Thermostability of vaccines

Every year the immunization services in developing countries around the world prevent more than three million deaths from measles, neonatal tetanus, and pertussis, as well as some 490,000 cases of childhood paralysis from poliomyelitis. That achievement is due in part to the progress that numerous countries have made in properly transporting and storing vaccines and in better maintaining the cold chain that helps preserve vaccines’ potency.

Nevertheless, those improvements have been far from uniform, and much still needs to be done to make the best use of the available vaccine resources. With that goal in mind, the Global Programme for Vaccines and Immunization of the World Health Organization (WHO) in December 1998 issued a new publication, Thermostability of Vaccines. It is an updated version of a 1989 WHO guide entitled Stability of Vaccines.

Doubts often arise as to whether or not to use stocks of vaccines that have been exposed to elevated temperatures for some period of time. Further, there is no easy, inexpensive method that can be used in the field to answer that question. Nevertheless, a knowledge of the stability of particular vaccines can help determine storage requirements and whether or not particular stocks should be used.

And that knowledge base has expanded greatly in recent years, particularly in comparison to periods in the past when all that was available was one fairly rigid set of guidelines for vaccine-handling worldwide. While that approach offered the benefit of simplicity, it led to a dogmatic view of the cold chain and prevented local health workers from making the best use of the actual heat stabilities of different vaccines. In addition, improvements in vaccines in recent years have made them more stable.

The stability of vaccines varies widely. Diphtheria and tetanus toxoids and hepatitis B vaccine have the best resistance to elevated temperatures; freeze-dried measles, yellow fever, and the BCG tuberculosis vaccines are in the middle; and oral poliomyelitis vaccine is the most fragile. Reconstituted vaccines against measles, yellow fever, and tuberculosis (BCG) are unstable and should be used as soon as possible after being reconstituted.
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Storage temperature (°C)</th>
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</thead>
</table>
| **Tetanus and diphtheria toxoids as monovalent vaccines or components of combined vaccines** | 0–8: Stable for 3–7 years  
22–25: Stable for months  
35–37: Stable for weeks  
Over 37: At 45 °C: stable for 2 weeks. At 53 °C: loss of potency after few days. At 60–65 °C: loss of potency after few hours. |
| **Hepatitis B vaccines** | 0–8: Stable for 2–4 years  
22–25: Stable for months  
35–37: Stable for weeks  
Over 37: At 45 °C: stable for days |
| **Measles vaccine** | 0–8: Stable for 2 years  
22–25: Retains satisfactory potency, up to 50%, for at least 1 month  
35–37: Retains satisfactory potency for at least 1 week, but may lose 20% and 50% of potency for 1–4 day and 2–6 day exposure, resp.  
Over 37: At 41 °C: 50% loss of potency after 2–3 day exposure. At 54 °C: 80% loss of potency after 1-day exposure. |
| **Yellow fever vaccines** | 0–8: Stabilized vaccines stable for 2–3 years  
22–25: 50% loss after 3–10 month exposure  
35–37: 50% loss after 10–20 day exposure  
Over 37: At 46 °C: about 50% loss in potency in 2 days. |
| **Pertussis vaccines** | 0–8: Stable for 18–24 months, in spite of continuous slow decrease in potency  
22–25: Stability varies: some vaccines stable for 2 weeks  
35–37: Stability varies. Some vaccines lose 50% of potency during storage for 1 week  
Over 37: At 45 °C: about 10% loss of potency per day. At 50 °C: rapid loss in potency. |
| **BCG vaccine** | 0–8: Stable for one year  
22–25: Stability varies: 20% to 30% loss of viability during 3-month exposure  
35–37: Stability varies; 20% loss of viability during 3–14 day exposure  
Over 37: Unstable. At 70 °C: 50% loss during 30-minute exposure. |
| **Oral poliomyelitis vaccine** | 0–8: Stable for 6–12 months  
22–25: Some vaccines may retain titer for 1–2 week exposure  
35–37: Unstable. VVMs in use. Loss of satisfactory titer in 1–3 days.  
Over 37: Very unstable. At 41 °C: 50% loss in one day. At 50 °C: loss of satisfactory titer after 1–3 hour exposure. |

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**Table 1. Stability of vaccines commonly used in national immunization programs**

a Data refer to freeze-dried measles, yellow fever, and BCG vaccines; other vaccines are presented in a fluid form. Reconstituted vaccines lose their potency quickly and they must be discarded at the end of an immunization session. Reconstituted BCG vaccine contains no bacteriostatic agent, and there is a risk of contamination. Reconstituted yellow fever vaccine should be administered quickly (up to one hour) after reconstitution. If the vaccine can be kept continuously in an ice bath, the reconstituted vaccine can be used within one immunization session. It must be discarded after the session.

b Vaccines adsorbed on aluminum salts. They should never be frozen.

c Optimal long-term storage is at −25 °C or less. Diluent should be kept separately and should not be frozen.
### TABLE 2. Stability of other bacterial and viral vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Storage temperature (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–8</td>
</tr>
<tr>
<td>Inactivated poliomyelitis vaccine</td>
<td>Stable for 1–4 years</td>
</tr>
<tr>
<td>Meningococcal polysaccharide vaccine</td>
<td>Stable for 2 years</td>
</tr>
<tr>
<td>Human diploid cell rabies vaccine</td>
<td>Stable for 3.5 years</td>
</tr>
<tr>
<td>Japanese encephalitis vaccine</td>
<td>Stable for one year; about 5% loss in potency during 52-week storage</td>
</tr>
<tr>
<td>Live oral typhoid Ty21a vaccine</td>
<td>Needs refrigeration. Shelf life depends on residual moisture content</td>
</tr>
</tbody>
</table>

<sup>a</sup> D-antigen content is measured in vitro by the ELISA test. IPV is standardized in D-antigen units; enhanced-potency IPV contains 40, 8, and 32 D-antigen units of types 1, 2, and 3, respectively.

<sup>b</sup> Half life: the time at which 50% loss of original potency occurs.

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Even with the most-stable vaccines, exposure to elevated temperatures results in some degradation. Table 1 provides guidelines for the vaccines that are most commonly used in national immunization programs, and Table 2 gives recommendations for other bacterial and viral vaccines. Of course, all vaccines should also be handled and used in line with their manufacturers’ storage recommendations and expiry dates.

The text sections of the new WHO document provide much more extensive detail on the stability of the vaccines listed in Table 1 and Table 2, and other vaccines as well.

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**SINOPSIS**

**La termoestabilidad de las vacunas**

En años recientes, muchos países han avanzado en el transporte y almacenamiento adecuado de las vacunas y han mejorado la cadena fría que ayuda a conservar su potencia. No obstante, estas mejoras se han producido de manera muy poco uniforme y aún falta mucho para que se aprovechen al máximo las vacunas disponibles. El conocer la estabilidad de ciertas vacunas puede ayudar a establecer las condiciones en que deben almacенarse y a saber si determinados lots deben usarse o no. En este trabajo se presentan dos cuadros donde se resumen muchos datos actualizados sobre la termoestabilidad de las vacunas, según informa una nueva publicación de la Organización Mundial de la Salud.