

RSV STRATEGIC PRIORITIES- BMGF PERSPECTIVES

WHO Global RSV Surveillance mid term review meeting
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RSV Initiative E2E strategy

| Strategic Goal | Strategic areas of work |
|--|---|
| <ul style="list-style-type: none">▪ Reducing RSV mortality in first six months of life | <ul style="list-style-type: none">▪ Clarify RSV disease burden▪ Appropriate interventions development<ul style="list-style-type: none">Maternal RSV vaccineNeonatal Passive prophylaxis RSV mAb▪ Develop global policy, standards and norms for RSV Vaccine Development▪ Enhance understanding RSV Disease▪ Vaccine Access, sustainable finance, delivery and country preparedness |

CLARIFY RSV DISEASE BURDEN

| Strategy Area | Challenges |
|---|--|
| <ul style="list-style-type: none">▪ Ensure RSV disease burden clarity in developing countries and identify risk groups▪ Develop global guidance for RSV surveillance, disease burden estimation and enhance data quality▪ Utilize the improved data for intervention business case for sustainable global support | <ul style="list-style-type: none">▪ Insufficient documentation and understanding of disease burden/mortality in infants < 6 months▪ Standardization Challenges in burden estimation, wide range in global mortality estimates▪ Standardization of clinical case definition▪ Stakeholders and policy makers unaware of RSV burden |
| Key studies and activities | |
| <ul style="list-style-type: none">▪ RSV burden of disease studies in various geographies (Latin America, Asia, Africa)▪ Improving Global mortality estimates (RSV-GEN)▪ Prospective birth Cohort Studies (Argentina, South Africa)▪ Multi-country Aetiology study of Neonatal Infections in South Asia (ANISA)▪ Multi-country Pneumonia Etiology Research in Child Health (PERCH)▪ Child Health and Mortality Prevention Surveillance (CHAMPS) Network▪ RSV Community Mortality Studies in multiple geographies (Argentina, India, Zambia, Pakistan)▪ RSV Global mortality registry (RSV-Gold) | |

Maternal RSV Vaccine Development

| Strategy Area | Challenges |
|--|---|
| <p>Vaccine Development for Maternal Immunization</p> <ul style="list-style-type: none"> Accelerate global R&D for RSV maternal Vaccines Develop intervention Target Product Profile Identify lead vaccine candidate and plan integrated Product development Ensure global access to developing countries. Scientific, Regulatory and technical issues related to licensure Vaccine trials in pregnancy | <ul style="list-style-type: none"> Developing new product for maternal indication? Mitigate the risk of historic legacy of enhanced vaccine diseases with early vaccine trials Data and policy gaps for interventions in developing countries Unclear regulatory path- developed and developing country regulators alignment Stakeholders and policy makers unaware of neonatal mortality due to RSV |
| <p>Key studies and activities</p> | |
| <ul style="list-style-type: none"> Global landscape analysis of RSV vaccines to identify lead and other candidates (PATH) Preclinical comparative immunogenicity with 7-8 candidates (PATH) With Lead candidate (Novavax) <ul style="list-style-type: none"> Complete preclinical/CMC development/COGS/Manufacturing issues Immunogenicity, dose/regimen formulation studies in non-pregnant women Reproductive Toxicity studies in animal models Evaluating and Developing clinical trial sites for anticipated phase 3 studies Landmark First in Pregnancy Safety and immunogenicity study First ever Phase 3 global licensure study for RSV maternal vaccine launched (Novavax) | |

RSV Vaccine Global Standards, Norms and Policy Development

| Strategy Area | Challenges |
|--|---|
| <p>Global Standards, Norms and Policy Development</p> <ul style="list-style-type: none">• Establish global guidance for RSV surveillance• Global RSV vaccine development standards• WHO RSV regulatory guidance for evaluation of RSV vaccines and monoclonals | <ul style="list-style-type: none">• RSV not yet a priority for global and national policy makers• No established WHO position on RSV R&D priority• Non-existence of surveillance mechanisms for RSV• Lack of clarity on standards for assays• Unclear regulatory path for maternal vaccines• No prequalification pathway for monoclonals |
| Key activities | |
| <ul style="list-style-type: none">• WHO PDVAC prioritization of RSV• WHO SAGE endorsement of strategies for reducing disease burden in first six month of life• WHO guidance of study design and end-points in maternal RSV vaccines• Establishment of WHO International standard serum for RSV and standardization of neutralization and PCA assays• Global policy roadmap for RSV vaccine• Joint Regulatory review mechanisms for global RSV vaccine trials• Launch of WHO Global RSV surveillance pilot in 14 countries• WHO guidance for adaption of maternal influenza immunization policy in developing countries | |

Enhanced understanding of RSV Disease

| Strategy Area | Challenges |
|--|--|
| <p data-bbox="369 301 1098 339">Enhanced understanding of RSV Disease</p> <ul data-bbox="369 391 1182 611" style="list-style-type: none"><li data-bbox="369 391 1182 462">• Assess the impact of acute consequences in key risk groups<li data-bbox="369 505 1182 539">• Understand longer term consequences of RSV disease<li data-bbox="369 582 1182 611">• Better assessment of RSV severity | <ul data-bbox="1294 291 2150 662" style="list-style-type: none"><li data-bbox="1294 291 2150 325">• Poorly understood disease in developing country setting<li data-bbox="1294 368 2150 402">• RSV- Asthma association indicated but not confirmed<li data-bbox="1294 445 2150 516">• Strength of association and RSV related Asthma phenotype not well defined<li data-bbox="1294 559 2150 594">• RSV attributable asthma burden is not modelled<li data-bbox="1294 636 2150 665">• Lack of appropriately powered long term follow-up studies |

Key studies and activities

- Foundation global convening on RSV and Asthma
- WHO SAGE endorsement of leveraging opportunity of planned phase 3 intervention trials for longer term follow-up for asthma
- Development of standards and norms for such long term studies
- Cross-sectional follow-up of intervention study for assessment of asthma inception at age 6
- RSV Severity Score and assessing Biomarkers for RSV disease severity for vaccine trials
- Acute and longer term consequences of RSV infection in children
- Long term follow-up of birth cohort for pneumonia mortality

Vaccine access, delivery, sustainable finance and country preparedness

Strategy Area

- **Ensure vaccine access through sustainable finance mechanism**
- **Vaccine Delivery roadmap**
- **Country Preparedness**

Key challenges

- GAVI only vaccine finance mechanism
- 2018 Vaccine investment strategy will consider new vaccines like RSV, Flu and Dengue but envelope of resources limited
- New mechanisms like Global Financing Facility/Health Impact Fund
- GAVI graduate countries need new finance mechanisms- tiered pricing?
- Vaccine resource prioritization only on cost-effectiveness considerations, need new tools like IOM's strategic multi-attribute ranking tool for vaccines' (SMART)
- Political changes impacts vaccine uptake sometimes in positive way like India resulting into global vaccine supply issues
- RSV vaccines need Accelerated Development and Introduction Plan (ADIP-like mechanism) for country adoption

Why is Surveillance important?

Strategy Area

- **Standardized Guidance for Global RSV surveillance**
- **Standardized disease burden data collection – baseline in pilot countries, preparing for launch and post-vaccine launch impact studies**
- **Useful data for investment case for sustainable finance and country policy decisions**

Key challenges

- Country level policy makers not aware of RSV disease burden, priority risk groups, RSV interventions in pipeline
- Standardized surveillance guidance not available
- Standardized clinical case definitions
- Establishment of RSV surveillance capacity at country level
- Quality laboratory capacity development
- Possibilities of pre and post vaccine impact assessment studies
- Virological monitoring of RSV after country wide launch of RSV interventions (mAbs) – escape mutants monitoring
- Possible longer term prospective cohort studies to understand acute and longer term consequences of early life RSV exposure.