Food and Drug Administration
Center for Biologics Evaluation and Research
SUMMARY MINUTES
VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE
Meeting # 105: December 14 - 15, 2005
Holiday Inn Select, Bethesda, MD

Committee Members
Dr. Gary D. Overturf, Chair
Dr. Walter Royal III
Dr. Ruth A. Karron
Dr. David Markovitz
Dr. Monica M. Farley
Dr. Steven Self **
Dr. Bonnie M. Word

FDA Participants
Dr. Norman Baylor
Dr. Rosemary Tiernan
Dr. Hector Izurieta
Dr. Patricia Rohan

Acting Industry Representative
Dr. Samuel Maldonado **
Dr. Seth Hetherington ***

Absent
Dr. Philip LaRussa
Ms. Cindy Lyn Province, R.N., M.S.N. *

Consultants
Dr. Bruce Gellin
Dr. Pamela McInnes **
Dr. Melinda Wharton
Dr. Thomas Fleming ***
Dr. Daniel Scharfstein ***
Dr. Michael Rowbatham ***

Guest Speakers
Dr. Mark Bagarazzi
Dr. Penny Heaton
Dr. David Gutsch
Dr. Jeffrey Silber

Executive Secretary
Christine Walsh, R.N.

Committee Management Specialist
Denise Royster

These summary minutes for the December 14 - 15, 2005 Meeting of the Vaccines and Related Biological products Advisory Committee were approved on _____.

I certify that I participated in the December 14 - 15, 2005 Meeting of the Vaccines and Related Biological Products Advisory Committee and that these minutes accurately reflect what transpired.

_____
Christine Walsh, R.N.
Executive Secretary

_____
Gary D. Overturf, M.D.
Chair

*Consumer Representative **Attended December 14 only ***Attended December 15 only

The Vaccines and Related Biological Products Advisory Committee (VRBPAC) met on December 14 - 15, 2005 at the Holiday Inn Select, 8120 Wisconsin Ave., Bethesda, MD. In open session on December 14, 2005, the committee heard presentations and made recommendations on the safety and efficacy of RotaTeq™ which is a live, oral rotavirus vaccine manufactured by Merck & Co. In open session on December 15, 2005, the committee heard presentations and made recommendations the safety and efficacy of ZOSTAVAX (Zoster Vaccine live [Oka/Merck]) manufactured by Merck & Co.

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/cber05.html#VaccinesandRelatedBiological.

Open Session

The Vaccines and Related Biological Products Advisory Committee meeting was called to order by the Chair, Dr. Gary D. Overturf, at 9:02 a.m. on December 14, 2005. Dr. Rosemary Tiernan, FDA, opened the meeting by welcoming the committee and providing a brief introduction to the days' topic; safety and efficacy of a Rotavirus Vaccine manufactured by Merck & Co., and ended by presenting questions being posed to the committee in the afternoon session. Following Dr. Tiernan, Dr. Mark Bagarazzi and Dr. Penny Heaton represented the sponsor, Merck &Co. in a presentation to the committee which summarized proposed indications of their product; RotaTeq™, global impact of rotavirus gastroenteritis, and provided an overview of their products clinical development program. Following the sponsor presentation, Dr. Tiernan presented for the FDA. Dr. Tiernan provided an overview for the panel which included epidemiology, the regulatory history of the product, and efficacy and safety factors. Immediately following Dr. Tiernan, Dr. Hector Izurieta, FDA, made presentation to the committee regarding a summary on intussusception following use of RotaShield® and an outline of pharmacovigilance plans for RotaTeq™. To open the afternoon session, an Open Public Hearing was offered. Dr. Paul M. Mendelman made presentation to the committee regarding the benefit of live attenuated vaccines for public health. No other public comment was made. After presentation of the questions again, the committee then held discussion and made recommendations regarding the days' topic.

The Advisory Committee began by considering the third question posed by the FDA which asked for assistance in identifying any additional issues that should be addressed including post-licensure studies.

Topics that were discussed included: intussusception, the Applicant's proposed pharmacovigilance plan, concomitant use with other routinely administered childhood vaccines and the use of the vaccine in immunocompromised children or other special populations.

The Committee recommended that the Applicant undertake a post-marketing program to monitor children for intussusception. The FDA Vacccine Safety Branch/Division of Epidemiology/Office of Biostatistics and Epidemiology/CBER (VSB/DE/OBE/CBER) recommended using a post-marketing site outside of the Vaccine Safety Datalink (VSD) for the phase 4 study and Merck stated that they were already pursuing plans to secure such a site. The VSB also expressed concern about the proposed sample size for the phase 4 study, and suggested that the issues related to the phase 4 post-marketing study could be discussed with the sponsors at a conference call.

Regarding concomitant use with other childhood vaccines, the committee agreed that it was important to finalize the assay validation data for the tetanus, diphtheria and pertussis vaccines. They also recommended that studies be done with concomitant vaccines other than the products that were used in the U.S. concomitant vaccine study. Merck explained that they already planned to do additional concomitant vaccine studies including studies overseas.

The committee recommended that additional populations to study with RotaTeq™ could include children with HIV infection, and children with underlying gastrointestinal disorders such as short guts or malabsorptive syndrome.

The committee was also concerned that additional post marketing studies needed to be done regarding the safety and efficacy of administering catch up immunizations. They also felt that once the vaccine was introduced it would be important to have ongoing surveillance to detect whether rotavirus serotype replacement occurs.
Based on information presented to the committee regarding available data adequate to support the efficacy of RotaTeq™ in preventing rotavirus gastroenteritis caused by serotypes G1, G2, G3, G4 and G serotypes that contain P1 (e.g. G9), when the first dose of vaccine is administered at 6 – 12 weeks of age, followed by two subsequent doses separated by 4 – 10 week intervals, the committee recommended:

- The committee unanimously recommended (10 votes in favor, 0 against, 0 abstained) that available data were adequate to support the efficacy of RotaTeq™. The acting committee Industry Representative abstained from making comment.

Based on information presented to the committee regarding available data adequate to support the safety of RotaTeq™ when used in a 3 dose vaccine series beginning with the first dose at 6 – 12 weeks of age, followed by two additional doses separated by 4 – 10 week intervals, the committee recommended:

- The committee unanimously recommended (10 votes in favor, 0 against, 0 abstained) that available data were adequate to support the safety of RotaTeq™. The acting Industry Representation abstained from making comment.

This completed committee discussions and recommendations. The Chair adjourned the meeting for the day at 3:08 p.m.

The Chair called day 2 of the meeting to order at 9:03 a.m. on December 15, 2005. The meeting opened with a brief presentation by Dr. Patricia Rohan, FDA. Dr. Rohan welcomed the committee and presented the questions for the day's topic: safety and efficacy of ZOSTAVAX™ (Zoster Vaccine live [Oka/Merck]) manufactured by Merck & Co. Dr. Rohan was followed by Dr. David Gutsch and Dr. Jeffrey Silber representing Merck & Co. Presentations from Merck representatives included product profile, proposed indications, and epidemiology and clinical program development. Following Merck, Dr. Rohan made a presentation to the committee providing an overview of the day's topic including the proposed indication, background, clinical development, and review of clinical studies. To begin the afternoon session, an Open Public Hearing was held; no public comment was offered. Prior to the committee's discussion and recommendations, Dr. Rohan again presented the questions being posed to the committee.

On the topic of question 1, "Are the available data adequate to support the efficacy of ZOSTAVAX™ when administered to person older than 50 years of age in: a) preventing herpes zoster, b) preventing post-herpetic neuralgia; preventing post-herpetic neuralgia beyond the effect on the prevention of herpes zoster, c) decreasing the sponsor-defined burden of illness (BOI); decreasing the sponsor-defined burden of illness (BOI) beyond the effect on the prevention of herpes zoster?"

- The Committee unanimously voted no (11 against, 0 for, 0 abstained). The Acting Industry Representative answered no in response to the question.

On the topic of question 2, "Are the available data adequate to support the safety of ZOSTAVAX™ when administered to persons at least 50 years of age?"

- 2 members of the Committee voted yes, 8 members voted no, but indicated that safety in persons at least 60 years of age was demonstrated, and 1 member voted no, commenting that he did not wish to vote on subgroups. The Acting Industry Representative provided a qualified yes in response to the question.

A revised question was then posed, "Are the available data adequate to support the safety and efficacy of ZOSTAVAX™ in preventing herpes zoster when administered to persons at least 60 years of age?"

- The Committee voted unanimously yes (11 yes, 0 no, 0 abstained), with 6 members indicating concerns regarding diminished efficacy in those at least 80 years of age The Acting Industry Representative answered yes in response to the question.

This completed committee discussions and recommendations. The Chair adjourned the meeting for the day at 4:01 P.M.