Food and Drug Administration
Center for Biologics Evaluation and Research

SUMMARY MINUTES
186th VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

September 20, 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.
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
Luis Jódar, Ph.D. ***

Consumer Representative
Jay Portnoy, M.D.*+

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

Committee Management Staff
Joanne Lipkind
Lisa Johnson

Temporary Voting Member
Anna Durbin, M.D.
Randy Hawkins, M.D. *>
C. Mary Healy, M.D.
Sarah Long, M.D.
Marcela Pasetti, Ph.D.
Melinda Wharton, M.D., M.PH.

Speakers and Guest Speakers
May ElSherif, M.D. M.P.H. (Canada)
Scott Halperin, M.D. (Canada)
Susan Hariri, Ph.D. (CDC)
Robert Read, M.D., FRCP (UK)

FDA Participants
Peter Marks, M.D., Ph.D.
David C. Kaslow, M.D. (Speaker)
Sudhakar Agnihothram, B. Pharm., Ph.D.
Tod Merkel, Ph.D. (Speaker)
Jay Slater, M.D.
E. Scott Stibitz, Ph.D. (Speaker)
Prabhakara Atreya, Ph.D.

+Not Attending
*Consumer Representative
*> Alternate Consumer Representative
***Industry Representative

These summary minutes for the September 20, 2024, meeting of the Vaccines and Related Biological Products Advisory Committee were approved on October 31, 2024.

I certify that I participated in the September 20, 2024, meeting of the Vaccines and Related Biological Products Advisory Committee and that these minutes accurately reflect what transpired.

-----X-----

Sussan Paydar, Ph.D.
Designated Federal Officer

------X-----

Hana El Sahly, M.D.
Chair

On September 20, 2024, at 8:30 a.m. Eastern Daylight Time (EDT), the 186th 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 related to the use of pertussis controlled human infection models [CHIMs] in pivotal studies to demonstrate effectiveness of pertussis vaccines for the purpose of licensure.

In the afternoon, for Topic II, the committee met in open session to hear an overview of the Laboratory of Mucosal Pathogens and Cellular Immunology (LMPCI) research program in the Division of Bacterial, Parasitic, and Allergenic Products (DBPAP), 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. EDT. 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 Kaslow, Director, Office of Vaccines Research and Review, Center for Biologics Evaluation and Research (CBER) followed by a 5-minute question and answer time (Q&A).

Next Dr. El Sahly called upon Dr. Susan Hariri, from Centers for Disease Control and Prevention (CDC) to speak on Pertussis Epidemiology in the Acellular Vaccine Era. The talk was followed by a 5-minute Q&A.

At 9:30 a.m. EDT, Dr. Hana El Sahly called upon Dr. Robert Read from University Hospital Southampton, United Kingdom who gave a 40-minute presentation on “A human challenge model of *Bordetella pertussis* infection” followed by a 10-minute Q&A.

Next Dr. El Sahly called upon Dr. Scott Halperin and Dr. May ElSherif, from Canadian Center for Vaccinology, Dalhousie University, Nova Scotia, Canada who together gave a 40-minute presentation on "The First North American Pertussis Controlled Human Infection Model Using the Pertactin-Producing D420 Isolate" followed by a 10-minute Q&A.

The committee took an approximately 10-minute break, reconvening at 11:00 a.m. EDT for a 30-minute FDA presentation, titled "Use of Controlled Human Infection Models (CHIMs) for Demonstration of Effectiveness of New Pertussis Vaccines" by Dr. Tod Merkel. The talk was followed by a 10-minute Q&A. The committee was given additional 20 minutes to discuss and ask questions from the morning presenters.

The Committee then took a 30-minute lunch break, reconvening at 12:30 p.m. EDT for the Open Public Hearing (OPH) session. The Chair, Dr. Hana El Sahly, read the Chair's Conflict of Interest statement. The floor was then assigned to Dr. Sussan Paydar who provided further OPH instructions. Four OPH participants attended the session. Two were members of the public and gave approximately 3-5-minute presentations. The other two OPH participants were industry public speakers from Sanofi and ILiAD each with PowerPoint Presentations. After the OPH session concluded, Dr. Sussan Paydar returned the floor to Dr. El Sahly to begin the next session.

Dr. El Sahly, opened the floor to the committee for Considerations for Development and Licensure of New Pertussis Vaccines. The Committee was shown two sets of Discussion questions as shown below:

1. Controlled Human Infection Model—*Disease Endpoint*
    a. Do *B. pertussis* controlled human infection models, in their current stage of development, produce signs and symptoms of disease that accurately and reliably reflect human disease caused by natural infection with *B. pertussis*?
    b. If yes, are *B. pertussis* controlled human infection models, in their current stage of development, sufficiently robust models of natural infection and disease to provide the primary human data to support effectiveness of new pertussis vaccines for booster vaccination of adults?

2. Controlled Human Infection Model—*Colonization Endpoint*
    a. Can prevention of *B. pertussis* colonization be considered a surrogate endpoint that is reasonably likely to predict clinical benefit, specifically prevention of pertussis disease?
    b. If yes, do *B. pertussis* controlled human infection models of colonization, in their current stage of development, accurately and reliably reflect colonization following natural *B. pertussis* exposure?

The committee discussed the Disease Endpoint and Colonization Endpoint questions for approximately 95 minutes before adjourning with Topic I at approximately 2:50 p.m. EDT.

Meeting Summary for Topic I:
The committee expressed overall excitement on the use of controlled human infection models with disease or colonization as endpoints. VRBPAC members discussed several considerations on the use of these models, including the relevance to pediatric populations, the limitations of these two CHIMs (e.g., differences compared with real-world pertussis disease), and the ability of these models to assess longer term effectiveness of pertussis vaccine candidates. Overall, the committee emphasized that clinical study design will be critical for using these models to assess effectiveness of pertussis vaccine candidates.

Disease Model: Although Committee members opined that additional work may add value in demonstrating the fitness-of-purpose of the disease model to assess effectiveness of pertussis vaccines, the VRBPAC consensus was that the model in its current state could be used in an adequately powered clinical study, with cough as a disease endpoint, to assess the efficacy of pertussis vaccine candidates. Committee members noted that other considerations on use of the disease model may include assessing durability of protection from vaccination and demonstration of noninferiority of pertussis vaccine candidates compared with currently licensed pertussis vaccines.

Colonization Model: Committee members opined that additional work may be needed to render the colonization model "fit-for-purpose" to support licensure of pertussis vaccine candidates through use of a surrogate endpoint reasonably likely to predict clinical benefit, specifically predicting prevention of real-world pertussis disease. Committee members cautioned that use of a sterilizing immunity endpoint in a colonization model may pose an unreachable outcome that risks impugning potentially effective pertussis vaccine candidates and noted that time to clearance of the challenge organism may provide a more tractable quantitative endpoint.

The meeting proceeded to Topic II at 3:00 p.m. EDT after a 10-minute break. The Committee met in open session to hear an overview of the Laboratory of Mucosal Pathogens and Cellular Immunology (LMPCI) research program in the Division of Bacterial, Parasitic, and Allergenic Products (DBPAP), 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 the brief roll call and reading of the COI Statement. Dr. Tod Merkel then explained the Site Visit Process and provided an overview of research conducted in CBER, OVRR, and DBPAP followed by a 5-minute Q&A.

Next Dr. El Sahly called upon Dr. Scott Stibitz, Chief and Principal Investigator from LMPCI, DBPAP, OVRR, who provided an "Overview of Research in the Laboratory of Mucosal Pathogens and Cellular Immunology (LMPCI)" followed by a 5-minute Q&A.

The presentations were followed by the Open Public Hearing (OPH) Session at 3:45 p.m. EDT, 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 3:45 p.m. EDT.

The Committee and CBER senior leadership then moved to the Closed Session for the Site Visit Report discussions.

Additional information and details may be obtained from the transcript and the recording of the webcast of the meeting that may be viewed at:
Vaccines and Related Biological Products Advisory Committee September 20, 2024 Meeting Announcement - 09/20/2024 | FDA