Developing a novel Group B Streptococcus (GBS) Vaccine

Patrick Tippoo
1. Overview of Biovac
2. GBS Project Overview
3. African Significance
Biovac Overview

- A Centre of Excellence rooted in Africa for the development and manufacture of cost-effective vaccines

Establish **end-to-end vaccine development** and **manufacturing capability** for local and export markets

...through **product development partnerships** and **technology transfer partnerships**
Vaccine Manufacturing Infrastructure

Pre 2003

2007

2017
Vaccine Manufacturing Infrastructure
People: Skills Development

Focused investment in developing local skills

Headcount Growth

- 2003: 30
- 2008: 78
- 2013: 156
- 2016: 195
- 2017 (to date): 213
Technology Transfer Partnerships

Established two key manufacturing technology transfer partnerships

**Sanofi**
- Hexavalent vaccine
- Fill/Finish

**Pfizer**
- Pneumococcal conjugate vaccine
- Formulation/Fill/Finish
Product Development

Step-wise capacity building...

- Hib Conjugate Vaccine
- Pneumo Conjugate Vaccine
- Recombinant Vaccines
- GBS Conjugate Vaccine

- Partnership with BioNet Asia
- Out-licensed to 2 Asian vaccine manufacturers
- WHO PQ

- PATH Partnership
- Chengdu Institute for Biological Products

- HIV/AIDS Vaccine Candidate (European partner)
- TB Vaccine candidate (US Partner)

Capabilities

- Bacterial Fermentation
- Polysaccharide purification
- Conjugation
- Analytics

...focused on conjugate vaccine platform technologies
Backward Integration

4th transition
Development of Group B Strep (GBS) with PATH / BMGF

3rd transition
Formulate, Fill, Finish with Pfizer

2nd transition
Fill, Finish with Sanofi

1st transition
Packaging

R&D → Clinical Development → Antigen Manufacture → Formulation → Filling → Packaging & Labeling → Cold chain and Distribution
Developing a novel
GBS Vaccine
GBS Disease

Group B streptococcus (GBS):

... a leading cause of **sepsis** and **meningitis** in neonates and young infants.

... can cause stillbirths

- **Maternal colonisation** in pregnancy has been found in a proportion of women (10–40 %) in **all geographical settings** evaluated.
GBS Disease

- **Reported incidence** of neonatal and infant invasive GBS disease **varies geographically.**

... The vast majority of the disease burden lies in **low-and-middle-income countries.**

... Estimates as high as **3 cases per 1000 live births** in some areas (excluding stillbirths).

... **Case fatality is high** (10 % and 50 %) particularly in **resource poor settings.**

Chances of a baby dying in Africa from GBS is 4-5 times higher than in America or Europe.
Intra-partum antibiotic prophylaxis

- In high income countries, risk- or screening-guided *intra-partum antibiotic prophylaxis (IAP)* reduces the incidence of early onset GBS disease.

  ... This prevention strategy is **not available or practical** in most resource-limited countries.

  ... **Not all women at risk are reached,** and a significant disease burden remains.

  ... IAP also raises concerns about **emerging antimicrobial resistance**.
Currently, **no vaccine exists** for prevention of GBS disease, but evidence suggests

- **maternal immunisation** with protein-conjugated GBS capsular polysaccharides
- may **reduce the disease risk** in neonates and young infants in a serotype-specific manner

**Ten GBS envelope polysaccharide-based serotypes** have been described,

- **five** of which (Ia, Ib, II, III, V) are estimated to account for the **vast majority of the disease burden**
GBS Project Partnerships and Goals

Collaborative partnerships

- **Biovac** and **PATH** with technical assistance provided by **Inventprise** and other partners
- Funding provided by the **Bill & Melinda Gates Foundation**

Project Goals

- Develop a **low-cost polyvalent GBS conjugate vaccine** that will significantly reduce neonatal mortality caused by GBS in sub-Saharan Africa and potentially other low-income regions of the world.
- **Capacity building** for **African vaccine development and manufacturing**
GBS Project Goals

- Develop a pentavalent GBS vaccine
  - Obtain licensure in SA
  - Obtain WHO PQ

- Build vaccine manufacturing capacity in Sub-Saharan Africa
  - Skills development (>30 additional staff)
  - Enhancement of Technology Platforms
GBS Project Objectives

Phase 1  5 Objectives

1. Development of production processes for polysaccharide and monovalent conjugates for GBS serotypes Ia, Ib, II, III & V.

2. Formulation development of the pentavalent GBS vaccine

3. GMP production and release of intermediates and pentavalent GBS vaccine for Phase 1 study

4. Preclinical evaluation of immunogenicity and toxicity

5. Regulatory engagement and conduct of First in Human Phase 1 clinical study
GBS Technology Packages

- Isolate and Clonal Selection
- Fermentation
- Purification
- Conjugation
- Formulation

Analytical Method Development

- Capsule → Polysaccharides → Glycoconjugate
- Sugar
Process Development

**Step 1**
- Isolate and clonal selection
- Fermentation development

**Step 2**
- Purification and isolation of antigen (polysaccharide)

**Step 3**
- Conjugation
- Formulation
Process Development Deliverables

Output 1
A pure, high yielding strain for each of the 5 GBS serotypes

Output 2
Purified capsular polysaccharide that meets required quality specifications

Output 3
A set of highly immunogenic conjugates that provides Ab protection from mother to baby
GBS Project Roadmap and Timelines

- **Stage Gates**
  - PCD: Pre-clinical Development
  - FIH: First in Human trial

- **Process Development**
- Pilot scale batches
- Toxicology studies
- cGMP batches
- First in human studies

- Partnerships formally established in Q1 2017 and work at Biovac began in Q2 2017.
- First-in-human trial expected 2020

2017 — 2021
## WHO GBS Vaccine PPC

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Preferred Characteristic</th>
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</thead>
<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>Prevention of laboratory-confirmed GBS stillbirth and invasive GBS disease in neonates and young infants.</td>
</tr>
<tr>
<td><strong>Target Population</strong></td>
<td>Pregnant women, in the second or third trimester of pregnancy.</td>
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<tr>
<td><strong>Schedule</strong></td>
<td>A one dose regimen is highly preferred.</td>
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<tr>
<td><strong>Safety</strong></td>
<td>Safety and reactogenicity profile at least as favourable as current WHO-recommended routine vaccines for use during pregnancy (influenza, tetanus toxoid, acellular pertussis).</td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td>Available evidence supportive of 80% protection against combined risk of laboratory-confirmed GBS (all serotypes) stillbirth and invasive disease in the offspring.</td>
</tr>
<tr>
<td><strong>Strain and serotype coverage</strong></td>
<td>The serotypes in the vaccine formulation must cover at least 90% of the current invasive disease isolates in the target region.</td>
</tr>
<tr>
<td><strong>Adjuvant Requirement</strong></td>
<td>Preference for the absence of an adjuvant.</td>
</tr>
<tr>
<td><strong>Immunogenicity</strong></td>
<td>Established correlate/surrogate of protection based on a validated assay measuring antibody levels/ functionality in the mother and/or the neonate.</td>
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<td><strong>Non-interference</strong></td>
<td>Demonstration of favourable safety and immunologic non-interference upon co-administration with other vaccines recommended for use in pregnancy. Demonstration of non-interference with immune responses to relevant vaccines from the Expanded Program of Immunisation in infants of vaccinated mothers.</td>
</tr>
<tr>
<td><strong>Route of administration</strong></td>
<td>Injectable (IM, ID, or SC) using standard volumes for injection as specified in programmatic suitability for PQ or needle-free delivery.</td>
</tr>
<tr>
<td><strong>Registration, prequalification and programmatic suitability</strong></td>
<td>The vaccine should be prequalified according to the process outlined in Procedures for assessing the acceptability, in principle, of vaccines for purchase by United Nations agencies. WHO defined criteria for programmatic suitability of vaccines should be met</td>
</tr>
<tr>
<td><strong>Value proposition</strong></td>
<td>Dosage, regimen and cost of goods amenable to affordable supply. The vaccine should be cost-effective and price should not be a barrier to access including in low and middle income countries.</td>
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GBS Project: African context and significance

- Last successful novel vaccine development project in South Africa was OPV in 1950s.
- GBS Vaccine Development Project is a significant milestone for vaccine development in Africa.
- Addresses specific African disease burden.
- Responds to an unmet health need.
- Contributes to socioeconomic development and the bioeconomy in Africa.
THANK YOU