Overcoming the challenges in Scale-up and Manufacturing of MenAfrivac

Dr Suresh Jadhav
Executive Director
SERUM INSTITUTE OF INDIA PVT LTD
PUNE, INDIA
The pathogen

- *Neisseria meningitidis* - Gram-negative bacterium, encapsulated diplococcus
- Strains identified by polysaccharide capsule
- Strict human pathogen - man only reservoir, carried on NP mucosa
- Transmitted through saliva, respiratory secretions, aerosolization
Advantages of Conjugate vaccines

POLYSACCHARIDE
- Stimulates T-independent immunity
- Not immunogenic in children ≤2 years old
- No booster response
- Short duration

CONJUGATE
- Stimulates T-dependent immunity
- Immunogenic in all age-groups including infants
- Repeat doses elicit booster response
- Long duration

Protein
Development and Manufacturing at SIIPL - Key to Success

- Very strong commitment on public health from Senior management, ensuring availability of high quality, low cost affordable vaccines for the masses
- Leveraging the advantage of operations at high scale
- Sophisticated equipment with high level of automation
- Use of latest technologies for conjugation and purification
- Highly committed, stable human resources with scientific expertise
Production overview

**Building SEZ1B Second Floor**
- Seed Lot
- Fermentation
- PsA Purification
- Conjugation
- Bulk Conjugate
- Formulated Bulk

**Building 7**
- TT

**Building SEZ1B Ground Floor**
- Filling
- Lyophilization
- Final Lot

**QC Testing and Release**
- QC Testing and Release
- QC Testing and Release
- QC Testing and Release
Leveraging the Scale up expertise at SIIPL

**Fermentation**
- 20 L
- 800 L

**Ps Purification**
- 60 L
- 800 L

**Conjugation**
- 100 mg
- 100 gm

**Lyophilization**
- ~2000 vials
- ~93500 vials
Production controls to ensure consistency in Scale up
NMR Characterization of Purified PsA

\[ \text{\`H NMR of PsA (ZMAP08002)} \]

\[ \text{\`H NMR of PsA (ZMAP08003)} \]

\[ \text{\`H NMR of PsA (ZMAP08004)} \]

\[ \text{\`P NMR of PsA (ZMAP08002)} \]

\[ \text{\`P NMR of PsA (ZMAP08003)} \]

\[ \text{\`P NMR of PsA (ZMAP08004)} \]
Concept to Licensure—an overview of timelines for MenAfrivac (10 mcg/dose)

<table>
<thead>
<tr>
<th>Sr No.</th>
<th>Stage</th>
<th>Year</th>
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<tr>
<td>1</td>
<td>Know how Transfer/Process development</td>
<td>2004</td>
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<td>2</td>
<td>Phase 1 CTM, PsA-TT-001 India</td>
<td>2004</td>
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<td>3</td>
<td>Phase 2 CTM, PsA-TT-002, Mali &amp; Gambia</td>
<td>2005-6</td>
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<td>4</td>
<td>Phase 2/3 CTM, PsA-TT-003, Mali, Senegal &amp; Gambia</td>
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<td>Infant dose ranging, PsA-TT-004, Ghana</td>
<td>2008</td>
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<td>6</td>
<td>Phase 3, PsA-TT-005, India</td>
<td>2008</td>
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<td>7</td>
<td>Marketing Authorization application submission</td>
<td>2009</td>
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<td>8</td>
<td>NOC to export based on African data</td>
<td>Dec 2009</td>
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<td>9</td>
<td>WHO on site evaluation</td>
<td>Mar 2010</td>
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<td>10</td>
<td>WHO PQ</td>
<td>Jun 2010</td>
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<tr>
<td>11</td>
<td>DCGI Licensure for India</td>
<td>Dec 2011</td>
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Use of Vaccine outside the Cold chain (CTC study)

• Cold chain maintenance is a challenge
• MenAfrivac was granted storage at room temperature NMT 25 deg C for 2 weeks or 40 deg C NMT 4 days, single period
MenAfrivac (5 mcg/dose)
(additional strength)

- New MenAfrivac vaccine (5 mcg/dose) received DCGI approval on 19th Nov and WHO PQ on 30 Dec 2014

- Age group 3 months to 24 months
  - 2 doses 3 months apart between 3 – 9 months
  - 1 dose after 9 months through 24 months

- Post licensure 2.5 mio doses of new presentation have already been manufactured and NRA lab released. This vaccine will be part of the routine immunization program from 2016 onwards
Partnerships for MenAfriVac development
It is not over yet..

- Despite of the success of MenAfrivac, Africa remains at high risk for meningitis caused by other strains.

- Baseline meningitis rates (outside epidemic years) are 10 to 100 times higher than Developed countries.

- There is no pathophysiologic explanation why meningococci cause epidemics under dry and dusty conditions in Africa and not elsewhere.

- As long as pathogenic *Neisseria* (C, Y, W135, X strains) freely circulate in unprotected Sub-Saharan Africans, the potential for major meningitis epidemics is always present.

- SIIL continues its Polymening and Pneumococcal development programs to address the global threat caused by Meningitis strains.
Thanks.

ssj@seruminstitute.com