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Developing a novel Group B Streptococcus (GBS) Vaccine

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Presentation

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

Biovac Overview

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- 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

Product Development | **Manufacturing**

- …through **product development partnerships** and **technology transfer partnerships**

Vaccine Manufacturing Infrastructure

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Vaccine Manufacturing Infrastructure

People: Skills Development

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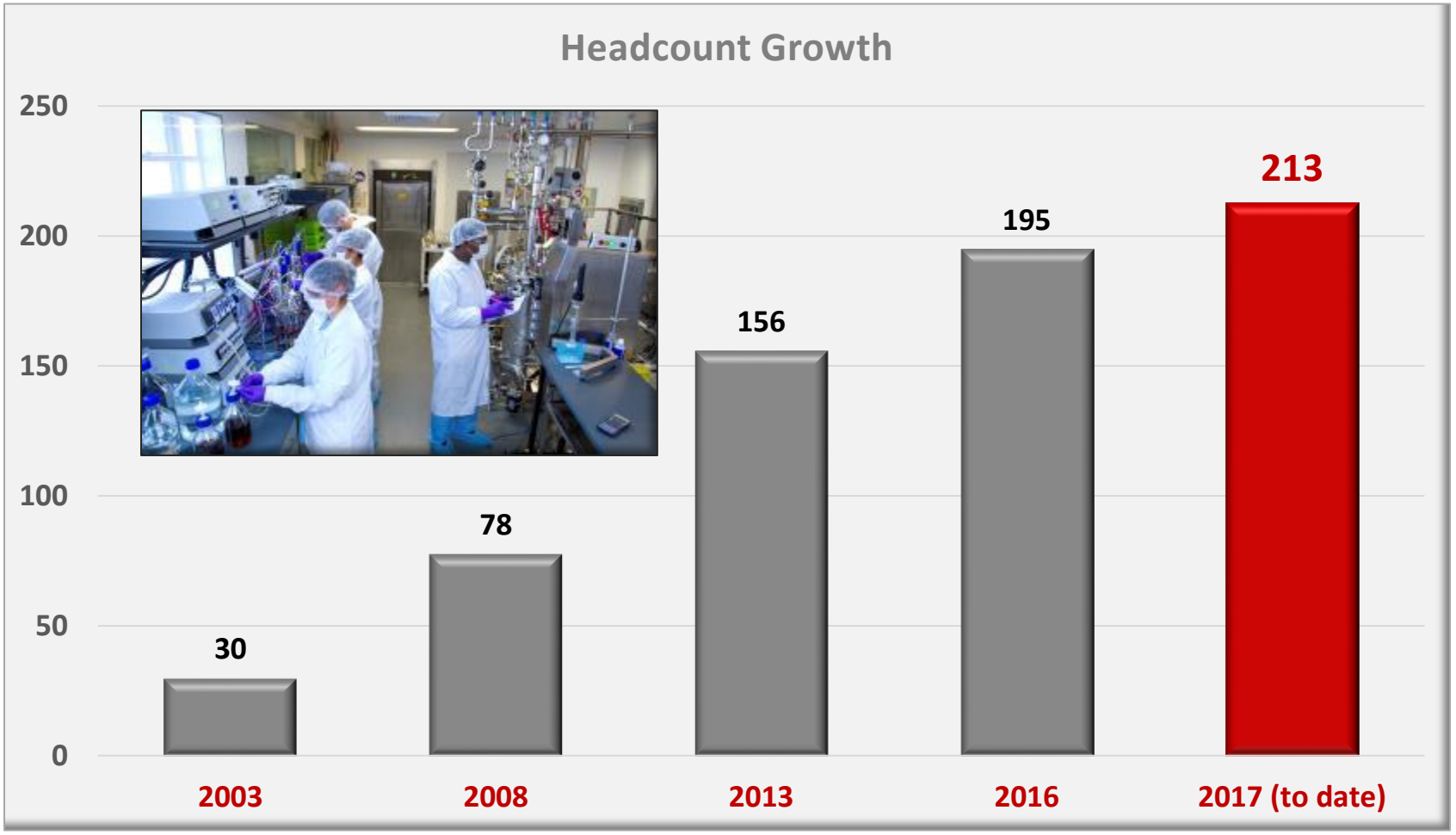
Focused investment in developing local skills



Technology Transfer Partnerships

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Established two key manufacturing technology transfer partnerships

Sanofi

- Hexavalent vaccine
- Fill/Finish

Pfizer

- Pneumococcal conjugate vaccine
- Formulation/Fill/Finish

Product Development

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Step-wise capacity building…

Hib Conjugate Vaccine

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

Pneumo Conjugate Vaccine

- PATH Partnership
- Chengdu Institute for Biological Products

Recombinant Vaccines

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

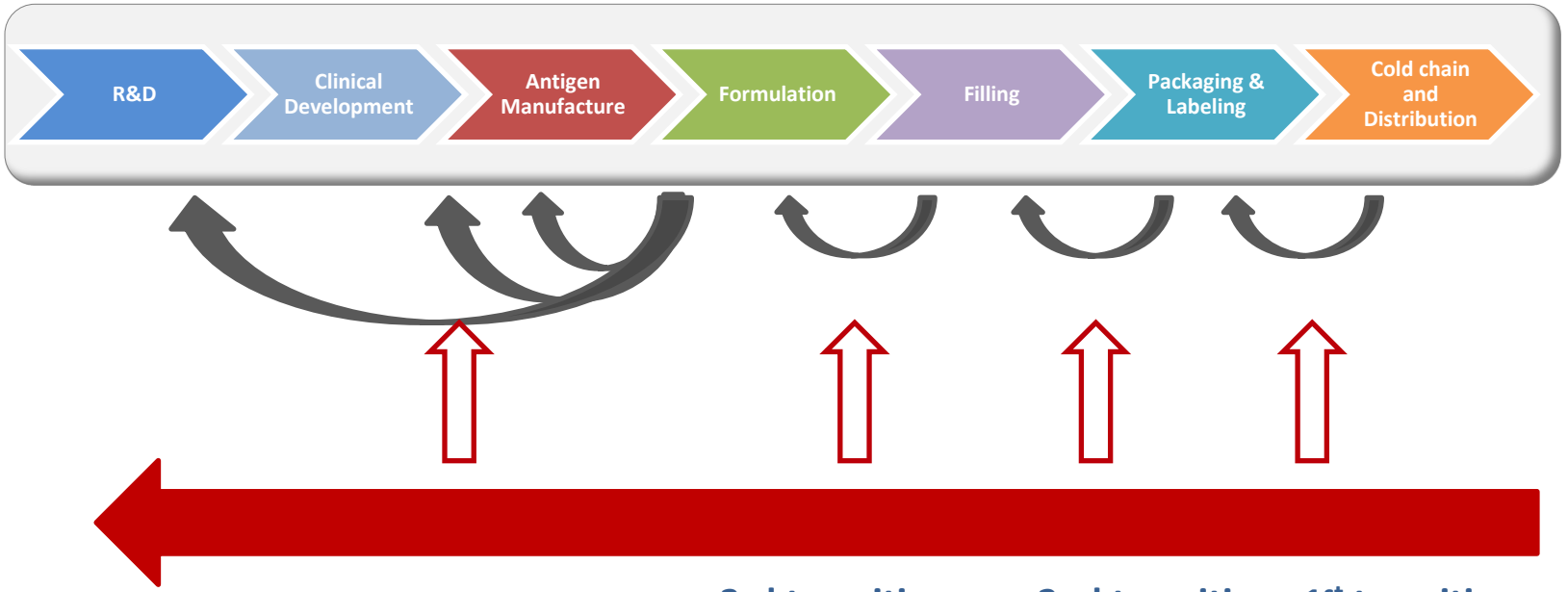
GBS Conjugate Vaccine

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

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Developing a novel GBS Vaccine

GBS Disease

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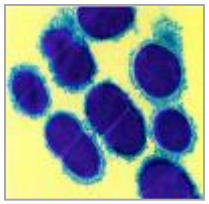
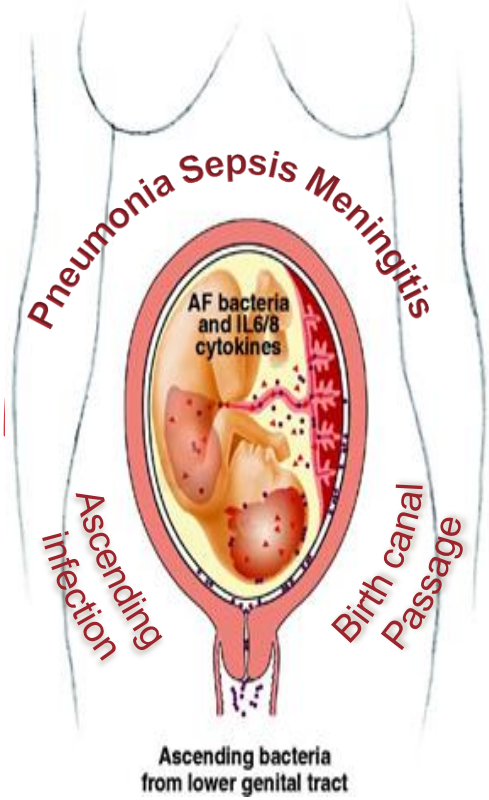
Group B streptococcus (GBS):



- … 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.



AF= amniotic fluid

Group B Streptococcus Vaccine Development Technology ROADMAP 2017 WHO/IVB/17.10

WHO Preferred Product Characteristics for Group B Streptococcus Vaccines 2017 WHO/IVB/17.09

GBS Disease

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- **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

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- 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**.

GBS Vaccine

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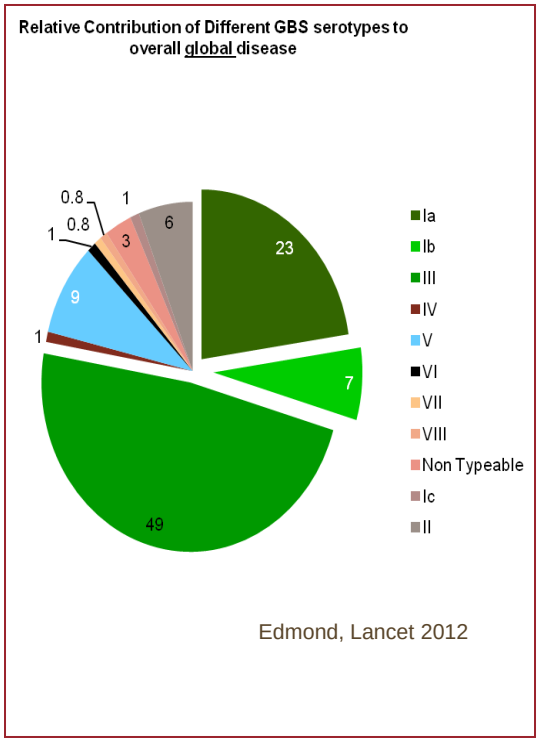
- Currently, **no vaccine exists** for prevention of GBS disease, but evidence suggests
  - … **maternal immunisation** with protein-conjugated GBS capsular polysaccharides
  - … may **reduce the disease risk** in neonates and young infants in a serotype-specific manner

- **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**

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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

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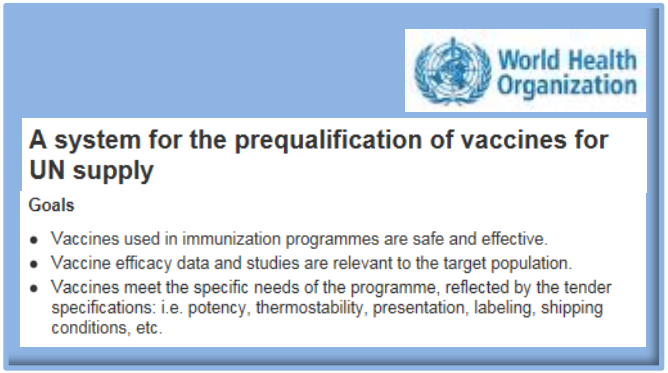
- ✓ **Develop a pentavalent GBS vaccine**
  - **Obtain licensure in SA**
  - **Obtain WHO PQ**



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

AVMI
AFRICAN VACCINE MANUFACTURING INITIATIVE

GBS Project Objectives

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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

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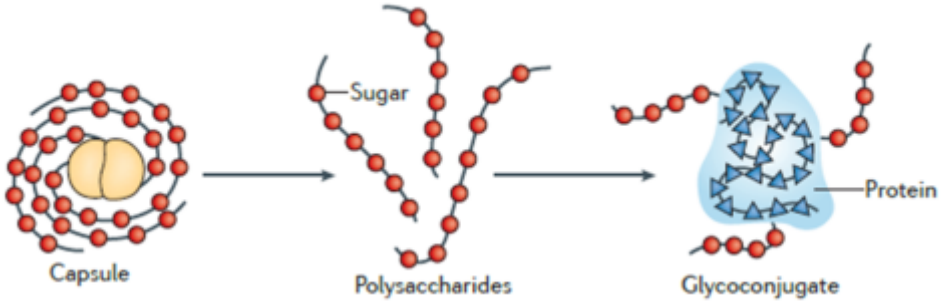
Isolate and Clonal Selection → Fermentation → Purification → Conjugation → Formulation

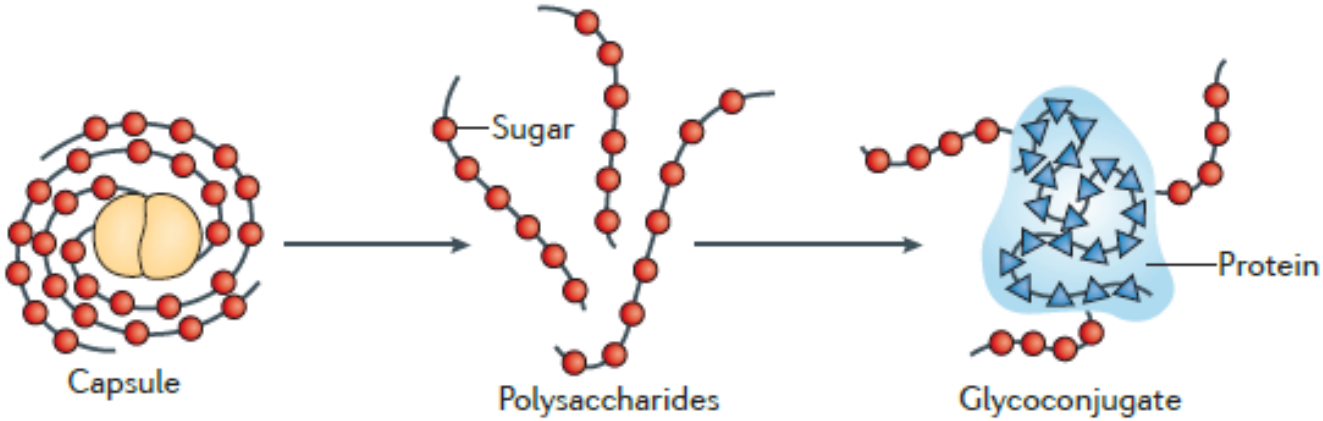
Analytical Method Development





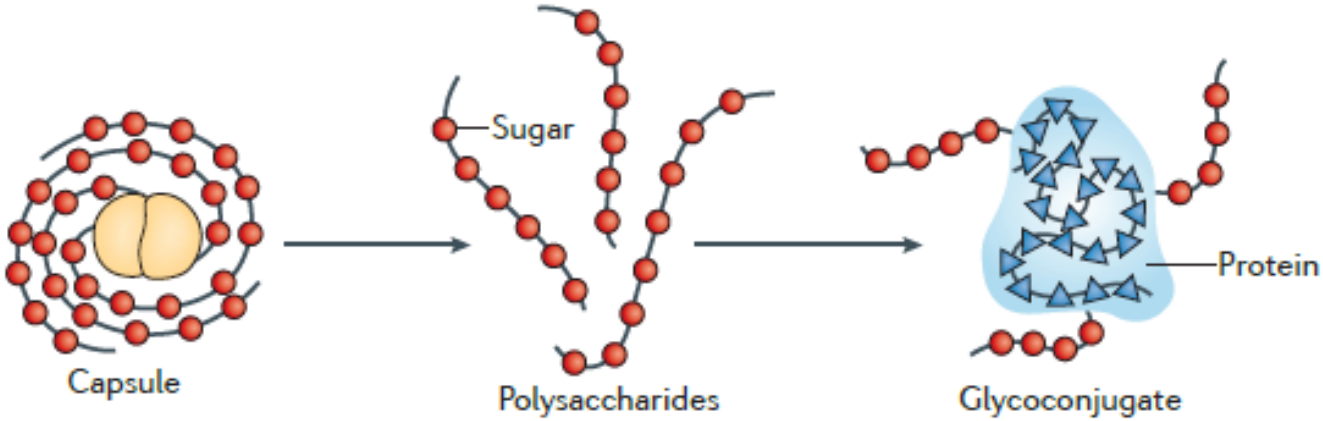


Process Development



Step 1	Step 2	Step 3
• **Isolate** and **clonal selection** • **Fermentation** development	• **Purification** and isolation of antigen (polysaccharide)	• **Conjugation** • **Formulation**

Process Development Deliverables



Output 1	Output 2	Output 3
A pure, high yielding strain for each of the 5 GBS serotypes	**Purified capsular polysaccharide** that meets required quality specifications	**A set of highly immunogenic conjugates** that provides Ab protection from mother to baby

GBS Project Roadmap and Timelines

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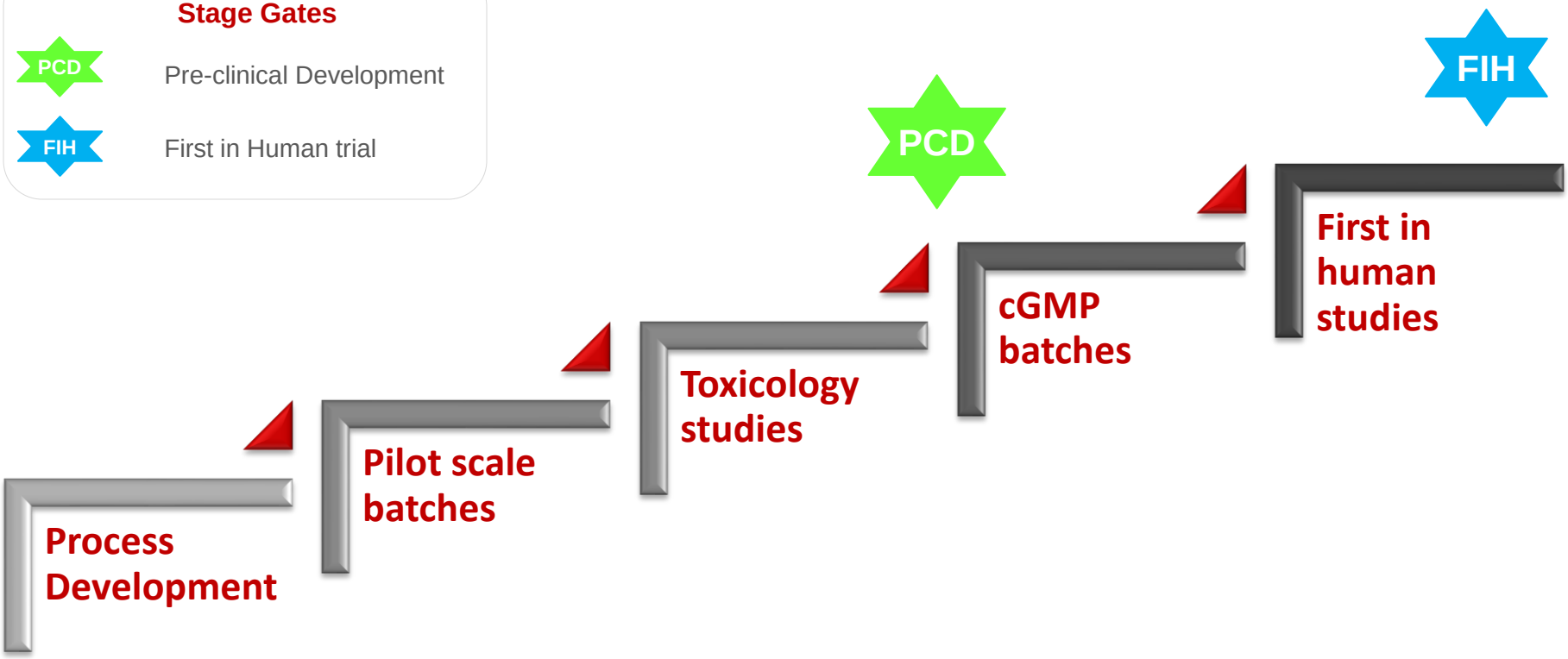
Stage Gates

PCD — Pre-clinical Development

FIH — First in Human trial



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

2017 ..... **2021**

WHO GBS Documents

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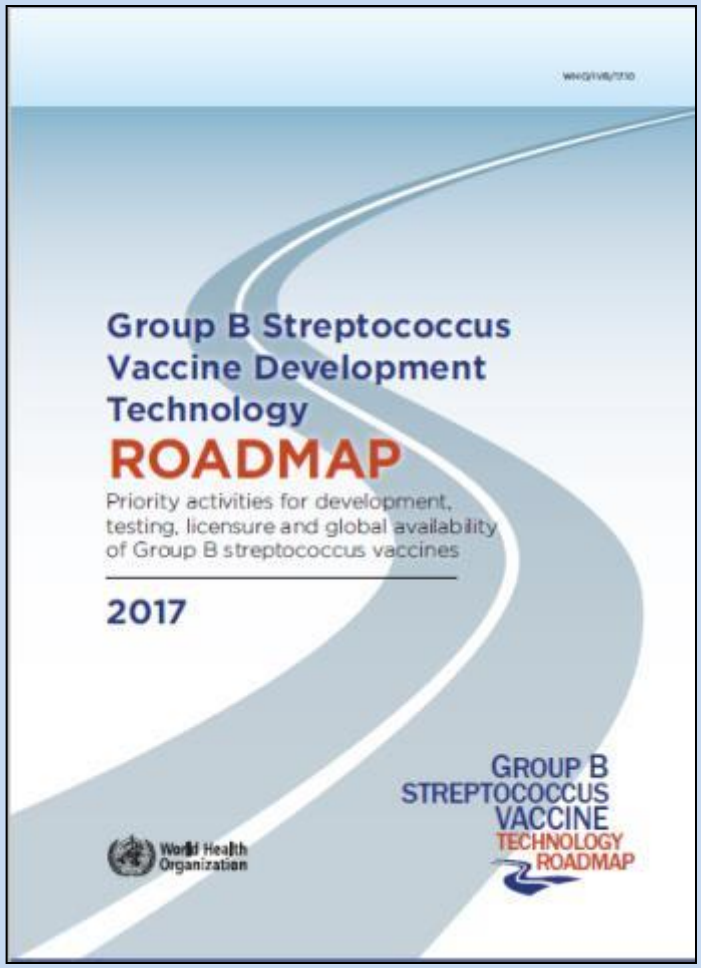

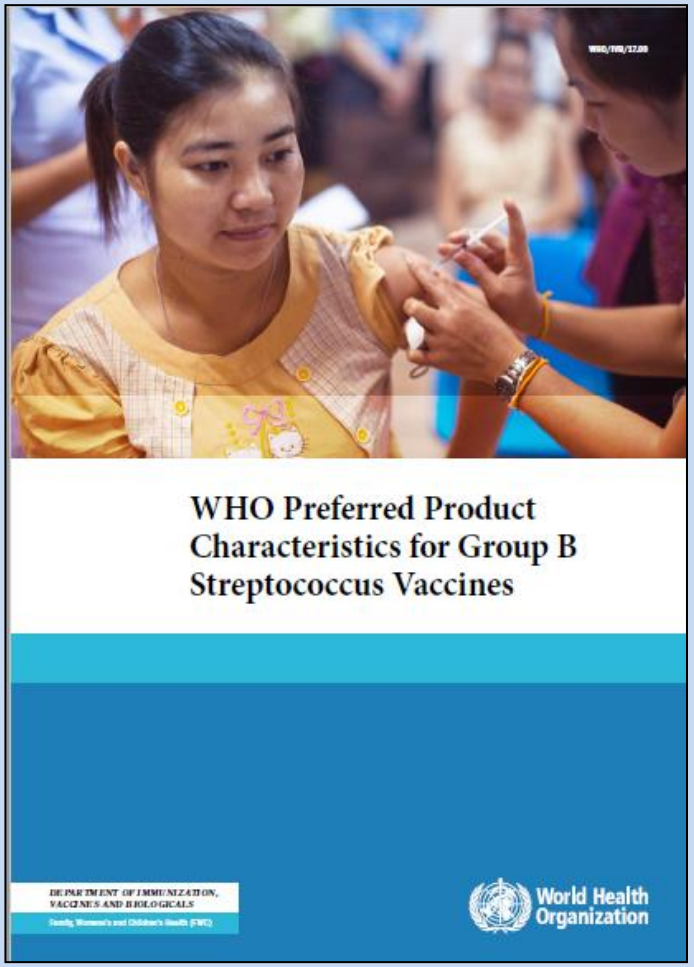

WHO GBS Vaccine PPC

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Parameter	Preferred Characteristic
Indication	Prevention of laboratory-confirmed GBS stillbirth and invasive GBS disease in neonates and young infants.
Target Population	Pregnant women, in the second or third trimester of pregnancy.
Schedule	A one dose regimen is highly preferred.
Safety	Safety and reactogenicity profile at least as favourable as current WHO-recommended routine vaccines for use during pregnancy (influenza, tetanus toxoid, acellular pertussis).
Efficacy	Available evidence supportive of 80% protection against combined risk of laboratory-confirmed GBS (all serotypes) stillbirth and invasive disease in the offspring.
Strain and serotype coverage	The serotypes in the vaccine formulation must cover at least 90% of the current invasive disease isolates in the target region.
Adjuvant Requirement	Preference for the absence of an adjuvant.
Immunogenicity	Established correlate/surrogate of protection based on a validated assay measuring antibody levels/ functionality in the mother and/or the neonate.

WHO GBS Vaccine PPC

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Parameter	Preferred Characteristic
Non-interference	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.
Route of administration	Injectable (IM, ID, or SC) using standard volumes for injection as specified in programmatic suitability for PQ or needle-free delivery.
Registration, prequalification and programmatic suitability	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
Value proposition	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.

GBS Project: African context and significance

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- **Last successful <u>novel</u> 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

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