WHO Guidelines on the international packaging and shipping of vaccines

UNICEF Vaccine Industry Consultation
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Carmen Rodriguez
Group lead, Vaccine Prequalification
Secure the existing supply of vaccines
Ensure that timely and safe delivery of vaccine to the consignee at country of destination,
Action to minimize wastage of vaccines, facilitate outreach (VVMs, MDVP, CTC)
How?

As per WHO TRS 978 Annex 6, 2013 requirements,

➤ Chapter 4: Vaccine composition, presentations and schedules
  • label intended to detect vaccine recommended storage temperature and “Do Not Freeze” warning,
  • Vaccine Vial Monitor (VVM): a label containing a heat sensitive material - Colour density changes indicator

➤ Chapter 9: Production and distribution
  • Packaging procedures for international shipments (including box sizes, packing volumes, etc.),
  • Validation protocols and reports of the shipping boxes used for United Nations supply
    – WHO WHO/IVB/05.23 Guidelines on the international packaging and shipping of vaccines should be followed,
  • Describe the arrangements for handling complaints and product recalls. Include provisions for informing WHO and the United Nations agencies.

➤ Chapter 7: Stability

Assessment of the stability profile of the vaccines at different temperatures is one of the main foci of the assessment by the prequalification program to guarantee the quality, safety and efficacy of the vaccine throughout the shelf life and considering the cold chain conditions of the NIP worldwide
  – Real Time condition @ 2 to 8°C, -20°C (0, 3, 6, 9, 12, 18 every 6 mths)
  – Accelerated condition @ 25°C (0, 30, 45, 60, 90...193 days)
  – Stress condition @ 37°C (0, 2, 7, 14, 21, 30 days)
## Types of vaccines

### Heat stable but **Freeze sensitive**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Heat sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP</td>
<td></td>
</tr>
<tr>
<td>DTaP–hepatitis B–Hib–IPV (hexavalent)</td>
<td></td>
</tr>
<tr>
<td>DTwP</td>
<td></td>
</tr>
<tr>
<td>DTwP–hepatitis B–Hib (pentavalent)</td>
<td></td>
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<tr>
<td>Hepatitis A</td>
<td></td>
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<tr>
<td>Hepatitis B</td>
<td></td>
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<tr>
<td>Human papillomavirus</td>
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<tr>
<td>Meningitis C (polysaccharide–protein conjugate)</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal (polysaccharide–protein conjugate)</td>
<td></td>
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<tr>
<td>TT, DT, Td</td>
<td></td>
</tr>
</tbody>
</table>

- Cholera (inactivated)
- Influenza (inactivated, split)
- Hib (liquid)
- Inactivated poliovirus
- Typhoid polysaccharide

*These vaccines are not damaged by freezing*

### Freeze stable but **Heat Labile**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Heat sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral poliovirus</td>
<td></td>
</tr>
<tr>
<td>Varicella–zoster virus</td>
<td></td>
</tr>
<tr>
<td>Influenza (inactivated, split)</td>
<td></td>
</tr>
<tr>
<td>Inactivated poliovirus</td>
<td></td>
</tr>
<tr>
<td>Japanese encephalitis (live)</td>
<td></td>
</tr>
<tr>
<td>Measles, mumps, rubella</td>
<td></td>
</tr>
</tbody>
</table>

- Cholera (inactivated)
- DTaP
- DTwP
- DTap–hepatitis B–Hib–IPV (hexavalent)
- DTwP–hepatitis B–Hib (pentavalent)
- Hib (liquid)

- Measles
- Rotavirus (liquid and freeze dried)
- Rubella
- Yellow fever

*These vaccines are not damaged by freezing*

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Heat sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillus Calmette-Guérin</td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td></td>
</tr>
<tr>
<td>Japanese encephalitis (inactivated)</td>
<td></td>
</tr>
<tr>
<td>TT, DT, Td</td>
<td></td>
</tr>
</tbody>
</table>

- Hepatitis A
- Hepatitis B
- Hib (freeze dried)
- Meningitis A (polysaccharide–protein conjugate)
- Meningitis C (polysaccharide–protein conjugate)
- Pneumococcal (polysaccharide–protein conjugate)
- Rabies
- Typhoid polysaccharide
Temperature deviations

**Heat exposure:**

All vaccines lose their potency over time, and heat accelerates this potency loss (Thermal stability studies),

Vaccine types vary in their sensitivity to heat, and the rate of loss is temperature-dependent

**Freeze exposure:**

Freezing can irreversibly damage vaccines that contain aluminium-salt adjuvants (i.e. DTP, Hep A, HepB, HPV),

Some non adjuvanted vaccines can also be damaged by freezing (i.e. Oral Cholera, IPV and Influenza)

Diluent for meningitis A conjugate vaccine contains an aluminium adjuvant.
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Background and history

• This is a very widely used document and is referenced by UNICEF and PAHO in all their invitations to bid for vaccine supplies and also by countries that directly procure their vaccines.

• First published in 1990, revised in 2005

• Since 2005 many new vaccines have been prequalified and there is a need to update the guidelines to reflect this fact.

• In addition to the introduction of new vaccines, technologies have advanced over the past 10 years

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Structure of the document

- Draft guidelines consist of 5 chapters:
  - Insulated packaging standards
  - Temperature monitoring devices
  - Labelling for international shipments
  - International shipping procedures
  - Vaccine arrival reports

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Proposed changes

• Informal consultation with PATH, UNICEF, WHO EPI and some vaccine manufacturers took place in June 2017 to identify areas that needed improvement.

• A section on insulated shipping standards and IATA time and temperature labelling has been added to the current draft.

• There were discussions around the rationale for the current alarm set points and the possibility of extending the electronic monitor recording periods (currently 20 days) but no agreements were reached.

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Ongoing public consultation

• The goal of this formal consultation is to receive suggestions from the global community on how to improve this document in light of new vaccines and improved information and communication technologies

• The current consultation is open till September 30th

• Target publication in December 2019

• Link on the WHO website for the consultation:

Conclusions

WHO PQ ensure programmatic suitability of vaccines at global level

**Vaccines**
Cold chain throughout the shelf life of the vaccine from manufacturing to vaccinees:
1. Assessment of quality data: Composition, stability
2. Review of labelling
3. Selection of Vaccine vial monitor.
4. Review of packaging procedures and shipping validation according to the type of vaccines.

**Immunization equipment**
1. Prequalification of shipping boxes
2. PQ of temperature monitoring devices: electronic devices, VVMs
3. Revision of shipping guidelines