Advisory Commission on Childhood Vaccines (ACCV)
Meeting and Conference Call

March 7-8, 2007

Minutes

Members Present

Don L. Wilber, M.D., Chair
Marguerite E. Willner, Vice-Chair
Tawny Buck
Loren G. Cooper, J.D.
Jaime Deville, M.D.
William P. Glass, Jr., J.D., via conference call
Robin Stavola, via conference call
Jeffrey M. Sconyers, J.D.
Tamara Tempfer, R.N-C, M.S.N., P.N.P.

Ex-Officio Members Present

Marion Gruber, Ph.D. for
Norman Baylor, Ph.D., Center for Biologics and Evaluation Research, Food and Drug Administration (FDA)
Dr. John Iskander, M.D., M.P.H., Acting Co-Director, Immunization Safety Office, Centers for Disease Control and Prevention (CDC)
Barbara Mulach, Ph.D., for
Carole Heilman, Ph.D./National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH)
Dr. Kenneth Bart, M.D., M.P.H., for
Dr. Bruce Gellin, M.D. Director, National Vaccine Program Office (NVPO)

Executive Secretary

Geoffrey Evans, M.D., Director, Division of Vaccine Injury Compensation (DVIC), Healthcare Systems Bureau (HSB), Health Resources and Services Administration (HRSA)

Staff Liaison

Cheryl Lee, DVIC, HSB, HRSA

Welcome and Opening Remarks

Dr. Don Wilber convened the 65th quarterly meeting of the Advisory Commission of Childhood Vaccines (ACCV) and welcomed all participants. Since this is his last meeting as ACCV Chair, he thanked Cheryl Lee, Tamara Overby and Dr. Geoffrey Evans for coordinating the ACCV meetings and obtaining information for the ACCV. He also thanked Loren Cooper and Marguerite Willner for serving as Chairs of ACCV Workgroups. The minutes of the October 24, 2006 meeting were approved.

Report from the ACCV Futures Work Group: Marguerite E. Willner, ACCV Member

Ms. Marguerite Willner stated that the ACCV Futures Workgroup (Workgroup) was formed to create a robust agenda for every ACCV meeting. More specifically, it was formed in response to the ACCV's belief that the National Vaccine Injury Compensation Program (Program) needs to be improved and modernized and, therefore, the ACCV should hold more meetings and each meeting held should be more productive. Ms. Willner noted that, in particular, many ACCV members were interested in following up presentations made to the ACCV by petitioners' attorney, Cliff Shoemaker, and others who advocated extending the statute of limitations. Many ACCV members felt the Program should be inclusive, rather than exclusive, and its success should be measured by how many vaccine-injured people file claims in the Program and receive compensation, rather than by how many do not or cannot.

Ms. Willner reported that the Workgroup was composed of six of the nine ACCV members. Of the six, two were new members: Tawny Buck and Jeff Sconyers; and four were veteran commissioners: Dr. Don Wilber (ACCV Chair), Loren Cooper, Dr. Jaime DeVille, and Ms. Willner (ACCV Vice-Chair). She also noted that the Workgroup was careful to keep the three non-Workgroup members informed of its work.

Ms. Willner mentioned that the Workgroup members devoted a substantial amount of time and effort to create the legislative recommendations to be presented today. Not only did they review hundreds of pages of literature, they met at least three times by conference call and met in Washington for a two-day face-to-face meeting on February 5th and 6th .

On February 5th, the Workgroup invited various Program participants and stakeholders to attend a "Roundtable Discussion" during which the Workgroup solicited their views on the past, present, and future of the Program and ways to improve it.

Invited guests included: Chief Special Master Gary Golkiewicz of the U.S. Court of Federal Claims; Jackie Noyes, former ACCV chair, and Karen Hendricks of the American Academy of Pediatrics; Sarah Depres from Congressman Waxman's Congressional Oversight Committee on Government Reform; Tom Powers, a plaintiffs' attorney currently representing petitioners in the Autism Omnibus Proceeding; and Randy Moss, partner of the law firm of Wilmer Hale who has represented vaccine manufacturers. Each guest provided valuable insight, and Ms. Willner thanks each for

their participation.

On February 6th, the Workgroup deliberated privately and subsequently developed the following set of legislative recommendations which are summarized in the Workgroup Report distributed this morning. Ms. Willner noted that each recommendation received unanimous Workgroup support and was now ripe for public discussion and ACCV action. Ms. Willner then proceeded to address each of the Workgroup's twelve recommendations, solicit a ACCV and public discussion, and hold a vote.

Dr. Wilber noted that these are general recommendations and those receiving a favorable vote will be sent to the Secretary of HHS, who may then decide to ask his staff to develop specific legislative language to be sent to Congress. Dr. Wilber thanked the Workgroup for its hard work.

Ms. Stavola stated at the outset that, after consulting the attorney who filed her claim, Mr. Stanley Kops, she is in favor of Recommendations Nos. 1 through 5, 11, and 12; she's uncertain about #7; and she is not in favor of Nos. 8-10.

(IMPORTANT NOTE: See attached 3/23/07 ACCV Letter to Secretary Leavitt for specific language of each Workgroup recommendation and outcome of ACCV vote [ATTACHMENT 1].)

1. Allowing Payment of Interim Fees and Costs to Petitioners' Attorneys.

Ms. Willner said that the Workgroup felt that it is important to recommend amending the Act to provide for the payment of interim fees and costs to petitioners' attorneys because it significantly affects the quality of representation petitioners receive. She noted that when the National Childhood Vaccine Injury Act of 1986 (Act) was passed, Congress contemplated that all claims would be resolved within 8 months and, win or lose, petitioners' attorney fees and costs would be promptly paid. Today, however, most claims take years to process and require the use of expensive expert witnesses. During these years, petitioners' attorneys' go without pay. This unduly burdens both petitioners and their counsel. The Workgroup, therefore, feels it would be much more fair to petitioners and their counsel to amend the Act to provide for the payment of interim fees and costs to petitioners' attorneys after the entitlement decision is made.

The ACCV voted unanimously in favor of this recommendation.

2. Procedure for Paying Fees and Costs Solely to Petitioner's Attorney.

Ms. Willner stated that when the Program pays fees and costs to petitioners' attorneys, the check now must be made payable to both the petitioner and his attorney. While normally this is not a problem, there have been some extraordinary circumstances, such as when the petitioner cannot be located, that this requirement has unfairly prevented the attorney from being paid. Therefore, to avoid this result, the Workgroup recommends amending the Act to provide that in certain extraordinary circumstances, the special master or court may order that the award check for fees and costs be made payable solely

to the petitioner's attorney.

The ACCV voted unanimously in favor of this recommendation.

3. Increased Benefits Caps for Death and Pain and Suffering.

Ms. Willner said that the Workgroup recommends increasing the $250,000 benefit cap for death and the $250,000 benefit cap for pain and suffering to account for inflation. Both benefit caps would be retroactively increased since 1988 to account for inflation and would increase annually to account for inflation using the Consumer Price Index-All Urban Wage Earners (CPI-U) as envisioned by Congress in the original Act in 1986.

The ACCV voted unanimously in favor of this recommendation.

4. Allowing Compensation for Family Counseling Expenses and Expense of Establishing and Maintaining Guardianships, Conservatorships, or Trusts.

Ms. Willner stated that the Workgroup wanted to make sure that counseling was made available to the families of those who had suffered a vaccine injury or death. Thus, it recommends amending the Act to provide compensation for reasonable and necessary, non-reimbursable expenses that have been or will be incurred for family counseling relating to a vaccine injury or death.

Similarly, the Workgroup believes that the Program, and not petitioners, should incur the significant expenses associated with setting up legal and financial vehicles necessary for the care of a petitioner who has prevailed in a Program case. Accordingly, it recommends amending the Act to provide compensation for reasonable and necessary, non-reimbursable expenses that have been or will be incurred establishing and maintaining a guardianship, conservatorship, or trust, approved by the Court, for the benefit of a person who has suffered a vaccine-related injury.

The ACCV voted unanimously in favor of this recommendation.

5. Appointment of Adult with Vaccine-Related Injury to ACCV.

Because approximately 50% of petitions are now filed by adults on their own behalf, Ms. Willner stated that the Workgroup recommends amending the Act to permit the Secretary of HHS to appoint an adult who has personally suffered a vaccine injury to one of the two ACCV posts currently reserved under the Act for parents or legal guardians of a child who has been injured by a vaccine.

Prior to the vote, Mr. Glass suggested adding language which would also allow the Secretary to appoint the spouse of a vaccine-injured adult to one of these posts. Accordingly, the Workgroup amended the recommendation as stated in its Report to allow, but not require, the Secretary to appoint an adult who has personally suffered a vaccine-related injury, or the guardian or family member of such an adult, to one of the

two posts reserved for the legal representative of a child who has suffered a vaccine-related injury or death.

The ACCV voted unanimously in favor of this amended recommendation.

6. Clarification: A Petitioner Who Establishes a Vaccine-Related Injury and Death is Entitled to Both Death and Injury Benefits.

Ms. Willner stated that the Workgroup wishes to clarify that a petitioner who establishes a vaccine-related injury and death is entitled to both death and injury benefits under the Act as written. Ms. Willner mentioned that this issue is currently being litigated by DOJ. The Workgroup, however, believes it is unwarranted and unfair to interpret the Act in such a way as to provide the same $250,000 death benefit to someone who dies instantly after receiving a vaccine as someone who dies years after suffering a vaccine-related injury and illness.

Prior to the vote, there was a discussion in which Ms. Stavola voiced her attorney's concerns, which were allayed by Mr. Glass and Ms. Willner.

The ACCV voted unanimously in favor of this recommendation.

7. Parent Petitions for Compensation.

Ms. Willner stated that the Workgroup believes that Program should be made available to parents and other third parties with vaccine-related damage claims. The Workgroup, therefore, recommends amending the Act to require a parent or other third party to file a petition in the Program before filing or maintaining a civil action against the vaccine manufacturer or administrator in state or federal court for damages, including claims for loss of consortium, society companionship or services, loss of earnings, medical and other expenses and emotional distress. This recommendation was premised upon on the Workgroup's belief that third party claimants would have a better chance of receiving compensation in the Program than in the tort system.

Prior to the vote, Ms. Stavola stated her opposition to the portion of the recommendation which requires a parent or other third party to file a petition with the Program before filing a civil suit.

The ACCV voted 8 to 1 in favor of this recommendation.

8. Clarification of Definition of Manufacturer.

Ms. Willner reported that the Workgroup recommends clarifying the definition of manufacturer by enlarging the current definition to include any corporation, organization, or institution whether public or private that manufactures, imports, processes or distributes any component or ingredient of any vaccine on the Vaccine Injury Table (Table). She added that this clarification would provide liability protection under the

Program to manufacturers of thimerosal or any other ingredient in a licensed vaccine listed on the Table.

Prior to the vote, a discussion ensued during which Ms. Willner and Ms. Cooper explained that this, along with the following two recommendations, were the Workgroup's adaptation of certain provisions in the Frist Bill. They are interrelated and purport to accomplish the same thing, that is, to eliminate collateral litigation surrounding the issue of whether the Program should capture claims alleging that a single ingredient or component of a vaccine caused an injury or death. In other words, it opens the Program to this type of claim.

Ms. Cooper noted that if this kind of recommendation is not made, manufacturers may not be able to procure the components needed to make vaccines. Ms. Willner noted that, as a practical matter, this recommendation simply codifies what is in practice today, as evidenced by the Autism Omnibus Proceeding, where the Program has been made available to claims that Thimerosal causes autism.

Mr. Glass stated that he would vote "no" out of deference to certain parents group who opposed the Frist Bill.

The ACCV voted 7 to 2 in favor of this recommendation.

9. Clarification of Definition of Vaccine-Related Injury or Death.

The Workgroup recommends that the definition of vaccine-related injury or death be clarified so that a component or ingredient approved for use in a Table vaccine by the FDA is not to be considered an adulterant or contaminant for purposes of the Act.

Prior to the vote, a discussion ensued. Ms. Willner and Mr. Sconyers reiterated that the idea behind this recommendation is to make the Program more accessible to those with component-injury claims. In other words, as long as a vaccine listed on the Table has been made according to its FDA product license, then any claim that an ingredient or component caused an injury or death is covered by the Program, as it cannot be considered an adulterant or contaminant. On the other hand, the Program would not cover an ingredient or component that the FDA has not approved in the product license.

Ms. Cooper further explained that when the FDA approves a vaccine, it looks at different things, including all of the ingredients that go into the vaccine. So if there is an ingredient or component that has been approved by the FDA, by definition that can't be considered an adulterant or a contaminant. Therefore, if the injury is alleged to have been a result of that component, then it doesn't fall outside the scope of a vaccine-related injury.

Dr. Gruber stated that the proposed wording in italics includes any component or ingredient listed in a vaccine's product license application or product label. Product license application is a regulatory term. The terms, "active ingredient, inactive

ingredient, component, byproduct, and residual," have certain definitions. The ACCV needs to be sure that it is using the appropriate terms.

Mr. Sconyers stated that the Workgroup intended to present an idea, not develop the definitive legislative language. The idea is that a component that is part of the approved formulation can't be an adulterant. Dr. Evans stated that, if the Secretary wants to develop this suggestion into a legislative proposal, the Department would certainly ask the FDA for its views and any necessary language would be incorporated.

Again Ms. Willner noted that ever since the Leroy decision, the vaccine court has held that allegations of injury from vaccine components or ingredients must go through the Program. So, as a practical matter, this recommendation simply codifies an existing practice.

Mr. Glass stated that he does not want to vote "no" to this recommendation, but he doesn't fully understand it and couldn't explain it to somebody. He then offered a motion to table this recommendation until the next meeting. His motion was not seconded.

The ACCV voted 7 to 2 (1 no; 1 abstention) in favor of this recommendation.

10. Add Definition of Vaccine.

The Workgroup recommends adding a definition of vaccine to the Act. The Act does not now define "vaccine," and the Workgroup felt that adding one consistent with its other definitional clarifications for "manufacturer" and "vaccine-related injury or death" has merit. Here again, we wanted to define vaccine in such a way that ingredients or components are not adulterants or contaminants for purposes of the Act.

Prior to the vote, Mr. Glass stated that he thinks that defining vaccine is out the ACCV's purview, and that the ACCV should just recommend to the Secretary there is a need for a definition of "vaccine." Mr. Sconyers asked Mr. Glass if he would like to offer a motion that the ACCV advise the Secretary to adopt a definition of vaccine that is consistent with the other provisions of the Act. Mr. Glass agreed with this suggestion. Ms. Willner stated the ACCV would ask the Secretary to add a definition of vaccine to the Act that includes all components and ingredients listed in the vaccine product license application and product label. Mr. Glass offered a motion to substitute Ms. Willner's suggestion for the definition above.

The ACCV voted 8 to1 in favor of this amended recommendation.

11. Extending the Statute of Limitations (SOL) for an Injury.

As the Workgroup's primary goal was to expand access to the Program, Ms. Willner emphasized that extending the statute of limitations (SOL) was the most important issue it faced. The Workgroup carefully studied this issue and agreed to recommend that the current 3-year SOL be extended to 8 years to correspond to the 8 years of retroactive

coverage currently provided under the Act when a new injury or vaccine is added to the Table.

For vaccine-related injuries, the SOL would be extended from three to eight years, but the Program would be the exclusive remedy for anyone who files a claim during the extended 5-year period. In other words, anyone who files a petition during the extended period cannot "opt out" to file a civil action. However, the opt-out remains available to anyone who files within the current 3-year SOL. The Workgroup recognized that those who failed to timely file under the current SOL, cannot opt out anyway – so they give up nothing for the benefit of having 5 additional years to file a claim.

Prior to the vote, Mr. Glass asked for some explanation of this provision. Mr. Sconyers replied that the Workgroup has proposed that the SOL be extended from its current three years to eight years, which matches the look-back period when either vaccines or injuries are added to the Table, but that for the additional 5-year period, the remedies under the VICP be exclusive (i.e., no opt-out for this period).

Mr. Glass noted that this provision would benefit parents because it opens the Program up to those parents with claims that do not meet the current SOL. He stated that he didn't like that the Program would be the exclusive remedy for the 5-year period. Mr. Sconyers stated that this recommendation reflects a range of views on the Workgroup, and is a compromise. It probably isn't exactly what any one member of the Workgroup would have designed from the start.

Ms. Buck stated that she had the same concerns as Mr. Glass about the opt-out, but that she wanted to reiterate what Mr. Sconyers just said. It is a reflection of a compromise. Ms. Stavola asked Tawny to explain what she meant by stating that it was a compromise. Ms. Buck replied that she would like to see the SOL extended without the Program being the exclusive remedy. Some of us thought that the SOL should be extended to the age of majority, while others didn't think that it should be extended at all. So, the Workgroup wanted to come up with a compromise that is better than what we have now.

Ms. Willner agreed, telling Mr. Glass and Ms. Stavola that "It is better than nothing. If our goal is to improve access, it does that, period."

The ACCV voted unanimously in favor of this recommendation.

12. <u>Extending the SOL for a Death.</u>

For vaccine-related deaths, the Workgroup recommends extending the SOL from 2 to 8 years following the death, with the Program being the exclusive remedy during the extended 6-year period. In other words, those who file during the extended period cannot opt out of the Program to file suit in civil court. Also, the SOL would be extended from 4 to 8 years after the first symptom of the vaccine injury from which the death occurred, with the VICP being the exclusive remedy for years 4 through 8. Again, these proposed extensions would benefit those now barred from filing claims with the Program, or in

civil court, because they have missed the Program's SOL.

Prior to the vote, Ms. Buck stated that she would like to see a more generous SOL, but this provision provides better access than what parents have now. It gives more people access to the VICP, so it is a good compromise.

The ACCV voted unanimously in favor of this recommendation.

Discussion of VICP Outreach Activities: Tamara Overby, MBA, Chief, Policy Analysis Branch, DVIC

Ms. Overby stated that she is making this presentation because the ACCV Workgroup has requested wanted information about the outreach efforts of the National Vaccine Injury Compensation Program (VICP). She discussed the VICP outreach activities in 2006 and plans for 2007.

In 2004, DVIC began the process of developing outreach materials. Before that time, there were not any brochures or booklets that described or gave information about the VICP in a succinct and easy to understand way. From 2004 to 2006, DVIC worked on developing documents which were easier for the public to understand than previously used materials. In 2004, DVIC awarded a contract to the Media Network, a communications company, to test the draft VICP materials with various populations. They tested the materials with parents, attorneys and health care providers, both English- and Spanish-speaking, to determine if the materials conveyed the intended messages.

As a result of this 2-year project, in February 2006, DVIC published the VICP brochure and booklet in English and Spanish. The brochure is intended to provide an overview of the VICP, whereas the booklet is intended to provide in-depth information in a question and answer format about the VICP. There have been 800 booklets in English, 900 brochures in English, 65 booklets in Spanish, and about 38 brochures in Spanish have been distributed by the HRSA Information Center.

In 2006, the VICP website was extensively revised to make the language easier for the public to understand. Before the revisions, the text of the website consisted of language from the legislation which created the VICP. This legislative language is hard for the average person to understand. The website was also reformatted to make it more user-friendly. Individuals can send DVIC questions by clicking on the "Ask HRSA" box, and responses are sent to them via the website. The website address changed to www.hrsa.gov/vaccinecompensation.

In terms of other outreach activities, DOJ has taken on sole responsibility for these efforts exhibiting at medical and legal conferences. In 2005, HRSA changed its policy on programs attending outside professional gatherings. Last year, DOJ exhibited at the National Academy of Physicians Assistants Conference, the Texas Bar Association Conference, and the American Academy of Pediatrics Conference.

Another effort includes the use of Vaccine Information Statements, which contain contact information about the VICP, and are distributed by the Centers for Disease Control and Prevention (CDC). This is one of the primary ways that parents and individuals receive information about the VICP.

Regarding future outreach strategies, DVIC and DOJ will continue the 2006 efforts. DVIC plans to develop press releases any time a new vaccine or injury is added to the VICP. The meningococcal vaccine was added to the VICP effective February 1. Once the Federal Register notice is published announcing that this vaccine has been added to the VICP, HRSA will issue a press release. A press release will also be released announcing that the 2-year filing deadline of July 1, 2007, is approaching for flu claims alleging injuries up to 8 years prior to the July 1, 2005, effective date of VICP coverage.

On another front, DVIC plans to proactively seek speaking engagements at annual conferences of legal and medical organizations. In the past, staff have spoken at the National Immunization Conference, the American Bar Association, and the National Bar Association. DVIC will continue efforts to publish information about the VICP in the AARP newsletter.

DVIC will pursue cost effective and efficient ways of distributing the VICP brochure and booklets. DOJ plans to continue to exhibit at professional meetings. In 2007, DOJ will exhibit at the Western Institute of Nursing, the American Academy of Nurse Practitioners, the American Bar Association, the California Bar Association and the American Academy of Nursing conferences. DVIC may also exhibit this year because HRSA appears to be revising its attendance at outside meetings policy. DVIC is open to any suggestions that ACCV members have and is always looking for creative and cost efficient ways to do outreach.

Dr. Deville asked if DVIC has ever exhibited at the American Academy of Pediatrics (AAP) and the Society of Pediatric Research (SPR) meetings. Dr. Evans replied that the AAP has probably been one of the most frequent meeting locations over the years, particularly in the 1990's. Dr. Deville asked if DVIC could explore getting in to a long term relationship with the AAP, so that the VICP has a presence at those meetings. If HRSA does change its policies in the future and funding is available, DVIC would certainly pursue participating in the AAP annual conference, rather than the more specialized pediatric research meetings.

Dr. Deville asked whether DVIC and DOJ participate only as an exhibitor or also presents updates about the VICP in presentations when exhibiting at meetings. Exhibits are often overlooked. Dr. Evans replied most of the time DVIC and DOJ are exhibitors. This is also an opportunity for the pediatric staff to receive continuing medical education credit and network. In the early '90s, Dr. Evans stated that he was an invited speaker at the "Meet the Red Book" session, which was a wonderful way to get information about the VICP to the pediatric community. This meeting usually has thousands of attendees and is a good forum for information exchange. In terms of speaking engagements, there

has been interest and efforts on our part to be invited to speak about the VICP. The American Academy of Family Physicians has been a difficult entry for the VICP, but will keep trying. It is tough to get in the plenary sessions, but it is easier to be invited to speak at workshop sessions. Of course, the audience attendance is much more limited. Dr. Evans stated that a list of organizations where DVIC has spoken can be provided to the ACCV.

Dr. Deville asked if DVIC could explore ways of getting into partnerships, perhaps with AAP, to mail the VICP brochures to pediatricians' offices, since a low number of them have been distributed, especially the Spanish version. Dr. Evans replied that DVIC will check with several organizations to determine their policies for distributing materials to their members between now and the next meeting.

Mr. Sconyers asked DVIC to describe the change in HRSA's exhibiting policy. Ms. Overby stated before 2005, bureaus within HRSA had their own exhibiting budgets and determined which conferences they would attend. Sometimes, the bureaus within HRSA were exhibiting at the same meeting. Therefore, HRSA's leadership decided to centralize exhibiting activities, including the budgets, for better use of resources. Instead of two bureaus going separately to these conferences, HRSA would exhibit as one entity. The leadership would determine which meetings the bureaus were allowed to go to. Therefore, the number of meetings for exhibiting was reduced from about 100 to ten, and the ten were not meetings attended by VICP's target audiences.

Mr. Sconyers stated that the VICP should find ways to attend more meetings, both legal and pediatric, because knowledge of the program is limited. It would be better for people who have been injured and potentially able to file a claim to know more about the VICP. Ms. Overby agreed and acknowledged that DVIC needs to be conducting more outreach activities on a regular basis. However, if HRSA's policy doesn't change, DVIC still has to find ways to get the word out. DVIC is definitely trying to think of creative and cost efficient ways to promote the availability of the VICP.

Mr. Sconyers asked about the audience for the VICP booklets and brochures. Ms. Overby replied that the booklets and brochures were designed for parents, health care providers who administer vaccines, and attorneys. Mr. Sconyers questioned DVIC's expectations about distributing these materials to patients, anyone receiving the vaccine, or any pediatrician who is treating a patient with signs of vaccine-related injury. Dr. Evans responded the Vaccine Information Statements (VIS's) are a superb mechanism for publicizing the availability of the VICP, at least in theory. By law, they should be given every time a covered vaccine is administered. Then, if more information about the VICP is needed, the patient could contact the VICP using the information on the VIS and the brochure or booklet would be sent to them at that time.

Mr. Sconyers asked how did people come to receive the brochure or booklet. Ms. Overby replied that people who have received the brochure or booklet have found out about the VICP and the HRSA Information Center sent the materials to them. DVIC is not sure of their source of information. Ms. Buck stated that it would be interesting to

know how they heard about the VICP. Presentations should be made to parent groups, at schools, to school nurses, and people who are dealing with kids and their shots.

Ms. Cooper suggested that DVIC could request national organizations to distribute the materials to their networks. One organization would be the American Public Health Association. She stated that the members are concerned that there is not enough awareness about the VICP and that there may be certain populations that are being underserved at this point. Having these materials available at clinics or wherever parents are showing up could be very helpful. Mass mailings don't work, but working with national organizations may be a more cost effective way to do it. Dr. Iskander suggested that another more targeted group would be the Association of Immunization Managers. Each state has an adverse event reporting coordinator.

Dr. Evans said that these are wonderful ideas, and DVIC is will contact these organizations. It is a immense challenge to get children and adults immunized. Sometimes people promoting immunization are not oriented to thinking about vaccine safety and liability. They are trying to convince people of the importance of vaccines, and it presents a dilemma for them, in terms of how one conveys both of these kinds of messages.

Dr. Deville said that he agrees and DVIC must reach the healthcare providers. He stated that for example, in the last two months, he has seen two patients after they received the MMR (measles-mumps-rubella) vaccine. One patient developed encephalitis which was probably associated with the mumps component of the vaccine, and the other one had arthritis probably from the rubella component of the vaccine. In both cases, he spoke with the pediatricians who referred these patients, and these doctors had no idea about the VICP. They were completely unaware of it. Ms. Stavola suggested placing the brochure on the AAP website under professional education and resources. Dr. Wilber responded that he has significant experience with AAP and that they would be very willing to participate in making it available nationally.

Ms. Overby stated that a few years ago, DVIC staff looked into how healthcare providers could earn continuing education credits learning about the VICP. It was much more involved than first thought. Dr. Iskander stated that Vaccine Adverse Event Reporting System (VAERS) has struggled with these same issues. VAERS has published several continuing education articles and has reached health professionals in this manner. The process has become more difficult over the years, but it is not an impossible. He suggested that this information could be made available through the CDC information line, so that they can either refer calls to the VICP or be able to provide information about the VICP. He asked Ms. Overby if there was any attempt to develop a message or core messages or develop a scientifically or evidence-based framework for doing outreach. VAERS has taken very similar approaches to what DVIC has done. Ms. Overby rephrased his question for clarification and stated that DVIC would like to develop an overall communication strategy, but does not have expertise in-house, and would like to award a contract to do this initiative. However, currently DVIC does not have the money to do so.

Dr. Evans stated that it was his understanding that reporters of serious events to VAERS are advised of the availability of the VICP in the initial follow-up at two months, as well as the 12-month letter. This is another way that the public is made aware of the VICP.

Dr. Iskander stated that there is always the issue of wanting to keep VAERS and the VICP as separate systems to avoid misunderstandings and to try to limit the frustration of people who think they are accessing both systems by accessing one. However, the two programs still could use some of the same types of outreach forums. There probably are messages that can be developed that would appeal to different audiences, specifically tag lines that could raise awareness of the VICP. He stated that he experienced a lot of these challenges at VAERS over the years.

VAERS was able to commission a nationally representative survey of providers to obtain quantitative information of overall levels of knowledge and the risk factors for knowing about the system (i.e., which providers are more likely to know about it). According to the survey, pediatric providers had much better knowledge of VAERS than adult providers. This type of survey,which takes some resources to complete, can be used to help determine how to best direct resources, such as which conferences to attend. He stated that he was not citing VAERS as a model or success story, but is sharing experiences that will hopefully benefit both programs.

Ms. Tempfer stated that so many health care providers rely heavily on the Internet for information. Medscape, a part of WebMD, offers ontinuing education unit credit programs all the time. They are always looking for new programs to put on their site. Dr. Deville suggested sending a letter to the pediatric organizations asking them to add a vaccine safety session to their meetings.

Dr. Wilber asked for public comments and there were not any comments.

After the discussion, Dr. Wilber stated to Mr. Paul Glass that we had notification of your father's passing, and as a representative of this committee, just let me convey the thoughts and prayers from all the committee members as well as the staff. Mr. Glass thanked Dr. Wilber and stated that several people called with prayers and thoughts, and he appreciated everybody's concern.

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

Dr. Evans welcomed everyone to the 65th quarterly meeting of the Advisory Commission on Childhood Vaccines (ACCV). He pointed out the new covers for the ACCV Meeting Book and that it is symbolic of the work of Cheryl Lee and Tamara Overby. He stated that there are several standout pictures on the cover, such as the little girl and boy that are in the second to the right vertical column, Jenna and Joshua, who are Jean Suthard's children, and Elijah Overby, Tamara’s son, who is in the second column from the left

towards the bottom. For phone messages, the conference control center phone number is 301-443-2585, and the conference center's fax is 301-443-2559. If you need any materials photocopied, please see Cheryl in the back.

Dr. Evans stated that following his presentation on the DVIC, the agenda items for today's meeting include: an update from the Department of Justice by Mark Rogers, and a presentation on the Vaccine Adverse Event Reporting System, including the requirements for the reporting of adverse events by Dr. Ann McMahon. In addition, our ex officio members will be providing updates -- Dr. Kenneth Bart from the National Vaccine Program Office, Dr. John Iskander from the Immunization Safety Office at the CDC, Dr. Barbara Mulach from the National Institute of Allergy and Infectious Diseases, NIH, and Dr. Marion Gruber from the Center for Biologics Evaluation and Research, FDA.

In your blue folders, there are several documents. On the right side is the obituary notice for Mr. William Paul Glass. Dr. Evans shared his condolences for the recent passing of Mr. Glass's father. On the left side are four articles. The first reconfirms the original CDC recommendation after reviewing the safety data on rotavirus vaccine, which was introduced in February 2006. There are articles on safety issues also under Tab G in the meeting book. The second article is entitled, "Merck to Stop Pushing to Require Shots", and the third and fourth articles are to be read in conjunction with Dr. McMahon's presentation on the VAERS later this morning.

He presented the statistics for the VICP under Tab D in the meeting book. Under claims filed, the significant trends are that autism claims have dropped and continue to do so. In terms of non-autism claims, the VICP has been receiving an average of about 140 to 160 over the past several years. So far this Fiscal Year, 58 claims have been filed and if it keeps on this pace, about 180 claims will be filed by the end year's end. This potential increase is not surprising because influenza vaccines were added to the VICP effective July 1, 2005, and claims for this vaccine are now starting to be filed. This vaccine is given to many more people than other routine childhood vaccines.

By adding influenza vaccine, the VICP covers a third more of the vaccines that are distributed in the U.S. Now, the VICP covers 95 to 96 percent of vaccines distributed. In terms of awards, the average is $58 million for petitioners' awards and $4 million for attorneys' fees and costs per year. The balance of the Vaccine Injury Compensation Trust Fund (Trust Fund) is between $2.4 and $2.5 billion. It is increasing at the rate of over $200 million per year and will continue to increase, especially since the flu vaccine has been added to the VICP and the amount of doses of this vaccine distributed and administered continues to increase. He expects that if 110 to 120 million doses of flu vaccine are given per year, which is the target, then Trust Fund revenue and interest will probably approach $300 million against average outlays of $58 or $60 million per year.

He stated that on December 20, 2006, the President signed into law the "Tax Relief and Health Care Act of 2006," which added meningococcal and human papillomavirus (HPV) vaccines to the VICP, by imposing a 75 cent excise tax on each dose that is administered.

The effective date of that excise tax is February 1, 2007. As a reminder, in order for a vaccine to be covered by the VICP, an excise tax must be imposed and the CDC must recommend the vaccine for routine administration to children evidenced by publication in the Morbidity and Mortality Weekly Reports (MMWR).

In the case of meningococcal vaccines, and there are two types of vaccines: the polysaccharide vaccine and the more recently licensed conjugate vaccine for young children. The routine use recommendation was published in the Morbidity and Mortality Weekly Report in May 2005. With the imposition of the excise tax, meningococcal vaccines are officially covered as of the effective date of February 1.

In terms of the HPV vaccine, Dr. Iskander stated that the routine use recommendation for HPV would be published on March 12. Once that is done, both prerequisites will have been met. The Secretary will publish a notice of coverage in the Federal Register notifying the public of this new addition to the Vaccine Injury Table (Table). Once the notice is published, it is listed in the last box of the Table. All newly-added vaccines are included in this last box until a final rule is published. Only after publishing a notice of proposed rulemaking, a 180-day public comment period, and publishing a final rule, will the new vaccine have a separate and distinct listing on the table, including the listing of any injuries or conditions found to be associated with the vaccine.

Once a vaccine or injury is added to the Table, there is eight years of retroactive coverage based on the effective date of coverage. Individuals have two years to file these claims, in addition to the regular statute of limitations.

For HPV, claims going back eight years would be for injuries sustained during clinical trials. Individuals participating in clinical trials for covered vaccines are able to file claims with the VICP, assuming they have not received compensation for their injuries previously. However, the VICP has never had a claim for injuries sustained during clinical trials. Now, the VICP covers 16 vaccines.

In other legislative news, on February 17, Representatives Dave Weldon and Carolyn Maloney reintroduced a bill entitled the "Mercury Free Vaccines Act of 2007." The bill requires that influenza shots given to children under age three and pregnant women contain no more than one microgram of mercury, beginning with the 2007-2008 influenza season. In addition, this bill requires that all other routinely administered childhood vaccines contain no more than one microgram of mercury by July 1. A copy of this bill is in Tab E3, and the "Tax Relief and Health Care Act of 2006" is in Tab E2.

In terms of meetings, in October 25, Dr. Indira Jevaji, a DVIC pediatric medical officer, attended the Advisory Committee Immunization Practices (ACIP) meeting in Atlanta. Of note, the ACIP recommended the use of Zostavax, a vaccine recently licensed by FDA for prevention of herpes zoster in older adults. This vaccine is recommended for individuals that are 60 or older. Because it is not recommended for routine use in children, this vaccine will not be covered by the VICP. In addition, Dr. Jevaji attended the ACIP meeting a few weeks ago. During that session, in addition to updates on

vaccines and thimerosal, there were updates on VAERS reports of intussusception following use of the new rotavirus vaccine, and of GBS after meningococcal conjugate vaccine. Information about two of these topics are under Tab G in the meeting book.

In addition, ACIP appears to be getting closer to expanding the immunization recommendation for influenza vaccine beyond five years of age, up to 18. The ACIP did not vote to do so, but keeps discussing it. There are some members of the ACIP who would like to have universal use of influenza vaccine and that would certainly increase excise tax revenues considerably. Since more companies are producing the vaccine now, and this is something that will probably happen.

Dr. Wilber asked if adults who receive the flu vaccine are covered by the VICP, even though one of the two prerequisites for adding a vaccine to the VICP is that it be recommended for routine administration to children. Dr. Evans replied that anyone of any age who received a VICP covered vaccine can file a claim.

Finally, in terms of points of contact, individuals can write the National Vaccine Injury Compensation Program at 5600 Fishers Lane, Parklawn Building, Room 11C-26, Rockville, Maryland 20857. The HRSA Information Center number is 1-800-338-2382. The VICP website address is www.hrsa.gov/vaccinecompensation. HRSA has done an excellent job of making the website much more user friendly, and there is a great deal of current information about the VICP on it. As the VICP changes, new information is added.

Lastly, in terms of public comment, anyone who would like to formally participate in ACCV meetings should contact Ms. Cheryl Lee. Notices are published in the Federal Register notifying the public of the meetings.

Mr. Sconyers stated that the ACCV received a letter from the Secretary thanking us for the recommendation that there be a periodic scientific review of the Vaccine Injury Table, and that a scientific panel be established for that purpose. He inquired about the status and whether there been such a panel established. Dr. Evans replied that a panel has not been established. Traditionally, the Institute of Medicine has been the body that has performed these studies, and would probably be one of the first choices for the Department to do further studies. To re-study the Table and all the vaccines that have been added since the Table was last studied, probably would cost about $2.5 to $3 million. DVIC does not have this amount of money in the budget. At this point in time, this is probably the most significant unmet need of the VICP.

Mr. Sconyers stated that updating the Table on a regular basis and on the basis of good science is crucial. The ACCV would like to support the program's efforts to request funding.

Another item from the prior minutes was that DVIC would provide the ACCV with a report of the compensable and non-compensable cases and time frames for adjudication of claims. Ms. Lee replied that she sent Mr. Sconyers these statistics to the Workgroup.

Mr. Sconyers responded that he would like these statistics to be a part of the regular statistics report. He stated that from Fiscal Year 1999 and beyond, the rate at which non-autism cases are filed and the rate at which they are adjudicated are different. Basically, the adjudication rate is not keeping pace with the filing. He would like to know how the VICP can improve the rate at which cases are resolved. He stated that he thinks claimants experience long delays, and it isn't good for the credibility of the VICP. Dr. Evans responded that in 1999, DVIC received 300 hepatitis B claims because the retrospective deadline was approaching in the summer of that year. The Court has not been to adjudicate these cases because of the lack of information about conditions allegedly related to hepatitis B vaccine. The Court has grouped these claims by the injuries alleged and is now just starting the adjudication process. DVIC understands the point of trying to increase the efficiency of the process. Over the years, DVIC has reported that, on average, it takes two to three years to adjudicate a claim. These hepatitis B claims will extend this average. The claims that can proceed are adjudicated in a fairly efficient manner. Mr. Sconyers said that at the June meeting that he would like to discuss which claims are delayed and why.

Report from the Department of Justice: Mark Rogers, Deputy Director, Torts Branch, Civil Division, Department of Justice

Staffing and Hiring

Deputy Director Mark Rogers returned from active duty in the Marine Corps, and gave the presentation for the Office of Vaccine Litigation, Department of Justice (DOJ). Since October, 2006, DOJ has hired two new attorneys, Vo Johnson, in attendance, and Robin Broderick. They are replacing two attorneys who have left DOJ. DOJ is hiring one more attorney.

Litigation

Mr. Rogers anticipates an increase in DOJ's workload based on two factors: 1) autism litigation will begin in earnest in June, and, 2) an expected increase in influenza claims because the statute of repose will expire in July, 2007 (as of July 1, 2005, trivalent influenza vaccines were added to the Table), which is two years after the flu vaccine was added to the Vaccine Injury Table.

All cases

The data is consistent with a steady state of approximately 200 petitions being filed annually; that number excludes autism petitions. Since the last meeting, and for this first part of the fiscal year, 69 cases were resolved. Of those, 32 cases were compensated. Of those, 25 cases were settled. Mr. Rogers explained that settlement means that the parties agreed upon a resolution, alternative to litigation. Crediting the Office of Special Masters, as well as counsel for petitioners and respondent, Mr. Rogers highlighted the benefits of settlement as an alternative to litigation. There were seven entitlement decisions for the petitioner; three of those were death cases where the respondent

conceded the case. Thirty seven cases were dismissed; seven of those were for procedural reasons, including jurisdiction. The statute of limitations is a leading basis for those dismissals, as are cases alleging a vaccine that is not listed on the Table. Four cases were withdrawn; one was non-autism while the other three alleged autism. There were 26 decisions where the Special Master found that causation had not been established. Of those, only eight involved a hearing. Mr. Rogers explained that, in many cases, petitioners do not request a hearing. In other words, petitioners request that the case be decided on the record without a hearing.

Mr. Rogers offered historical data spanning the last five years to show that the computed average adjudication time of a case is 1,026 days, which translates to approximately 2.8 years for an average case to be resolved in the Program. The median adjudication time, which removes outlying cases, is 2.2 years, which signals that there are more outliers at the long end of the cases. Mr. Rogers opined that the outliers consist of hepatitis B claims that are currently being resolved. The hepatitis B claims were initially filed as a group two years after hepatitis B was added to the Table, under the two year statute of repose. The claims, which are now six-seven years old, were essentially dormant until very recently. Mr. Rogers noted a lack of capacity in the Office of Special Masters and within the Program to process such a voluminous surge in filings. The claims are finally being processed, which accounts for the skewed statistics.

Mr. Rogers also presented statistics reflecting average case adjudication time for 2000 through 2005. For 2000, average adjudication time was 2,437 days, which captured the very end of the retrospective cases, cases where the vaccine was administered from the beginning of the Act through history. Because of the large volume of claims filed, those claims took nearly ten years to process. For 2001, average adjudication was 1,195 days; for 2002, average case adjudication took 970 days; 2003, it was 1,005; for 2004, it was 1,006; and for year 2005, it was 1,033. Mr. Rogers acknowledged that the time period is climbing and emphasized DOJ's desire to process claims faster. Citing to the hepatitis B claims currently being processed, Mr. Rogers suggested that the median may represent a more significant statistic. According to DOJ's computation, the average award is $961,000 per case.

Autism

There are approximately 4,750 claims pending in the Autism Omnibus Proceeding; approximately 300 have been resolved by dismissal or withdrawal. Two additional Special Masters have been appointed to oversee the proceedings along with Special Master Hastings: Special Master Campbell-Smith and Special Master Vowell. Mr. Rogers expressed his current understanding of the proceedings. The first trial is scheduled to begin in June. The first trial will comprise the first of the three component causation theories proposed by petitioners. The Special Masters have decided that all three special masters will hear the evidence of the first causation theory in the context of one "test" case, Cedillo, with Special Master Hastings issuing his decision on that petition. The first theory, in essence, is that thimerosal containing vaccines in combination with the MMR vaccine causes autism spectrum disorder.

Over the next three months, Special Masters Vowell and Campbell-Smith will each take another representative single case, and hear the evidence specific to that case. Thus, there will be three trials on petitioners' first theory of causation. The goal is to have three decisions by the three Special Masters, then proceed through the appeals process, if appropriate. Mr. Rogers' understanding of the strategy is to develop case precedent, known as *stare decisis*, which would provide the parties with some knowledge into how the cases should proceed. Mr. Rogers did not know whether or not the Special Masters would issue their decisions simultaneously; presently, Mr. Rogers was aware that they intended to review the evidence as to their respective fact patterns, then render a decision. As for future trials, Mr. Rogers understood that the three Special Masters would convene three similar hearings for each of the petitioners' next two theories of entitlement. Petitioners' Steering Committee filed their expert opinions in Cedillo on February 20, 2007, and the government's were due on April 24, 2007.

Hepatitis B vaccine

Regarding the hepatitis B litigation, Mr. Rogers advised that there were approximately 400 cases, which, in large part, comprise the 700 total cases that are in backlog. He reiterated that these cases are currently being decided. While he hopes that these cases will be resolved by the end of the calendar year, Mr. Rogers considered that prediction somewhat optimistic. Mr. Rogers explained that those cases were divided into eight subgroups according to particular injuries alleged. Some representative groups include demyelinating disorders, GBS, and CIDP, which have largely been resolved. As a representative group, sixty-six cases comprise the neurodevelopmental cases. Of that group, seven have been resolved. One was resolved in favor of the petitioners, while five were dismissed, and one settled. Thus, thirty-seven claims remain active; the Special Master has started to take evidence and convene status conferences. Twenty-two claims are still waiting for processing at this point.

Appeals

There is one case before the Supreme Court on a writ of certiorari. In the Program, where a party loses before the Federal Circuit Court of Appeals (Federal Circuit), the party may petition the Supreme Court for review. The petition for writ of certiorari was filed by petitioners in the case of Pafford v. HHS. There, the Federal Circuit upheld a Special Master's determination that petitioners had not proven causation. The key issue involved evidence of another cause.

At the Federal Circuit, two cases, both appealed by petitioners, are pending: Walther v. HHS and Marks v. HHS. In Walther, the Special Master held that petitioner's medical expert was not credible and the Court of Federal Claims affirmed. Oral arguments were held on November 8, 2007, and the decision is pending. In the Marks case, the Special Master held that petitioner's claim was not supported by medical records or opinion. The Court of Federal Claims affirmed. That appeal was filed last month.

Three cases were decided by the Federal Circuit since the last ACCV report: Aull v. HHS, Wiley v. HHS, and Markovich v. HHS. Of these, all three were appeals filed by petitioners. In Aull, the Federal Circuit affirmed the Special Masters' dismissal of a vaccine petition because petitioner had pending a simultaneous state civil action against the vaccine manufacturer or vaccine administrator for a vaccine-related injury. Under the Vaccine Act, a party cannot maintain those simultaneous actions. In the Wiley case, the Federal Circuit affirmed a Special Master's dismissal of a time-barred case – a case filed too late under the Vaccine Act. The Markovich case also involved the interpretation of the Vaccine Act's three year statute of limitations.

The Federal Circuit issued a published decision affirming the Special Master's dismissal of the petition. The key issue was when the three-year (or 36 month) limitations period starts to run under the Vaccine Act. The Special Master held that the limitations period begins with the first sign or symptom of manifestation of onset of a condition, regardless of whether it is recognized as a sign or symptom of an injury at that time. Petitioners argued that the first sign or symptom of manifestation of onset means something that is manifest, i.e., something that is understood to be a sign or symptom of a vaccine injury. The Special Master and Court of Federal Claims rejected petitioners' argument, the Federal Circuit affirmed, holding that the standard is objective, not subjective.

At the Court of Federal Claims level, Mr. Rogers reported that there are five cases pending. All five petitions for review were filed by petitioners and dispute a finding of no causation. In other words, petitioners disagree with a Special Master's decision. Four cases were decided by the Court of Federal Claims since the last ACCV report. In emphasizing that these appeals were filed by petitioners, Mr. Rogers explained that respondent only seeks appeal under criteria where it is important in advancing Program goals. In Sauer v. HHS, petitioners voluntarily dismissed their case; thereafter, they discovered additional evidence and requested that the Special Master re-open the case.

The Special Master found that petitioners' claims were untimely. On appeal, the Court of Federal Claims reversed, and stated that the petitioners claim should be re-opened. In the remaining three cases, the Court of Federal Claims ruled for the respondent. In Avera v. HHS, the Court declined to adopt a "forum rule" (Washington, DC hourly rates) argument or allow the payment of interim attorneys' fees, which the Court found to be unavailable under the Vaccine Act. In Way v. HHS, the Court of Federal Claims upheld a Special Master's dismissal of a petition for failure to prove causation. In Smith v. HHS, the Court of Federal Claims upheld a Special Master's dismissal of a petition as time-barred.

Civil Litigation

Mr. Rogers reported on a decision issued in the Rivard v. AHIP case, which was filed outside of the Program, in the Superior Court of New Jersey. Mr. Rogers summarized that petitioners filed a claim in state court alleging that the oral polio vaccine contained a monkey virus, SV-40, and that the monkey virus caused a brain tumor in their child. The defendant argued that plaintiffs' claim should have been filed in the Vaccine Program.

Plaintiffs maintained that their claim belonged in state court because the monkey virus was a contaminant that should not have been in the vaccine and could have been eliminated had the defendants exercised due diligence in manufacturing the vaccine. The trial court agreed with the plaintiffs' arguments. The appellate court reversed on appeal and ruled consistent with defendant manufacturers that the case should have been filed in the Vaccine Program first. In short, the appellate court held that the monkey virus was a normal component incidental to the manufacturing process. It was not intentionally added to adulterate or to contaminate the vaccine. Mr. Rogers offered his view that the Rivard ruling takes the thimerosal cases a step further, and reflects a tendency by civil courts to find that these cases are properly before the Vaccine Program.

Overview of the Vaccine Adverse Event Reporting System and the Requirements for Reporting of Adverse Events: Dr. Ann McMahon, M.D. M.S., Division of Epidemiology, Center of Biologics Evaluation and Research, Office of Biostatistics and Epidemiology, Food and Drug Administration (FDA)

Dr. Ann McMahon provided an overview of the Vaccine Adverse Event Reporting System (VAERS). Post-licensure safety surveillance is necessary because pre-licensure trials have limitations, such as the size and duration of the clinical trials, and the population in these trials which may be limited by age, co-morbidity or severity of various conditions. There are often exclusions in the pre-licensure trials; and therefore, certain subpopulations are not included in the clinical trials.

VAERS was established as one of the changes made to the U.S. vaccine safety infrastructure in the National Childhood Vaccine Injury Act of 1986 (Act). It was established in 1990. It is a passive surveillance system operated collaboratively by the CDC and FDA. Reports to VAERS are submitted by health professionals, vaccine manufacturers and the public.

What are some of the strengths of VAERS? VAERS detects rare adverse events. It has a large surveillance area, the United States, and in some instances, international surveillance. The data are often available in a timely fashion. This tool can be used for hypothesis generation which is generally the way that it is used at the FDA and CDC.

VAERS also has its weaknesses. VAERS is often missing data or has inaccurate data. There is underreporting to VAERS. Accuracy rates are not known. VAERS is better at detecting events that occur in close time proximity with vaccination, than events with long latency periods. There is a lack of an accurate denominator or number of people that are vaccinated. There is also a lack of a control group. All of these weaknesses result in the near inability to assess causality.

The serious adverse events reported to VAERS, as defined by 21 CFR 600.80, are death, life threatening events, initial hospitalization or prolongation of hospitalization, events with significant or persistent disability/incapacity, congenital anomalies or birth defects, and medical events that may require intervention to prevent one of those from occurring.

What are the reporting requirements to VAERS? In 21 CFR 600.80, the requirements for vaccine manufacturers are the following. Licensed manufacturers with approved Biologics License Applications (BLAs) are required to report serious and unexpected adverse events regardless of presumed causation from U.S. and foreign sources. Unexpected means if it is not included in the product's label. Other adverse events are also required to be reported if they occur in the U.S. Adverse events from studies, where there is a reasonable possibility that the adverse event was caused by the product, are also required to be reported. When must adverse events be reported by the manufacturers of biologic products? A 15-day alert reports are required for both serious and unexpected adverse events, and quarterly for three years after licensure, and then annually for other adverse events.

What events are required to be reported to VAERS by health care providers? The Act requires that health care providers report any event listed in the manufacturer's package insert as a contraindication to further doses of the vaccine, and any event in the reportable events table that occurs within the specified time period after immunization.

What is the efficiency of reporting to VAERS? There were two different manuscripts published on this subject several years ago. They were done using different tools. "The Reporting Sensitivities of Two Passive Surveillance Systems for Vaccine Adverse Events" paper by Steven Rosenthal, M.D., M.P.H. and Robert Chen, M.D., M.A. in the American Journal of Public Health, December 1995 compared the rate of reporting of various adverse events after various vaccines in VAERS divided by a denominator, which is described in the paper. Then, they compared that rate with rates published in the literature of these adverse events that were associated with one or another vaccine. They came up with a reporting efficiency number for these various adverse events.

For example, they found that vaccine associated polio after oral poliovirus vaccine had a reporting efficiency of 68 percent, which is relatively high, whereas rash after measles-mumps-rubella vaccine had a reporting efficiency of less than one percent. Generally, the observation could be made that the more severe the vaccine associated event is, then the higher the reporting efficiency. However, this observation is clouded by issues, such as whether there is stimulated reporting by other events that are occurring during this period of time. For example, publicity may have been given to one event and one vaccine more so than another.

Another paper looked at reporting efficiency in a slightly different way. The "Enhancing Vaccine Safety Surveillance: A Capture-Recapture Analysis of Intussusception after Rotavirus Vaccination" by Thomas Verstraeten paper in the American Journal of Epidemiology in 2001 looked at intussusception after vaccination with the rotavirus vaccine (trade name: Rotashield). This study looked at the number of cases reported to VAERS and compared to the number of cases that were found in clinical trials that had been ongoing during the same period of time. They found that the VAERS reporting efficiency was 47 percent for intussusception after Rotashield.

How does the FDA use VAERS? There are a number of quantitative methods for signal detection in a system such as VAERS. Several that are used frequently in the Vaccine Safety Branch at the FDA are the following: 1. Comparison of reporting rates to VAERS with background rates. Reporting rates are derived from number of adverse events reported to VAERS and some estimate of the number of persons vaccinated. Background rates are commonly derived from reports in the literature, but other methods are also used, such as querying health maintenance organization databases. 2. The FDA also uses "data mining" to identify adverse events reported to VAERS more commonly after one product than after others. It is important to be aware in applying any of these quantitative methods that the results can be impacted by reporting artifact or biases in reporting. In addition, it is important always to use medical knowledge and independent confirmation of results of quantitative methods."

So data mining is a term that is often used in this context to refer to identifying events reported more commonly for one product as compared to another product. So using a database with numerators, such as VAERS which does not have denominators, what can be done to quantify proportionality? There are different ways of doing data mining. Proportional reporting ratios and empirical Bayesian geometric means are methods used by FDA. Medical knowledge and review of the reports after the numbers are generated is usually necessary.

Other than those means, how does the FDA generate hypotheses in VAERS? There are a wide range of possibilities. For example, only one case could be used if it is a positive-rechallenge case, or a case where someone had an adverse event after one dose of vaccine and had the same adverse event after a second dose of vaccine. This might be very compelling, and it might generate a hypothesis. Or there may be a clustering of adverse events occurring eight to 12 days after vaccination. When looking at clusters of adverse events, background rates must be considered because some adverse events may be extremely common, such as depression, versus adverse events that are quite rare, like aplastic anemia.

It is important to consider the health impact of an adverse event, both the severity of the event and the number of people impacted, in determining a public health response. Additionally, it is important to consider both potential costs and benefits of any public health intervention. The interventions that might be considered if appropriate are: updating the package insert, sending a “Dear Doctor Letter” or public health advisory; presenting at professional meetings; publishing peer-reviewed articles; designing and implementing a risk management program; and rarely, withdrawing the product. Dr. McMahon thanked Dr. Robert Ball and Dr. Miles Braun for their help with the presentation, and asked if anyone had questions.

Mr. Sconyers had questions about how is VAERS publicized to likely reporters, such as pediatricians, how do they know about VAERS, and how do they know that they have a requirement to report certain things. Dr. McMahon replied that information about VAERS is sometimes publicized in journals. Dr. John Iskander replied that there are a variety of strategies that are used annually. “Dear Doctor Letters” can contain VIS with

information about VAERS. Information about VAERS can be exhibited at meetings. Certain resources that are very commonly used by pediatricians, for example, the American Academy of Pediatrics Red Book (Red Book) contain a sample VAERS form and contains information about adverse event reporting. All of the ACIP statements now contain standard language and recommendations about adverse event reporting. Again, VAERS is certainly amenable to constructive suggestions about new and different and innovative ways of promoting reporting.

Dr. Evans replied that there is an entity called the Reportable Events Table (RET), which probably confuses more than helps some people. If you look at the back of the Red Book, it combines both the Vaccine Injury Table (Table), as well as the RET. The VAERS RET is very similar to the VICP Table, but has slightly different time intervals based on the Act. It is a reminder that anything that is on the RET must be reported to the VAERS. It also includes those events that are in the Contraindication section of the package inserts. Also, more recently, the harmonized schedule that is published in the January edition of *Pediatrics* and family practice journals now has a footnote which reminds practitioners that any clinically significant events that occur after any vaccines should be reported to VAERS. Hopefully, this may have boosted the awareness of practitioners of the importance of getting reports to VAERS.

Mr. Sconyers asked whether any of the FDA adverse event responses have occurred. Dr. McMahon replied these responses have been implemented at various times. The peer reviewed publications of VAERS and adverse events are done all the time. Presentations at professional meetings are also done all the time. "Dear Doctor Letters" are done when required. Package insert label are reviewed regularly, and changed as needed. Dr. Gruber replied that last year, FDA updated the package insert for the Menatra (a meningococcal vaccine) to include the Guillain Barre Syndrome reporting.

Mr. Glass wanted to know whether health care providers required to report and if unexpected events required to be reported by them. Dr. McMahon replied that the rule about serious and unexpected events is in 21 CFR 600.80, and refers to the manufacturers. But unexpected events, that is, events that are not in the label, are not required to be reported by health professionals. Mr. Glass questioned the reasoning for that, or the benefit of not reporting them? Dr. Evans replied that health care providers are required to report events listed in the contraindications section of the manufacturer's package insert and events on the reportable events table. There is not any punitive action if they don't report these events, but by law they are required to be report them. Language was added, and it appears in all the footnotes of the Reportable Events Table, sometimes bolded and underlined, that anything that is clinically significant that occurs after any vaccine should be reported, whether by a parent or a physician. However, passive reporting systems, historically, suffer from underreporting, despite best efforts.

Dr. Iskander replied that FDA/CDC have never quantified it precisely. In fact, most of the events reported to VAERS are voluntary rather than mandatory reporting. Ms. Buck inquired about how does VAERS identify who made a report, whether it is a manufacturer or a member of the public. Dr. McMahon replied that who filed that report

is on the reporting form.

Update from the National Vaccine Program Office: Dr. Kenneth Bart, M.D., M.P.H., National Vaccine Program Office

Dr. Bart stated that on April 10-11, the National Vaccine Program Office and the four agencies that are responsible for vaccine safety -- NIH, HRSA, CDC, and FDA -- are planning a vaccine safety evaluation meeting focusing on post-marketing safety surveillance. It will be announced in the Federal Register and is a public meeting. The purpose of the meeting is to discuss the ideal vaccine safety evaluation system. The meeting will focus on vaccine safety methodologies, what we can do to improve, and how we can enhance the vaccine safety evaluation process. This is a follow-up to a meeting which occurred in the year 2000 for pre-marketing surveillance. This meeting was sponsored by FDA, and examined what is done prior to the formal licensing of a vaccine to demonstrate the accumulation of data on safety of a vaccine.

The meeting will look at strengths and limitations of each agency's vaccine safety monitoring tools. International speakers, the European Regulatory Agency, countries, such as the U.K. and Denmark, that have large and in some cases country-wide databases accessible to them have been invited. Interested is focused on the strengths and limitations of these systems. These systems and ongoing research will be systematically reviewed over the two days of the meeting.

Invitations have been sent to ACCV members. Please come to the meeting and invite interested others to attend as well. If you are going to make a presentation, you should inform the organizers in advance, so that time is made available for your presentation. Register on-line because of the security procedures on the NIH campus.

Agenda Item: Update on the Immunization Safety Office (ISO), Centers for Disease Control and Prevention (CDC): Dr. John Iskander, M.D., M.P.H., Acting Co-Director, ISO, CDC

Dr. Iskander stated that Dr. Robert Davis, who has addressed the committee previously, has accepted a position with Georgia Kaiser Permanente effective March 12. As of February 26, Kristin Pope and Dr. Iskander are serving as acting co-directors of the Immunization Safety Office, CDC. Dr. Iskander provided a brief background about himself. He has worked in vaccine safety at CDC for the past seven years and has served as project officer and team leader for VAERS, and most recently was Associate Director for Science. Kristin Pope is a senior policy analyst who has worked at CDC since 2000, and has worked with immunization safety since 2003 on a variety of challenging policy and management issues.

ISO research agenda development, as outlined by Dr. Davis at the last ACCV meeting,

will be proceeding. An external scientific consultant panel will meet in Atlanta May 10-11. Their recommendations will be only one of several inputs that will be considered in drafting a research agenda. The National Vaccine Advisory Committee (NVAC) will be involved in the latter stages of the research agenda development process. In February 2007, a progress update was presented to the NVAC, and there were several constructive suggestions that ISO will consider implementing.

The Advisory Committee on Immunization Practices (ACIP) met in February. This was a relatively short meeting, and at the same time, a meeting with a great deal of safety related content presented. A joint ISO and National Center for Immunization and Respiratory Disease analysis was presented which indicated that the risk of intussusception after vaccination with Rotateq was not elevated in either the seven- or 21-day period following vaccination. Using the Vaccine Safety Datalink (VSD), no cases of intussusception have been detected after about 28,000 doses were given. This implies that the risk with Rotateq, if there is a risk, is less than that seen with Rotashield. The open question is whether there might be a risk on the order of one in 100,000 or even rarer, which will take ongoing analyses and accumulation of dose experience to determine. Details of this analysis are posted at www.cdc.gov/nip/acip, and will also be published in a forthcoming MMWR (www.cdc.gov/mmwr).

Additional safety issues discussed at the ACIP included an update on Guillain-Barre Syndrome following the meningococcal conjugate (Menactra) vaccine. Post-licensure safety summaries of Tdap and zoster vaccines and a status report on the VSD's autism case control study were discussed. Medimmune presented safety data on FluMist, the nasal spray influenza vaccine, which indicated that children between one and five years of age with prior history of wheezing or asthma may be at risk to wheeze again following Flumist. Published data from VAERS previously indicated that wheezing episodes reported following Flumist were associated with previous wheezing. Currently, Flumist is licensed only for healthy 5 to 49-year-olds. However, Medimmune is interested in expanding use to children under age five and has a BLA pending with FDA.

Dr. Iskander reported that both he and Melinda Wharton will be presenting on behalf of CDC at the NVPO post-marketing surveillance meeting in April.

A safety update on human papillomavirus (HPV) vaccine was provided at the ACIP meeting as well. To date, reporting to VAERS has been very vigorous, which we expect for a vaccine which is both new and of a novel type, and perhaps being given by providers who are not as experienced as pediatric providers with giving vaccines. Relatively, few serious adverse events have been reported to date. There has been discussion about syncope (fainting) following vaccination, but this seems to be an issue of vaccination in general, especially vaccination of adolescents of both genders. There doesn't seem to be anything disproportional about these episodes happening after HPV. Media attention has focused primarily on concerns about mandates. About 18 states are considering legislation regarding mandates.

Dr. Deville asked about the kinds of adverse events have been reported, particularly in

the older adolescents, after Tdap vaccine has been given. Dr. Iskander replied that the overall safety profile looks quite favorable with local and systemic reactions of a self-limited nature, comprising up to 90 to 99 percent of the reports. The issues which came to ISO's attention were administration errors, product mix-ups because of Tdap, DTaP, TD, and variety of vaccines that can be said or abbreviated in similar ways with similar packaging. None of those have resulted in any serious clinical outcomes, but it is an issue involving both immunization program administration and vaccine safety. About five percent of the reports have involved fainting or near fainting episodes, without documented serious outcomes (such as intracranial bleeding) having occurred.

Dr. Deville asked if Dr. Iskander has seen a significant amount of arm swelling in the adolescents receiving Tdap. Dr. Iskander replied that whole limb swelling has been observed with booster doses of DTaP given to children getting their pre-school shots, which sounds quite frightening, but in practice resolves spontaneously and is very difficult to study because parents rarely even bring their children in for medical attention when this happens. It has also been observed with a variety of vaccines, including Td, (tetanus and diphtheria toxoids), and hepatitis B vaccines. CDC's Clinical Immunization Safety Assessment (CISA) Centers have undertaken a couple of studies to determine the pathophysiology of this. So far, there have been a variety of theories and no clear cause has been found, and the continued observation has been that these reactions seem to occur following a variety of vaccines. They peak in their clinical presentation within about 48 hours, and they resolve spontaneously, and do not have ongoing sequelae.

Dr. Deville asked about those cases where adolescents have been given the DTaP vaccine accidentally, and if there is a higher incidence of adverse events. Dr. Iskander replied that this issue as been looked at preliminarily. To date, the information doesn't suggest that those vaccine mix-ups have resulted in any serious consequences. The concern is that people exposed to the higher diphtheria toxoid content in DTaP, especially people vaccinated more recently with diphtheria toxoid containing vaccines, might be more at risk for serious local reactions.

There have been now some post licensure observational studies that have been done--one in Canada and one in New Hampshire--which looked at intervals between diphtheria toxoid containing vaccines as short as 18 months to two years. It doesn't appear that there is any increased risk of serious local reactions with these shorter intervals. This suggests that using Tdap for a pertussis outbreak could be a reasonable strategy to pursue, where the potential benefits of a vaccine are more apparent.

Dr. Wilber explained the difference between DTaP and Tdap vaccines. DTaP is given to children and Tdap is given to adults and adolescents. Dr. Iskander stated that on the vaccine schedule, "D" indicates a higher diphtheria toxoid content. The "d" indicates that there is less diphtheria toxoid content. Menactra contains diphtheria toxoid, not as an immunizing antigen, but as a carrier protein, and it is a "D". There has been is a lot of concern about different schedules of vaccines containing diphtheria, tetanus and acellular pertussis.

Dr. Deville asked about problems being reported in children receiving a fourth dose of Hepatitis B even though it is recommended that they get only three doses of vaccine. They get the first dose at birth, and then, they could potentially get their second, third and fourth doses with the Pediarix, which is a vaccine containing Diphtheria and Tetanus Toxoids, Acellular Pertussis, Hepatitis B and Inactivated Poliovirus Vaccine for children. Dr. Iskander responded that the ISO is aware of this concern. He said that he is not aware of any analyses done by VAERS looking specifically at the fourth dose given and that fourth dose would fall within what is allowed under the general recommendations on immunization. It may be that with a newer combination vaccine many providers move to a schedule or change products so a fourth dose would be eliminated. Dr. McMahon replied that Soju Chang, who works with VAERS, has been looking at something related to this issue.

Dr. Evans stated that Rotateq, a rotavirus vaccine, has been licensed for a year, and the VICP has not received a claim alleging injuries from this vaccine yet, although some may be filed soon with cases of intussusception being reported through VAERS. On the Vaccine Injury Table, there are two boxes that contain rotavirus vaccine. Box XI contains the general category of rotavirus vaccine with no condition specified. Rotateq is covered under this category. Box XII contains the live, oral, rhesus-based rotavirus vaccine (trade name: Rotasheild) with the injury of intussusception, which is no longer in effect because Rotashield withdrew its vaccine from the market in 1999. In the near future, the VICP may publish a technical change notice to remove Box XII, and then, only the general category of rotavirus vaccine will remain on the Table. The VICP will certainly look at ongoing data being gathered and make a decision about whether there is any proven evidence of a relationship between Rotateq and intussusception. With Rotateq, there is no presumption of causation at this point.

Update on National Institute of Allergies and Infectious Diseases: Dr. Barbara Mulach, Ph.D., National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health

Dr. Babara Mulach stated that in December 2006, scientists as the Vaccine Research Center (VRC) within NIAID began a small Phase I study of an H5N1 avian influenza DNA vaccine. This clinical trial will enroll 45 volunteers between the ages of 18 and 60. Unlike conventional flu vaccines, which are developed by growing the influenza virus in eggs and then administered as a weakened or killed form of the virus, DNA-based vaccines contain only portions of the influenza virus' genetic material. This vaccine is aimed at newer clade II strains of the H5N1 virus that currently pose a threat in Indonesia. To read the full press release, please visit: http://www.nih.gov/news/pr/jan2007/niaid-02.htm.

The National Children's Study has issued a request for proposals to award contracts to up to 20 new study centers. This study seeks to examine the effects of environmental influences on human health and development by enrolling a representative sample of more than 100,000 infants from across the United States and following them from before birth until age 21. The study is led by a consortium of federal agencies: the U.S.

Department of Health and Human Services—including the National Institute of Child Health and Human Development (NICHD) and the National Institute of Environmental Health Sciences at the NIH, and the Centers for Disease Control and Prevention—and the Environmental Protection Agency. The National Children's Study has received an appropriation of $69 million from Congress for fiscal year 2007 to support the implementation of the study. Detailed information on the National Children's Study is available at http://www.nationalchildrensstudy.gov.

The following are new NIAID publications- 1) *NIAID Biodefense Research for CDC Category A Agents-2006 Progress Report* is now available in hard copy or on the NIAID web site; 2) *The Jordan Report: Accelerated Development of Vaccines 2007* will be available soon (Spring 2007). Hard copies of this report (as well as the web link) will be made available to the ACCV when the document is completed.

Dr. Deville asked about the status of the DNA-based avian flu vaccine research and kinds of immunogenicity seen in preliminary avian flu studies. Dr. Mulach replied that the Vaccine Research Center (VRC) has been doing several different products with their DNA platform. So far, in animal studies, the VRC has seen immunogenicity and safety. But with the avian flu, there is the added complication of not really knowing what an avian influenza clade II vaccine might draw in immune response. In animal studies, it has shown promise. The VRC is really trying to see whether a DNA vaccine strategy can be used, then it will be fairly easy to change what is put into the DNA vaccine. This will make it very versatile in terms of the evolution and the changing of the strains that are actually circulating.

Dr. Deville stated the concern with this approach will be the same concern that resulted in the failure of the HIV vaccine which was that responses are extremely weak. Dr. Mulach responded that the VRC is investigating the use of prime boost strategies with their DNA vaccines. There are a lot of strategies that can be used and this is just a first indication of what it is might be possible. With the avian flu vaccines, it has been difficult to get a strong immune responses to begin with, so there may be multiple strategies that are examined in the future. Currently, the VRC is focusing on a very limited population for safety and initial immune response. Dr. Deville asked about the number of people involved in the study. Dr. Mulach replied that 50 people are involved in the study so far.

Dr. Wilber asked about the clade. Dr. Mulach responded that clade is the different strain of influenza that is circulating. Dr. Wilber asked is it H5N1 also. Dr. Mulach replied it is H5N1, but it is called clade II which is what people are concerned about now. In Indonesia, the clade II's are circulating. The concern is with clade I vaccines that were made a couple of years ago because the further away you get from what is circulating, then, there is going to be less of an immune response.

NIH and HHS are looking at multiple types of avian flu vaccines to determine what works the best. It may be ultimately that there is some mixture, but it is important to understand the different clade vaccines.

Update on Food and Drug Administration Vaccine Activities: Dr. Marion Gruber, Ph.D., Center for Biologics and Evaluation Research, Food and Drug Administration (FDA)

Dr. Gruber stated that on January 25, 2007, the FDA's Vaccines and Related Biologics Product Advisory Committee (VRBPAC) met to discuss whether the data that were submitted to the biologics license application (BLA) for Pentacel, a new combination vaccine that includes diphtheria, tetanus, acellular pertussis, inactivated polio and haemophilus influenza type b antigens, would support the safety and the effectiveness of this product in the indicated population. The proposed indication is for prevention of diphtheria, tetanus, pertussis, poliomyelitis and invasive disease caused by *Haemophilus influenza* type B, in infants and children six weeks through six years of age.

FDA noted in its presentation to VRBPAC that the response to pertactin (one of the pertussis antigens present in the vaccine) was statistically inferior following Pentacel relative to the control DTaP vaccine and the response to the Hib component showed inconsistent results derived from 2 clinical studies performed. In its discussions, the committee took into consideration data from Canadian post-marketing experiences with the product. The committee voted in favor of the safety of Pentacel. While the committee voted that the data were adequate to support the efficacy of Pentacel, some members expressed concern regarding the efficacy of the Hib and pertussis component. Members suggested post-licensure evaluation of the effectiveness of the Hib and pertussis components of Pentacel.

Dr. Gruber stated that it is her understanding that if this vaccine is licensed, there will be an ACIP workgroup that will further review the safety and immunogenicity data of this vaccine to develop recommendations to update the recommended childhood immunization schedule.

On February 27, 2007, the VRBPAC met to make recommendations on the safety and effectiveness of an H5N1 inactivated influenza vaccine manufactured by sanofi pasteur and to have discussions on clinical development of influenza vaccines for pre-pandemic uses. The BLA for the H5N1 A/Vietnam/1203/2004 vaccine, an influenza virus with pandemic potential and manufactured by sanofi pasteur, is the first U.S. license application for a vaccine against H5N1 influenza virus strain. This vaccine, if licensed, will be the first vaccine available against H5N1 strain in the interim until other influenza vaccines against H5N1 are developed and licensed. VRBPAC recommended approval of this vaccine for use during a pandemic or in situations of high risk exposure.

On February 28, 2007, VRBPAC considered which influenza viruses should be included in vaccines for use in the 2007-2008 influenza season. Based on surveillance data, responses to current vaccines and availability of strains, VRBPAC recommended trivalent influenza vaccines, consisting of three different types - two influenza A types and one B type. There will be a strain change regarding the H1N1 subtype A, the H3N2 subtype A will stay the same, and the B-like virus will also stay the same compared to the 2006-2007 season. These recommendations for influenza vaccine composition to be used

in the upcoming 2007-2008 season in the U.S. are identical to those recommended by the World Health Organization when they met February 14, 2007. Dr. Gruber stated that she tried to get information on the projected amounts of influenza vaccine doses that will be available, but data were not available to her.

There are several BLAs under review, namely those for Pentacel and the H5N1 influenza vaccine. FDA also has a BLA for Flumist, a live attenuated influenza virus vaccine currently indicated for use in persons five to 49 years. Medimmune seeks to extend the currently licensed age indication to the pediatric population (i.e., children less than five years). The FDA also has a BLA for a live attenuated smallpox vaccine for immunization of persons who are at risk for smallpox infection.

Dr. Wilber asked about when FDA will make a decision about the BLA for expanding the use of Flumist to a broader pediatric population. Dr. Gruber replied the BLA is currently under review, and the FDA has certain time lines that have to be met. So if approved, it would happen in early summer. However, the availability of this vaccine for the coming season is not known. With Flumist, there are also still issues under discussion. Dr. Iskander mentioned wheezing after receipt of this vaccine. Therefore, the data have to be further analyzed to determine the age range for use of this vaccine. Dr. Iskander stated that wheezing is a very common condition in young children, but that has to be balanced against the fact that the efficacy and effectiveness of this vaccine in young children appear to be very, very good, and would potentially be an improvement over inactivated vaccines. This is going to be another risk versus benefit calculation.

Dr. Evans stated that any pandemic vaccine will be a monovalent vaccine. According to the excise tax language that Congress passed in 2004, only trivalent influenza vaccines are covered by the VICP. Therefore, the avian influenza vaccines that Drs. Barbara Mulach and Marion Gruber discussed for the stockpile, or for general distribution if there ever should be an emergency, would not be vaccines covered by the VICP unless Congress were to expand the excise tax language.

Dr. Wilber asked if VRBPAC was reviewing data about the serologic markers which did not meet non-inferiority criteria for the Hib and pertussis components for Pentacel. Dr. Gruber responded that for Pentacel, efficacy is inferred by determining the adequacy of pre-defined immune endpoints. The antibody response to the Hib components showed inconsistent results derived from 2 clinical studies performed. For the Hib antigen, there is a correlated of protection. Even though two different clinical trials gave inconsistent results based on statistically predefined criteria, in both cases the antibody response was above what is considered protective. For the pertussis antigen, no correlate of protection has been established. The response to pertactin, one of the pertussis components present in the vaccine, was statistically inferior following Pentacel relative to the control DTaP vaccine.

Dr. Deville asked another question about the Pentacel vaccine. He stated that for years, there have been attempts to mix the acellular pertussis vaccine with Hib, and for the most part these have failed. How is this vaccine different? Which antigen of pertussis doesn't

show similar titers to the one in the licensed vaccine? Dr. Gruber replied there are different pertussis components in various licensed vaccines. They are all different. In this case, there are several pertussis components included in Pentacel, and one of them is pertactin, and the antibody response to the pertactin component was statistically inferior. Dr. Deville stated that it is believed to be the most protective antigen by many. Dr. Gruber responded that she thinks opinions differ on this issue. Some people believe it is really the pertussis toxin component which is the most protective component. However, she stated that Dr. Deville raised important issues that the FDA is grappling with in terms of reviewing this data. There has been an issue when the Hib vaccine is mixed with other antigens because there has been suppression in the immune response to the Hib components, which is why some companies do not develop these Hib combination vaccines. It is difficult to know why the immune response of the Hib component is the way it turned out to be in the clinical trials.

Dr. Deville stated that there are two issues. One is the *Haemophilus influenza* disease, which for the most part eliminated from of this country. If we introduce a vaccine that is not as immunogenic, that might create a problem, especially with travelers to other parts of the world. These children might not be as protected. Dr. Gruber replied that the FDA is currently discussing this concern. This is an issue that was raised at the VRBPAC meeting. Also, an ACIP workgroup is going to be formed to analyze this issue. One consideration is to conduct post-marketing studies in the US to determine the efficacy of the Hib component to see if there has been a surge in Hib disease. However, it might not be feasible to do these studies given the low incidence of Hib disease currently in the United States.

Dr. Iskander stated that what would make such studies difficult would be the greater than 99 percent reduction in Hib disease in the U.S. The other factor that would make it potentially difficult is that there is a lot of non-type *Haemophilus* disease based on data from 2007 the National Immunization Conference. Non-typable is a type. Non-typed means it is *Haemophilus,* but the category that it fits into is not known. According to the data, 70 percent of isolates across the country are not typed at all. There are eight active surveillance sites, but even if data from all sites were combined it is uncertain whether an increase of disease, if indeed occurring, would be detected.

Dr. Deville asked for an update on the status of the pneumococcal vaccine and the herpes simplex vaccine. Dr. Gruber replied that she could not provide an update on these vaccines because of the confidentiality issues. Mr. Sconyers asked whether there have been Canadian studies on the effectiveness of Pentacel and specifically on the pertussis effectiveness. Dr. Gruber replied, that post-marketing surveillance is ongoing in Canada. That data was presented at that VRBPAC meeting and it was reassuring. However, there is the question of the comparability of the subject population, the geographic areas, the density of population in Canada versus the United States. There are questions of whether one can apply the Canadian experience to the United States.

Mr. Sconyers asked about what does the Flumist protect against and how does it account for seasonal variation. Dr. Gruber responded that it will have the same seasonal influenza

strains as those in the inactivated vaccine.

Selection of ACCV Chair and Vice Chair: Dr. Don Wilber, M.D.

Tawny Buck nominated Jeff Sconyers to be the ACCV Chair and Dr. Jaime Deville to be Vice Chair. Mr. William Paul Glass seconded both nominations. Dr. Wilber called for a vote and the ACCV unanimously supported these nominations. Dr. Evans thanked the three retiring members, Loren Cooper, Marguerite Willner and Dr. Wilber, for their service and informed them that they would be receiving certificates in the mail from the Secretary of Health and Human Services.

Public Comment: Dr. Wilber

There were not any comments from the public.

Future Agenda Items: Dr. Wilber

Dr. Wilber asked about future agenda items. Mr. Sconyers replied that the ACCV Workgroup did a lot of work and did set aside several issues for discussion in the future. They include vaccine safety, questions about access of minorities and underserved groups to the VICP, and effectiveness of outreach programs. Therefore, he suggested that a subsequent workgroup be formed, an include one of the new members.

ATTACHMENT 1

Don L. Wilber, M.D.
Oklahoma City Clinic
600 National Avenue
Midwest City, OK 73110

March 23, 2007

The Honorable Michael O. Leavitt
Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Leavitt:

The Advisory Commission on Childhood Vaccines (ACCV) is a nine member advisory commission appointed by the Secretary of Health and Human Services (Secretary), as required by § 2119 of the Public Health Service Act, to advise and make recommendations to the Secretary on matters related to the implementation of the National Vaccine Injury Compensation Program (Program).

The National Childhood Vaccine Injury Act of 1986 (the Act) created the Program. The Act's overarching public health policy objective was to eliminate vaccine-preventable disease by encouraging the use of vaccinations. Toward that end, the goal of the Program was to stabilize the nation's vaccine supply by creating a federal cause of action whereby the U.S. government assumes liability for injuries or deaths resulting from the administration of certain vaccines mandated for childhood use. Thus, the direct beneficiaries of the Program were to be vaccine manufacturers (industry), vaccine administrators (healthcare providers) and those claiming vaccine-related injuries (petitioners).

For petitioners, the Program was to be an appealing "no-fault" alternative to the tort system in which the process of receiving compensation would be faster, less adversarial, and more compassionate. The House Report on the Act called for a compensation program that administers awards "quickly, easily, and with certainty and generosity."

For industry, the Program was to provide a broad measure of liability protection by requiring any person claiming a vaccine-related injury to file a petition in the Program before "opting out" to directly sue a manufacturer or provider in state or federal court.

The Program is privately funded by the imposition of a 75-cent excise tax per disease prevented (per dose) which is paid by the vaccine consumer, collected by the manufacturer, and deposited into the Vaccine Injury Compensation Trust Fund (Fund).

The un-obligated balance of the Fund is expected to reach almost $2.6 Billion by year end, which far exceeds current Program obligations.

The Program is administered jointly by the Department of Health and Human Services (Health Resources and Services Administration), the Department of Justice, and the U.S. Court of Federal Claims (Court). The Program was to be "fair, simple and easy to administer" and "to compensate persons with recognized vaccine injuries without requiring the difficult individual determinations of causation of injury." Accordingly, the Act provides for informal procedural rules, limited discovery, and requires petitions to be decided within 240 days (8 months).

On average, 125 petitions are filed with the Program each year.[1] For Fiscal Years 2002-06, on average, about 44% of all claims received compensation; compensated claims took, on average, 3.3 years to process, even though 67% are settled. For the same period, claims which were dismissed took, on average, 2.4 years to process. Since the inception of the Program in 1988, the average post-1988 Act injury award is $961,738 and the average fee paid to petitioners' attorneys is $37,460 which is about 4% of the average annual award paid to petitioners.

The statute of limitations (SOL) for filing a petition in the Program is three years from the date of the first symptom of the injury, even if the petitioner reasonably would not have known at the time that the vaccine had caused the first symptom. Thus, the Program stands in stark contrast to most state SOLs which do not run against a plaintiff until he is aware of both the injury *and* its cause and which suspend the SOL for minors and the disabled.

At its March and October 2006 meetings, the ACCV heard presentations highlighting concerns about the Program's SOL. To respond to these concerns and to study other proposals to improve the Program, the "ACCV Futures Workgroup" (Workgroup) was formed to develop a specific set of recommendations to present to the full ACCV for action at its next public meeting.

The Workgroup was composed of six ACCV members and was chaired by the ACCV Vice Chair, a representative of the general public. As ACCV Chair and a physician representative, I was also a member of the Workgroup along with another physician representative, a representative of the general public who is the parent of a vaccine-injured child, a general attorney representative, and an attorney who specializes in representing vaccine manufacturers.

The Workgroup met regularly from November 2006 to March 2007. It carefully studied and discussed both internal and external proposals to improve the Program, and reviewed

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[1] There are currently about 4,800 autism claims awaiting adjudication in the "Omnibus Autism Proceeding".

hundreds of pages of documents, and sought the advice of outside experts.

For example, on February 5th, the Workgroup held a Round Table Discussion to solicit the ideas and feedback from representatives from the Congressional Oversight Committee on Government Reform, the Court , the American Academy of Pediatrics, an attorney with expertise in both constitutional law and experience representing the vaccine industry, and a plaintiffs' attorney who is also a member of the Petitioner's Autism Steering Committee. (For list of attendees and agenda, please see pages 9-10.)

The Workgroup's efforts yielded significant results – it developed and garnered support for a list of 12 legislative recommendations to improve the Program.

At the March 7th ACCV meeting, the Workgroup presented the following list to the full ACCV, stressing its conclusion that the Program must be made more accessible and inclusive. After discussion and public comment, the ACCV voted overwhelmingly to support all 12 recommendations -- with 8 receiving unanimous support. The summary of these recommendations and the voting outcomes is enclosed.

This result, along with the fact that this is the first time in over eight years that the ACCV has felt compelled to proactively create and send to the Secretary an affirmative set of recommendations, underscores both the value and urgency with which the ACCV commends them for your consideration.

In conclusion, Mr. Secretary, we urge you to adopt these recommendations as your own and present them as legislative proposals to Congress at your earliest convenience. We firmly believe that passing such legislation will ensure that this Program remains viable and above reproach.

The ACCV wants you to know that it greatly appreciates your leadership and support, and we await your reply.

Sincerely,

(signature)

Don L. Wilber, M.D.
Chair, ACCV

Recommendations to Amend the National Childhood Vaccine Injury Act

Presented by the ACCV Futures Workgroup
to the
Advisory Commission on Childhood Vaccines for Action
on March 7, 2007

The ACCV Futures Workgroup, having itself unanimously agreed to support them, presented the following list of 12 recommendations to amend the Act to the full ACCV for a vote at its public meeting on March 7, 2007. (Voting results are noted in red.)

1. Allowing Payment of Interim Fees and Costs to Petitioners' Attorneys.

   After the special master or court has determined that a petitioner is entitled to compensation, the petitioners' attorney may seek an award for reasonable fees and costs incurred in the proceeding. The "interim award" shall be promptly paid by the Secretary pursuant to the special master's or court's order and without need of a final disposition of the case.

   ACCV VOTE: UNANIMOUSLY SUPPORTED.

2. Procedure for Paying Fees and Costs Solely to Petitioner's Attorney.

   When a special master or court awards attorneys' fees or costs, it may order them payable solely to the petitioner's attorney if the petitioner expressly consents or the special master or court determines that (i) the petitioner cannot be located or refuses to respond to a request by the special master or court for information and there is no practical alternative means to ensure that the attorney will be reimbursed for such fees and costs expeditiously, or (ii) there are other exceptional circumstances and good cause for paying such fees and costs solely to the petitioner's attorney.

   ACCV VOTE: UNANIMOUSLY SUPPORTED.

3. Increased Benefits Caps for Death and Pain and Suffering.

   Increase the $250,000 benefit cap for death and the $250,000 benefit cap for pain and suffering to account for inflation. Both benefit caps would be retroactively increased since 1988 to account for inflation and would increase annually to account for inflation using the Consumer Price Index - All Urban Wage Earners (CPI-U), as envisioned by Congress in the original National Childhood Vaccine Injury Act of 1986.

   ACCV VOTE: UNANIMOUSLY SUPPORTED.

4. Allowing Compensation for Family Counseling Expenses and Expense of Establishing and Maintaining Guardianships, Conservatorships, or Trusts.

   The Act shall provide compensation for reasonable and necessary, non-reimbursable expenses that have been or will be incurred for (a) family counseling determined to be reasonably necessary and that results from the vaccine-related injury and/or death for which the petitioner seeks compensation; and (b) compensation for reasonable and necessary non-reimbursable expenses, including attorneys' fees, that have been or will be incurred to establish and maintain a guardianship, conservatorship, or trust, approved by the U.S. Court of Federal Claims, for the benefit of an individual who has suffered a vaccine-related injury.

   ACCV VOTE: UNANIMOUSLY SUPPORTED.

5. Appointment of Adult with Vaccine-Related Injury to ACCV.

   Amend the Act to permit, but not require, the Secretary to appoint an adult who has personally suffered a vaccine-related injury, or the guardian or family member of such an adult, to one of the two ACCV posts reserved for the legal representative of a child who has suffered a vaccine-related injury or death.

   ACCV VOTE: UNANIMOUSLY SUPPORTED.

6. Clarification: A Petitioner Who Establishes a Vaccine-Related Injury and Death is Entitled to Both Death and Injury Benefits.

   Amend 42 USC § 300aa-15(a)(2): In the event of a vaccine-related death, an award of $250,000 for the estate of the deceased, *in addition to the benefits provided in Sections 15(a)(1), 15(a)(3) and 15 (a)(4). (new words in italics)*

   ACCV VOTE: UNANIMOUSLY SUPPORTED.

7. Parent Petitions for Compensation.

   Amendment to require parent or other third party to file a petition in the Program before filing or maintaining a civil action against a vaccine manufacturer or administrator in a Federal or State court for damages relating to a vaccine-related injury or death, including but not limited to damages for loss of consortium, society, companionship or services, loss of earnings, medical or other expenses, and emotional distress, and no court may award damages in such an action unless the action is joined with a civil action brought by the person whose vaccine-related injury is the basis for the parent's or other third party's action.

   ACCV VOTE: 8 FOR; 1 AGAINST (parent rep.): SUPPORTED.

8. Clarification of Definition of Manufacturer.

   Enlarges the current definition of manufacturer (42 USC § 300aa-33(3)) to include any corporation, organization, or institution (public or private) which manufactures, imports, processes, or distributes *any component or ingredient* of any vaccine set forth in the Vaccine Injury Table.

   ACCV VOTE: 7 FOR; 2 AGAINST (parent rep. and petitioners' attorney rep.): SUPPORTED.

9. Clarification of Definition of Vaccine-Related Injury or Death.

   Clarifies that a component or ingredient approved for use in a Table vaccine by the FDA is not to be considered an adulterant or contaminant for purposes of the Act. (42 USC § 300aa-33(5))

   New Definition: Vaccine-related injury or death means an illness, injury, condition, or death associated with one or more of the vaccines set forth in the Vaccine Injury Table, except that the term does not include an illness, injury, condition, or death associated with an adulterant or contaminant intentionally added to such a vaccine. *For purposes of the preceding sentence, an adulterant or contaminant shall not include any component or ingredient listed in a vaccine's product license application or product label. (new words in italics)*

   ACCV VOTE: 7 FOR; 1 AGAINST (parent rep.); 1 ABSTENSION (petitioners' attorney rep.): SUPPORTED.

10. Add Definition of Vaccine to 42 USC § 300aa-33.

    The Act currently contains no definition of "vaccine." To complement the above clarifications – that ingredients and components are not adulterants or contaminants for purposes of this Act – the Workgroup recommends that the Secretary add a definition of "vaccine" to the Act that includes all components and ingredients listed in the vaccines' product license application and product label.

    ACCV VOTE: 8 FOR; 1 AGAINST (parent rep.): SUPPORTED.

11 and 12. Extending the Statute of Limitations ("SOL").

The Workgroup's goal was to expand access to the Program; therefore, it recommends extending the SOL to correspond to the 8 years of retroactive coverage when a new vaccine or injury is added to the Vaccine Injury Table:

11. For vaccine-related injuries:

    Extend the SOL from 3 to 8 years, but make the Program the exclusive remedy for any petitioner who files during the extended period (no opt out). There would be no change in the current 3 year SOL, including the right to opt out. However, the Program would be the exclusive remedy for any petition filed during the extended 5-year period (year 3-8).

    ACCV VOTE: UNANIMOUSLY SUPPORTED.

12. For vaccine-related deaths:

    Extend the SOL from 2 to 8 years following a death, with the Program being the exclusive remedy for the extended 6-year period (no opt out); and extend the SOL from 4 to 8 years from injury, with the Program being the exclusive remedy from year 4-8 (no opt out).

    ACCV VOTE: UNANIMOUSLY SUPPORTED.

ACCV Futures Workgroup Round Table Discussion

February 5, 2007
The Jefferson Hotel
Washington, D.C.

Participants:

ACCV Workgroup Members:

Marguerite Evans Willner, Workgroup Chair, ACCV Vice-Chair

Tawny L. Buck

Loren G. Cooper, J.D.
GlaxoSmithKline Biologicals, SA

Jaime G. Deville, M.D.
Department of Pediatrics Infectious Diseases, University of California

Jeffrey M. Sconyers, J.D.
Children's Hospital & Regional Medical Center

Don L. Wilber, M.D., ACCV Chair
Oklahoma City Clinic

Invited Guests:

Sarah Despres
Congressman Waxman's Congressional Oversight Committee on Government Reform

Chief Special Master Golkiewicz
U.S. Court of Federal Claims

Karen Hendricks
Asst. Director, Government Affairs, American Academy of Pediatrics

Randy Moss, J.D., WilmerHale

Tom Powers, J.D., Williams, Love O'Leary, Craine & Powers, P.C.

Staff: DVIC, Healthcare Systems Bureau, HRSA

Cheryl Lee, Principal Staff Liaison

Tamara Overby, M.B.A., Chief, Policy Analysis Branch

Staff: HHS Office of the General Counsel

Elizabeth Saindon, J.D., Senior Attorney

ACCV Futures Workgroup
Agenda
Monday, February 5, 2007

9:30 Welcome

Topics:

1. The Original Purposes, Policies, and Goals of the National Childhood Vaccine Injury Act of 1986 ("the Act")

2. How have the Act and the Table changed over the last 20 years?

   Legislative Changes to the Act and Agency Rule-Making Changes to the Vaccine Injury Table ("the Table") (*Tamara Overby, M.B.A.*)

3. How has the Act been interpreted by the courts over the last 20 years?

   Althen and Capizzano (relaxed standards of proof)

4. What impact have these changes had on petitioners, industry, the Vaccine Injury Compensation Trust Fund, and those entrusted with implementing the Program?

5. Does the Act currently fulfill its promises to stakeholders?

   to petitioners: to provide a no-fault compensation program in which awards can be made "quickly, easily, and with certainty and generosity"

   to industry: to provide a broad measure of liability protection

   to the public (including petitioners): to perfect vaccines, monitor adverse events, promote public health by ensuring a stable vaccine supply and improving immunization rates

6. Do differing perceptions concerning the purpose of compensating vaccine-associated injuries threaten the Program?

7. Does the "Table" reflect a tension among competing interests with incompatible goals and values and disproportionate political power (Congress, government agencies, the general public, petitioners, and industry)?

8. Does the Program provide an "appealing alternative" to the traditional tort system? If not, what are the implications?

9. Discussion of legislative solutions.

   5:00 Adjourn.

_____	_____
Jeffrey Sconyers, J.D. ACCV Chair	Dr. Jamie Deville ACCV Vice-Chair
_____	_____
Geoffrey Evans, M.D. Executive Secretary, ACCV	Date
