Food and Drug Administration
Center for Biologics Evaluation and Research

SUMMARY MINUTES
VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

Meeting # 91: May 21, 2002

Committee Members
Dr. Robert Daum, Chair
+Dr. Michael Decker
Dr. Pamela Diaz
Dr. Walter Faggett
*Ms. Barbara Loe Fisher
Dr. Judith Goldberg
Dr. Diane Griffin
Dr. Sam Katz
Dr. David Markovitz
Dr. Gary Overturf
Dr. Julie Parsonnet
Dr. David Stephens
Dr. Rich Whitley

Temporary Voting Members
Dr. Mimi Glode
Dr. Richard Schwartz
Dr. Dixie Snider
Dr. Holli Hamiliton

Sponsor Presenters
Dr. Steven Black
Dr. George Siber
Dr. Terhi Kilpi

FDA Participants
Dr. Karen Midthun
Dr. Susan Ellenberg
Dr. Norman Baylor
Dr. Karen Goldenthal
Dr. Douglas Pratt
Dr. Patricia Rohan
Dr. Jingyee Kou

Committee Members Absent
Dr. Estuardo Aguilar-Cordova
Dr. Audrey Manley
Dr. Peter Palese

Executive Secretary
Dr. Jody Sachs

These summary minutes for the May 21, 2002 meeting of the Vaccines and Related Biological Products Advisory Committee were approved on _____ .

I certify that I participated in the May 21, 2002 Meeting of the Vaccines and Related Biological Products Advisory Committee and that these minutes accurately reflect what transpired.

_____
Jody Sachs, D.P.M.
Executive Secretary

_____
Robert S. Daum, M.D.
Chair

* Consumer Representative
+ Non-Voting Industry Representative

The 91th meeting of the Vaccines and Related Biological Products Advisory Committee was called to order at 8:30 a.m. EST on May 21, 2002 by the Chair, Dr. Robert Daum. The meeting addressed in **Session #1:** Prevnar? for indication in acute ottitis media, and **Session #2:** Update on GSK Lyme Disease Vaccine (LYMErix?). Both Session 1 and 2 were open sessions.

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/02acsdocs.htm. A copy of the agenda is attached.

Session #1-Open Session
Prevnar® for Acute Otitis Media (AOM) Indication

The committee discussed an additional proposed indication for Prevnar? "for active immunization of infants and toddlers against otitis media caused by *Streptococcus pneumoniae* due to capsular serotypes included in the vaccine (4, 6B, 9V, 14, 18C, 19F and 23F)."

Data supporting this indication were provided from two controlled clinical trials:

1) Finnish Acute Otitis Media Trial (FinAOM)
2) Northern California Kaiser Permanente Efficacy Trial (NCKP)

Efficacy Against Otitis Media

	FinAOM (%)	NCKP (%)
Vaccine Serotype AOM	57 (44,67)	69* (0.4,93)
Vaccine Related Serotype AOM	51 (27,67)	
Non Vaccine Serotype AOM	-33 (-81,1)	
All Pnc AOM	34 (21,45)	
Recurrent AOM	16 (-6,35)	12 (7,16)
All AOM	6 (-4,16)	7 (4,9)
Tube Placement	44[1] (19,62)	24 (12,35)

* Spontaneous TM rupture

In the Finnish study, vaccine efficacy was 57% (95%CI: 44%, 67%) for AOM episodes due to vaccine serotypes, and 34% (95%CI: 21%, 45%) for all AOM episodes caused by pneumococci, regardless of serotype. The Finnish study included myringotomy and cultures of the middle ear, this was not true of the Kaiser study. Vaccine efficacy for all causes of AOM, regardless of etiology, was 7% (95%CI: 4.1%, 9.7%), based on evidence from the Kaiser study, and 6% based on evidence from the Finnish Study.

[1] Fin AOM follow up

In summary, the Committee concluded that data derived from two efficacy trials are adequate to demonstrate efficacy of Prevnar® against AOM caused by vaccine serotype. However, the committee expressed concern about the low efficacy (7%) of the vaccine against AOM regardless of etiology and concluded that substantial clinical benefit of Prevnar in reducing AOM regardless of etiology had not been demonstrated. The Committee cautioned against including an indication statement as proposed by the sponsor into the label and suggested using qualifying language if an indication for AOM regardless of etiology were to be added. Committee members cautioned against promoting prevention of AOM as a benefit of Prevnar? in direct-to-consumer advertising because of concerns about unrealistic public expectations. The Committee was concerned that promoting Prevnar? as an "AOM vaccine" could potentially compromise confidence in the existing recommendations for the vaccine and trust in the labeling that FDA puts on a vaccine. It was noted that an AOM indication for Prevnar® could set precedence for licensure of additional pneumococcal conjugate vaccines for prevention of AOM.

Discussion points included:

- The Kaiser Study demonstrated only a vaccine efficacy of 7% against AOM regardless of etiology. The significance of this efficacy was discussed.
- The Finnish Study and the Kaiser Study used different endpoints. By the use of different endpoints, some felt that the supporting results from the Kaiser Study may/may not support the findings of the Finnish Study.
- The vaccine serotype efficacy of 19F was discussed. The Finnish Study demonstrated that the AOM episodes due to individual vaccine serotypes (6B, 18C, 14, 23F, 4, 9V, 19F) ranged from 80% to 10%; 19F being the lowest.
- Reduction in the use of antibiotics was discussed as a positive outcome with the use of the vaccine.
- Prevnar® is currently recommended for all children under the age of 2 years. Immunization is already advised for children and toddlers, and children are given the vaccine. The two trials show consistent efficacy.
- Would the suggested change in the current label accurately communicate all the information necessary to the families of the AOM patients treated, as well as, the doctors treating AOM patients? Many members discussed their concerns with this issue. Promotional materials are based on the approved labeling. Inaccurate marketing would do more harm than good. The committee members felt that this was not an "AOM vaccine". Many felt that it would be a mistake by the company and FDA to have this marketed as an "AOM vaccine".
- There is no minimum level of efficacy required for licensure of a preventive vaccine addressed by the FDA regulations or guidelines.

Recommendations were as follows:

- ?? Additional clinical trials for the prevention of AOM with the vaccine, using serology and analyzing serotypes, would be helpful to further evaluate the consistency of the results of the two studies. Continuous monitoring of serotypes is needed and more data need to be generated for analysis.
- ?? Further evaluation of the vaccine serotype 19F was suggested to find out why the 19F vaccine component was not effective.
- ?? Tympanostomy tube placement can easily be followed by ICD coding. Long-term tympanostomy tube follow-up on AOM vaccine patients was recommended.
- ?? Phase 4 studies might be useful. Serotype 19F efficacy, tube placement, antibiotic resistance, and the pursuit of non-serotype replacement of nasopharyngeal colonization are important issues to pursue.
- ?? Careful wording and qualifying language be used if the AOM indication efficacy data were to be included on the current label of Prevnar®. (Suggestions included using the wording that "the vaccine efficacy was only 7% in treating all AOM, regardless of etiology".)
- ?? The vote was 13 to 3 to agree that the data support the efficacy of Prevnar® for active immunization in infants and toddlers for the prevention of AOM caused by *S Pneumoniae* due to capsular serotypes included in the vaccine (4, 6B, 9V, 14, 18C, 19F and 23F).

Session #2 – Open Session
FDA Update on the GSK-Lyme Disease Vaccine (LYMErix?)

The FDA informed the committee members that GSK voluntary withdrew LYMErix? from sale in February of 2002 and distribution was discontinued. GSK cited poor sales as the reason for withdrawal. No further vaccinations are recommended, clinical trial vaccination ended, Dear Doctor/Investigator letters were sent, and refunds were given for returned vaccine. Complete safety follow-up will be completed for all clinical studies and the Phase 4 post-marketing study is to be completed in 2006.

Open Public Hearings

Two Open Public Hearing sessions were announced. No one requested time to speak in Session #1. For Session #2 there were eight requests for speaking.

Session #2-Open Public Hearing
Public Speakers on Lyme Disease:

1. Karen Vanderhoof-Forschner (Lyme Disease Foundation)
2. Dr. Norman Latov
3. Dr. Mark Geier
4. David Geier

5. Stephen Sheller, Esq.
6. Kathy Shepanski
7. Pat Smith (Lyme Disease Assoc.)
8. Jenny Marra

Proceedings were adjourned at approximately 3:30 p.m. EST on May 21, 2002.