RSV vaccine research and development: WHO technical roadmap

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WHO Initiative for Vaccine Research

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What is WHO’s Initiative for Vaccine Research (IVR) role?

Acceleration of vaccine development and increasing access to vaccines, in low and middle income countries (LMICs)
WHO Initiative for Vaccine Research
Bridging R&D, licensure, policy, financing, use

WHO IVR guidance

Research & Product development
Licensure

WHO Policy Decision
WHO PQ

Procurement Financing
Country processes
Regulatory and Policy Perspectives: optimize public health impact

<table>
<thead>
<tr>
<th>Regulatory</th>
<th>Policy perspective</th>
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<tr>
<td>• Quality</td>
<td>• Safety</td>
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<tr>
<td>• Manufacturing consistency</td>
<td>• Efficacy &amp; effectiveness</td>
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<tr>
<td>• Safety</td>
<td>• Impact, often modelled</td>
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<tr>
<td>• Efficacy, sometimes inferred from immunogenicity</td>
<td>• Feasibility of implementation</td>
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<tr>
<td>• Initial licensure databases for new vaccines have varied from 6,000 to 40,000 or so</td>
<td>• Health economic evaluations</td>
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<td>• Risk/Benefit profile</td>
<td>• Role of the intervention in the context of existing interventions</td>
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<td>• Broader perspectives including equity, community acceptability</td>
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How to prioritize investments?
Value proposition

- End to end perspective:
  - R&D investments required
  - Manufacturing and pricing
  - Costs related to implementation and use
  - Health benefits & Health Systems impact, societal impacts
  - Beyond cost-effectiveness

Cost of vaccine preventable disease burden
Cost of development, procurement, delivery
Consultations on RSV vaccine development, 03/2015, 04/2016

- Reviewed burden of disease and vaccine R&D landscape
- Identify gaps in knowledge, clinical development challenges for both maternal, paediatric vaccines and mAbies
- Case definitions
- Launch of
  - Vaccine R&D Technical Roadmap
  - Preferred product characteristics documents
SAGE April 2016 recommendations regarding RSV vaccines

- RSV surveillance to better characterize **RSV disease burden**
- Assessment of the **long term effects of RSV interventions**
- Derive **impact and cost effectiveness** estimates
- Strengthening of the **maternal immunization platform**
- Establishing a **WHO PQ pathway for monoclonal antibodies**
- Initiate **early discussions with financing bodies**

www.who.int/wer/2016/wer9121.pdf
RSV Vaccine R&D Technology Roadmap

Vision and goal:
High quality, safe, effective, affordable & accessible vaccines that prevent severe disease and death in infants <12 months & reduce morbidity in children <5 years, appropriate for LMICs.

Priority approaches:
1. Maternal vaccines leading to trans-placental antibody transfer & prevention of RSV disease in neonates & young infants
2. Paediatric vaccines to prevent RSV disease in infants & young children.

Note: Focus on vaccines, but most considerations are relevant to the development of mAbs

Reference:
Consensus research priority activities

• Improve global estimates of disease burden and potential vaccine impact
  – Age stratified data in the very young
  – Identify risk factors (including co-infections) for adverse outcomes
  – Clarify relationship with wheeze, reactive airway disease, asthma
  – Estimate vaccine impact on disease (by various vaccination scenarios)
  – Estimate health economic impact and reduction of antibiotic use

• Increase availability and quality standards of pre-clinical tools for evaluating candidate RSV vaccines

• Develop quality-assured standard reference immune assays
Consensus clinical development priority activities

- Define key elements of trial design & development progression steps
  - Establish consensus on staged clinical development plans for vaccine evaluation in pregnancy and for RSV seronegative infants
  - Define optimal dose, schedule, timing of vaccination during pregnancy and the need for re-vaccination during subsequent pregnancies.
  - Define safety and efficacy endpoint case definitions and standard data capture methodologies relevant and applicable in LMICs, allowing comparisons across studies.
  - Define relevant immunological assays in clinical trials, with the goal of determining correlates of protection.
  - Determine an appropriate strategy for assessment of the long term effects of vaccination on recurrent wheezing & reactive airway disease
Key capacities

- Investigator networks
- Baseline data: surveillance, preparation for post-introduction studies

Consensus policy and delivery activities

- Comprehensive health economic value proposition
- Develop functional program delivery strategy & platforms
  - ANC/EPI
  - Role of season-based delivery?
  - Surveillance
- Understand barriers to uptake
Preferred Product Characteristics

- Provides guidance to scientists, regulators, funding agencies & industry groups developing RSV vaccine candidates to help define their suitability & value proposition for LMICs.

  - Preferred characteristics related to indication; target population; schedule; vaccine platform & adjuvants; safety; efficacy; strain specify; Immunogenicity; Non-interference/co-administration; Route of Administration; Registration, prequalification and programmatic suitability; Value Proposition.
## PPC notes (ie. Maternal immunization)

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<thead>
<tr>
<th>Parameter</th>
<th>Preferred Characteristic</th>
<th>Notes</th>
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<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>Prevention of severe RSV disease in neonates and early infancy</td>
<td>Published WHO proposed case definitions</td>
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<tr>
<td><strong>Target population</strong></td>
<td>Pregnant women, second or third trimester</td>
<td>Preference for increased range</td>
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<tr>
<td><strong>Schedule</strong></td>
<td>One dose</td>
<td>Role of two doses?</td>
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<tr>
<td><strong>Safety</strong></td>
<td>No indication of ERD in offspring</td>
<td>Safety stage gates? Safety in HIV Bridge to pregnancy immunization initiatives</td>
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<tr>
<td><strong>Efficacy</strong></td>
<td>70% against severe RSV disease in the offspring, 0-4m</td>
<td>Other endpoints of interest: Non severe RSV disease Long term respiratory health Protection of mothers Reduction of AB use</td>
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<tr>
<td><strong>Strain specificity</strong></td>
<td>A and B subtypes</td>
<td>Impact of variability, polymorphism</td>
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<tr>
<td><strong>Immunogenicity</strong></td>
<td>Established correlate/surrogate of protection</td>
<td>Assay development needed</td>
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<tr>
<td><strong>Value proposition</strong></td>
<td>See programmatic recommendations</td>
<td>Comprehensive health economic research needed</td>
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GAVI: Vaccine candidates are evaluated and prioritised, guiding investment decisions

Approach for vaccines for endemic diseases (criteria to be reviewed by Gavi Board in Nov 2017)

Vaccine Analyses

- Main product characteristics
- Efficacy
- Impact
- Likely vaccination strategy
- Uptake in countries
- Target population
- Coverage
- Price
- ...

Funding decisions

E.g.
- Financing vaccines for routine immunisation
- Catalytic (operational) support for introduction
- Stockpile
- Learning agenda
Thank you

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