History, implementation and impact of MenA conjugate on disease burden in Africa

First Regional Meningococcal Symposium, 19-20 March 2012
Buenos Aires, Argentina

Co-hosted by the Sabin Vaccine Institute and the Pan American Health Organization

Dr Marie-Pierre Preziosi
The African Meningitis Belt
Definition and characteristics

For > 100 years, meningitis outbreaks occur each year in the "meningitis belt", extending from Senegal to Ethiopia. Periodic epidemics occur, explosive with attack rates 100-800/100,000 affecting mostly < 30 year-olds.

Periodicity and seasonality - over 2-3 dry seasons with interruption during wet season, mainly serogroup A (C, W135 and X also), devastating social and economic consequences.

Strategic approach for > 30 years: epidemic response
Early detection of cases and response with mass vaccinations of at-risk populations with polysaccharide vaccines.
Epidemic Meningitis in Africa

Epidemic curve 1950-2010

Number of cases

Year

Meningitis Vaccine Project

MVP is a Partnership between WHO and PATH

Confidential & Proprietary Information
The Meningitis Vaccine Project (MVP)

Early development

- **Early 2000**, a WHO expert group concluded that development of a meningococcal conjugate vaccine offered an attractive strategy for epidemic control in sub-Saharan Africa.
- **April 2000**, a group of international experts and delegates from African ministries of health endorsed the initiative.
- **June 2001**, the Bill & Melinda Gates Foundation agreed to fund MVP:
  - 10-year partnership between WHO and PATH
  - Goal of eliminating epidemic meningitis as a public health problem in sub-Saharan Africa through the development, testing, licensure and widespread use of conjugate meningococcal vaccines.
- **2001-2002 Project constraints**, discussions with African public health officials who emphasized the key importance of a low vaccine price for a sustainable supply (< $ 0.5 USD per dose).
The Meningitis Vaccine Project (MVP)

**Development model**

PsA produced by SynCo BioPartners, Amsterdam, Netherlands for initial development then transferred to SIIL

Serum Institute of India (SIIL) process development and manufacturing

Conjugation method developed at CBER/FDA, Bethesda, USA, transferred and scaled-up at SIIL

Lyophilization and stabilization tech transfer from Aerial, France to SIIL

Target price US$ < 0.50/dose
The Meningitis Vaccine Project (MVP)
Preparation and characterization of a meningococcal conjugate vaccine

• PsA-TT, MenA polysaccharide (Ps) conjugated to a protein carrier: tetanus toxoid (TT)

A crosslinked lattice structure
formed from activated MenA PS containing multiple aldehyde groups randomly distributed along the chain of the molecule with activated TT containing multiple hydrazide groups

⇒ conjugates with higher crosslinkage are more stable and immunogenic

• Comprehensive product development according to international standards for Good Practices: Manufacturing (GMP), Laboratory (GLP), Clinical (GCP)…

MenAfriVac Regulatory Pathway
Licensure and WHO prequalification

- Marketing Authorization in the country of manufacture
  Drugs Controller General of India – December 2009
- WHO prequalification certificate – June 2010
  - Indication: 1 to 29 year olds
- Post-licensure and prequalification requirements
  - Completion of two phase III studies: lot-consistency in India, safety in Mali
  - Post-marketing surveillance plans implemented in countries
- Licensure variation – development ongoing
  - Indication: infants
MenAfriVac Clinical Development Program
Summary Implementation

- Expert support (statistics, serology, carriage, pharmacovigilance)
- Expert review and continuous monitoring of clinical program
  - Expert Panel (pharma and clinical)
  - Project Advisory Group (clinical and introduction)
  - Independent scientific peer review of all study protocols
- Multiple ethical clearance (IRBs, IECs in country & at study sites)
- Multiple regulatory clearance (Indian and African Authorities)
- Conduct of trials according to ICH/GCP, regulatory requirements
- Comprehensive GLP serologic testing at reference laboratories
- Independent GCP audits and regulatory inspections of trial sites
Meningococcal A Conjugate Vaccine (PsA-TT) Clinical Development

MenAfriVac developed by MVP and Serum Institute of India Ltd.

**1 to 29-year-old Indication**

Infant (< 1-year-old) Indication

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Phase II/III

Senegal  Mali  The Gambia

2-29-year-olds

Aug 07 - Apr 09

Phase II

India

18-35 year-olds

Aug 05 - Oct 06

Phase I

Safety

Immunogenicity

Carriage

Phase II

Senegal  Mali  The Gambia

2-29 year-olds

Aug 07 - Apr 09

Phase II/III

India

1-29 year-olds

Feb 10 - Jan 11

Phase III

India

5-10 year-olds

Jan-Jun 10

Phase III

Mali

1-29 year-olds

Feb 10 - Jan 11

Phase II

Ghana

Infants

Nov 08 - Jul 13

Phase II/III

India

2-10 year-olds

Aug 07 - Nov 08

Phase II

The Gambia

12-23 month-olds

Sep 06 - Apr 09

Phase I

India

18-35 year-olds

Aug 05 - Oct 06

Indian Licensure for Export and for India WHO Prequalification

Licence in three countries in Africa*

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Expanding Safety Database

Confirming Lot Consistency

Confirming Schedule

Expanding Safety Database

Immune Persistence

4 years after 1 dose

Immune Persistence

5 years after 1 dose

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Expedited procedure for licensing of WHO prequalified vaccines

*Burkina Faso, Mali, Niger

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Schedule Evaluation
Summary of Results from studies

MenA conjugate vaccine safety and immunogenicity in 1-29 year-olds

**Safety**
- about 10,000 subjects in trials
- safe and well tolerated, no safety concern in any age group

**Immunogenicity after a single dose of MenAfriVac**
- superior immune response vs. licensed polysaccharide vaccines in all age groups (1 to 29 year-olds indication)
- bactericidal antibody sustained to 2 years and evidence of immune memory
- response consistent between vaccine lots
- boost of the anti-tetanus immunity

**NEJM publication (with web-only suppl. appendix, all protocols and statistical analysis plans) with free access at**


Immunogenicity and safety of a meningococcal A conjugate vaccine in Africans
MenAfriVac
A Meningococcal A Conjugate Vaccine
The ongoing phased introduction of the vaccine in countries of the African meningitis belt will allow further characterization of its safety and evaluation of its efficacy.
MenAfriVac Introduction

Strategy

• Mass vaccinations of 1-29 year olds with a single dose of Men A conjugate to induce strong herd immunity

• Protection of new birth cohorts
  ➢ Follow-up campaigns every 5 years of 1-4 year olds or
  ➢ Routine immunization in infants / toddlers
  ➢ Pediatric indication, development ongoing
A total of 20 Million persons aged 1 to 29 years were vaccinated in 3 countries in 2010 with > 95% overall vaccine coverage and no safety issues.

Promising initial data post vaccine introduction:
- **Dramatic fall in cases of MenA disease** in the 3 countries who reported the lowest number of confirmed MenA cases ever recorded during a meningitis epidemic season.
- **Dramatic effect on carriage** (both elimination and prevention of MenA carriage) shown in Burkina Faso.
The Big Day – 6 December 2011

"This historical event marks the beginning of the end of a disease that has caused the suffering of generations in Africa."
Seydou Bouda, Minister of Health, Burkina Faso
MenAfriVac Roll-out Plan 2010 – 2012
Mass vaccination campaigns among 1 to 29 year-olds

2010
~20 Million vaccinated
Burkina Faso, Mali, Niger
September 2010: Pilot introduction ~1 M
passive + active surveillance of serious AEFIs
December 2010: Introduction ~19 M

2011
~35 Million vaccinated
Mali, Niger
+ Nigeria, Cameroon, Chad
Mali and Niger: country-wide completion
Nigeria, Cameroon, Chad: priority districts/states

2012
~55 Million to be vaccinated
Nigeria, Cameroon, Chad
+ Senegal, Ghana, Benin, Sudan

High vaccine coverage: reached among all age groups in all countries (administrative coverage 92-100%, coverage surveys 63-98%)
No safety concern: serious AEFIs mostly coincidental or when related, anaphylactic or expected
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MenAfriVac Introduction

Some of the challenges...

• Country co-financing
  ✓ identification and timely release of funds (delays)

• Country preparedness: issues and delays
  ✓ cold-chain capacity+++, human resources and coordination, planning and training, social mobilization (e.g. weakest coverage among 15-29 year-olds), vaccine distribution, vaccination cards, waste management, AEFI monitoring and case management (e.g. availability of drugs), monitoring and evaluation (e.g. standardization of tools)

• Surveillance…(strengthening, funding,…)

→ Continuing surveillance for cases of meningitis and monitoring of vaccination coverage will be crucial to confirm the effects of the vaccine as it is introduced across the meningitis belt, and the relative importance of disease caused by other serogroups

→ defining a sound pediatric indication will be key to ensure protection of new birth cohorts