Food and Drug Administration
Center for Biologics Evaluation and Research

SUMMARY MINUTES
188th VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

December 12, 2024

Committee Members
Hana El Sahly, M.D., Chair
Adam Berger, Ph.D.
Andrea Shane, M.D., M.P.H., M.Sc.+
Archana Chatterjee, M.D., Ph.D.+
Arnold Monto, M.D.
Michael Nelson, M.D. Ph.D.
Eric Rubin, M.D. Ph.D.+
Henry Bernstein, D.O. MHCM, FAAP
Hayley Gans, M.D.
Jay Portnoy, M.D.
Holly Janes, Ph.D.
Paul Offit, M.D.
CAPT. Sarah Meyer, M.D., M.P.H.
Stanley Perlman, M.D., Ph.D.
Steven Pergam, M.D., M.P.H.+

Industry Representatives
Robert Janssen, M.D. ***

Consumer Representative
Jay Portnoy, M.D.*

Designated Federal Officers (DFO)
Sussan Paydar, Ph.D.
Kathleen Hayes, MPH

Committee Management Staff
Joanne Lipkind

Temporary Voting Member
Karen Kotloff, M.D.
Sarah Long, M.D.
Allison Malloy, M.D., MSc
Tracy Ruckwardt, Ph.D.

Speakers and Guest Speakers
Fatimah Dawood, M.D. (CDC)
Pedro A. Piedra, M.D. (Baylor)
Christine Shaw, Ph.D. (Moderna)
Matthew Snape, MBBS, M.D. (Moderna)

FDA Participants
Peter Marks, M.D., Ph.D.
David C. Kaslow, M.D. (Speaker)
Karin Bok, M.S., Ph.D.
Sudhakar Agnihothram, B. Pharm., Ph.D.
Rebecca Reindel, M.D.
Mark Connelly, M.D.
Prabhakara Atreya, Ph.D.

+Not Attending
*Consumer Representative

***Alternate Industry Representative

These summary minutes for the December 12, 2024, meeting of the Vaccines and Related Biological Products Advisory Committee were approved on January 13, 2024.

I certify that I participated in the December 12, 2024, meeting of the Vaccines and Related Biological Products Advisory Committee and that these minutes accurately reflect what transpired.

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Sussan Paydar, Ph.D. Designated Federal Officer	Hana El Sahly, M.D. Chair

On December 12, 2024, at 8:30 a.m. Eastern Standard Time (EST), the 188th meeting of the Vaccines and Related Biological Products Advisory Committee (VRBPAC) convened to discuss two topics.

In the morning, for Topic I, the committee met in open session to discuss considerations for Respiratory Syncytial Virus [RSV] vaccine safety in pediatric populations.

In the afternoon, for Topic II, the committee met in open session to hear overviews of the Laboratory of Immunoregulation (LI) and Laboratory of Retroviruses (LR) research programs in the Division of Viral Products (DVP), Office of Vaccines Research and Review (OVRR), Center for Biologics Evaluation and Research (CBER). After the open session was completed, in the latter part of the afternoon, the meeting was closed to the public to permit committee deliberations, disclosure of which would constitute a clearly unwarranted invasion of personal privacy (5 U.S.C. 552b(c)(6)).

Dr. Hana El Sahly, the Chair, called the meeting to order at 8:30 a.m. EST. The Designated Federal Officer (DFO), Dr. Sussan Paydar made administrative remarks, conducted roll call, and invited the committee members to introduce themselves. She read the Conflict of Interest (COI) statement for the public record.

The meeting began with a 15-minute FDA Introduction by Dr. David C. Kaslow, Director, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research (CBER).

Next Dr. El Sahly called upon Dr. Fatimah Dawood, from Centers for Disease Control and Prevention (CDC) to speak on Epidemiology of Respiratory Syncytial Virus in U.S. Children. The talk was followed by a 5-minute Q&A.

At 9:20 a.m. EST, Dr. Hana El Sahly called upon Dr. Pedro Piedra from Baylor College of Medicine, Houston, Texas who gave a 30-minute presentation on "Clinical and Nonclinical Aspects of RSV Vaccine Safety in Young Children" followed by a 15-minute Q&A.

Next Dr. El Sahly called upon Dr. Christine Shaw and Dr. Matthew Snape from Moderna who together gave a 40-minute presentation on "Review of Investigational RSV (mRNA-1345) and RSV/hMPV (mRNA-1365) Vaccines in Infants and Children < 2 Years" followed by a 15-minute Q&A.

The committee took an approximately 5-minute break, reconvening at 11:03 a.m. EST for approximately a 30-minute FDA presentation, titled "Imbalance in Severe Respiratory Syncytial Virus (RSV) Cases in a Clinical Trial of an RSV vaccine in Infants and Young Children" by Dr. Mark Connelly. The presentation was followed by a 12-minute Q&A. The committee was given additional 10 minutes to discuss and ask questions from the morning presenters.

The Committee then took a 20-minute lunch break, reconvening at 12:15 p.m. EST for the Open Public Hearing (OPH) session. The Chair, Dr. Hana El Sahly, read the Chair's OPH Chair Statement. The DFO Dr. Sussan Paydar provided further OPH guidance. Four OPH participants attended the session. Two speakers were members of the public and gave approximately 3-6-minute presentations. The other two OPH participants were industry public speakers from Blue Lake Biotechnology and Sanofi, respectively, each with PowerPoint Presentations. After the OPH session concluded, some of the Committee members asked Sanofi OPH presenters clarifying questions.

After the OPH session was concluded, Dr. El Sahly, opened the floor to the committee for Considerations for Respiratory Syncytial Virus (RSV) Vaccine Safety in Pediatric Populations. The Committee was shown two sets of Discussion Topics as shown below:

1. **RSV Vaccine Safety in Pediatric Populations**

1.1 Please discuss whether the currently available evidence indicates a potential safety concern more broadly applicable to the evaluation of RSV vaccine candidates in infants and toddlers. Please discuss the applicability to:

a. different vaccine technologies (e.g., live-attenuated RSV, viral-vectored, mRNA, and subunit protein vaccines); and

b. different antigenic conformations (e.g., stabilized preF or other RSV protein prototypes).

1.2 Based on the currently available evidence, please discuss current nonclinical and clinical safeguards, and recommend whether any additional nonclinical and clinical information should be considered and/or precautions taken when evaluating RSV vaccine candidates in infants and toddlers.

2. Sequential Administration of RSV Monoclonal Antibodies (mAbs) followed by RSV Vaccines in Infants and Toddlers

2.1 Please discuss whether currently available evidence suggests potential RSV mAb (e.g., nirsevimab) - RSV vaccine interactions that may affect active immunization in infants and toddlers.

2.2 Based on currently available evidence, please discuss and recommend whether any additional factors and data should be considered when evaluating RSV mAb - RSV vaccine interactions, including potential impact of administration of RSV mAbs on safety and/or effectiveness of subsequent parenteral or mucosal administration of RSV vaccines.

The committee held a discussion for approximately 120 minutes before adjourning with Topic I at approximately 3:00 p.m. EST. Dr. El Sahly thanked the temporary voting members before moving to Topic II.

Meeting Summary for Topic I: FOR OVRR to fill in

VRBPAC agreed that the clinical trial safeguards implemented, based in part on discussion and recommendations made at the May 2017 VRBPAC meeting, were effective in identifying the potential safety signal observed in a clinical trial of investigational RSV vaccines in infants and children younger than two years of age. VRBPAC noted that additional information is needed to determine whether the safety signal is causally related to the investigational RSV vaccines and that data from pending analyses to be submitted by the sponsor would be informative in that regard. VRBPAC acknowledged the observation of a potential safety signal associated with administration of the human metapneumovirus (hMPV, closely related to RSV) vaccine in the same trial but cautioned that because the number of trial participants was small and safety follow up was still ongoing, no conclusion on the vaccine relatedness of this potential safety signal could be made at this time. VRBPAC emphasized several points for future consideration including the need for detailed understanding of the humoral and cell-mediated immunity following natural RSV infections versus vaccine-associated severe disease, evaluation of mucosal immune responses elicited by RSV/hMPV vaccines, and assessment of risk and genetic factors that may predispose individuals to vaccine-associated severe disease. VRBPAC also noted that investigational RSV vaccines manufactured using different vaccine technologies (including live-attenuated RSV vaccines) should be considered on a case-by-case, and that careful age-escalation approaches that incorporate appropriate nonclinical studies and clinical trial safeguards, and demonstration of benefits of vaccination in older RSV-naïve and RSV-experienced trial participants should also be considered prior to evaluation of investigational RSV vaccines in RSV-naïve infants younger than 2 years of age.

VRBPAC noted that insufficient information was available to comment on RSV vaccine – RSV mAb interactions or on the clinical significance of the observed immune blunting. VRBPAC recommended that studies evaluating effectiveness of investigational RSV vaccines in the context of prior RSV mAb administration should focus on timing of vaccine administration following RSV mAb treatment, route of RSV vaccine administration, and likely other factors to

better understand the clinical significance of RSV vaccine – RSV mAb interactions. VRBPAC highlighted that understanding RSV disease burden in the coming years in the context of well-established patterns of passive immunization measures will be critical to understanding the significance of RSV vaccine development in addressing unmet medical needs for infants.

The meeting proceeded to Topic II at 3:10 p.m. EST after a 10-minute break. The Committee met in open session to hear overviews of the Laboratory of Immunoregulation (LI) and the Laboratory of Retroviruses (LR) research programs in the Division of Viral Products (DVP), Office of Vaccines Research and Review (OVRR), Center for Biologics Evaluation and Research (CBER).

The VRBPAC Chair called the meeting to order and welcomed everyone, and then handed the meeting over to the DFO for a brief roll call and reading of the COI Statement.

Dr. Karen Elkins provided an "Overview of CBER Research and Site Visits" conducted in CBER.

Dr. Tod Merkel provided an overview of "Office of Vaccines Research and Review and Division of Viral Products" in CBER.

Next Dr. El Sahly called upon Dr. Carol Weiss, Chief and Principal Investigator from LI, DVP, OVRR, who provided an "Overview of the Laboratory of Immunoregulation" followed by a 5-minute Q&A.

Dr. El Shaly then called upon Dr. Hana Golding, Chief and Principal Investigator from LR, DVP, OVRR, who provided an "Overview of Laboratory of Retroviruses" followed by a 5-minute Q&A.

The presentations were followed by the Open Public Hearing (OPH) Session at 4:10 p.m. EST, for which there were no pre-registered OPH speakers. Dr. El Sahly announced that there were no pre-registered OPH speakers and concluded the open session of Topic II at 4:10 p.m. EST. She then thanked the Alternate Industry representative and handed the meeting over to CBER senior leadership, Dr. Marks and Dr. Kaslow who thanked the Committee for their contributions. The meeting moved to the Closed Session for the Site Visit Report discussions at approximately 4:15 p.m. EST.

Additional information and details may be obtained from the transcript and the recording of the webcast of the meeting that may be viewed at:

https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-december-12-2024-meeting-announcement