

# RSV Vaccine Research and Development Technology **ROADMAP**

Priority activities for development, testing, licensure and global use of RSV vaccines, with a specific focus on the medical need for young children in low- and middle-income countries

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## 2017



World Health  
Organization

RESPIRATORY  
SYNCYTIAL  
VIRUS (RSV)  
VACCINE  
**TECHNOLOGY  
ROADMAP**

A stylized blue wave graphic, consisting of three curved lines that sweep upwards and to the right, positioned below the text.

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## WHO secretariat

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## Credits

Page 3: CDC/Dr. Craig Lyerla

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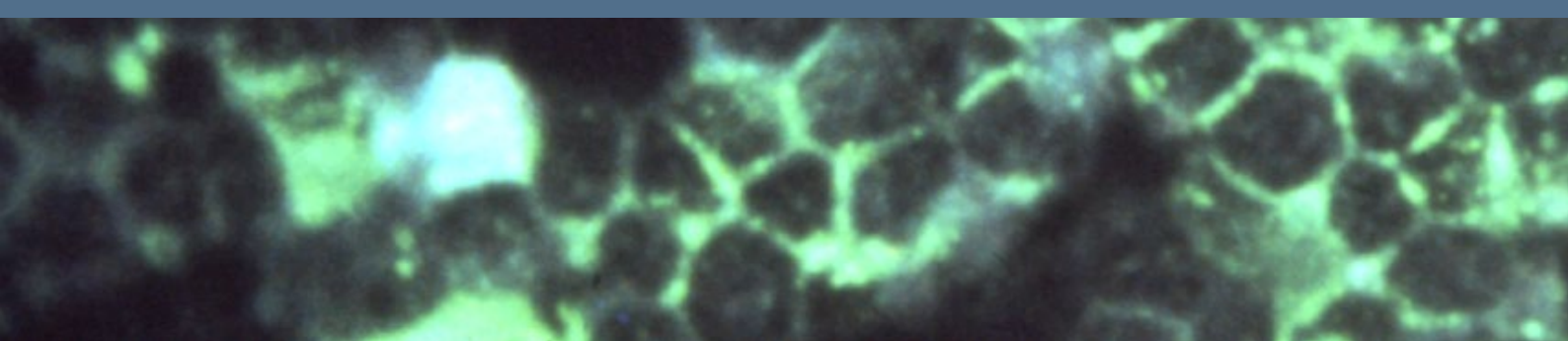
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## .....> Background

Respiratory syncytial virus (RSV) is the most common cause of lower respiratory tract infection in neonates and young infants. The risk of severe outcome is highest in the first months of life, but RSV causes significant morbidity throughout childhood. A vast majority of the disease burden lies in low- and middle-income countries (LMIC). Seasonal incidence variations are marked in temperate climates, more than in tropical areas. Important gaps in epidemiological characterisation remains, including data to define the long term impact of RSV infection on respiratory health.

Symptomatic supportive care constitutes the cornerstone of severe RSV disease clinical management. One licensed monoclonal antibody used for passive immunization is recommended and available for prevention of severe RSV in selected high-risk groups in high-income countries. However, this intervention is generally not accessible in lower resource settings due to its cost and monthly dosing delivery logistics. Second generation candidate monoclonal antibodies, with improved pharmacokinetics, pharmacodynamics and/or lower cost are being evaluated.

RSV vaccine research and development activities have been re-vitalised in the last years, as the field advanced beyond the legacy of enhanced RSV disease caused by immunization with crude formalin-inactivated whole virus vaccine in the 1960s. In March 2015 and April 2016, WHO convened consultations with RSV subject matter experts from academia, industry, government and regulatory authorities to formulate guidance on RSV vaccine development. The need to prepare in anticipation of RSV vaccine licensure in years ahead, to identify and address gaps in the pathway to prequalification, policy recommendation and implementation, was highlighted. Significant progress was made on developing strategic goals, drafting candidate case definitions, and identifying development pathways for RSV vaccines – particularly those administered through maternal immunization and targeting protection of young infants in the first months of life.

To ensure meaningful vaccine impact where it is most needed in the shortest timeframe possible, a number of key research and product development activities need to be undertaken. These priority activities are outlined in this document. Many activities presented here are relevant to the field of prophylactic monoclonal antibody development, and some specific needs to support the development of passive immuno-prophylaxis for use



in LMIC are highlighted herein, but more detailed priorities are beyond the scope of this document. While vaccine development activities targeting protection against RSV disease in the elderly are ongoing, this population is currently not prioritized within the scope of this document.

Outlined below, the RSV vaccine ‘Vision’ articulates the prioritized public health need and the ‘Strategic Goals’ describe two vaccination strategies designed to realize that vision.

Updates to this Roadmap will be formally considered following significant research findings, product development events, or changes to key underlying assumptions that warrant reassessing this stated vision, strategic goals or priority activities. WHO will encourage implementation of the finalised roadmap by the RSV vaccine community.

## » Vision

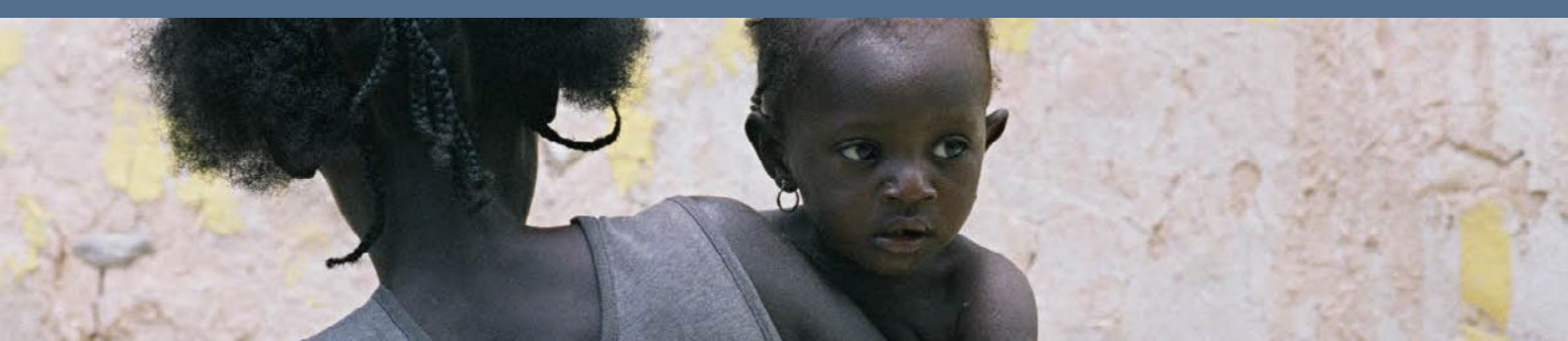
**There is a need for high-quality, safe, effective, affordable and accessible RSV vaccines that prevent severe disease and death in infants less than 12 months of age and reduce morbidity in children less than 5 years of age, appropriate for use in LMICs.**

## » Strategic Goals

**Develop and license high-quality, safe and effective RSV vaccines that prevent severe disease and death in infants less than 12 months of age and to reduce morbidity in children less than 5 years of age, and to ensure they are available and affordable for global use including in LMICs.**

Two priority approaches are identified:

- ❶ Development of vaccines for maternal immunization during pregnancy leading to trans-placental antibody transfer and prevention of severe RSV disease in neonates and young infants.
- ❷ Development of vaccines for paediatric immunization to prevent RSV disease in infants and young children.



## .....> Consensus priority activities

### Research

#### **Improve global estimates of disease burden and potential vaccine impact.**

- Improve global RSV surveillance platforms and conduct epidemiology studies to generate estimates of age-stratified disease burden (especially in the first months of life) including mortality; identify risk factors (including co-infections) for adverse outcomes; clarify the relationship between RSV and recurrent wheezing, reactive airway disease and asthma; improve understanding of RSV transmission dynamics to identify potential target groups for prevention of transmission; describe local seasonality patterns to inform seasonal vs age-based vaccination strategies.
- Develop RSV disease burden (considering co-infections) and transmission mathematical models for further estimation of potential vaccine impact and selection of vaccine strategies and target population.
- Estimate the potential benefit of RSV vaccines in reducing antibiotic use and antimicrobial resistance.

#### **Increase availability and quality standards of pre-clinical tools for evaluating candidate RSV vaccines.**

- Better define the relevance of existing tools for preclinical safety and efficacy evaluation towards establishment of a consensus pre-clinical evaluation strategy and down-selection criteria for prioritization of vaccine candidates to progress to clinical evaluation.
- Ensure access to relevant preclinical tools and comparability of results between laboratories.





#### Develop quality-assured standard reference immune assays.

- Develop international reference standards to facilitate the comparison of immune responses to candidate RSV vaccines, including RSV-neutralizing antibody activity as measured by a variety of assays including plaque reduction neutralization, microneutralization, reporter virus, and epitope-specific assays.
- Establish accessible standard assay guidance and/or protocols to encourage harmonization and results comparability.

### Vaccine development

#### Define key elements of clinical development progression steps and vaccine clinical trial design.

- Establish a consensus on staged clinical development plans for vaccine evaluation in pregnancy (maternal immunization) and RSV seronegative (previously unexposed) infants (pediatric immunization), minimizing exposure to a risk of post-vaccination enhanced disease caused by subsequent natural RSV infection.
- Define optimal dose, schedule, timing of vaccination during pregnancy and the need for re-vaccination during subsequent pregnancies (maternal immunization).
- Define safety and efficacy study endpoint case definitions and standard data

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