. Dr. Evans noted that a request for proposals based on those specifications had been released and that a contract should be executed within a couple of weeks. The purpose of the contract is to develop an outreach plan that would address the needs of parents, the general public and healthcare providers. He added that funding from the DVIC budget should be available for this one-year contract.

Dr. Fisher commented that the Workgroup, with the review and approval of the Commission members, had created a brief paragraph describing the VICP and that it had been placed in a number of strategic publications, including the Pediatric Infectious Disease Newsletter and the web site of the New Jersey chapter of the American Academy of Pediatrics (AAP). It will also be added to the main AAP web site in the near future. Finally, she noted that a review she had written about H1N1 virus for the Pediatric Infectious Disease Journal included a paragraph specifically discussing pediatric vaccines and the compensation program. Ms. Castro-Lewis suggested that Dr. Fisher provide any information available about each exposure and the approximate size of the readership.

Dr. Herr explained that he was working with Dr. Evans on a letter about the VICP that would be reviewed in the Journal of the AAP. Dr. Evans added that the AAP Journal would probably also be interested in a discussion of the Countermeasures Injury Compensation Program (CICP), pointing out the differences between the two programs.

Institute of Medicine Project on Vaccines and Adverse Events
Rosemary Johann-Liang, M.D., Chief Medical Officer, DVIC, and
Kathleen Stratton, Ph.D., Study Director, IOM

Dr. Johann-Liang briefly explained that the purpose of the IOM study is to review current science with regard to vaccine adverse events in order to update the current table of injury, which provides the presumption of causation for claims under the VICP. The original charge to the IOM was to review four vaccines -- influenza, hepatitis B, human papillomavirus and varicella vaccine. Recent additional funding has allowed the additional review of four more vaccines -- meningococcal vaccine, diphtheria-tetanus-toxoid andacellular pertussis (and other tetanus-containing vaccines), hepatitis A vaccine, and measles-mumps-rubella (MMR) vaccine. That list of adverse events was initially developed by the medical officers reviewing vaccine injury petitions plus a literature search of vaccine adverse events. The list was then presented to the Inter-Agency Vaccine Group for input by other federal agencies including CDC and FDA. The final list was provided to the IOM for consideration. There is on-going opportunity for public comment through the IOM web site. She noted that the Committee could add to the list of adverse events proposed by VICP.

Dr. Stratton explained that the charge to the IOM was based on an earlier congressional mandate to conduct two reviews of vaccine adverse events (in 1991 and 1994) in order to submit recommendations to the Secretary for consideration in developing the vaccine injury table. Although not congressionally mandated, the current review is in consonance with the previous review process. The charge to the IOM is to assess scientific evidence related to vaccine adverse events, including a look at epidemiology, clinical trials and other clinical studies, as well asbasic researchregarding possible

pathophysiologic mechanisms of vaccine reactions that has gone well beyond what was available in the early nineties during the previous IOM reviews for the VICP

Dr. Stratton described the selection of committee members, who represent a wide variety of fields. Expertise includes epidemiology, biostatistics, pediatric and adult neurology, pediatric and adult rheumatology, allergy, developmental immunology, developmental biology, and immunotoxicology.. . Dr. Stratton explained that the selection process involves review of a much large number of experts than is finally selected, and that each committee member must conform to a stringent conflict of interest standard. For example, a member may not have served on a federal advisory committee on vaccine injury, approval, or use. She noted that the committee members were volunteers, not paid for their participation, even though they commit to a substantial amount of time to attend meetings, review materials and write report drafts.

Over 5,500 citations have been identified in a literature search regarding the first four vaccines, and each will be considered.

During discussion, asked about whether VAERS reports might appear in the literature, Dr. Stratton commented that the source of the 5,500 citations might include published reviews of some of the VAERS reports, but that many of the VAERS reports are of recent origin and would not yet be published. Asked about the uses of the HRSA funding, Dr. Stratton explained that, although the volunteers received no remuneration, travel and lodging expenses were reimbursed, and there were costs related to holding meetings, for the staff required to support the study, for the purchase of research reprints, and for the printing of the final report. Asked about the use of VAERS data and the disposition of various claims filed by vaccine-injured parties, Dr. Stratton explained that passive surveillance reports are included in the data collected, as are some VICP disposition information, but only insofar as the VICP decisions might provide leads as to proposed mechanisms of an adverse event. She added that the committee would not consider the outcome of the proceeding to be within its purview and would not consider the causal rationale that might be associated with any case.

Finally, the committee may look at interval from time of vaccination to time of adverse event onset, whether an adverse event is related to the vaccine or the process of administration, the differences between reactions related to live or inactivated vaccines, vaccine interaction with the immune system, the influence of repeat vaccinations, and whether there may be vulnerable populations that are more or less susceptible to adverse reactions. Asked about whether the committee would address the need for multiple vaccinations, Dr. Stratton explained that consideration of efficacy was not in the committee's charge, only the issue of adverse events.

Dr. Stratton explained that the committee would meet perhaps eight or nine times over two and a half years. Several of the meetings will be public workshops and/or open to the public and material associated with the meetings, including verbatim transcripts, will be available on the committee web site. The committee has access only to publicly available information and, except for proprietary information submitted by meeting participants, will make that information available. It has no access to information not publicly available. Finally, she indicated that the final report would be released in mid-2011, and that (in accordance with National Academies policy) there would be no interim report. The report will not comment on the need for future similar reviews by the IOM, that recommendation considered being self-serving

Report on Countermeasures Injury Compensation Program (CICP)
Vito Caserta, M.D., M.P.H., Director, CICP

Dr. Caserta explained that the purpose of the CICP is to provide liability coverage for those entities involved in getting countermeasures to victims of a terrorist incident or a pandemic, and to provide compensation for those victims to supplement any compensation the victims might receive from other sources (insurance companies, health insurers, etc.). Victims could receive unreimbursed medical costs, payment of lost wages, and/or a death benefit (of about $300,000). The liability coverage applies to manufacturers, distributors, program administrators, public health official if they are involved in a response to an eligible incident.

The CICP covers only the monovalent influenza vaccine that is associated with a possible pandemic or specific terrorist attack, and not the trivalent flu vaccine that is aimed at seasonal flu. To be eligible for compensation the specific countermeasure must be identified by declarations issued by the Secretary of DHHS under the provisions of the Public Readiness and Emergency Preparedness (PREP) Act of 2005. Those declarations must identify the specific injury and cause of injury, the countermeasure used, and usually a geographic area and a time frame for administration of the countermeasure. The adverse event must be serious (life threatening or liable to cause permanent injury or disability).

The CICP may also cover other adverse events from countermeasures for anthrax, botulinum, smallpox and radiation poisoning. The vaccines covered include those for H1N1 and H5N1, as well as H2, H6, H7 and H9. Tamiflu and Relenza are covered, as are diagnostic products. Finally, the program covers adverse events related to the use of mechanical respirators. Dr. Caserta stated that the adverse event could be related to either the device or the vaccine or both. Importantly, Dr. Caserta added, the program does not cover efficacy of either vaccines or devices, only serious adverse events caused by either.

Mr. Sconyers expressed serious concern that a health care worker, for example, could don a malfunctioning respirator and, as a result, contract a serious disease and yet not be covered by the CICP. Dr. Caserta conceded that was true and agreed to communicate the concern to the Secretary. Ms. Levine added that, although the health care provider might not be covered under the compensation program, there could be protection from liability under the PREP Act.

In closing, Dr. Caserta compared the CICP and the VICP. The CICP is administrative, not judicial and decisions on causation are made based on scientific evidence as assessed by a Public Health Service physician and not by a ruling based on evidence presented by plaintiffs. Legal fees, if any, are not paid by the CICP as they are by the VICP. There is no payment for pain and suffering as with the VICP, and there is a single appeal step under the CICP, unlike the judicial appeal to higher courts available under the VICP. Those injured under CICP can only sue the manufacturer of a drug for willful misconduct, a difficult standard to pursue. The deadline for filing a claim under CICP is one year versus three years for the VICP. The CICP covers only monovalent pandemic flu vaccine and the VICP covers only the trivalent seasonal flu vaccine. Finally, the CICP is funded by appropriated funds and the VICP is funded through dose taxes that accumulate in a trust fund.

Public Comment

Ms. Castro-Lewis invited public comment.

Mr. James Moody, representing Safe Lives, commented that Congress had causation standards for vaccine injury, affirmed *in Althen, Capizanno*, and *Pafford,* which relied on the preponderance of evidence and not scientific proof of causation. Mr. Moody suggested that the IOM study should rely on that those standards, and not those that might be required in the tort environment, when the IOM reviews adverse events in anticipation of making recommendations for revisions in the vaccine table of injury. He added that it would also be appropriate, if not imperative, that both the ACCV and the IOM would endorse the importance of developing baseline data in children not vaccinated in order to assess adverse events in vaccinated children.

Future Agenda items and Adjournment

Ms. Castro-Lewis noted that reports from the two work groups would be on the next agenda. One work group is looking at a proposal to allow the program to make more than one payment for pain and suffering and medical costs; the other work group is looking at a proposal to the Secretary to develop an approach to resolving off table cases consistent with the ruling in *Andreu*. Ms. Hoiberg reiterated her request that the Secretary of Department of Health and Human Service (DHHS) be present at some future meeting. She also volunteered to be on the agenda committee. Finally, in response to a question about whether CDC will publish a vaccine information sheet (VIS) for H1N1, Dr. Caserta confirmed that, although not required, such a VIS will be published.

On motion duly made and seconded, there was unanimous agreement to adjourn. The meeting adjourned at 11:30 p.m.

Magdalena Castro-Lewis ACCV Chair	Sherry K. Drew ACCV Vice-Chair
Date Geoffrey Evans, M.D. Executive Secretary, ACCV	Date