Introduction of Typhoid Vaccine: Cold Chain & Logistics Implications

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IVI Meeting on Typhoid Vaccination
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Vaccine demand forecasting for typhoid vaccines: # of doses to be procured

- Defining and estimation of eligible population—2-5 years or 5-10 years, all population > 2 years
- Number of doses—one single dose in lifetime or multiple doses every 3 years
- To be provided through routine system or in a campaign approach covering broad age group every 3-5 years
- Or a combination approach—cover 2-5 years in first year of introduction; then cover 2 years old in following years
  - Estimate a fraction of older kids that may not come at 2 years of age
Calculation of # of doses required

- May become complicated if routine vaccination is done for broad age groups
- Difficult to make coverage assessments—what should be the denominator
- May run into overstock or under-stock situation

In 2008:
- Total 2-5 year old population: 350

In 2009:
- Total 2 year old population: 100 + 10% of 3-5 year old population

<table>
<thead>
<tr>
<th>Year</th>
<th>2</th>
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<th>3</th>
<th>4</th>
<th>5</th>
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<tbody>
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<td>2008</td>
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<td>2009</td>
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<td>4</td>
<td>5</td>
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</tbody>
</table>

2008: yr of intro
What is EPI logistics?

A complex system comprised of equipment and staff who ensure the proper storage and transport of vaccines at adequate temperatures, from the vaccine producer to the point of administration.

The vaccine cold chain

For every child
Health, Education, Equality, Protection
ADVANCE HUMANITY

unicef
### WHO recommended vaccine storage conditions

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Primary</th>
<th>Intermediate Region</th>
<th>District</th>
<th>Health Centre</th>
<th>Health Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPV</td>
<td></td>
<td>-15°C to -25°C</td>
<td></td>
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<tr>
<td>BCG</td>
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<tr>
<td>Measles</td>
<td></td>
<td>WHO no longer recommends that freeze-dried vaccines be stored at -20°C. Storing them at -20°C is not harmful but it is unnecessary. Instead, these vaccines should be kept in refrigeration and transported at +2°C to +8°C.</td>
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<tr>
<td>MMR</td>
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<td></td>
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<tr>
<td>MR</td>
<td></td>
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<tr>
<td>Yellow Fever</td>
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<tr>
<td>Hib freeze-dried</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>HepB</td>
<td></td>
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<tr>
<td>DTP-HepB</td>
<td></td>
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<tr>
<td>DTP-Hib</td>
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<tr>
<td>Hib liquid</td>
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<td>DTP</td>
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<td>Td</td>
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</tbody>
</table>

All the currently available typhoid vaccines are recommended to be stored at this temperature as well.

*Diluent vials must NEVER be frozen. When the manufacturer supplies a freeze-dried vaccine packed together with its diluent, ALWAYS store the product at between +2°C and +8°C. Where space permits, diluents supplies separately from the vaccine may safely be stored in the cold chain at between +2°C to +8°C.*
Vaccine Temperature Sensitivity

Heat sensitivity

Days at 37°C

2

7

14

30

Most sensitive

Heat sensitive

Freeze sensitive

Most sensitive

However, can not use the heat stability feature of Typhoid vaccines if the vaccine does not come with VVM
Cold chain equipment & devices

1. Storage & transportation equipment
   - Cold rooms (+2c to +8c degrees and -10c to -15c)
   - Freezers (OPV storage, production of frozen icepacks)
   - Refrigerators (storage of all types of vaccines)
   - Cold boxes and vaccine carriers (transport, vaccination sessions, outreach)
   - Refrigerated trucks

2. Systems and devices for temperature monitoring
The stakes are higher

Newer vaccines are much bulkier and much more costly

* UNICEF and PAHO Revolving Fund Vaccine Prices
** GAVI Price Estimate (2008)
Example: Rotavirus vaccines

- **$635.50**
  - 4100 doses of Polio and Measles Vaccines
  - Rural hospital storage, Mozambique

- **$4,687.50**
  - 625 doses of Rotavirus Vaccine
  - District vaccine store, Brazil

* Source: WHO. Guidelines on the international packaging and shipping of vaccines. 2002; WHO/V&B/01.05.

** Based on $7.50/dose for Rotarix and $0.155 per dose for polio and measles
Vaccine Volume

Volume of a vial
Volume of a packaged dose

Measurements:
Length of box: 15 cm
Width of box: 12 cm
Height of box: 7 cm
# vials per box: 20 vials
# of doses per vial: 10 doses

Volume per dose =
Length X Width X Height

------------------------------------- = 1260/200 cm³
# Vials x Total doses per vial
The vaccine volume per dose varies according to vaccine type and across manufacturers.

The current guidelines need to be updated to include volume required for typhoid vaccines.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Doses per vial</th>
<th>Volume per dose in cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG freeze dried</td>
<td>20 doses</td>
<td>1.2</td>
</tr>
<tr>
<td>DTP</td>
<td>10 doses</td>
<td>3.0</td>
</tr>
<tr>
<td>OPV</td>
<td>10 doses</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>20 doses</td>
<td>1.5</td>
</tr>
<tr>
<td>Measles</td>
<td>10 doses</td>
<td>3.0</td>
</tr>
<tr>
<td>MR</td>
<td>10 doses</td>
<td>3.0</td>
</tr>
<tr>
<td>MMR</td>
<td>10 doses</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>1 dose</td>
<td>19</td>
</tr>
<tr>
<td>TT</td>
<td>10 doses</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>20 doses</td>
<td>3.0</td>
</tr>
<tr>
<td>Hep B</td>
<td>10 doses</td>
<td>3.8</td>
</tr>
<tr>
<td></td>
<td>6 doses</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>2 dose</td>
<td>17.5</td>
</tr>
<tr>
<td></td>
<td>1 dose</td>
<td>35.0</td>
</tr>
<tr>
<td></td>
<td>UNIJECT</td>
<td>24.6</td>
</tr>
<tr>
<td>DTP-HepB</td>
<td>10 doses</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>2 doses</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td>1 dose</td>
<td>9.7</td>
</tr>
<tr>
<td>DTP-Hep-Hib</td>
<td>10 dose</td>
<td>5.3</td>
</tr>
<tr>
<td></td>
<td>2 doses</td>
<td>9.7</td>
</tr>
<tr>
<td></td>
<td>1 dose</td>
<td>19.4</td>
</tr>
</tbody>
</table>
New Vaccines: Current Presentations

**Prevnar PCV-7:** One box contains 10 pre-filled syringes without needle
Storage volume per dose: **55.9cm³**

**Rotarix:** One box with 2 blisters of 5 syringes of diluents, 1 plastic bag with ten transfer adapter + 1 box with ten vials of vaccine
Storage volume per dose: **156.0cm³**

**Typhim Vi:**
One box of 1 pre-filled glass syringe vial of
Storage volume per dose: **91.3cm³**
Typhoid vaccines: current Presentations

• Vi Polysaccharide vaccine:
  – Prefilled single dose syringe (GSK vaccine Typherix™; Sanofi’s Typhim Vi™) in singel box:
    • space requirements higher than current 7-valent pneumococcal vaccine-91.3 cm³
  – 5-dose vials (by Bharat Biotech, India)
    • Space requirement similar to DPT vaccine (~5-6 cm³)
  – 20-dose vial (IVAC, Vietnam)

Application of multi-dose vial policy: ????
Live attenuated Ty21a vaccine

Licensed in 56 countries

Produced by Berna Biotech – Switzerland
  – Presented as phthalate-coated gelatin capsules
  – A liquid formulation is also available (with sachet and buffer)
  – Administered as three doses 2 days apart

• Cold chain space requirement: Needs to be calculated!
Current & anticipated vaccines volumes per FIC

**Current & anticipated vaccines volumes per FIC**

- **TV + Penta_liq + PCV-7**
  - Today's requirements: 20
  - New target: 36
  - Initial target: 21

- **TV + Penta + PCV-2-dose vial + Rota**
  - Today's requirements: 20
  - New target: 240

- **TV + Penta + PCV-7**
  - Today's requirements: 20
  - New target: 240

- **TV + Penta**
  - Today's requirements: 20
  - New target: 177

- **Tradi Vax**
  - Today's requirements: 32

**Legend:**
- Traditional Vax
- dtp/hepB/Hib combo
- PCV
- Rota

**Volumes, cm³**

- 0 50 100 150 200 250 300 350 400

- Traditional Vax
- dtp/hepB/Hib combo
- PCV
- Rota
Lead Time Required

- Assessing the need → 3 months
  - Central & intermediate → 1-2 months
  - Intermediate & service → 2-3 months

- Preparing & ordering equipment → 6-9 months

- Receiving, installation, training → 3-6 months

- Can take at least 12 months to upgrade needed cold chain capacity for new vaccines introduction
Challenges Ahead

- Emerging vaccine products with non-standard characteristics
  - Challenging existing policies (MDVP, VVM)
  - Increased waste disposal
  - Service delivery strategies (expanded age groups)

- Increased volume of safe injection supplies stored at ambient temperatures
  - Adequate bundling and distribution of matched supplies

- Radical implication for training & supportive supervision:
  - Improved skills logistics managers at all levels
  - Health worker training and supportive supervision
Ongoing Efforts

- WHO Vaccine Presentation and Packaging Advisory Group (VPPAG): Input to future presentation development
  
  [see http://sites.google.com/site/vppagp]

- WHO/PATH ‘Optimise’ Project: Future of technologies and logistics

- Tools for country-decision-making and planning
  - Vaccine volume calculator
  - Stock management tool (Access and Excel Based)
  - Equipment inventory tools (Access and Excel Based)
  - EVSM and VMA assessment tools
The Logistics System

1. Staffpower:
   - Logisticians
   - Technicians
   - Users

2. Management:
   - Policies, norms, procedures
   - Training and supervision
   - Monitoring & reporting

3. Materials:
   - Equipment/devices
   - Consumables

4. Money:
   - Costs of manpower, materials & management
     - Other financial costs
The PQS (Performance Quality & Safety) gives all specifications about cold chain equipment (WHO – UNICEF web catalogue):

http://www.who.int/vaccines-documents/
2. Continuous temperature records are available, and these records demonstrate that vaccines have been stored correctly in both permanent and temporary cold stores.

2.1.1 Store all vaccines and diluents at the correct temperature

Method: Interview staff, inspect training records

Q1: Critical indicator: Does the storekeeper know the correct storage temperature range for each of the vaccines on the schedule (see note 1)? [YES=1, NO=0] 1 5.00

Q2: Critical indicator: Does the storekeeper know the freezing temperature of all the freeze-sensitive vaccines on the schedule (see note 2)? [YES=1, NO=0] 15.00

Q3: Has the storekeeper received formal or on-the-job training in how to look after vaccines? [YES=1, NO=0] 0 0.00

Q4: Have all other staff who are responsible for looking after vaccines received such training? [YES=1, NO=0] 0 0.00

Commentary: Q3 & Q4: Interviews with staff suggest that training in vaccine management is weak.

2.1.2 Use stock records to demonstrate that all vaccines and diluents have been stored in accordance with current WHO storage temperature recommendations.

Method: Inspect stock records

Q5: Critical indicator. Collect the following information to establish the percentage of doses that have been discarded as a consequence of incorrect storage conditions during the review period (note 3).

A. Record number of doses of all vaccines in stock at the start of the review period. 1,000,000
B. Record number of doses of all vaccines received during the review period. 1,000,000
C. Record number of doses issued during the review period. 0
D. Record number of doses of all vaccines discarded because of incorrect storage temperatures. 5,000
E. Record number of doses of all vaccines in stock at the end of the review period. 2,000,000

END BALANCE CHECK: Based on these figures, the end balance should be 1995000 doses. If it is not, query the stock records.

F. If the percentage discarded is greater than 1% score is set = 0. If equal to or less than 1%, score = 5. 5.00

Commentary: Discrepancy of 5000 doses could not be reconciled. Refer to Qs on stock management for further comments on this topic, showing weaknesses in this area of store management.

Over a period of 12 months, all vaccines have been stored within WHO recommended temperature ranges.

Note to assessors: There are a number of unforeseen ways in which vaccine may be damaged or lost during storage which do not necessarily reflect badly on the system - for example, accidental damage during handling. To take account of such events, questionnaires and/or interviews should be included with appropriate critical indicators and additional questions where necessary.
# Vaccine Volume Calculator

<table>
<thead>
<tr>
<th>ANTIGENES</th>
<th>Nbre doses flacon</th>
<th>Volume par dose (cm3)</th>
<th>Nbre doses du calendrier</th>
<th>Facteur perte</th>
<th>Volume net de stockage in cm3 par Enfant Compl. Vacciné</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>B</td>
<td>C</td>
<td>D</td>
<td>E</td>
<td>F</td>
</tr>
<tr>
<td>Pentavalent Lyo/liquid</td>
<td>2</td>
<td>9,7</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hib liquid</td>
<td>10</td>
<td>13,8</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hib liquid</td>
<td>1</td>
<td>32,3</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Hib lyophilised</td>
<td>1</td>
<td>9,7</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>BCG</td>
<td>20</td>
<td>1,5</td>
<td>1</td>
<td>2</td>
<td>3,0</td>
</tr>
<tr>
<td>DPT</td>
<td>20</td>
<td>2,5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DPT</td>
<td>10</td>
<td>3,0</td>
<td>3</td>
<td>1,18</td>
<td>10,6</td>
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<tr>
<td>DT or Td</td>
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<tr>
<td>Measles</td>
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<td>3,0</td>
<td>1</td>
<td>1,33</td>
<td>3,99</td>
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<td>Polio</td>
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<td>4</td>
<td>1,18</td>
<td>11,80</td>
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<td>Polio</td>
<td>20</td>
<td>1,5</td>
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<tr>
<td>Yellow F.</td>
<td>10</td>
<td>3,0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Yellow F.</td>
<td>20</td>
<td>2,5</td>
<td>1</td>
<td>1,33</td>
<td>3,3</td>
</tr>
<tr>
<td>Tetanus toxoid (par ECV)</td>
<td>10</td>
<td>3,0</td>
<td>2</td>
<td>1,18</td>
<td>7,1</td>
</tr>
<tr>
<td>Tetanus toxoid (par ECV)</td>
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<td>2,5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Volume net de stockage Cm3 par ECV</strong></td>
<td>24,0</td>
<td>15,8</td>
<td>39,8</td>
<td></td>
<td></td>
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</tbody>
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