Beyond the cold chain...

Meningitis A conjugate vaccine in a controlled temperature chain (CTC): Experience from Benin

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WHO recommended storage temperatures

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>National 6 to 12 months</th>
<th>Regional / Provincial / District Up to 3 months</th>
<th>District / Health Facilities 1 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPV</td>
<td>-15°C to -25°C</td>
<td></td>
<td>+2°C to +8°C</td>
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<tr>
<td></td>
<td>OPV is only vaccine can be safely frozen and unfrozen repeatedly</td>
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<tr>
<td>BCG</td>
<td></td>
<td>WHO does not recommend storing freeze-dried vaccines at –20°C. Storing them at –20°C is not harmful to the vaccine but it is not a necessity.</td>
<td>+2°C to +8°C</td>
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<tr>
<td>Measles, MR</td>
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<td>YF, Meningitis</td>
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<tr>
<td>Hib lyophilised</td>
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<tr>
<td>DTP-HepB-Hib</td>
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<td>DTP / DT / TT/Td</td>
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<tr>
<td>Pneumo</td>
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<td>Rotavirus</td>
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<tr>
<td>HPV</td>
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</table>

The diluent must NEVER be frozen. If the vaccine is supplied freeze-dried pre-packed with the diluent, the whole package must be stored at +2°C to +8°C. When supplied separately, diluents should be stored separately at +2°C to +8°C.
Can we learn from other countries?

Menjugate (Men C)- Novartis (Canada)
- Alternative storage condition (before reconstitution):
  - Do not store above 25°C. Do not freeze. Protect from exposure to light. The product should be used or discarded within 6 months of the date of removal from refrigerator (+2 to +8°C) or on reaching the other carton expiry date (whichever comes first).

Prevnar-13 (Pneumo) – Wyeth (South Africa)
- Store at 2°C - 8°C - Do not freeze.
- Prevnar 13 has been shown to be stable at temperatures of up to 40°C for 4 days (…). These data are not recommendations for shipping or storage (…)

Gardasil (HPV)- Merck (USA)
- Store at 2°C - 8°C - Do not freeze.
- GARDASIL can be out of refrigeration (at temperatures at or below 25°C/77°F), for a total time of not more than 72 hours.

Cervarix (HPV)- GSK (EU)
- Store at 2°C – 8°C - Do Not Freeze
- ...Stability data ... remains stable... up to 3 days between 8°C and 25°C and up to one day between 25°C and 37°C
Cold chain challenges and solutions

- **Challenges**
  - 2013: 23,000 facilities with missing equipment
  - Lack of maintenance systems
  - $350-650M funding gap for 2014-2020
  - Significant amount of vaccines exposed to freezing

- **“Equipment” Solutions**
  - Short term: expanding the cold chain to unequipped Health facilities
  - Support development of new cold chain equipment
    - Emerging technologies: passive devices, solar technology, etc

- **“Thermostability” solutions**
  - Short term: Taking advantage of existing stability
  - Explore new technologies that may offer a way to better stability in the future
    - Addition of excipients
    - Drying
    - Novel formulations (antigen coating, etc)
October 2012

MenAfriVac obtains a license variation from its regulatory agency, DCGI, and is prequalified by WHO, for use in a **Controlled Temperature Chain (CTC)**

License allows for use of MenAfriVac for up to 4 days at temperatures of up to 40°C
December 2012
MenA national campaign in Benin

- CTC implemented in one district: Banikoara
  - Strict 2-8°C cold chain maintained from national to the district level
  - Special training and supervision in the district, with emphasis on adverse events monitoring
  - 155,000 individuals vaccinated without cold chain
  - Administrative coverage 106%
  - No significant wastage due to CTC practice (only 9 vials discarded)
Three strategies for taking advantage of CTC used in Benin

1. **Functional cold chain at health centre, nearby populations**
   Vaccines are removed from the cold chain for day of vaccination (*no ice packs needed, no risk of freezing diluent*)

2. **Remote and hard to reach areas**
   Teams are able to stay overnight for 3 days, enabling them to reach all those in the target population (*rather than returning each night to the health centre*)

3. **No cold chain/ lack of cold chain space at health centre level**
   Vaccines can be stored in a CTC for 4 days (*eliminating up to 8 trips to the district level*)
What we learned

• No serious AEFIs and no increase in AEFIs reported
  – Active surveillance study implemented by AMP

• Teams felt CTC helped them increase coverage

• No ‘confusion’ in future campaigns
  – Cold chain conditions properly used for Polio NID implemented 10 days after MenA campaign in Banikoara

• Specific guidance needed
High levels of CTC acceptance

<table>
<thead>
<tr>
<th>Is the CTC practice useful?</th>
<th>Vaccinators (n=77)</th>
<th>Supervisors / district staff (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very useful</td>
<td>74%</td>
<td>81%</td>
</tr>
<tr>
<td>Relatively useful</td>
<td>26%</td>
<td>19%</td>
</tr>
<tr>
<td>Not useful</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

When given a choice, **100% of supervisors and 98.7% of vaccinators would prefer to conduct their next campaign using CTC, if possible.**

Zipursky et al. Benefits of using vaccines out of the cold chain: Delivering Meningitis A vaccine in a controlled temperature chain during the mass immunization campaign in Benin. Vaccine 2014
CTC has the potential to reduce costs

Modelling of MenA CTC in Chad indicate potential savings of 50%

- No need for ice & cold boxes
- No need to "touch base" every morning and evening

Lydon et al, Bull. WHO 2014: Economic benefits of leveraging the true stability of vaccines: The case of Meningitis A in Chad
Lessons learned - CTC

- CTC approach well suited to campaigns and special strategy situations, single antigen setting
  - Can this current focus be extended?
- CTC has the potential to reduce cold chain costs and Health care worker time spent on logistics during campaigns
- Collaboration key to success
  1) manufacturer engagement
  2) WHO regulatory and programmatic guidance
  3) Country engagement and implementation
- Need to accelerate licensure of other appropriate vaccines in a CTC
  - Cholera, HPV and yellow fever in the pipeline
“Finding solutions to reducing the cost and logistical challenges of reaching people living in remote areas would remove a major constraint to achieving universal coverage of vaccine beyond MenAfriVac,”
Michel Zaffran, EPI coordinator WHO

“This is really quite revolutionary”
Marie-Pierre Preziosi, MVP director

Mikael, age 11, in Banikoara

Mikael was the first person ever vaccinated with MenAfriVac in a CTC. When he grows up, he wants to be a doctor.