

Food and Drug Administration
Center for Biologics Evaluation and Research

SUMMARY MINUTES
VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

Meeting # 93: December 20, 2002

Committee Members

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

Members Not Present

Dr. Audrey Manley
Dr. Peter Palese
Dr. Rich Whitley
Dr. Diane Griffin

FDA Presenters

Dr. ChrisAnna Mink

FDA Participants

Dr. Karen Midthun
Dr. Douglas Pratt

Consultants

Dr. Nancy Cox
Dr. Kathryn Edwards
Dr. Theodore Eickhoff
Dr. Bruce Gellin
Dr. Holli Hamilton
Dr. Martin Myers
Dr. Dixie Snider
Dr. Mark Steinhoff

Executive Secretary

Dr. Jody Sachs

These summary minutes for the December 17, 2002 Meeting of the Vaccines and Related Biological Products Advisory Committee were approved on _____ .

I certify that I participated in the December 17, 2002 Meeting of the Vaccines and Related Biological Products Advisory Committee and that these minutes accurately reflect what transpired.

* Consumer Representative

+ Non-Voting Industry Representative

Jody Sachs, D.P.M.
Executive Secretary

Robert S. Daum, M.D.
Chair

The Chair, Dr. Robert Daum, called the 93rd Meeting of the Vaccines and Related Biological Products Advisory Committee to order at 8:30 a.m. EST on December 17, 2002. The meeting addressed the review and discussed the safety, efficacy, and proposed indications for the product, FluMist, a cold-adapted, live attenuated, trivalent influenza vaccine for the prevention of influenza sponsored by MedImmune Vaccines, Inc.

The Meeting was held at the Bethesda Marriott Hotel, 5151 Pooks Hill Road, Bethesda, Maryland 20814.

An Open Public Hearing session was announced. No 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/02acsdocs.htm>. A copy of the agenda is attached.

Proceedings were adjourned at approximately 4:30 p.m. EST on December 17, 2002.

Open Session

FluMist™ Influenza Virus Vaccine, Trivalent, Types A & B, Live, Cold Adapted

On December 17, 2002, the Vaccines and Related Biological Products Advisory Committee (VRBPAC) met to discuss safety and efficacy data intended to support licensure of FluMist? , Influenza Virus Vaccine Live, intranasal, manufactured by MedImmune Vaccines. FluMist? contains 3 strains of cold-adapted, temperature sensitive influenza viruses: 2 type A (H1N1 and H3N2) and one type B. FluMist? was previously discussed at VRBPAC in July 2001.

The indication proposed by the sponsor and discussed at the December 2002 VRBPAC was for active immunization for the prevention of disease caused by influenza A and B viruses in healthy children, adolescents, and adults from 5 years (? 60 months) through 64 years of age. This age range differed from that discussed in July 2001; the sponsor's proposed age range at that time was 1 to 64 years of age. FluMist? is administered as a 2-dose regimen (60 ± 14 days) for first use in children 5 through 8 years of age, and 1 dose for individuals 9-64 years of age.

Data from a clinical safety trial completed since the July 2001 VRBPAC were presented, which suggested that children under the age of 5 years appear to be at increased risk of asthma and upper respiratory illnesses following receipt of FluMist? . New data relating to transmission and shedding of FluMist? among children attending daycare were also presented. Efficacy and effectiveness data, from studies previously discussed, were also reviewed.

The committee was asked to vote on the adequacy of safety and efficacy data to support use of FluMist? in healthy individuals in each of three age groups: 5-17 years, 18-49 years, and 50-64 years. Advice relating to these specific age groups was requested based on the design of pivotal

studies (children/adults), and recommendations of the Advisory Committee on Immunization Practices (ACIP) for use of influenza vaccine in healthy persons older than age 50 years, who are considered to be at high risk for influenza and are targeted for annual vaccination. Eighteen committee members and consultants were eligible to vote.

On the question of safety, the committee voted that the data were adequate to support safety of FluMist? for individuals in the three age groups, i.e., safety data were judged to be adequate for ages 5-64 years. Eight of 18 committee members and consultants voted that the safety data were inadequate for the 50-64 year age group. Concern was expressed about the small amount of safety data available for individuals over 50 years of age (N= 622).

On the question of efficacy, the committee voted that the data were adequate to support efficacy or effectiveness for individuals 5-17 years and 18-49 years. However, for the 50-64 year age group, the committee members and consultants voted 14 (no) to 4 (yes), on whether efficacy/effectiveness data were adequate. Among the concerns expressed regarding the efficacy/effectiveness data in the older age group were: lack of data related to annual revaccination, lack of culture-confirmed efficacy data, little evidence of effectiveness from a subgroup analysis in individuals over age 50 years and possible biological plausibility for such a finding, and no data from trials comparing FluMist? to a licensed trivalent influenza vaccine for this higher risk age group.

The committee was asked to discuss the design and endpoints used in a clinical study intended to identify lack of attenuation of new strains that may be incorporated into FluMist? annually. In general, the committee concurred with the study design and endpoints, and supported the conduct of such studies moving forward.

The committee was also asked to comment on what additional information should be collected from post-marketing studies. Additional information was requested about the following: 1) annual revaccination; 2) shedding, transmission and genetic stability of FluMist? strains; 3) use among individuals at high-risk of influenza complications; 4) the risk of asthma and wheezing in children; 5) comparative safety and efficacy to a licensed inactivated influenza vaccine, especially for adults over 50 years of age; 6) immune correlates; and 7) annual monitoring of efficacy, possibly through influenza surveillance and case-control studies.