Advisory Commission on Childhood Vaccines

March 4-5, 2010

Day One

Minutes

Members Present
Magdalena Castro-Lewis, Chair
Sherry K. Drew, J.D., Vice Chair
Tawny Buck (via teleconference)
Margaret Fisher. M.D.
Charlene Gallagher, J.D.
Thomas Herr, M.D.
Sarah Hoiberg
Elizabeth Saindon, J.D.
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. Castro-Lewis called the meeting to order and after introductions, expressed appreciation for the planning and preparation for the meeting by both staff and Commission members, noting especially the provision of meeting materials in advance of the meeting. She presented the Chairperson's report, noting that she had attended the NVAC meeting and provided an update on ACCV activities.

Ms. Castro-Lewis called for approval of the minutes of the September 15-17, 2009 meeting. Mr. Sconyers commented that the minutes may have failed to convey the frustration of some Commission members with regard to the failure of staff to provide, either in advance of the meeting or at the meeting, a copy of the contract which was the subject of the Banyan presentation. He noted that the frustration was clearly expressed by some Commission members during that presentation. On motion duly made and seconded, the minutes of the September 15-16 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 75th meeting of the ACCV. He reviewed the agenda and the meeting materials provided to the Commissioners prior to the meeting.

Providing an update on the program statistics since the last meeting, Dr. Evans noted that filings for autism injuries were significantly below the same period last, only eight claims in the first four months of fiscal year 2010. Conversely, claims for non-autism injuries dramatically increased – 142 in the first four months. He added that autism filings peaked in 2003 (2,437 claims) and then declined through 2006, after which there were fewer than 200 claims a year, but then increased slightly in 2007 and 2008 because of publicity surrounding the test case hearings.

Influenza vaccine was added to the Table in 2005, and there was a peak in 2007 when the 2-year deadline for the filing of claims dating back 8 years expired, and a recent surge in 2009 because of the expanded flu vaccination program. Thus far this fiscal year, 44% of non-autism claims are for influenza vaccines, with all others far behind – HPV 9%, ETAP 7%, DTaP 6%, "other" less than 5%. In addition, because most influenza claims are filed on behalf of adults, there has been a shift in overall claims from children to adults. Asked about specific injuries, Dr. Evans explained that demyelinating conditions were predominate, mainly Guillain Barré Syndrome, transverse myelitis and chronic inflammatory polyneuropathy. Asked about the ratio of flu vaccinations between children and adults, Dr. Evans referred the question to Dr. Fisher, who commented that the ratio (adults received the majority of flu vaccines) will probably shift toward children as recommendations from advisory groups for universal coverage begin to affect the distribution of vaccines. Other adverse events in adults may also begin to occur later than the current demyelinating conditions that typically have relatively rapid onset.

In response to a question about concurrent claims filed with VICP and the Countermeasures Injury Compensation Program (CICP), Dr. Evans explained that the CICP is in the process of becoming an active compensation program and only "requests" or "notices to file" can be submitted. Concerning its longevity, Dr. Evans stated that the program is permanently authorized and should remain in effect for an extended period of time. He added that the program covers H1N1 vaccine as well as other antivirals designated by the Secretary DHHS -- anthrax, smallpox and other vaccines that might be required to respond to a bioterrorist threat. Currently the only requests submitted have been for H1N1, which will be included in the next year's seasonal vaccines, and therefore covered under the VICP.

Concluding his report, Dr. Evans noted that adjudications are slightly behind last year's level, as are awards, most of which continue to be based on settlement, although both concessions and court decision have increased slightly since last year. However, the amount of awards thus far indicates that total awards may exceed $100 million, the highest level since 2003. Dr. Evans stated that the VICP Trust Fund is currently $3.2 billion.

Finally, Dr. Evans commented that he and Ms. Castro-Lewis provided VICP updates at the February 3-4 National Vaccine Advisory Committee. He also attended the February 24-25 Advisory Committee on Immunization Practices, which voted to recommend to CDC that everyone over the age of six months receive the seasonal flu vaccine. He added that Commission member Tammy Tempfer attended the ACIP meeting, representing the National Association of Pediatric Nurse Practitioners.

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

Personnel

Previously, Mr. Rogers indicated that the office was hiring two attorneys. The office recently made those selections and Mr. Rogers hoped to have them on board by the next ACCV meeting. Vince Matanoski, an assistant director, is on extended duty in the Congo. One attorney is on a detail assignment to another section of the Department of Justice ("DOJ"), and should be back within a couple of months.

Power Point Presentation Summary

Mr. Rogers referenced the Power Point materials, entitled March 4, 2010, Department of Justice Power Point Presentation ("DOJ PP"), as part of his presentation.

Statistics

As in past presentations, Mr. Rogers emphasized that DOJ offers a slightly different snapshot of the statistics than the Department of Health and Human Services (HHS). DOJ uses the time reference of one ACCV meeting to the next. Mr. Rogers recommended using HHS statistics if looking for a "macro" perspective, and using DOJ statistics for a quick "snapshot" of what has happened recently. Since the last meeting, 91 petitions were filed. Of those, 4 were autism petitions and 87 were non-autism petitions. (DOJ PP, p. 3). More claims are being filed for adults than for children.

Mr. Rogers explained, in response to a question posed by Mr. Sconyers during HHS' presentation, that damages awarded in an adult claim vary a great deal, but damages awarded in a child's claim are more predictable. Since adults have a reduced life expectancy, future costs and medical expenses will be less expensive than those same costs for a child, who is expected to live longer. However, wage loss calculations vary in adult cases. For a child who filed a petition under age eighteen, a standard formula is used to predict the value of lost wages. Adult wage losses are calculated based on his/her career and skill set, so there is a great deal of variation. For example, an award for an adult who is in a high income bracket could be higher than an award for a lesser paid individual. The award for an adult or child in a death claim is the same.

There were 33 petitions adjudicated, of which 16 were compensable. (DOJ PP, p. 4). Of those, 4 were concessions. There were 12 petitions that were not conceded. Of those not conceded, 9 were resolved by settlement, 2 were decisions by the special master, and 1 was a proffer. In a proffer, both sides submitted evidence that the special master then accepted as dispositive of the level of damages.

There were 17 petitions that were not compensable. (DOJ PP, p. 4). Of those, 8 were autism petitions and were typically were dismissed for jurisdictional reasons as untimely or withdrawals.

Mr. Rogers reviewed the glossary of terms that has been presented in the past. (DOJ PP, pp. 5-6). Turning to the Processing Chart at DOJ PP, p. 7, Mr. Rogers noted that, for this time period, more cases were conceded and moved down the right side of the chart.

Autism

Mr. Rogers noted that Cedillo v. HHS and Hazlehurst v. HHS, two of the three test cases for the Theory One autism claims (whether thimerosal containing vaccines combined with the MMR vaccine to cause autism spectrum disorders), were in the briefing process before the U.S. Court of Appeals for the Federal Circuit ("Federal Circuit").

As for the Theory Two autism claims (whether thimerosal-containing vaccines alone can cause autism), Mr. Rogers noted that nothing had changed since the last meeting. The cases were still pending before the Special Masters. Responding to a question from Dr. Herr, Mr. Rogers commented that he expected decisions in the near future, but that the long wait was likely due to the voluminous records involved, and an intent perhaps by the three special masters to publish their respective decisions simultaneously.

Appeals

Since the last meeting, there were two new appeals to the Federal Circuit. Those cases, filed by petitioners, were Riggins v. HHS and Masias v. HHS. (DOJ PP, p. 10). Both appeals involve attorneys' fees and costs. Three cases, appealed by petitioners, were affirmed by the Federal Circuit: Hocraffer v. HHS, Wilkerson v. HHS, and Moberly v. HHS. (DOJ PP, p. 11). Hocraffer involved a case where the special master awarded $5,000 in damages and the appeal involved whether or not the award should have been higher. It was affirmed by the U.S. Court of Federal Claims ("Court of Federal Claims") and by the Federal Circuit. Wilkerson was a statute of limitations case where the Federal Circuit affirmed the dismissal of the petition as untimely. Moberly was an entitlement decision that was affirmed by the Federal Circuit in favor of the respondent. Mr. Rogers recommended the case to the ACCV because the case addressed the presentation by Professor Gray, several meetings prior, where she discussed some uncertainly in the Federal Circuit decisions about whether traditional tort litigation standards apply to cause-in-fact cases in the vaccine program. The Federal Circuit in Moberly addressed that issue and found that those standards apply here. Mr. Rogers cautioned that there is an asterisk next to Moberly as petitioners have moved for a rehearing en banc, meaning that they have asked for the entire Federal Circuit sitting en banc to rehear the case. Such a review is rarely granted, however, it has been requested and Mr. Rogers hoped to report further on this at the next meeting.

Ms. Castro-Lewis asked about the percentage of appeals on a daily basis and how many of those are reheard. Mr. Rogers had a sense that most cases appealed to the Federal Circuit are affirmed, while reversals are unusual. A rehearing en banc, by the full Federal Circuit to decide to rehear a three judge panel's decision, is very, very unusual. Mr. Rogers explained that when a case is appealed to the Federal Circuit it normally is assigned to a panel of three judges. When a case is asked to be reheard before the full Federal Circuit, the full Federal Circuit has the authority to reverse the three judge panel's decision. The full Federal Circuit also has the authority to look at all of the other panel decisions on the issue and decide which one is right, wrong, or reconcile them as they see fit. The full Federal Circuit review is what petitioners are requesting in Moberly.

Responding further to Ms. Drew's request to explain the levels of review, Mr. Rogers elaborated that a special master initially decides the case, then there is a right to appeal that decision within 30 days and seek review by the Court of Federal Claims. The Court of Federal Claims judge decides the case. Within 60 days of that decision, a party must file a Notice of Intent to Appeal the decision to the Federal Circuit. If a party appeals to the Federal Circuit, which has more than 12 judges (some of whom are senior status), a panel of three judges is assigned to hear the case. The three judge panel decides the case. At that point the case is normally over, however, a party could petition for *certiorari* before the U.S. Supreme Court. As an intermediate step, Mr. Rogers reiterated that a party could move for rehearing en banc, asking the full Federal Circuit to rehear the case, which is what petitioners have done in Moberly. In the history of the Program, only one case had gone to the U.S. Supreme Court -- Whitecotton v. HHS -- which, incidentally, was denied rehearing en banc by the Federal Circuit.

Responding to Ms. Castro-Lewis' question about the posture of the Cedillo case, Mr. Rogers stated that the Cedillo case has been decided by the Court of Federal Claims against petitioners and they have appealed it to the Federal Circuit. Once all briefs are in, the case will be assigned to a three judge panel. We will not know the identity of those judges until the morning of the oral argument. That panel will have all of the parties' briefs, will hear argument, spend a few months considering everything, and write a decision. Once the decision is issued, the time starts for seeking rehearing before the full Federal Circuit or a request that the U.S. Supreme Court hear the case. Mr. Rogers clarified that the Snyder v. HHS case from Theory One in autism was not appealed. Responding to Mr. Sconyers' question on briefing, Mr. Rogers confirmed that oral argument is scheduled in Hazelhurst for April 8, 2010. (DOJ PP at 14).

At the Court of Federal Claims level, Mr. Rogers stated that about half of the appellate activity pertained to attorneys' fees and costs. (DOJ PP, p.13). A large part of the fees and costs litigation involves deciding interim fees: when they are appropriate and how much is appropriate.

Settlements

In response to a request by the ACCV about settlements, Mr. Rogers presented a list of stipulations filed by DOJ in claims adjudicated between December 7, 2009 and February 22, 2010. (DOJ PP, pp. 15-17). The information is taken from filed stipulations, which reflect settlement agreements between the parties for an award. Each stipulation includes a statement taken from petitioners' allegations in the petition, i.e., that petitioner received a vaccine, suffered an alleged injury, and seeks compensation. Each stipulation also contains a paragraph of respondent's position contesting entitlement to compensation, and notwithstanding the parties' respective differences, they are settling the case. For purposes of this presentation and using the stipulations, Mr. Rogers provided several caveats. First, HHS may not agree that in any of these cases the alleged vaccine was even given -- an extreme example. Second, and more commonly, HHS may not agree that petitioner suffered the injury alleged. It is also possible that the initial, alleged injury morphed into some other injury. Thus, Mr. Rogers cautioned, this information must be used "with a grain of salt" in that it reflects information based on initial petitions. It is also possible that HHS did not consider the petition timely filed. The common denominator is that HHS found enough risk to settle the claim. Notwithstanding these caveats, this information is provided with the hope that it will be useful to the ACCV. Mr. Rogers further emphasized that complete stipulations are published on the Court of Federal Claims website.

Ms. Hoiberg asked whether the time that the petition was filed could be listed along with the time that the stipulation was filed. Mr. Rogers believed that DOJ could provide that information. Dr. Salmon asked whether the columns listing the vaccine matched the alleged injury, to which Mr. Rogers replied that they do. Responding to a question from Dr. Gidudu about whether cases involved multiple injuries and multiple vaccines, Mr. Rogers indicated that the stipulations only reflect what was initially alleged and sometimes we could not glean a specific injury from the petition. Normally, during litigation and further investigation, the claims, alleged injuries and vaccines become honed. From a time management standpoint, DOJ is providing information taken from the petition. Responding to Ms. Hoiberg's question about ADEM, Dr. Fisher defined ADEM as acute disseminated encephalomyelitis.

Mr. Sconyers, Ms. Buck, and Ms. Castro-Lewis each expressed appreciation for the information gathered, and for providing it in advance of the meeting.

Transparency of the National Vaccine Injury Compensation Program and the ACCV Web Page
Sherry Drew, J.D., ACCV Co-Chair

Ms. Drew invited an open discussion which addressed transparency within the federal structure (VICP, DVIC, ACCV, DOJ, the courts), transparency as it affects the members of the Commission and the interaction of the Commission with the public, and the potential of the ACCV web site.

A primary concern of the Commission members was availability of information and consultation by DVIC when important issues under the purview of the ACCV are decided. There was consensus that the Commission should receive information about all such issues, and concerning agenda items, in advance of each meeting so that Commissioners would have the opportunity to review that information before being expected to comment in the open meeting sessions. There were also suggestions that the Commission members should be consulted before decisions are made about programs and policies that involve the VCIP. Commission members identified two issues that might have been more effectively addressed by an increased consultation with the Commission – the outreach contract and the IOM contract.

In discussion by Commission members, some of the issues relating to transparency with the public overlapped with those involved with transparency within the federal structure. There was consensus that, for the benefit of Commission members who may attend meetings via teleconference and for those members of the public who listen in, posting meeting materials (agendas, PowerPoint presentations, and some handouts) on the web before the meeting convenes would be very helpful. It was noted that encouraging those who make presentations or otherwise contribute to meeting content can be challenging, given the fact that many are very busy, and there are often last minute updates to

presentation data. Nonetheless, it was suggested that deadlines be established for submission of meeting materials, as well as deadline established internally to insure that minutes and transcripts are posted to the web site in a timely manner. Minutes should be approved by the Commission before posting. It was also observed that in some cases a federal clearance process is required before information can be released.

There was an extended discussion of web site content, accessibility and ease of use. Dr. Evans explained that the ACCV web site was available through a link on the main HRSA home page (*http://www.hrsa.gov/vaccinecompensation/accv.htm).* The ACCV web site contains a brief explanation of the mission of the ACCV, the minutes and transcripts of past meetings, the charter, and a link to a listing of the roster of Commission members and staff. Commission members made several suggestions for new information on the web site – a contact person (including e-mail and telephone contact information) should be available; a "contact us" link might be an effective tool to increase access to the Commission; and the roster of members and staff could be expanded to include personal contact information. There was also a suggestion that links to other germane sites could be added (e.g., the US Court of Federal Claims page on which the stipulations are listed and explained in some detail). In the interest of ease of use, there was a suggestion that the link include a brief explanation of how to find and interpret the information on the other end of the link.

There was a suggestion that a method by which the public can submit questions and comments to the Commission should be developed, with some way to respond. Ms. Hoiberg, as chair of the Outreach Working Group, indicated she would be willing to field the questions and provide some response. The questions and comments might contribute to the development of future agendas. There was also a suggestion that a mechanism be developed to allow the public to submit questions and comments during the meetings, perhaps by e-mail.

Dr. Evans commented that the Policy Branch currently monitors comments and questions received by e-mail and the toll-free telephone number and provides responses. Ms. Hoiberg suggested that the Commission should receive a copy of that information, or perhaps a future agenda item could be crafted that would update the Commission on those e-mails and calls.

Ms. Hoiberg interjected a comment concerning her experience with a Freedom of Information Act (FOIA) inquiry. She stated that the information she received was incomplete. Dr. Evans explained that certain information is redacted (e.g., personal information that would violate an individual's privacy and proprietary information from public sources), but that in that specific case the information included the charge and methodology of the subject involved. In response to a comment that the ACCV was a federal entity and that members should be entitled to such information on the same basis as the DVIC, he explained that the individual members (even though "special federal employees") were considered members of the public and therefore subject to FOIA limitations.

Finally there was a brief discussion of creating a webcast of the meetings. However, Dr. Salmon, relying on his experience with the NVAC, explained that it was a complicated process requiring multiple cameras and a professional sound system and that it was a very expensive undertaking. He suggested that a real-time sound feed with coordinated webcast of the PowerPoint illustrations might be a more practical approach. Its success depends largely on the IT competence of the site, in this case the technicians at the Parklawn Building.

In closing discussion, Ms. Gallagher commented that challenges of transparency and open communications are directly proportional to the size of the organization, and with the federal government the challenges are significant. She suggested that a small group of the Commission members might take on the task of identifying actions that could increase transparency and visibility of ACCV proceedings. Perhaps legal counsel could be part of the process to determine which actions are legally acceptable.

Dr. Evans agreed to look into all of the suggestions and comments made during the discussion of transparency. He added that the Outreach Working Group might become more active in the process.

Finally, Commission members requested that the ACCV be kept posted on the activities of the outreach contractor, Banyan, perhaps with short briefings at the regular Commission meetings.

National Vaccine Plan Update
Ray Strikas, M.D., NVPO

Dr. Strikas discussed the national vaccine system and its relation to the National Vaccine Plan that was first published in 1994. The U.S. vaccine and immunization enterprise includes the impact of vaccines, which begins with research and development of vaccines, their licensure and subsequent manufacture, purchase and distribution to the appropriate segments of the U.S population. As the vaccines are administered their positive and negative effects are monitored, which provides the data required to continue the process. The ultimate goal is to provide a level of vaccine availability that protects the public from infectious diseases, with a resultant reduction in mortality and morbidity from those diseases, and with the lowest level of adverse effects possible. Aside from its primary mission of providing compensation to those who may be injured by vaccines, the VICP also provides important feedback of data related to adverse events to support ongoing research efforts to improve vaccines.

Dr. Strikas explained that under the original 1994 National Vaccine Plan there were four goals – to develop improved or new vaccines; enhance safety of the vaccines and of vaccination practices; inform vaccine decision making by policymakers, the public and providers; and to insure a stable and efficient supply of vaccines and support development of more effective programs to prevent disease through vaccinations. Subsequently a fifth goal was added, to support U.S. efforts to promote global programs to prevent infectious diseases in other countries.

An effort to revise and update the National Vaccine Plan has been under way for some time and In October 2008 the first draft of that plan was published. After that draft was published, further development of that draft considered 466 comments from the public, information gathered by NVAC after holding three open public meetings, and a major report by the Institute of Medicine released in December 2009. The second draft will add in the next few months information collected at the NVAC meeting in February to look at priorities. After the second draft is completed, public comment will again be solicited, and stakeholder input will be collected by an outside contractor, the Rand Corporation, which will inform the final version of the Plan. Dr. Strikas noted that the Plan currently has the five goals mentioned, 36 specific objectives and more than 140 strategies. The second draft should be released in April. Then during the summer an implementation plan will be developed, perhaps by the end of the year or shortly thereafter.

Dr. Strikas commented on the IOM's recommendations, which amplified the basic recommendation of the 2008 draft of the National Vaccine Plan. Goal One, vaccine development, should include prioritization of disease targets and vaccine research, which would be a departure from the historical ad hoc approach driven by the pharmaceutical companies and by specific NIH grant programs. In addition, the vaccine development strategy should include noninfectious diseases, such as nicotine addiction and Alzheimer's disease. Dr. Strikas noted that the NVPO is limited by its charter to vaccines that are targeted to infectious diseases.

Goal Two, vaccine safety – the IOM recommended a coordinated and prioritized agenda for vaccine safety research, which Dr. Strikas indicated was interpreted as a unified scientific agenda. Goal Three – similarly the IOM recommended an overarching national communications strategy to enhance the national understanding of the importance of the vaccine system in the U.S. Finally, goal Four – the IOM recommended assuring a stable vaccine supply, elimination or reduction of financial barriers, a more active federal role in the national health information initiative, which is funded at the state level by the American Recovery and Reinvestment Act of 2009, and a continued assessment of the current health reform legislation as it affects the National Vaccine Plan.

Dr. Strikas noted that the IOM report addressed the new fifth goal, global vaccine issues, urging support for building capacity to implement vaccine programs in low and middle income countries, and providing expertise and resources for new vaccines and infrastructure to achieve higher vaccination levels.

The NVAC has begun looking at the IOM recommendations, particularly the assessment of prioritization. The Committee is basing its deliberations on financial and technical feasibility, potential impact on health (morbidity and mortality), strategic opportunities (ability to involve stakeholders) and relevance to the public response in terms of priorities. One priority that evolved from deliberations by the DHHS agencies was the importance of public awareness of the Vaccine Injury Compensation Program, and a goal has been suggested that, by 2015, 90% of the public should be aware of the Program's existence and its basic purpose.

During discussion, Mr. Sconyers commented that the 90% goal might be a bit ambitious, considering there may be no federal programs that are that well known. He also suggested that the drafters of the goal should ask what achieving the goal would accomplish. Dr. Strikas agreed that the draft goal could be reconsidered and revised, by extending the deadline, for example. He added that there is no baseline data that his office could identify, which would offer a starting point that would be useful in the discussions.

Dr. Herr suggested that there should be a focus on the vaccine distribution system, which functioned poorly during the past flu season. He noted that even in the Vaccines for Children (VFC) Program the availability of vaccines was unreliable. Dr. Strikas agreed, but added that flu vaccines are particular challenging to reliably produce and that accounted for a significant share of the problem in supply. He added that a positive outcome of the program during the fall was the enlistment of over 120,000 potential provider participants, who were ready to administer the vaccines had they been available. That corps of providers is still available for future campaigns.

Concerning the VFC program, Dr. Strikas noted that eligible children, mainly uninsured or underinsured children, may receive even expensive vaccines. However, children who may not qualify but who are still in the lower income families may not be able to obtain such vaccines, an issue that merits consideration. Dr. Fisher added that, although the VFC program is outstanding as written, the administrators are still the states and some do a better job than others of administering the program at the state level. She added that a national infrastructure, such as outlined in the Plan, would be helpful in resolving that inequity.

Mr. Sconyers supported the notion of a coordinated research agenda, especially as it would relate to vaccine safety. Dr. Strikas agreed that such a coordinated effort at the highest federal level would be desirable. He added that research on vaccine safety relies on the surveillance systems in place, and it might be appropriate to assess the value and contributions of each. Ms. Buck supported the idea that systems, such as VAERS and CISA, should be more visible to the health care community and the public. Dr. Strikas agreed, adding that by congressional mandate the FDA is charged with having 100 million individuals under surveillance by 2012, a charge that may or may not be feasible.

Dr. Strikas concluded his comments, reiterating that the second draft should be available the first week in April, with a set of ten-year priorities listed. (NOTE, since the ACCV meeting, we have encountered multiple revision needs, and don't expect the second draft will be available until late May).

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

Dr. Gidudu reviewed the objectives of the ISO 2009 H1N1 influenza vaccine safety monitoring process – to identify clinically significant adverse events resulting from vaccination of the 2009 H1N1 vaccine in a timely manner; to immediately evaluate serious or an unusual increase in adverse events and inform public health decisions; to determine if there is a risk of Guillain Barré syndrome (GBS) associated with the H1N1 vaccine; and to communicate pertinent information to the public health community and the public in general in a clear and transparent way.

Dr. Gidudu also reviewed the various surveillance programs in place to identify public health risks related to the pandemic vaccine. The Vaccine Adverse Event Reporting System (VAERS), jointly administered by CDC and FDA, invites voluntary reporting of adverse events from any source and primarily serves as a

signal detection system. VAERS receives reports from the entire US (305 Million) The Vaccine Safety Datalink is an active surveillance system that monitors the populations of eight managed care programs covering about 9.5 million participants. A total of over 1.2 million H1N1 doses were administered during the past season. CDC and Johns Hopkins run the Real-Time Immunization Monitoring System which focuses on children, health care workers and pregnant women. The system tracked 7,000 doses, the majority of which were inactivated vaccine.

The Defense Medical Surveillance System, operated by the military, monitors safety in 1.4 million active duty personnel, and the Veterans Affairs Database covers a population of 1.2 million veterans. The Centers for Medicare and Medicaid Services (CMS) covers about 38 million through Medicare/Medicaid data reports. About 1.7 million doses were distributed to that population. The Indian Health Service monitors 1.4 million Native Americans who received over 200,000 doses. None of these surveillance systems has identified a signal related to adverse events from the H1N1 vaccination programs. The Post-Licensure Rapid Immunization Monitoring System (PRISM), is an active surveillance covering about 30 million with 17 million registries enhanced to monitor safety of the H1N1 vaccine.

Dr. Gidudu turned to detailed data from VAERS. There have been a number of recent enhancements that have improved the analysis and timeliness of data reports coming out of the data collected by VAERS. The number of VAERS reports was reasonably well correlated with the number of vaccine doses distributed during the first half of the flu season (October through December). Dr. Gidudu discussed the most recent report of adverse events from VAERS data, noting that reports were categorized by vaccine type. She noted that live attenuated vaccines comprised about a quarter of vaccines distributed to date, with inactivated vaccines comprising the rest (with a very small number of vaccines that were not specified in the VAERS reports). She described the reports under four headings – serious fatal, serious non-fatal, non-serious and GBS. The numbers were also broken down further into H1N1 and seasonal adverse events.

The breakdown showed that serious fatal adverse events reported by February 26th 2009 were less than 1%; serious non-fatal about 7%; and non-serious slightly over 90%. The GBS reports amounted to slightly over 1% and in none of the categories was a signal detected.

Dr. Gidudu also showed data by age group for adverse events in all categories. Dr. Fisher noted there were adverse events from live attenuated vaccine in the over 50 age group, adding that the vaccine is not licensed for those over 50. It was noted that a drug administered in error can be reported as an adverse event even though no actual adverse event occurs, which might have been the reason they showed up in those categories (50-64 and 65 and over). Dr. Gidudu added that the data is also automated and that entry error could be an issue.

Finally, Dr. Gidudu showed data related to adverse events which had been followed up with a chart review, including 51 verified deaths. The effort is supported by state health officers and thus far no deaths have been associated with the vaccines administered.

Asked about the definition of "signal," Dr. Gidudu explained that various methods are used to arrive at the decision of a signal. If adverse events in a particular vaccine exceed that the expected level, it is considered a signal (if the numbers exceed background rates). If that signal occurs it could be a false signal, so a more in depth analysis of data is performed to confirm if a signal exists. Ms. Buck commented that, although there may not be a population-level indication or signal related to the distribution of H1N1 vaccine, it does not mean that there are no vaccine-related injuries.

In closing, Dr. Gidudu briefly reviewed three publications. There was a discussion of H1N1 safety from licensure on in the November 24, 2009, MMWR that showed the safety profile was similar to the seasonal vaccines, in both VAERS and VSD surveillance, with no safety signals identified. A paper in the American Journal of Epidemiology looked at a study that validated the useof near real-time surveillance for selected specified adverse events following H1N1 and seasonal flu vaccinations when monitored in a system such as the VSD, where data is updated at least weekly. The last publication reviewed a recall of Haemophilus *influenzae* type b conjugate vaccine which was determined to be contaminated with

potential Bacillus . cereus bacteria. VAERS received 75 reports on the vaccine and, through enhanced surveillance, including lab-based surveillance, FDA and CDC confirmed that B. cereus was not a contaminant in any of the reports. The process demonstrated that the enhanced surveillance procedures could contribute to public health response in vaccine safety emergencies.

During discussion, Dr. Fisher commented that Europeans use adjuvanted vaccines and wondered if any signals had been generated in that population. Dr. Gidudu, noting that she was a participant in the global conversations that occur weekly, stated that no signals had been detected globally. Dr. Gruber added that the Europeans do not include live attenuated vaccine in their vaccination programs.

Finally, Dr. Gidudu noted three recent ACIP recommendations – universal annual influenza vaccine for adults 19 to 49 years of age; replacement of PCV-7 with the 13-valent pneumococcal vaccine, Prevnar; and a new contraindication for rotavirus vaccine for infants with severe combined immunodeficiency (SCID). Dr. Fisher commented that the ACIP recommendation came immediately after FDA approval, but that the ACIP review group for the vaccine had been looking at data for over two years and that there was no rush to market in that recommendation.

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

Dr. Mulach stated that she had no new information for the Commission, adding that she was involved at NIAID in some of the web site development processes and would be pleased to provide advice and counsel to DVIC staff working on the ACCV web site.

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

Dr. Gruber reported that there had been two FDA approvals of vaccines since the last ACCV meeting. The first on February 19th was approval of a meningococcal conjugate vaccine, *Menveo* manufactured by Novartis, for individuals 11 to 55 years of age, to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y and W-135. Now there are three such vaccines, the other two manufactured by Sanofi Pasteur (Menactra and MedImmune).

As previously mentioned during the meeting, Dr. Gruber confirmed the approval of Prevnar-13 for the active immunization to prevent invasive pneumococcal disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5,6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F, and for the prevention of otitis media caused by serotypes 4, 6B, 9V, 14, 18C, 19F and 23F when administered to children 6 weeks to 5 years of age. The vaccine is approved for children six weeks to five years of age, given in four spaced doses.

Finally, the Vaccines and Related Biological Products Advisory Committee (VRBPAC) met on February 22nd to consider which influenza viruses should be included in vaccines for use in the 2010-2011 influenza season in the US. The committee recommended that influenza vaccines for 2010-2011 should be trivalent and also recommended **two** strain changes:
The 2009 pandemic H1N1 vaccine strain will replace the H1N1 vaccine strain contained in the 2009-2010 seasonal vaccine. The current influenza A H3N2 vaccine strain will be replaced with a Southern hemisphere vaccine H3N2 like-virus, A/Perth/16/2009. The current Influenza B strain will be retained. The influenza vaccine compositions to be used in the 2010 - 2011 season in the US are identical to those recommended by WHO February, 2009.

Mr. Sconyers asked about the prevalence of the influenza strain A (H3N2) and Dr. Gruber confirmed that it was very low, but the H3N2 vaccine strain will be included in the seasonal flu formulation as a precaution. She added that the surveillance data mentioned before had shown that the H3N2 was a different strain than previously circulating; it is a Southern Hemisphere A/Perth strain.

Public Comment

The meeting agenda was completed ahead of time. The Commission agreed to pause until the appointed time for public comment, during which time there were a number of comments. Ms. Castro-Lewis commented that the charge to the Outreach Working Group had been expanded and that additional members might be appropriate. She volunteered to participate, as did Dr. Fisher. Ms. Gallagher suggested that the title of the working group might be expanded to "Communications and Outreach."

With regard to Dr. Gidudu's presentation, Dr. Fisher requested additional follow-up information on the serious non-fatal adverse events, specifically anaphylaxis and Guillain Barré syndrome, and more explanation regarding the apparent off label use in patients over 50. Dr. Herr noted the slight increase in adverse events in 18-19 year olds receiving the live attenuated vaccine and wondered if some explanation was available, and whether or not some data on doses actually given was available.

At the time specified in the agenda for public comment the teleconference operator confirmed that there were no members of the public on the call interested in making a comment. There was a final brief discussion about whether adjournment should be delayed to conform to the agenda time schedule for public comment. There was agreement that the public comment period is provided so that the public can comment on what has transpired during the meeting. It was noted that the practice of some committees was not to delay early adjournment, but to offer an opportunity for public comment at the end of the meeting, even if the meeting ends earlier than specified in the agenda. Dr. Evans agreed that, if the end of the meeting is not significantly early, it would be acceptable to provide an opportunity for public comment and then adjourn if no requests materialize.

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

Advisory Commission on Childhood Vaccines

March 4-5, 2010

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, J.D.
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 and Unfinished Business from Day One
Magdalena Castro-Lewis, ACCV Chair

Ms. Castro-Lewis called the meeting to order and announced that, as agreed at the end of the previous day, the public comment opportunity would be at the end of the meeting, regardless of the time of adjournment.

Update from the National Vaccine Program Office/H1N1 Safety Working Group Update
Dan Salmon, Ph.D., M.P.H., NVPO

Dr. Salmon presented a brief report on the NVAC meeting, describing several reports that were presented – a report on the National Vaccine Plan and an update by the Vaccine Safety Risk Assessment Working Group

The Vaccine Safety Risk Assessment Working Group is charged with reviewing safety data on H1N1 vaccines as it accumulates and provide comment as issues emerge. The Group, which meets every two weeks, is not concerned with the influenza disease burden or the efficacy of the vaccines. The membership consists of representatives of the five FACA groups involved in monitoring H1N1, plus a number of external members who provide specific expertise. The Group receives information for all major surveillance systems (VAERS, CMS, VSD, DoD, VA, Indian Health Service, etc.). In addition there are monitoring systems developed specifically for H1N1, such as PRISM, the Post-Licensing Rapid Immunization Safety Monitoring System. PRISM collects data from five major health plans covering eight states and New York City and from various registries, both of which provide information on actual immunizations. CDC has established a monitoring group that focuses on Guillain Barré syndrome in nine states. About once a month the Group develops a status report and submits it to the Assistant Secretary for Health and, if approved, it is posted online. Primarily the Group looks for signals or indications of issues related the H1N1 vaccines, and so far there have been none. Finally, there is a monitoring group looking at pregnancy outcomes.

Dr. Fisher commented on the value of immunization registries for children and the importance of supporting such registries for adults as well, since adults are becoming a major recipient of vaccines, and because the provision of flu vaccines is so diverse – airports, pharmacies, etc.

Dr. Salmon mentioned that NVAC has a Vaccine Safety Working Group, of which Ms. Buck is a co-chair, which recently completed its first project; a review of ISO's research agenda. The second project is to prepare a white paper on the US vaccine safety system that will try to define adverse event prevention strategies, timely detection, and a method of developing a timely safety profile for vaccines, which should enhance public confidence in vaccines. The NVAC Safety Working Group held its first open meeting in July 2009, inviting a wide variety of experts to discuss safety issues related to the National Vaccine Plan. The meeting broke into five subgroups, three content-focused and two process-focused. The content-focused groups discussed structure and governance, biological mechanisms, and surveillance. The process-focused groups looked at stakeholder engagement and implementation. The implementation subgroup considered a Rand Corporation report to try to develop ideas that would set the stage for acceptance of the Plan.

There are so many stakeholders in the vaccine area that NVAC is planning to hold small meetings to elicit recommendations in the form of white papers on specific issues and to hold a large meeting on June 1st, the day before the NVAC meets, to allow stakeholders to comment. The issues discussed will relate to the functions of the current vaccine safety system – accountability and coordination, surveillance, research licensing –and assessing key attributes of these functions, such as effectiveness, efficiency, transparency and evidence-based processes. NVAC anticipates having a report ready for release by September 2010. That deadline will make the report useful to NVAC in its work on the National Vaccine Plan.

Dr. Salmon stated that the mission of NVPO is to coordinate activities within DHHS for prevention of disease through vaccinations and reduction or prevention of adverse events as a consequence of vaccination. NVAC provides support for that mission

Asked about international aspects of the H1N1 vaccines, Dr. Salmon explained that there are biweekly meetings sponsored by the World Health Organization and coordinated in the U.S. by FDA, to provide all participating countries with data updates and signal detection. So far there have been no such signals of problems with vaccines anywhere in the world. There is an international study looking at Guillain Barré syndrome as it might relate to H1N1 vaccines that includes participants in both low- and middle-income countries. Dr. Fisher mentioned the Brighton Collaboration involving over 10,000 scientists and physicians, whose task is to devise definitions of adverse events for various vaccines – a task which she said was complex and difficult. Dr. Salmon agreed, noting that Guillain Barré syndrome is a rare event, perhaps occurring at the rate of less than one in a million vaccinations. That makes a specific definition for reporting purposes very important.

Ms. Buck commented that many of the surveillance systems were developed in response to the pandemic and she asked if the systems could be maintained in the future. Dr. Salmon commented that many of the systems were in place before the pandemic or were evolved out of systems that were pre-existent.

Dr. Salmon concluded his remarks by highlighting other topics discussed at the February NVAC meeting – an ISO update, a financing update and discussion of first dollar coverage, a report from the Adult Working Group, a description of the NVPO communications plan including approaches to coordinating communications across agencies, and an update on the vaccine stockpile, including H1N1 and seasonal flu vaccines.

ACCV Outreach Workgroup Report
Sarah Hoiberg, Chair

Ms. Hoiberg introduced the agenda item by inviting comments on the main objective to expand public awareness of the program, mainly to health professionals and the public. In a general discussion of the outreach program and the contract with the Banyan Group a number of observations were made.

The early information from the Banyan contractor indicates concurrence that providers (doctors) and parents are the main audience for the outreach effort. The actual descriptors from Banyan were: parents, parents to be, health care professionals, older adults, caretakers and others who may be vaccinated in their lifetimes. At this point Banyan is trying to find out how those who know about the program found out about it in the first place. Dr. Evans commented that the contractor would rely on the focus groups to define the best questions to ask in a broader subsequent survey, but would also be eliciting information about attitudes and perspectives.

Commission members offered a number of suggestions concerning the process – that the Workgroup would appreciate being able to review the questions to be asked during the focus groups, that the target audience might be too narrow (it is currently older adults), and that the ACCV should have a more participative role in the focus group effort. Ms. Hoiberg noted that the contractor had been responsive to the Workgroup's recommendation and sensitive to the firm belief that the project should be focused on the VICP and not on either vaccine safety or recognizing or reporting adverse events.

Mr. Sconyers questioned the wisdom of trying to educate too broad a target population. He mentioned that educating the public is an expensive process that probably needs to be focused and since most people learn on a just-in-time basis, a useful product of the Banyan effort might be to determine just how people would best learn about the VICP. He added that he felt that the education effort should be focused first on the most influential group, those who provide vaccine-related care for individuals, and then on those who may experience an adverse event.

Although there was interest in education about the causes of vaccine injury and how health care professional can recognize adverse events when they happen, as well as promoting vaccine acceptance by the public, there was general agreement that the purpose of the Banyan contract is to support an increased awareness of the VICP among the public and health care professionals. Dr. Fisher commented that awareness of the VICP could serve two purposes – first, to increase awareness that adverse events can happen with vaccination; and second, to increase the likelihood that an adverse event would be reported.

There was a brief discussion about whether the outreach is more effective as a long-term education process, where individuals absorb the message before the issue of vaccines becomes a part of their personal lives, or whether the focus should be on education at the time of the event (e.g., through more effective use of the VIS at the time of vaccination).

An analogy was drawn between the VICP and programs in other areas, such as the banking industry's FDIC program to insure personal assets held in banks. It was noted that most individuals are aware that some form of insurance is available for deposits if a banks fails, even though the details may not be clear to them. A similar analogy is homeowner's insurance. Most homeowners know it is there and become involved when there is a damaging event. Dr. Evans commented that his office had received many letters and calls over the years from congressional staff and parents stating lack of knowledge of the program, usually related to failure to file before the statute of limitations period ends. He stated that even creating a vague awareness of the VICP, like that of FDIC or homeowner's insurance, should be considered an outreach program success.

Ms. Hoiberg, recalling personal experience, stated that health care professionals may downplay the possibility that an event is related to a vaccine. A common response is that adverse events are rare, with the implication that what is happening to your child is probably not an adverse event. She added that in her case her child's neurologist recommended filing a VAERS report, and the pediatrician involved

actually filed a VAERS report without informing her of the filing. Neither discussed with her the VICP. Ms. Drew commented in support of focusing education on the medical community, noting that although lawyers have an ethical obligation to inform a vaccine-injured client about the VICP, those in the medical community do not. Awareness of the benefits of the program would enhance the likelihood that doctors would provide that information. Dr. Evans noted that VAERS sends follow-up letters to those who report an adverse event classified as "serious." These letters, which are sent at 2 months and 12 months after the VAERS report is submitted, seek the status of the injured individual and also include contact information on the VICP. However, they are sent to the reporter of the incident and often not the parent or individual who experienced the adverse event.

If the health care professionals are considered the primary target of outreach, Dr. Evans suggested it might be helpful to understand if the VICP is included in any of the medical and nursing school curricula. In the past there's been some discussion about including the VICP, VAERS and other vaccine safety information in pediatric residency training programs, and having board examination questions on these topics. Dr. Fisher added that, with the shift to more adult vaccinations internists will become a more important conduit for information about vaccines, including the VICP.

Dr. Salmon noted that CDC was responsible for most of the health-related educational messages from the federal government. As an example he mentioned a future supplement on vaccines to be published in *Pediatrics* that would provide health care professionals with information on vaccine surveillance, and the roles of FDA and NIH in vaccines. It will include an article by Dr. Evans and Kay Cook on the VICP. He added that there is legislation that requires that a vaccine information statement (VIS) be made available whenever an individual receives a vaccination. Each VIS mentions the VICP. Dr. Gidudu commented that CDC has a communications group that includes in its program an effort to inform providers about the process of filing an adverse event report.

Concerning Banyan's responsibilities to the ACCV, Dr. Evans explained that the contractor had been given a defined set of deliverables under the federal contract and that, thus far, they have been keeping the Outreach Workgroup informed. However, there is nothing in the contract that mandates a particular level of interaction with the ACCV and there are resource limitations involved. For example, there is a cost related to Banyan attending a meeting to provide an update. He assured the Commission that Banyan would be fully informed of the comments and recommendations that come out of the Commission's discussions at each meeting, and that he would encourage feedback from Banyan as the process continues. At the same time, the contract is a work-in-progress and much of the detailed information of interest will be contained in Banyan's final report, which the ACCV will receive and review later this year.

Dr. Evans noted that the contractor had been cooperative in keeping the Outreach Workgroup informed of its current efforts to develop focus groups. There had been two conference calls prior to each of the last two ACCV meeting to inform the Workgroup so that an update could be provided to the full Commission.

Election of Chair and Vice Chair

Ms. Tempfer, chair of the nominating committee, conducted the election of officers for the next term. She noted that three Commissioners had been nominated for the position of chair – Ms. Gallagher, Ms. Hoiberg, and Ms. Drew. There was a brief discussion about the number of votes required to decide the election. As specified in the Charter, a majority of those present at the meeting (including Commissioners who may be attending via teleconference) is required to establish a decision by the Commission. Ms. Saindon, as counsel to the Commission, noted that

the nominating committee's proposal had been amended to conform to the technical requirements of the Charter. On motion duly made and seconded, the Commission members present unanimously approved the conduct of the election in accordance with the report of the nominating committee for the instant election only. Following custom, each of the nominees offered a brief comment concerning her qualifications and her willingness to serve. At the conclusion of those remarks Ms. Tempfer called for a secret ballot and, after the ballot was counted, announced the results of that ballot, that Ms. Gallagher received a majority of the votes and would be Commission Chair for the next term.

In accordance with custom, Ms. Tempfer called for a secret ballot for the election of the Vice Chair, and after that ballot was counted announced that Ms. Drew received a majority of the votes and would be Vice Chair of the Commission for the next term.

Public Comment

Paul King requested an opportunity to make a public comment. He stated his opinion that vaccination programs should be cost effective, noting that the chicken pox vaccine program was an example of a program that was not cost effective. He noted that the chicken pox vaccine program was approved for administration of a single dose, but that it was currently a three-dose program. He estimated the cost of the unnecessary doses at $700 million.

Adjournment

There being no other business, on motion duly made and seconded, the meeting was adjourned by unanimous consent 11:30 a.m.

_____
Charlene Gallagher
ACCV Chair

_____
Sherry K. Drew
ACCV Vice-Chair

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

_____
Date