

Introduction

188th Vaccines and Related Biological Products Advisory Committee (VRBPAC) Meeting

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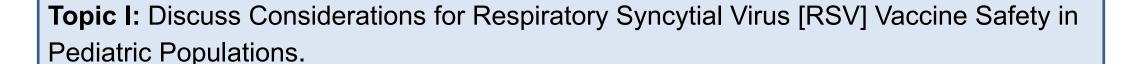
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188th VRBPAC Meeting Topics



Topic I: Discuss Considerations for Respiratory Syncytial Virus [RSV] Vaccine Safety in Pediatric Populations.

Topic II: Overview of Research Programs in the Laboratory of Immunoregulation (LI) and the Laboratory of Retroviruses (LR) in the Division of Viral Products (DVP | OVRR | CBER).





Current Context

- Observation in 1960's of enhanced respiratory disease (ERD) following RSV infection in formalin-inactivated RSV (FI-RSV) vaccinees cast a long shadow over RSV vaccine development.
- Recent advances in vaccine technologies and structural immunology, and plausible immune mechanisms that may explain FI-RSV vaccine-associated ERD (VAERD) facilitated RSV vaccine development and evaluation, respectively, including in adult, pregnant, and pediatric populations.
- Licensure of products that provide passive RSV immunity during infancy have partially addressed the unmet need for pediatric RSV vaccines.

New Considerations

- An imbalance in severe RSV lower respiratory tract disease has been observed following administration of mRNA-based RSV vaccine candidates to infants, the cause and mechanism of which have not been established.
- A potential RSV mAb RSV vaccine interaction has been observed that may impact active immunization in infants and toddlers.

Topic I: Discuss Considerations for Respiratory Syncytial Virus [RSV] Vaccine Safety in Pediatric Populations.



- CDC: Epidemiology of Respiratory Syncytial Virus in U.S. Children
 - Dr. Fatimah S. Dawood, CDC
- Clinical and Nonclinical Aspects of RSV Vaccine Safety in Young Children
 - Dr. Pedro A. Piedra, Baylor College of Medicine
- Review of Investigational RSV (mRNA-1345) and RSV/hMPV (mRNA-1365) Vaccines in Infants and Children < 2 Years
 - Drs. Christine Shaw and Matthew Snape, Moderna
- FDA: Imbalance in Severe Respiratory Syncytial Virus (RSV) Cases in a Clinical Trial of an RSV Vaccine in Infants and Young Children
 - Dr. Mark Connelly, FDA
- Open Public Hearing
- Committee Discussion and Recommendations

Topic I: Discuss Considerations for Respiratory Syncytial Virus [RSV] Vaccine Safety in Pediatric Populations.



Discussion Topics

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.

Topic I: Discuss Considerations for Respiratory Syncytial Virus [RSV] Vaccine Safety in Pediatric Populations.



Discussion Topics

- 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.

Considerations for Pediatric RSV Vaccine Development under U.S. IND



Considerations for enrollment of presumed RSV-naïve infants and children for RSV vaccine candidates under U.S. IND include:

- 1. If and how our current understanding of FI-RSV VAERD pathophysiology may inform benefit-risk assessments of other vaccine technologies
- 2. What critical additional assessments may further characterize the observed safety signal
- 3. What additional data may help stratify potential VAERD risk across vaccine technologies and antigenic compositions
- 4. How nonclinical studies may further inform potential VAERD risk in clinical studies
- 5. What additional risk mitigation/management strategies may address potential VAERD risk in clinical studies
- 6. How benefit-risk assessments may incorporate vaccine candidate benefits in RSV-experienced children, uncertainties regarding potential VAERD risk, and available preventative interventions (e.g., RSV mAb and maternal immunization)
- 7. How to address potential RSV mAb RSV vaccine interactions in clinical development plans and pediatric clinical study designs

