Food and Drug Administration
Center for Biologics Evaluation and Research
SUMMARY MINUTES
VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE
Meeting # 109: January 25, 2007
Doubletree Hotel, Bethesda, MD

Committee Members
Dr. Ruth Karron, Chair
Dr. Walter Royal III
Dr. Philip LaRussa
Dr. Bonnie Word
Dr. John Modlin
Dr. Lisa Jackson
Dr. Jack Stapleton
Ms. Cindy Lyn Province, R.N., M.S.N.*
Dr. Seth Hetherington**
Dr. Monica Farley
Dr. Steven Self

FDA Participants
Dr. Theresa Finn
Dr. Karen Farizo
Dr. Kathryn Carbone
Dr. Norman Baylor
Dr. Michael Brennan
Dr. Jerry Weir
Dr. Richard Walker
Dr. Jesse Goodman

Temporary Voting Members
Dr. Erik Hewlett
Dr. Pamela McGinnes
Dr. Bruce Gellin
Dr. Melinda Wharton
Dr. Jay Butler

Sanofi Pasteur Participants
Dr. Luc Kuykens
Dr. Michael Decker
Dr. Scott Halperin
Dr. David Greenberg

Executive Secretary
Christine Walsh, R.N.

Committee Management Specialist
Denise Royster

These summary minutes for the January 25, 2007 Meeting of the Vaccines and Related Biological products Advisory Committee were approved on ___2/20/07_____.

I certify that I participated in the January 25, 2007 Meeting of the Vaccines and Related Biological Products Advisory Committee and that these minutes accurately reflect what transpired.

_____/s/_____
Christine Walsh, R.N.
Executive Secretary

_____/s/_____
Ruth Karron, M.D.
Chair

*Consumer Representative
** Non-Voting Industry Representative

The Chair, Dr. Ruth Karron, called the one hundred and ninth Meeting of the Vaccines and Related Biological Products Advisory Committee to order at 8:07 a.m. ET on January 25, 2007. In Session 1, the meeting addressed the safety and immunogenicity of Diphtheria & Tetanus Toxoids & Acellular Pertussis Adsorbed, Inactivated Poliovirus and Haemophilus b Conjugate (Tetanus Toxoid Conjugate) Vaccine Combined (DTaP-IPV/Hib), Pentacel™, manufactured by Sanofi Pasteur. In Session II, the meeting addressed the Overview of the Office of Vaccines Research and Review, CBER followed by a closed session to discuss the report of the Office of Vaccines Research and Review Office Site Visit from May 19, 2006.

An Open Public Hearing was announced. Public comment was offered via an electronic message from B. Sachau. Copies of the comment were provided to committee members, displayed in the public notebook at the meeting, and a copy was made part of the official meeting record. No other public comment was offered.

Following is a summary of the discussion. Additional information and specific details may be obtained from the transcript of the meeting. The transcript may be viewed on the World Wide Web at:
http://www.fda.gov/ohrms/dockets/ac/cber07.html#VaccinesandRelatedBiological.

Proceedings were adjourned at approximately 5:00 p.m. ET on January 25, 2007.

**Open Session**

Dr. Theresa Finn, FDA, opened the morning session, safety and immunogenicity of Diphtheria & Tetanus Toxoids & Acellular Pertussis Adsorbed, Inactivated Poliovirus and Haemophilus b Conjugate (Tetanus Toxoid Conjugate) Vaccine Combined (DTaP-IPV/Hib), Pentacel, with a short introduction and background. Dr. Finn also presented the questions that would be asked of the committee later in the day.

Following Dr. Finn, the sponsor, Sanofi Pasteur then made presentation. Speakers for Sanofi Pasteur included Dr. Luc Kuykens, Dr. Michael Decker, Dr. Scott Halperin, and Dr. David Greenberg. Included in their presentation were safety and immunogenicity data, information on Canadian post-marketing effectiveness, and U.S. perspective. In his conclusion statements, Dr. Kuykens summary included that Pentacel is safe when administered alone or concomitantly with other age-recommended vaccines and immune responses were similar when Pentacel was administered alone or concomitantly with other vaccines.

Dr. Karen Farizo then presented for CBER, FDA. CBER presented safety data from four pivotal clinical studies. In these studies, a total of 5,980 subjects received at least one dose of Pentacel. Of these subjects, 4,198 were from three U.S. studies of four consecutive doses of Pentacel administered at 2, 4, 6, and 15-16 months of age, and 1,782 were from a study that evaluated the fourth dose only in subjects who had previously

received three doses of Pentacel in Canada. In two of the studies, the safety of four doses of Pentacel was compared to separately administered control vaccines: HCPDT (non U.S. licensed DTaP component of Pentacel), POLIOVAX and ActHIB in one study, and DAPTACEL, IPOL and ActHIB in the other.

In addition to the pivotal safety data, supportive post-marketing safety data were presented from a 9-year period in which approximately 13.5 million doses of Pentacel were distributed, primarily in Canada.

Directly following Dr. Farizo, Dr. Theresa Finn, FDA presented next for CBER. CBER presented immunogenicity data provided in the license application to support the efficacy of the diphtheria, tetanus, polio, Hib and pertussis components of Pentacel when administered at 2, 4, 6 and 15-16 months of age. CBER's presentation focused on the immune responses to the Hib and pertussis components of Pentacel, as concerns were identified regarding the data to support the efficacy of these components. The response to the Hib component was inconsistent in two controlled studies. In one pivotal study infants administered three doses of Pentacel had lower antibody levels to the Hib component than those administered U.S. licensed ActHIB vaccine separately. In the other study the response of infants administered three doses of Pentacel was similar to those administered ActHIB although both groups had lower antibody levels than seen in the first study. With respect to the pertussis component the immune response to one of the antigens (pertactin) did not meet the statistical criteria to demonstrate non-inferiority when four doses of Pentacel were compared to either three doses of a U.S. licensed DTaP vaccine (DAPTACEL) used in a clinical trial in Sweden or four doses of DAPTACEL when given to US children.

An Open Public Hearing was offered. Written comment was submitted by B. Sachau. No other public comment was made.

Following the Open Public Comment, the committee held discussion with the FDA and the sponsor on the topic prior to a vote taken.

Based on information presented to the committee regarding the safety and immunogenicity of Pentacel, the committee recommended:

- The committee unanimously recommended (15 votes in favor, 0 against, 0 abstained) that the data were adequate to support the safety of four doses of Pentacel administered at 2, 4, 6, and 15-18 months of age.

Based on information presented to the committee regarding the data to support the efficacy of Pentacel, the committee recommended:

- The committee unanimously recommended (15 votes in favor, 0 against, 0 abstained) that the data were adequate to support the efficacy of Pentacel. While overall agreeing that the data were adequate to support the efficacy of Pentacel,

some members made comment regarding the Hib (PRP-T) component stating there is inconsistent performance of a comparative vaccine.

After voting, the committee discussed issues which should be addressed in post-licensure studies if Pentacel is licensed. Recommendations made by the committee included concerns about HIB with possible labeling for public information, surveying populations with highest risk, and Hib and pertussis surveillance.

Session 1 was then adjourned.

After lunch, the committee was given an overview of the Office of Vaccines Research and Review, CBER. Dr. Kathryn Carbone, FDA opened the afternoon session with an overview of CBER Research Programs. Dr. Norman Baylor followed presenting an overview of the Office of Vaccines Research and Review. Subsequent presentations were made by Dr. Michael Brennan, FDA, Dr. Jerry Weir, FDA, and Dr. Richard Walker, FDA regarding the Office of Vaccines Research and Review Research Program, overview of the Division of Viral Products, and an overview of the Division of Bacterial Parasitic and Allergenic Products respectively.

An Open Public Hearing was offered. No public comment was made.

The open session was of the meeting was then adjourned.

**Closed Session**

The committee discussed the Office Site Visit Report from the May 19, 2006 review of the Office of Vaccines Research and Review. The report was approved as written.

The meeting was adjourned at 5:00 p.m. ET.