Beyond the cold chain…

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

World Health Organization

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GVRF | Washington DC | March, 2014

WHO recommended storage temperatures

<table>
<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>
<tr><td>OPV</td><td colspan="2">-15℃ to -25℃
OPV is only vaccine can be safely frozen and unfrozen repeatedly</td><td rowspan="8">+2℃ to +8℃</td></tr>
<tr><td>BCG</td><td colspan="2" rowspan="4">WHO does not recommend storing freeze-dried vaccines at –20℃. Storing them at –20℃ is not harmful to the vaccine but it is not a necessity.</td></tr>
<tr><td>Measles, MR</td></tr>
<tr><td>YF, Meningitis</td></tr>
<tr><td>Hib lyophilised</td></tr>
<tr><td>DTP-HepB-Hib</td><td colspan="2" rowspan="5">+2℃ to +8℃</td></tr>
<tr><td>DTP / DT / TT/Td</td></tr>
<tr><td>Pneumo</td></tr>
<tr><td>Rotavirus</td></tr>
<tr><td>HPV</td></tr>
<tr><td colspan="4">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 +2C to +8C. When supplied separately, diluents should be stored separately at +2C to +8C</td></tr>
</table>

Can we learn from other countries?

Menjugate (Men C)- Novartis (Canada)

- *Alternative storage condition (before reconstitution):*
- *Do not store above 25^{0}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^{0}C) or on reaching the other carton expiry date (whichever comes first).*

Prevnar-13 (Pneumo) – Wyeth (South Africa)

- *Store at 2^{o}C - 8^{o}C - Do not freeze.*
- *Prevnar 13 has been shown to be stable at temperatures of up to **40^{o}C for 4 days** (…) These data are not recommendations for shipping or storage (…)*

Gardasil (HPV)- Merck (USA)

- *Store at 2^{o}C - 8^{o}C - Do not freeze.*
- *GARDASIL **can be out of refrigeration (at temperatures at or below 25^{o}C/77^{o}F), for a total time of not more than 72 hours**.*

Cervarix (HPV)- GSK (EU)

- *Store at 2^{o}C – 8^{o}C - Do Not Freeze*
- *…Stability data … remains stable… up to 3 days between 8^{o}C and 25^{o}C and up to **one day between 25^{o}C and 37^{o}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,e tc)

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**
  - http://www.who.int/immunization/documents/WHO IVB 13.04 5 6/en/index.html

High levels of CTC acceptance

Is the CTC practice useful?

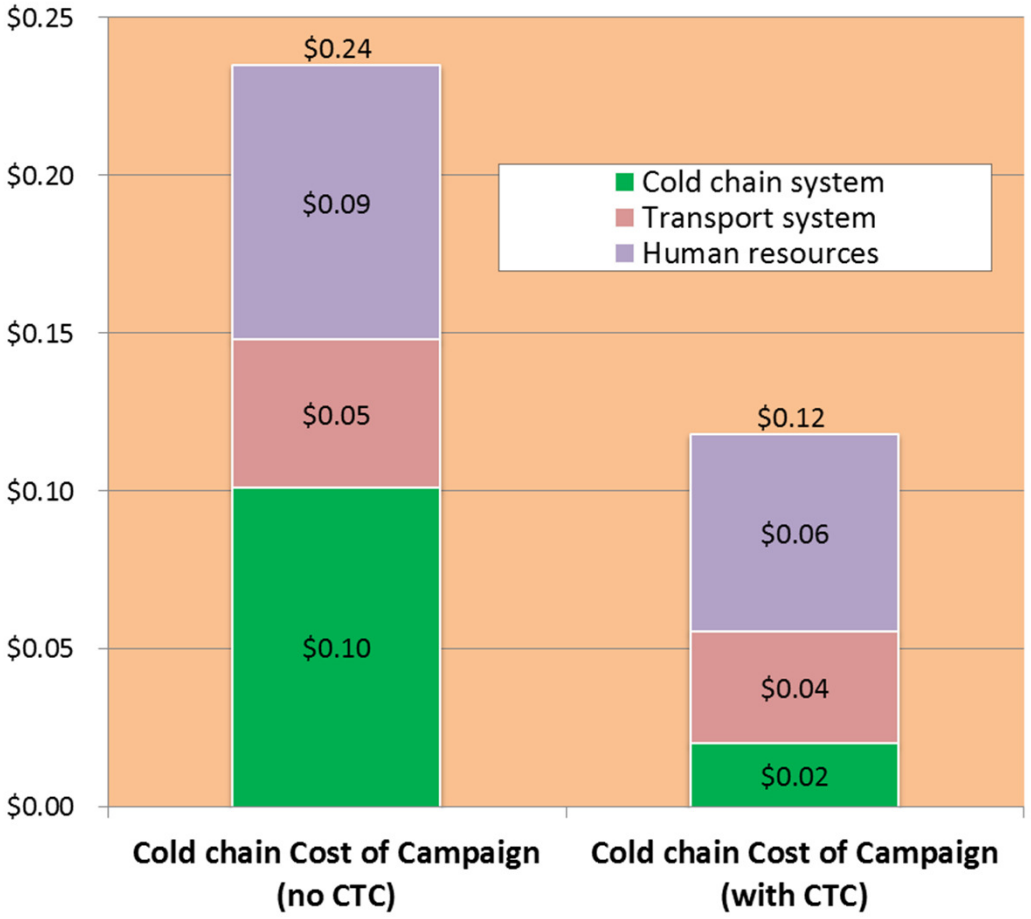
	Vaccinators (n=77)	Supervisors / district staff (n=21)
Very useful	74%	81%
Relatively useful	26%	19%
Not useful	0	0

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**

Thank you | Merci | Gracias | Obrigado

“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.