

Group B Streptococcus Vaccine Development Technology **ROADMAP**

Priority activities for development,
testing, licensure and global availability
of Group B streptococcus vaccines

2017



World Health
Organization

**GROUP B
STREPTOCOCCUS
VACCINE
TECHNOLOGY
ROADMAP**

A stylized blue wave graphic consisting of three curved, overlapping shapes that resemble a road or a path leading forward.

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Credits

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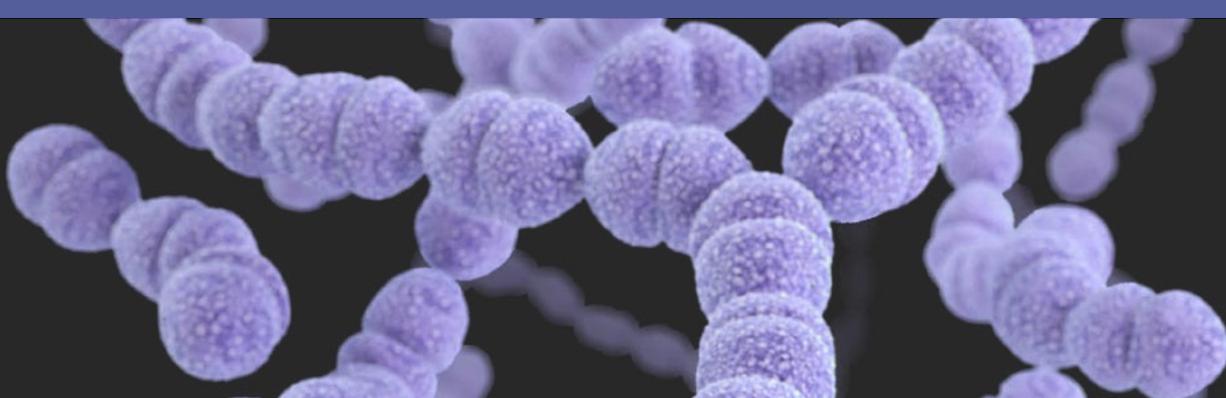


Background on Technology Roadmaps

Vaccine development technology roadmaps produced by the World Health Organisation (WHO) aim to provide a strategic framework underpinning priority activities for vaccine researchers, funders and product developers, with the goal to address globally unmet medical needs.

The present roadmap states the vision and strategic goals for Group B streptococcus (GBS) vaccine development from WHO, with input from public health agencies, academia, industry, regulators, ethicists and financing bodies amongst others. The GBS vaccine 'Vision' articulates the prioritized public health need, and the 'Strategic Goal' describes a vaccination strategy that will enable realization of that vision. The roadmap also lays out priority activities in the categories of research, product development, key capacities and policy, commercialization and delivery. The objective of this comprehensive framework is for the global GBS vaccine research and development community to accelerate timelines to licensure and use of GBS vaccines, especially in low- and middle-income countries where they are most needed. The present document is not intended to be product- or product type-specific.

WHO will encourage implementation of the finalised roadmap by the GBS vaccine community. Progress in the field will be monitored and if there are significant changes that warrant reassessing the vision, strategic goals or priority activities, the roadmap will be updated.



Introduction

GBS colonization during pregnancy occurs in some women in all geographical settings evaluated. GBS is a leading cause of sepsis and meningitis in neonates and young infants. The neonatal and infant disease incidence varies by country but can be as high as 3 cases per 1000 live births, with the case fatality rate ranging between 10% and 50% even when modern intensive care is available. GBS is also a cause of stillbirth, premature delivery, maternal and elderly disease, but precise disease burden estimates are lacking. The vast majority of the disease burden lies in low- and middle-income countries.

In high income countries, risk- or screening-guided intra-partum antibiotic prophylaxis reduces the incidence of early onset GBS disease, but not late onset GBS disease. Not all women at risk are reached, and a significant disease burden remains. This prevention strategy is not available or practical in most resource-limited countries.

Currently, no vaccine exists for prevention of GBS disease, but maternal immunization with multiple serotypes of protein-conjugated GBS capsular polysaccharides may reduce the disease risk in neonates and young infants through trans-placental passage of protective immunoglobulins. Protein-based vaccine candidates are also under evaluation.

» Vision

A safe, effective and affordable vaccine available for global use, to prevent GBS-related stillbirths and invasive GBS disease in neonates and young infants.

» Strategic Goal

To develop and license safe, effective and affordable GBS vaccines for maternal immunization during pregnancy to prevent GBS-related stillbirth and invasive GBS disease in neonates and young infants, appropriate for use in high-, middle- and low-income countries.



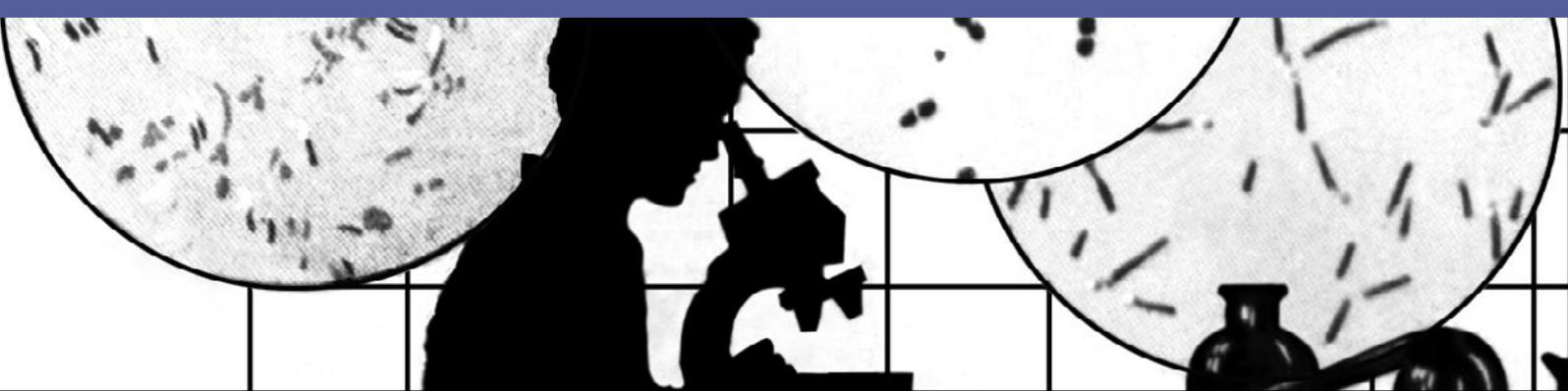
Research

Further quantify the unmet medical need for a GBS vaccine and its potential public health impact.

The global disease burden needs to be better defined, with characterization of serotype-specific distribution, especially in some geographical areas including South and South-East Asia, to guide required vaccine composition in terms of serotype diversity coverage. In addition to early- and late-onset disease, the burden of GBS-related still-birth, preterm birth and maternal disease needs to be further investigated. Rates of colonization recurrence, strain replacement, capsular switching, multiplicity of infection, and potential implications of vaccine introduction should be assessed. The potential impact of vaccine introduction on perinatal antibiotic use is a critical aspect and needs to be estimated, given the global problem of antimicrobial resistance and emerging data on the importance of preserving the neonatal microbiome.

Pursue efforts towards the development of vaccines with the potential to overcome serotype diversity and serotype-specificity of protection.

Protein-based vaccine candidates with the potential to induce protection independently of the capsular polysaccharide serotype are under development. Sequence polymorphisms in the target protein(s) also need to be considered.



Vaccine development

Develop quality-assured immunologic correlate(s)/surrogate(s) of protection.

The evidence base for correlates of protection can be derived from efficacy trials with nested immunogenicity evaluation or from the study of the association between maternal antibodies acquired following natural exposure and risk of neonatal and infant GBS disease in sero-epidemiologic studies, using quality-assured antibody capture and quantitative functional assays, with standardized procedures and reagents. Standard assays using reference reagents facilitate comparability assessments. Conservation of trial samples in anticipation of potential future use with innovative new platforms may be valuable.

The respective role of clinical efficacy estimation and immune correlate(s)/ surrogate(s) of protection in the pathway to licensure and recommendation for use should be defined, in consultation with regulators and policy makers.

Characterize key candidate vaccine immunogenicity parameters.

Serotype-specific vaccine immunogenicity in pregnant women should be characterized, including determination of the evolution of antibody titres over time in vaccinated mothers and in neonates, from birth through the at-risk period; of the IgG antibody transfer ratio from the mother to the newborn; of the optimal timing of immunization and other maternal factors influencing the transfer ratio; of the role of IgA antibodies and breastfeeding. The optimal vaccine dose, schedule, and requirements for adjuvants need to be determined, considering the preference for a one-dose regimen requiring no adjuvant or only adjuvants with established favourable safety for vaccination during pregnancy. The roles of past natural exposure, of pre-pregnancy priming, of a second dose in pregnancy, of boosters during subsequent pregnancies need to be defined. Immunogenicity upon co-administration with recommended vaccines for use in pregnancy, and impact on immune responses to relevant infant vaccines (considering both the target antigen and potential presence of a protein carrier) need to be evaluated.



Define pivotal clinical trial design

Case definitions and ascertainment methodologies need to be standardized, including detailed swabbing procedures for assessment of maternal and neonatal colonization, collection of hemocultures, CSF and other biological samples in subjects alive as well as in case of stillbirth or fatality. Optimal microbial culture and identification methods should be defined. Standardization should support the comparability of trial results.

Appropriate standards of care for maternal and infant infectious risk management in the context of a GBS vaccine efficacy trial should be defined, considering local standards of care and WHO recommendations.

Ensure appropriate data dissemination

GBS vaccine trial results should be made publicly available within 12 months of the last subject's last visit pertaining to primary endpoint data (<http://www.who.int/ictcp/results/reporting>).



Key capacities

Establish networks of investigators including research centres in low- and middle-income countries with Good Clinical Practices (GCP) trial research capacity and appropriate regulatory and ethical oversight; establish baseline rates of disease and common adverse obstetric and neonatal outcomes to prepare for optimal safety and efficacy surveillance.

Strengthen and use existing adapted recommendations and ongoing initiatives on safety surveillance for vaccines for use in pregnancy.

The Global Alignment of Immunization safety Assessment in pregnancy (GAIA) is an established partnership between WHO and the Brighton Collaboration aiming to provide standards and tools that strengthen and harmonize safety oversight, with specific focus on obstetric and neonatal outcomes in low and middle income countries (<http://gaia-consortium.net>).

Access to low cost vaccine manufacturing under current Good Manufacturing Practices (cGMP) for late stage development and commercial production.



Policy, commercialization and delivery

Establish cost-effectiveness and develop research and implementation financial investment scenario to support appropriate funding and policy decision-making at the global and national level, considering the full scope of costs and benefits.

A better understanding of the investment case may encourage responsible stewardship and support for vaccine development and implementation. A comprehensive business case analysis would need to include an estimation of research, development and manufacturing costs, market assessments and demand forecast, cost-effectiveness analyses, in a way that would support decision-making from manufacturers, research and implementation funders, WHO, and countries. Analyses should consider settings with different standards of care for infection prevention, including countries where a systematic intra-partum antibiotic prophylaxis strategy is not implemented.

Ensure availability, affordability, and acceptability of a functional, cost-effective delivery platform for immunization during pregnancy.

Potential barriers to access and uptake should be understood, taking into account health care providers' perspectives, community acceptance, user concerns. Communication and advocacy plans should be developed accordingly to reduce the risk of missed opportunities to immunize. Strategies towards implementation of various existing and future vaccines for use in pregnancy need to be developed.

Develop effectiveness and pharmacovigilance platforms for post-implementation surveillance. Strain replacement, capsular switching and the emergence of new virulent strains should be monitored. Monitoring of the impact of vaccine introduction on relevant current practice including reduction of antibiotic use is of particular interest.



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