MenAfrivac°, a long-waited vaccine for Burkina Faso

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Burkina Faso: landlocked sub-Saharan country

Area: 274 200 km²
Population: 14 330 584
Health system: 63 districts < 13 regions < Central
A. Introduction

Meningitis in Burkina Faso

- Burkina Faso is part of the ‘meningitis belt’.
- A major cause of morbidity and mortality
  - 10% of lethality.
  - A quarter of survivors suffer permanent damage—most commonly hearing loss, mental retardation, or epilepsy.
- Recurrent outbreaks occurs during the annual dry season (december to june).
- Meningitis epidemics occurs with predominantly *Neisseria meningitidis* serogroup A.
Global distribution of *N. meningitidis* serogroup A
Nov. 2006-June 2007 Epidemic Season

Burkina Faso the hardest-hit countries in Africa

Areas with *N. meningitidis* serogroup A disease
Areas with high serogroup A disease (where either another organism was the predominant identified cause of meningitis or no typing data was available.)
Areas with high serogroup A disease (where *N. meningitidis* group A is the predominant meningitis-causing typeable organism.)
A. Introduction

- For over 30 years, the control of meningitis epidemics is based on epidemiological surveillance and **response mass** immunization campaigns with **Polysaccharide vaccine**.

- A vicious cycle of outbreaks and reactive vaccinations, interrupting routine health services and consuming public health resources year after year...

- And before “reactive vaccination” starts up, it is too late for so many!
Limitations of Polysaccharide (PS) vaccine:

- Because PS vaccines immunity lasts only 2 or 3 years, their administration is only reactive after an outbreak is underway.
- Because PS vaccines do not provide long-lasting immunity and no herd immunity, the reactive mass vaccination campaigns must be repeated outbreak by outbreak.
- PS vaccine is not or little immunogenic in infants, an age group at risk.

But Polysaccharide vaccine was the only affordable and available vaccine for developing countries.
A. Introduction

• By 2001, three vaccine manufacturers had developed a group C meningococcal conjugate vaccine for the UK.
• Since then, introduction of Men C conjugate vaccines in industrialized countries has led to an almost complete disappearance of group C disease.
• But Group A meningococcus is nonexistent in industrialized countries, and returns on investment were too low for western companies to commit their resources to the development of vaccines for use mainly in Africa.
• Whereas only “conjugate vaccines” could allow controlling the disease in a preventive and therefore more effective manner!
B. Developing a group A meningococcal conjugate vaccine for Africa

• To overcome these obstacles to developing an affordable and effective conjugate vaccine for Africa, the Meningitis Vaccine Project (MVP) was created in 2001.

• MVP is a partnership between PATH and WHO, aims to eliminate meningitis as a public health problem in sub-Saharan Africa through the development and widespread use of conjugate meningococcal vaccines.
B. Developing a group A meningococcal conjugate vaccine for Africa

• Because group A *Neisseria meningitidis* is the pathogen responsible for most epidemics in the meningitis belt, **MVP with African public health officials have decided to develop a monovalent group A conjugate vaccine for Africa.**

• To make the conjugate vaccine accessible for African countries, MVP has collaborated with several partners for the development of a conjugation technology, and **Serum Institute of India Ltd (SIIL)** for vaccine production.

• SIIL agreed to manufacture a Group A meningococcal conjugate vaccine **at a target cost of US$0.40 per dose.**
B. Developing a group A meningococcal conjugate vaccine for Africa

• **Conjugation technology** was transferred to SIIL in Dec. 2003.
• In 2004, SIIL prepared test lots and clinical batches of the study vaccine.
• **Animal testing**, including toxicity, local tolerance, and immunogenicity of the study vaccine was completed in 2004.
• Since 2005, immunogenicity and safety have been evaluated in **7 clinical trials** (3 are ongoing) in 5 countries (India, Gambia, Ghana, Mali and Senegal).
• **These study results show that MenAfrivac° is safe and highly immunogenic.**
C. Regulatory stages before introduction of MenAfriVac° in Burkina Faso

1. Licensing by Indian regulatory authorities in December 2009
2. Pre-qualification by WHO on 23 June 2010
4. Marketing authorization granted by Burkina Faso NRA on 7 Sept. 2010
5. Enhancement of postmarketing surveillance, including monitoring of adverse events following immunization (AEFI)
On January 21, the Maharashtra state FDA officially granted SIIL the marketing authorization enabling MenAfriVac™ to be exported and used in Africa.

This decision approved a December 2009 request by the Drugs Controller General of India (DCGI) that MenAfriVac™ be made available for meningitis belt countries in Africa.

The DCGI decision was based on an extensive review of the two-part, 13,000-page dossier that had been submitted by SIIL in April/July 2009.

Following market authorization of MenAfriVac™, SIIL have began a large-scale production.
C2. Prequalification by WHO

- Prequalification is a process to provide advices to UN agencies that guarantees that individual vaccines meet international standards of quality, safety, and efficacy.
- MenAfrivac° was prequalified by WHO on 23 June 2010.
- PQ authorizes UN agencies to purchase the vaccine for use in African countries.
- PQ was based on:
  - Appropriate review of the Product Summary File.
  - Evaluation of the final product characteristics.
  - Site inspection of the SIIIL facilities (8 – 12 March 2010).
  - Follow-up of implementation of recommendations made by WHO reviewers during the evaluation.
The WHO prequalification is not a substitute for regulatory approval by the NRA of the importing country.

This is a mandatory to register all medicines in BF even for WHO prequalified vaccines furnished by UN agencies.

Especially for MenAfriVac®, a fast track regulatory process to obtain marketing authorization in BF, Mali and Niger was implemented before the introduction planned for sept. 2010.

A workshop was organized at WHO’s HQ (20-22 july 2010) to support NRA in the implementation of a procedure for expedited review of imported MenAfriVac°. (WHO/IVB/07.08)
C3. Implementation of an expedited procedure for regulatory approval by Burkina Faso

- Such expedited procedure consists in an abbreviated regulatory process building on the WHO prequalification procedure, that allows an NRA to provide regulatory approval for imported WHO’s prequalified vaccines for use in national immunization programmes.
Main steps of fast track procedure for regulatory approval of Menafrivac° - 1

1. Examination of prequalification reports:
   – **Product summary file**:
     - General information about the manufacturer
     - Information about the personnel and facilities
     - Vaccine composition
     - Production chain vaccine
     - Quality control of vaccine
     - Stability studies
   – **Clinical data reviewed** by WHO’s experts
   – **Site inspection visit** by WHO’s regulators
2. **Examination of product samples**, product inserts, NRA lot release certificates from the country of origin and summary lot protocols of 3 final lots derived from 3 consecutive bulk lots for consistency determination.

3. **Conduct a visual inspection of the samples** for consistency determination with respect to colour, freedom from particulates, vial size, vial filling, labels, etc.

4. **Review the product leaflet**, label and inner box for consistency with national norms.
5. Check that the specifications met by the product provided in the summary lot protocol match those in the appropriate WHO Technical Report Series.

6. Assure the presence of the Vaccine Vial Monitor (VVM)

7. Prepare a report based on the review indicating compliance or non-compliance with national norms using a standardized checklist provided by WHO. Annex 1d
C4. Marketing authorization in BF

• On the basis of this « expedited review » and of a strenghtening plan for postmarketing surveillance, the « national committee for registration of medicines » has granted marketing authorization for MenAfrivac° on the 7 september 2010.
C5. Enhancing postmarketing surveillance

- Before 2008: PV monitoring only during mass vaccination campaigns and EPI.
- Since 2008: Implementation of a Pharmacovigilance system within Ministry of health (DGPML).
- From Q4-2009 to Q2-2010, DGPML has convened several meetings with WHO representatives to review the pharmacovigilance protocol in preparation for the introduction of MenAfrivac°.
- On December 4, 2009, PV protocol was presented to the WHO Global Advisory Committee on Vaccine Safety (GACVS) at Geneva.
Objectives of the PV protocol are:

- To detect new, unusual, or rare vaccine adverse events up to 30 days after MenAfriVac™ vaccination
- To Investigate and treat all reported serious AEFIs
- To take corrective measures where necessary during the vaccination campaign
- To estimate the AEFI reporting rate for minor and serious AEFIs among vaccinated individuals in the community

Surveillance system is performed through:

- Active case finding for potential serious AEFIs
- Passive case reporting for any potential AEFI
C5. Enhancing postmarketing surveillance

- Pharmacovigilance conducted thus far in the vaccinated district continues to indicate that MenAfriVac° is a safe vaccine.
- All safety-related data will be reviewed by national committees and by the WHO “Global Advisory Committee on Vaccine Safety”.

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D. MenAfrivac° introduction in african countries

- Burkina Faso, Mali, and Niger have been selected for the first introduction of MenAfriVac™ on the basis of several criteria including disease burden, the ability to organize mass campaigns, and participation in clinical trials to develop the vaccine.

- In each of these first introduction countries, MenAfriVac™ is introduced in two stages:
  - Pilot vaccination campaigns of 1- to 29-year-olds at the district level (September 2010).
  - Country-wide vaccination campaigns of all 1- to 29-year-olds (December 2010).
## D. MenAfrivac° introduction in african countries

- District-level introduction of MenAfriVac™ in Burkina Faso started on September 2010. Around 400,000 people have been immunized against group A meningococcal meningitis.
- Lessons learned from these district-level immunization campaigns will be critical for implementing country-wide introduction.
- The official country-wide launch of MenAfriVac° will take place in Ouagadougou on the 6 December 2010.

- The launch will be the start of mass vaccination campaigns in Burkina Faso, Mali, and Niger that will continue into 2011 and aims to protect 33 million 1- to 29-year-olds from group A meningococcal meningitis.
E. Conclusion

✓ Advantages of the model of development of Menafrivac° by MVP consortium:

• It permits to produce a low-cost vaccine.
• It includes a north-to-south transfer of technology and capacity.
• It allows creation of a custom-made product for Africa:
  Ex : Menafrivac° has been formulated in ten-dose vials containing preservative, which is best suited for mass immunization campaigns but which would have limited use in industrialized countries.
E. Conclusion

✓ Benefits of the procedure of expedited review for imported prequalified vaccines:
  ▪ It would recognize the contribution of the WHO prequalification process, while facilitating development of NRA capacity.
  ▪ It allows for NRA to develop its relevant function of adverse events surveillance.
Thank you for your attention