RSV Vaccine
Preferred Product Characteristics

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Background

• PPCs describe WHO preferences for parameters of vaccines to priority pathogens for which there is unmet public health need:
  • Indications & target populations
  • Immunization strategies
  • Clinical and laboratory features of safety and efficacy

• Differ from Target Product Profiles (TPPs) in that they focus on preferences, do not include minimally acceptable criteria, and are generally applied to vaccines earlier in the pipeline

• Focus of WHO PPC is on LMIC perspective
RSV Vaccines: a WHO Strategic Priority

• RSV is the most common cause of lower respiratory infection in neonates and infants.

• RSV is globally prevalent but children living in LMICs bear a disproportionate burden of severe disease outcomes.
WHO report

WHO consultation on Respiratory Syncytial Virus Vaccine Development Report from a World Health Organization Meeting held on 23–24 March 2015

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Indications

• Prevention of severe or very severe RSV (A/B) lower respiratory tract infection (LRTI)

• Focus on preventing disease in seronegative infants and children less than 5 years old.
Target Populations

1) Maternal/passive immunization to prevent RSV disease in infants less than 6 months old

2) Pediatric immunization to prevent RSV disease in infants and young children after protection afforded by maternal immunization wanes
Safety

• Initial evaluation in multiple animal models (e.g. mouse, rat, cotton rat, bovine)

• Infants
  • Legacy of FI-RSV enhanced disease
  • Age de-escalation to the very young & seronegative

• Pregnant women
  • Safety database for 1st in class vaccine to prevent disease in infants by immunizing pregnant women

• No minimum number for approval but past databases included 6K – 40K participants
# Efficacy – Endpoints/Case Definitions

<table>
<thead>
<tr>
<th>Severe RSV LRTI</th>
<th>Very Severe RSV LRTI</th>
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<tbody>
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<td>An infant or young child presenting to a health facility that is part of the case ascertainment system for the phase III trial who fulfills both the laboratory <strong>AND</strong> clinical criteria below:</td>
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<td><strong>Laboratory criterion</strong> RSV infection as confirmed by a fit-for-purpose, fully validated PCR assay with high specificity and sufficient sensitivity on upper respiratory samples.</td>
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<td><strong>Clinical criteria</strong> Respiratory Infection defined as Cough or Difficulty Breathing <strong>AND</strong> LRTI defined as FAST BREATHING by WHO criteria <strong>OR</strong> SpO2 &lt; 95% <strong>AND</strong> ≥ 1 OF THE FOLLOWING FEATURES OF SEVERE DISEASE: Pulse oximetry &lt; 93% <strong>AND/OR</strong> lower chest wall in-drawing</td>
<td><strong>Clinical criteria</strong> Respiratory Infection defined as Cough or Difficulty Breathing <strong>AND</strong> LRTI defined as FAST BREATHING by WHO criteria <strong>OR</strong> SpO2 &lt; 95% <strong>AND</strong> ≥ 1 OF THE FOLLOWING FEATURES OF VERY SEVERE DISEASE: Pulse oximetry &lt; 90% <strong>AND/OR</strong> Inability to feed <strong>AND/OR</strong> Failure to respond/unconscious</td>
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Durability & Safety Follow Up

- Follow-up should extend through at least 2 RSV seasons:
  - To evaluate for durable immunogenicity and protection & cross protection against viral strains
  - To detect unexpected adverse events in children who were protected against severe RSV infection during their 1\textsuperscript{st} season but may experienced RSV infection during the 2\textsuperscript{nd} season
Clinical development pathway: Pregnant women

- Safety/Immunogenicity
- Safety/Immunogenicity/Formulation
- Proof-of-Concept/Efficacy

**High Income Settings**
- Phase I Healthy Adults
- Phase IIa Healthy Adults
- Phase IIa Pregnant Women
- Phase IIB/III Pregnant Women

**Low/Middle Income Settings**
- Phase I Healthy Adults
- Phase IIa Healthy Adults
- Phase IIa Pregnant Women
- Phase IIB/III Pregnant Women
Pre-Qualification

• The vaccine should be WHO pre-qualified according to the process outlined in: *Procedures for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies*
### Live Attenuated

- **RSV**
  - NIH (Synthetic RSV)
  - RSV F and G VLP
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  - RSV F and G VLP
  - RSV F and G VLP

### Vectored

- **Influenza-A/RSV**
  - Boivin/human PV-RSV

### Whole Inactivated

- **NanoR**
  - RSV

### Particle

- **Virus like particle**
  - Fraunhofer RSV F or G VLP
  - RSV F Site II VLP
  - Newcastle disease virus F/G VLP

### Subunit

- **Fusion protein (Pre)**
  - NIH RSV Stabilized Pre-F
  - Uncloned F monomer
  - Conformationally constrained F
  - Tomato expressed RSV F

- **Fusion protein (Post)**
  - RSV Prototype F/TLR agonist / Host defense peptide
  - Tomato expressed RSV F
  - Intermediate F
  - Novartis Post-F

- **Fusion protein (Intermediate)**
  - Conformationally constrained F
  - Tomato expressed RSV F
  - Intermediate F
  - Novartis Post-F

### G protein

- Conformationally constrained F
  - Tomato expressed RSV F
  - Intermediate F
  - Novartis Post-F

### SH protein

- Self-amplifying RNA in lipid nanoparticle

### Combination surface proteins

- Renaptyx Vaccines
  - RSV peptides
  - DPX-RSV, Adjuvant surface proteins

### Nucleic Acid

- **DNA**
  - NIH RSV Synthetic Construct

- **RNA**
  - RSV mRNA
  - Self-amplifying RNA in lipid nanoparticle

### Recombinant Vector

- **Adenovirus**
  - RSV expressing RSV F
  - Replication-deficient Ad5 expressing RSV F
  - Ad5 expressing RSV F
  - Replication-deficient Ad5 expressing RSV F

- **Modified Vaccinia Ankara (MVA)**
  - MVA expressing RSV A
  - Replication-deficient MVA expressing RSV A

- **Alphavirus**
  - Replication-deficient VEE VLP expressing RSV F
  - Replication-deficient VEE VLP expressing RSV F or G

- **Sendai virus**
  - Sendai expressing RSV F

### Combination Platform

- DNA prime/Protein boost
  - RSV F DNA & Protein

### Passive Prophylaxis

- Anti-Pre-F MAb