U.S. FOOD & DRUG ADMINISTRATION

Introduction

186th Vaccines and Related Biological Products Advisory Committee Meeting

David C. Kaslow, M.D.
Director, Office of Vaccines Research and Review/CBER/FDA
September 20, 2024

Since the 185th VRBPAC Meeting
(5-June-2024)

Allergenic Products Advisory Committee

- The Allergenic Products Advisory Committee (APAC) was terminated on July 9, 2024. For more information, please refer to the Federal Register Notice. FR Document Number 2024-15136 was published on July 10, 2024.
- All topics previously brought before the terminated APAC will now be addressed by the Food and Drug Administration's Vaccines and Related Biological Products Advisory Committee (VRBPAC).

Source: https://www.fda.gov/advisory-committees/blood-vaccines-and-other-biologics/allergenic-products-advisory-committee

186th VRBPAC Meeting Topics

Topic I: Use of pertussis controlled human infection models [CHIMs] in pivotal studies to demonstrate effectiveness of pertussis vaccines for the purpose of licensure.

Topic II: Overview of the research program in the Laboratory of Mucosal Pathogens and Cellular Immunology (LMPCI | DBPAP | OVRR | CBER).

* “effectiveness” refers to the regulatory determination that is made on the basis of clinical efficacy and other data

Topic I: Use of pertussis controlled human infection models [CHIMs] in pivotal studies to demonstrate effectiveness of pertussis vaccines for the purpose of licensure.

Proposed Problem Statement

- Pertussis remains a public health threat in the acellular pertussis vaccine era.
- New safe and effective pertussis-containing vaccines that increase the duration of disease protection and/or prevent transmission of *B. pertussis* may address an unmet medical need.
- Prospective randomized, controlled clinical efficacy endpoint studies adequate to demonstrate vaccine effectiveness may be infeasible to conduct.
- There are no scientifically well-established immunologic markers of protection for pertussis.
- Alternative approaches to demonstrate vaccine effectiveness may facilitate licensure of new pertussis-containing vaccines.

Topic I: Use of pertussis controlled human infection models [CHIMs] in pivotal studies to demonstrate effectiveness of pertussis vaccines for the purpose of licensure.

Focus of Today's VRBPAC Topic I

Discussion on the use of pertussis controlled human infection models [CHIMs] for the purpose of licensure of new pertussis vaccines for use as a booster dose in adults, including

- Traditional approval
- Accelerated approval

Generally, the following *product-specific* topics are out-of-scope today:

- Immunobridging to other population (children, immunocompromised, older adults, etc.)
- Licensure of combination vaccines containing new pertussis vaccine components
- Postmarketing studies (e.g., confirmatory studies as a condition of accelerated approval)

Topic I: Use of pertussis controlled human infection models [CHIMs] in pivotal studies to demonstrate effectiveness of pertussis vaccines for the purpose of licensure.

- Introduction
- Pertussis Epidemiology in the Acellular Vaccine Era
  - Dr. Susan Hariri, CDC
- Controlled Human Infection Models
  - A human challenge model of *Bordetella pertussis* infection
    - Dr. Robert Read, University Hospital Southampton
  - The First North American Pertussis Controlled Human Infection Model Using the Pertactin-Producing D420 Isolate
    - Dr. Scott Halperin, Dalhousie University
    - Dr. May ElSherif, Dalhousie University
- Use of Challenge Human Infection Models (CHIMs) for Demonstration of Effectiveness of New Pertussis Vaccines
  - Dr. Tod Merkel, FDA
- Additional Q & A
- Open Public Hearing
- Committee Discussion of Considerations for Development and Licensure of New Pertussis Vaccines

Topic I: Use of pertussis controlled human infection models [CHIMs] in pivotal studies to demonstrate effectiveness of pertussis vaccines for the purpose of licensure.

Discussion Questions

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?

186th VRBPAC Meeting Topics

Topic I: Use of pertussis controlled human infection models [CHIMs] in pivotal studies to demonstrate effectiveness of pertussis vaccines for the purpose of licensure.

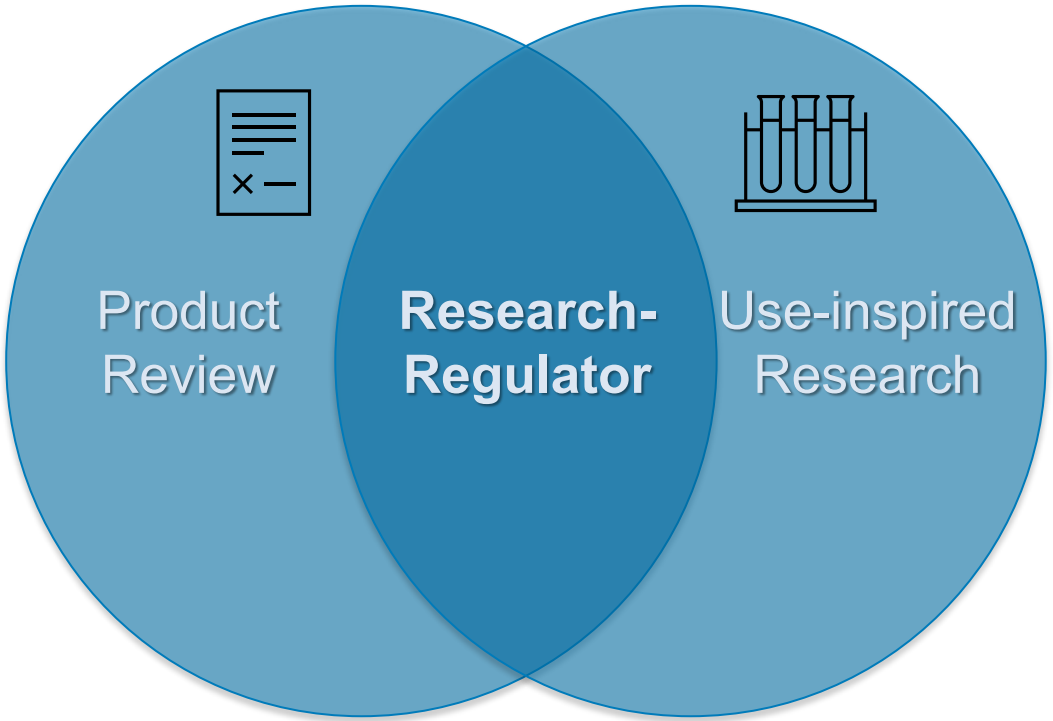
Topic II: Overview of the research program in the Laboratory of Mucosal Pathogens and Cellular Immunology (LMPCI | DBPAP | OVRR | CBER).

Topic II: Overview of the research program in the Laboratory of Mucosal Pathogens and Cellular Immunology (LMPCI | DBPAP | OVRR | CBER).

- Opening Remarks: Call to Order and Welcome
  - Dr. Hana El Sahly
- Roll call, Conflict of Interest Statement
  - Dr. Sussan Paydar
- Site Visit Process and Overview of Research conducted in CBER, OVRR, and DBPAP
  - Dr. Tod Merkel
- Overview of Research in the Laboratory of Mucosal Pathogens and Cellular Immunology (LMPCI)
  - Dr. Scott Stibitz
- Open Public Hearing
- Closed Session: Committee Discussion, Recommendation and Voting

OVRR Regulatory Use-Inspired Research

- Product review and 11 regulatory use-inspired research laboratories focused in two divisions:
  - **Division of Bacterial, Parasitic and Allergenic Products** (DBPAP)
    - Laboratory of Bacterial Polysaccharides
    - Laboratory of Immuno Biochemistry
    - Laboratory of Respiratory and Special Pathogens
    - Laboratory of Mucosal Pathogens and Cellular Immunology
  - **Division of Viral Products** (DVP)
    - Laboratory of DNA Viruses
    - Laboratory of Hepatitis Viruses
    - Laboratory of Immunoregulation
    - Laboratory of Method Development
    - Laboratory of Pediatric and Respiratory Viral Diseases
    - Laboratory of Retroviruses
    - Laboratory of Vector Borne Diseases
- Current FTEs: 166




FDA
U.S. FOOD & DRUG
ADMINISTRATION

Effectiveness v Efficacy

- The terms *"effectiveness"* and "*efficacy"* are used variably and often interchangeably by the scientific and regulatory communities.
- For purposes of FDA presentations at today's VRBPAC meeting, the term "*effectiveness"* is being used because it is the more commonly cited term in the Code of Federal Regulations.

Source: https://www.fda.gov/media/72335/download