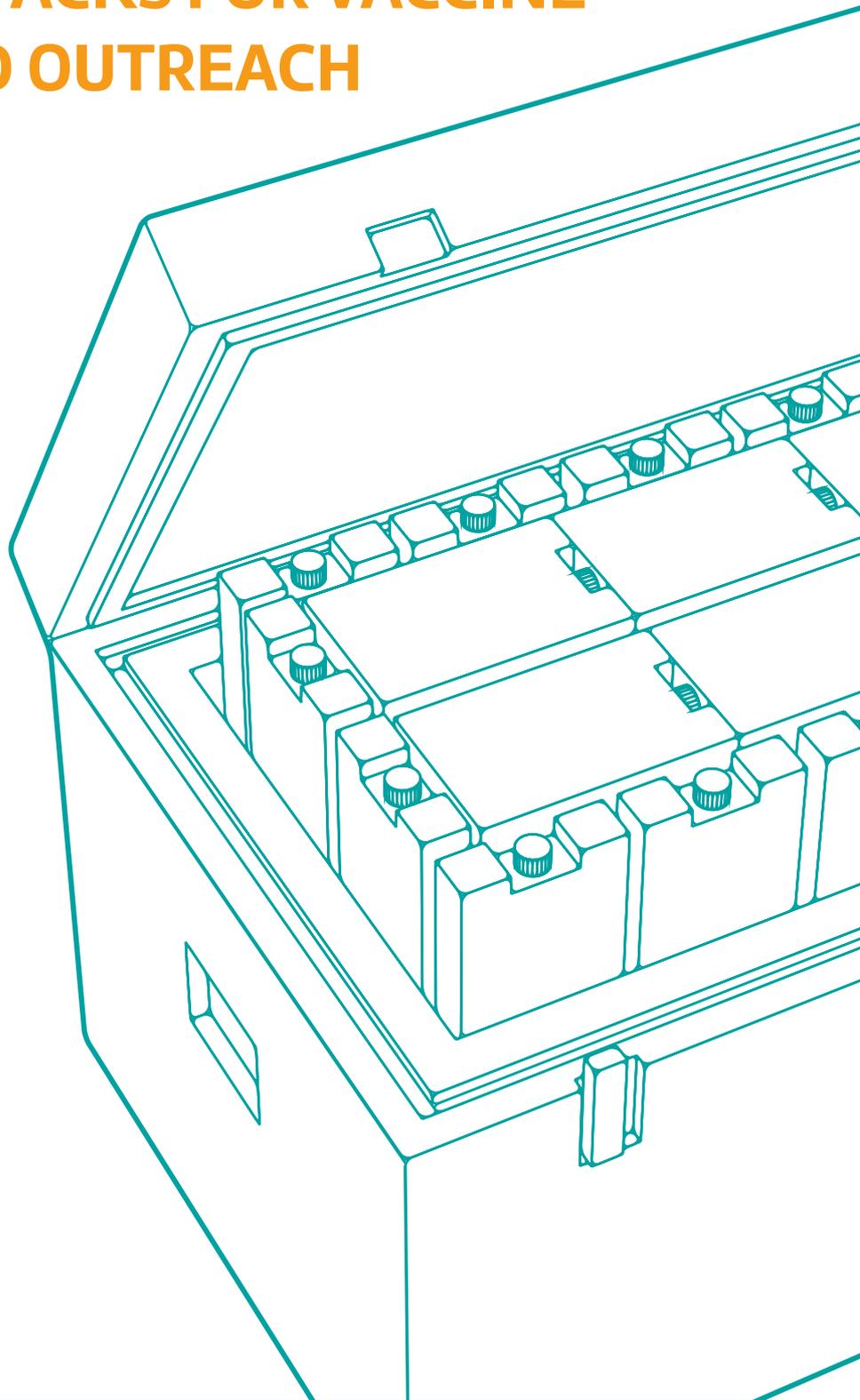




# HOW TO USE PASSIVE CONTAINERS AND COOLANT-PACKS FOR VACCINE TRANSPORT AND OUTREACH OPERATIONS

July 2015

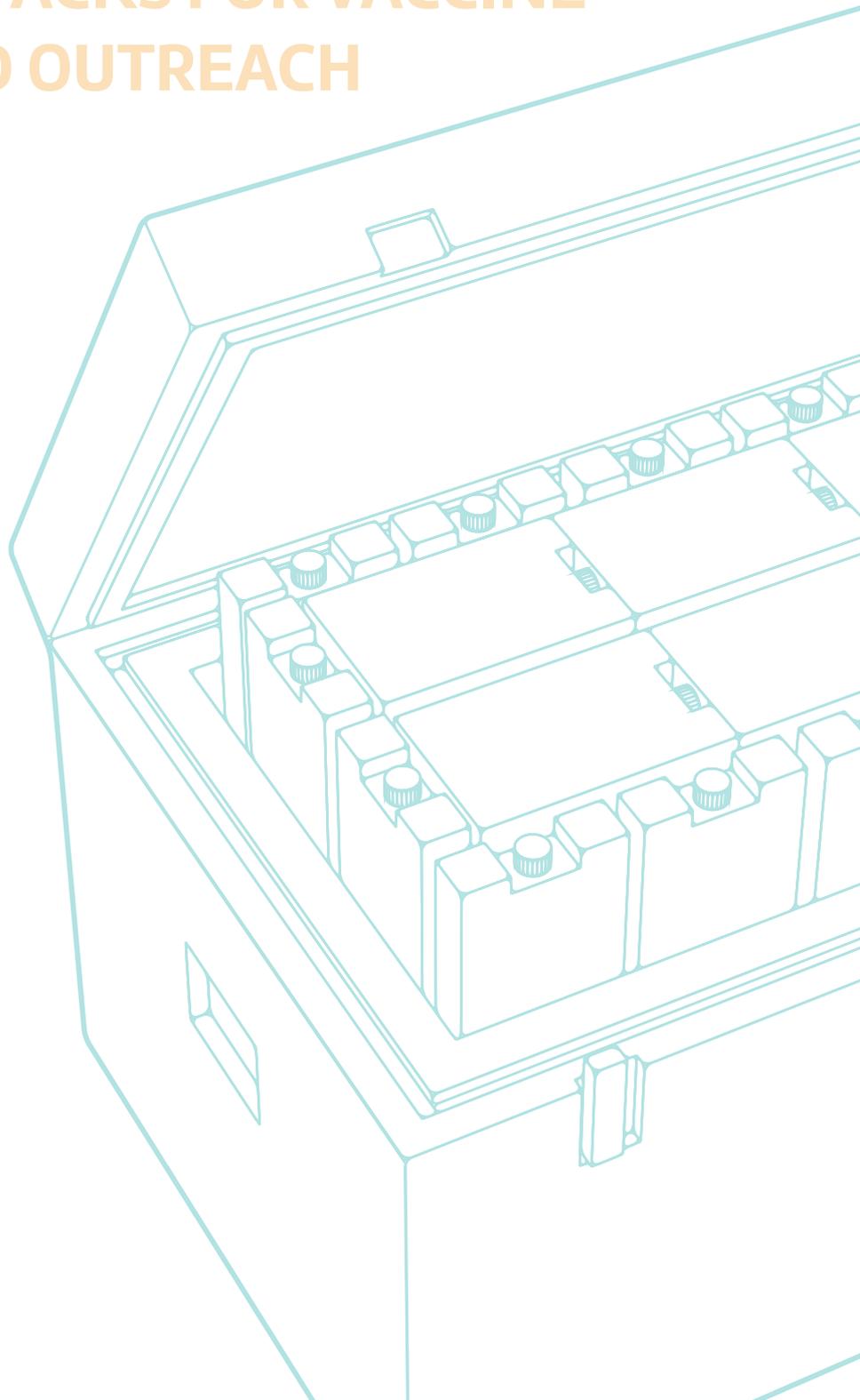






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July 2015



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## How to use this module

This module of the WHO Vaccine Management Handbook (VMH) is a component of the World Health Organization/United Nations Children's Fund Effective Vaccine Management (EVM) Initiative. The handbook is written for decision-makers at national and subnational levels; its purpose is to provide technical advice on key topics related to immunization logistics to help countries develop and refine national policies. For more detailed guidance on specific operational activities, readers should refer to the EVM Model Standard Operating Procedures.<sup>1</sup>

Advice in the VMH generally conforms to the guidance on good storage and distribution practice given in WHO Technical Report Series No. 961, 2011, Annex 9: Model guidance for the storage and transport of time- and temperature-sensitive pharmaceutical products.<sup>2</sup>

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<sup>1</sup> Effective Vaccine Management (EVM) Initiative Model Standard Operating Procedures. Geneva: World Health Organization, 2015 ([http://www.who.int/immunization/programmes\\_systems/supply\\_chain/eum/en/index2.html](http://www.who.int/immunization/programmes_systems/supply_chain/eum/en/index2.html), accessed 30 March 2015).

<sup>2</sup> WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-fifth report. Geneva: World Health Organization, 2011: Annex 9 (WHO Technical Report Series No. 961; <http://apps.who.int/medicinedocs/documents/s18683en/s18683en.pdf>, accessed 30 March 2015).

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## Abbreviations

DT	diphtheria and tetanus toxoid vaccine
DTaP	diphtheria, tetanus, and [acellular] pertussis vaccine
DTwP	diphtheria and tetanus toxoid (whole cell) and pertussis vaccine
EVM	Effective Vaccine Management (initiative)
Hib	<i>Haemophilus influenzae</i> type b vaccine
IPV	inactivated poliovirus vaccine
OPV	oral poliovirus vaccine
PCM	phase-change material
PQS	performance, quality and safety
SOP	standard operating procedure
Td	tetanus and diphtheria vaccine with reduced diphtheria content for adults
TT	tetanus toxoid
TTM	time-temperature monitoring device
VMH	Vaccine Management Handbook
VVM	vaccine vial monitor
WHO	World Health Organization

## Glossary

**Cold life (test):** The empty *passive container* is stabilized at +43°C and loaded with *icepacks* frozen at -25°C. *Cold life* is measured from the moment when the container lid is closed until the temperature of the warmest point in the *vaccine storage compartment* first reaches +10°C, at a constant ambient temperature of +43°C.

**Conditioned ice-pack:** An *ice-pack* that has been allowed to warm at ambient temperature until some water is present inside the pack. The pack is correctly conditioned as soon as the ice core is able to move inside the pack when it is shaken. The effective temperature of a *conditioned ice-pack* in this state is 0°C.

**Cool life (test):** The empty *passive container* is stabilized at +43°C and loaded with *cool water-packs* that have been stabilized at +5°C for a minimum of 24 hours. *Cool life* is measured from the moment when the container is closed until the temperature of the warmest point inside the *vaccine storage compartment* first reaches +20°C, at a constant ambient temperature of +43°C.

**Cool water-pack:** A *water-pack* cooled to a temperature between +2°C and +8°C before use.

**Coolant-pack:** A purposely designed leak-proof container, typically complying with performance, quality and safety (PQS) specification PQS/E005/IP01, filled with tap water or with a *phase-change material* (PCM).

**Diluent:** A liquid used to mix with a lyophilized (powder) vaccine in order to reconstitute the lyophilized vaccine and provide the final vaccine for administration.

### Important clarification of the use of the word diluent in this module

**In this module diluent means:** A liquid product which is pharmacologically inactive or another vaccine used to reconstitute (for dissolution) a lyophilized vaccine.

**Heat of fusion:** The amount of heat that must be added to convert a unit of mass of a solid into a liquid at its melting-point temperature, or the amount of heat that must be removed to convert a unit of mass of a liquid into a solid at its freezing-point temperature.

**Ice-pack:** A *water-pack* that has been frozen to a temperature of between -5°C and -25°C before use.

**Passive container:** A container that maintains a temperature-controlled environment inside an insulated enclosure, generally without thermostatic regulation, using *frozen ice-packs*, *conditioned ice-packs*, *cool water-packs* or *warm water-packs*. Chilled or 'frozen' PCM-packs are also used.<sup>3</sup> *Passive containers* in this context include reusable insulated cold boxes and vaccine carriers as well as single-use insulated cartons.

**Phase-change material:** A substance (other than water) with a high heat of fusion that melts and solidifies at a certain temperature and is capable of storing and releasing large amounts of energy. Heat is absorbed or released when the material changes from solid to liquid and vice versa. The *phase-change materials* used for vaccine transport typically change state at around +5°C.

**PCM-pack:** A purposely designed leak-proof **coolant-pack** filled with a *phase-change material*.

**Primary container:** Vial, ampoule, prefilled device, plastic dispenser or tube containing vaccine or diluent.

**Primary vaccine store:** A store that receives vaccine deliveries from the vaccine manufacturer, generally the national vaccine store. However, this may also be a state- or regional-level store in larger countries.

**Secondary packaging or secondary carton:** Carton containing one or more *primary container* units.

**Standard operating procedure:** Detailed written and/or visual instructions designed to ensure that a specific task or function is carried out in a consistent and uniform manner.

**Storage temperature:** The temperature range for vaccine storage as stated by the manufacturer on the primary container label and the package insert, and within the regulatory filings for the product. Some manufacturers also provide a temperature range for vaccine transport.

**Temperature excursion:** An excursion event during which a vaccine is exposed to temperatures outside the range(s) prescribed for storage and/or transport. Temperature ranges for storage and transport may be the same or different; they are determined by the product manufacturer based on stability data. In situations in which *cool water-packs* are used for vaccine transport, an excursion up to a maximum of +20°C is acceptable.

**Transport temperature profile:** Anticipated ambient temperature variation and duration to which a *passive container* may be exposed during packing, transport and unpacking operations.

**User-programmable temperature logger:** An electronic device primarily used for temperature monitoring studies. The user is able to start and stop the device and set the frequency of temperature recordings and alarms.

**Utilization percentage:** The average percentage of the measured *vaccine storage capacity* of a *passive container* that can be used in practice, taking into account the dimensions of the primary containers or *secondary cartons* that are being transported.

**Vaccine storage capacity:** The volume of the *vaccine storage compartment* within a *passive container* measured in litres with the recommended number of **coolant-packs** in place.

**Vaccine storage compartment:** The zone within a *passive container* that is designated by the manufacturer as suitable for storing vaccine when the container is loaded with the recommended number of **coolant-packs** required to achieve the container's maximum rated *cold life*.

**Warm life (test):** The empty *passive container* is stabilized at +18°C and loaded with *warm water-packs* that have been stabilized at the same temperature for a minimum of 24 hours. *Warm life* is measured from the moment when the container is closed until the temperature of the coldest point inside the *vaccine storage compartment* first reaches 0°C at a constant ambient temperature of -20°C.

**Warm water-pack:** A *water-pack* typically stabilized at room temperature, up to a recommended maximum of +24°C. Warm water-packs are used for the transport of freeze-sensitive vaccines when the ambient temperature is below 0°C.

**Water-pack:** A **coolant-pack**, typically complying with PQS

<sup>3</sup> WHO does not currently recommend PCM-packs for in-country transport but continues to keep this technology under review.



specification PQS/E005/IP01, filled with tap water.

# 1. Introduction

This module describes the correct use of passive containers [cold boxes and vaccine carriers] for in-country transport and outreach operations.

In order to avoid loss of potency and reduced shelf life, vaccines must be protected from exposure to excessively high or low transport temperatures. This protection can be achieved by taking the following actions:

- develop standard operating procedures for vaccine packing and transport, and train staff to observe these procedures;
- understand the heat and freeze sensitivity of every vaccine in the national schedule;
- know the duration of the journeys and the transport temperature profiles of all the routes over which the vaccines will be transported;
- choose passive containers with performance characteristics that suit documented transport temperature profiles;
- choose the correct type and quantity of **coolant-packs** to protect freeze-sensitive vaccines against freezing and heat-sensitive vaccines against heat damage;
- where passive containers are used during immunization sessions, ensure that opened vials of vaccines are protected from temperatures above +8°C. This condition applies to both lyophilized vaccines that have been reconstituted and liquid vaccines that do not contain preservative; and
- maintain temperature and/or vaccine vial monitor status records to demonstrate compliance.

There is no single recipe for transporting vaccines safely in passive containers. Every method carries risks, and these risks have to be identified, understood and managed in the specific operational context. A method that works well for short urban deliveries may not be suitable for long-distance transport to remote rural locations. The more field evidence that can be gathered on actual temperatures experienced during transport, the more the risks of vaccine damage can be reduced. Good management and effective training will further reduce these risks.

Some vaccines are damaged by freezing; others are particularly vulnerable to heat exposure [see **Annex 1**]. Vaccines are often exposed to sub-zero temperatures during transport, largely due to the use of frozen ice-packs.<sup>4</sup> However, heat damage can also occur when proper precautions are not taken.

This module provides guidance on how to develop a transport strategy that minimizes these risks through the correct use of passive containers and their associated **coolant-packs**. It covers vaccine transport down to the health facility level and transport for outreach operations.

## 1.1 Objectives of this module

The objectives of this module are to:

- a. describe the risks to vaccines from cold chain-induced temperature damage and the actions that should be taken to minimize these risks;
- b. introduce the concept of *transport route profiling* and provide references and resources to help countries follow this approach;
- c. describe existing passive container and **coolant-pack** technologies and how to make appropriate choices in a country context;
- d. provide guidance on choosing the correct type and quantity of **coolant-packs** to protect freeze-sensitive vaccines against freezing and heat-sensitive vaccines against heat damage;
- e. describe how opened vials of unpreserved liquid vaccine and reconstituted vials of lyophilized vaccine can be stored at temperatures between +2°C and +8°C when passive containers are used during immunization sessions;
- f. recommend a shortlist of standard operating procedures [SOPs] for vaccine packing and transport, and the staff training needed to make sure that these procedures are observed; and
- g. describe the temperature and/or vaccine vial monitor [VVM] status records needed to demonstrate compliance with good distribution practice.

## 1.2 Target audience

This module is intended to be read by Expanded Programme on Immunization managers and supporting partners, and those responsible for:

- a. overall planning of in-country vaccine transport and outreach operations;
- b. implementing a safe and effective vaccine transport plan based on the use of passive containers;
- c. routine management of in-country vaccine transport and outreach operations; and
- d. purchasing cold chain equipment.

<sup>4</sup> See, for example: Matthias DM, Robertson J, Garrison MM, Newland S, Nelson C. Freezing temperatures in the vaccine cold chain: a systematic literature review. *Vaccine*. 2007;25(20):3980-6.

## 2. Passive containers and coolant-packs

Passive container systems consist of a thermally insulated container with an opening lid and a compatible set of **coolant-packs** that line the inside of the container. Depending on the operational conditions, **coolant-packs** may be frozen, conditioned, cooled or warmed before use in order to maintain safe temperatures within the container for the transport period required.

This section describes existing World Health Organization (WHO)-prequalified passive containers and **coolant-packs** and summarizes their strengths and weaknesses and the risks associated with their use. It does not cover forthcoming technologies such as cold boxes and vaccine carriers with freeze-prevention technology.

### 2.1 Passive container risks

A passive container system has to control heat flow through the container walls so that vaccines remain within the recommended storage temperature range to prevent damage from temperature extremes. This temperature range, including allowable temperature excursions, must be maintained from the moment the vaccine load is packed until it is removed at the end of the journey, even when the ambient temperature fluctuates widely.

Adverse events most commonly arise when **coolant-packs** are used incorrectly, the wrong type of container is chosen for the conditions of the intended journey or the journey takes longer than anticipated. Failure to manage these risks can result in:

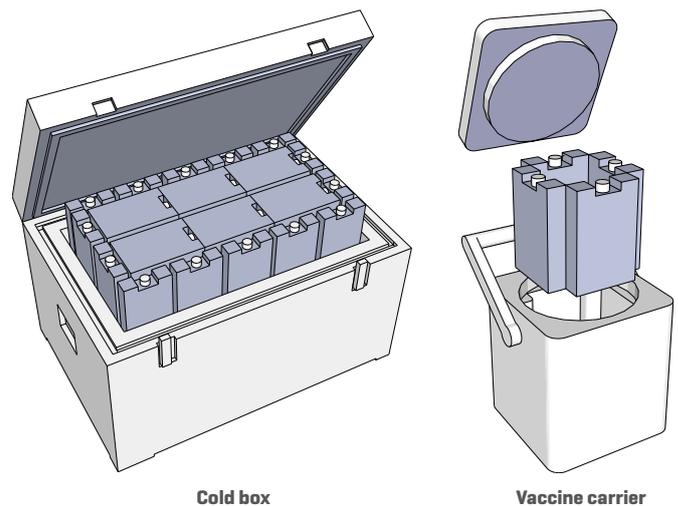
- exposure of freeze-sensitive vaccines to sub-zero temperatures, causing loss of potency (if alum-containing vaccines are frozen, they lose their potency and must be discarded);
- exposure of heat-sensitive vaccines to temperatures above +8°C for extended periods, causing loss of potency; and
- increased risk of microbial growth in opened vials of vaccine, which can occur if reconstituted preservative-free vaccines or opened vials of liquid vaccines that do not contain preservative are exposed to temperatures above +8°C during immunization sessions.

### 2.2 Prequalified passive containers

The current generation of WHO-prequalified passive containers are robust, insulated, and reusable<sup>5</sup> and hold WHO-prequalified water-packs. Cold boxes have hinged lids; vaccine carriers generally have separate lids, although hinged lids are optional

[see Figure 1]. Typically, the container has rigid moulded plastic inner and outer shells between which there is a foam-plastic insulating core.<sup>6</sup> Some products are constructed using soft materials. The water-packs provide the thermal mass needed to maintain a safe storage temperature range for the required transport period.

Figure 1. Cold box and vaccine carrier with coolant-packs



As part of the WHO prequalification process, containers are laboratory tested under controlled conditions. These tests assess whether the product is robust enough to withstand long-term use and establish its cold life, cool life, and warm life.

Cold life and cool life are measured at a constant ambient temperature of +43°C and warm life is assessed at a constant ambient temperature of -20°C. The cold life test uses frozen ice-packs, the cool life test uses refrigerated cool water-packs and the warm life test uses water-packs at room temperature. It is important to note that the current tests DO NOT measure cold life with conditioned ice-packs.

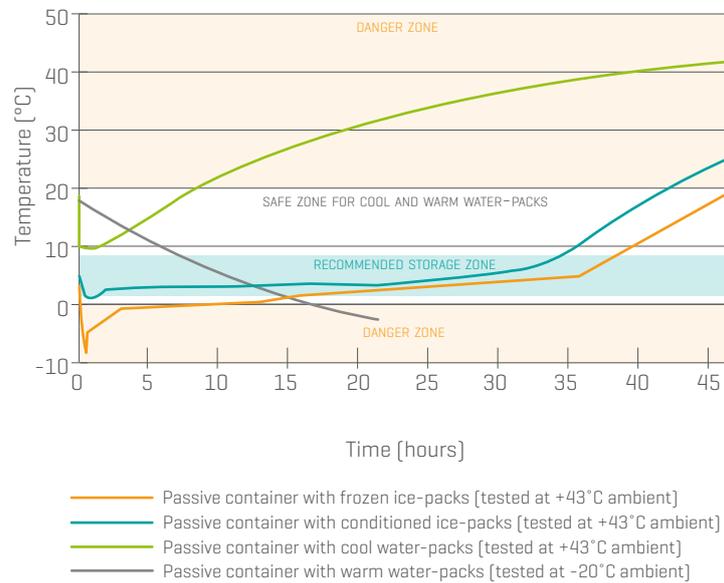
Figure 2 illustrates the temperature profiles inside a vaccine vial placed in the center of a typical vaccine carrier for the three PQS test conditions (a conditioned ice-pack temperature profile is also shown). Actual profiles will differ depending on the container design, the ambient temperature experienced along the transport route, and the thermal mass of the cold vaccine placed in the container. The temperature profile measured when the vaccine carrier is packed with cool-water packs stays in the safe zone for 6 to 7 hours. The negative temperatures shown in Figure 2 when the vaccine carrier is packed with frozen ice-packs demonstrate why WHO guidance requires that conditioned ice-packs be used to transport a freeze-sensitive vaccine or diluent.<sup>7</sup>

<sup>5</sup> Disposable passive containers are widely used for in-country transport in higher-income countries, but they are not specifically considered in this guideline.

<sup>6</sup> Insulation foams, such as polyurethane, are widely used in passive container construction. Countries should be aware that the thermal performance of some types of foam reduces as the gas foaming agent gradually escapes and is replaced by air. This means that the rated cold, cool and warm life of older containers, especially those that have damaged shells, may shorten over time. This factor needs to be considered during transport route planning.

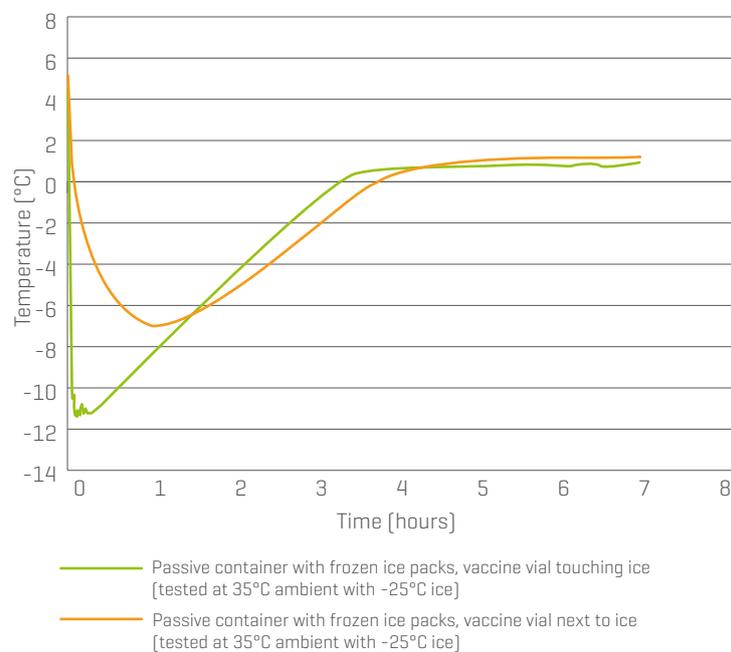
<sup>7</sup> Conditioning frozen icepacks (EVM-SOP-E7-04). In: Effective Vaccine Management (EVM) Initiative Model Standard Operating Procedures. Geneva: World Health Organization, 2015. ([http://www.who.int/immunization/programmes\\_systems/supply\\_chain/eum/en/index2.html](http://www.who.int/immunization/programmes_systems/supply_chain/eum/en/index2.html), accessed 30 March 2015).

**Figure 2.** Temperatures inside vaccine vials placed in the centre of a vaccine carrier packed with four types of water-packs



**Source:** Illustrative data from PATH laboratory tests using a WHO prequalified vaccine carrier [2014].

**Figure 3.** Temperatures inside vaccine vials adjacent to and in contact with frozen ice-packs inside a vaccine carrier



**Source:** PATH laboratory test results for a WHO-prequalified vaccine carrier [2014].

Figure 3 illustrates the temperature profiles inside a vaccine vial placed next to the inside wall of a vaccine carrier filled/loaded with frozen ice-packs. The temperatures drop well below zero, especially when the vial is touching the frozen ice-pack.

**Annex 2** shows the range of performance for the various types of prequalified passive containers. The best-performing cool life for current cold boxes is 51 hours, compared with 156 hours for the best cold life. For vaccine carriers, the corresponding figures are 18 hours and 50 hours.

**Coolant-packs** can be prepared for use in four different ways, as follows:

- **Frozen ice-packs** taken directly from a freezer are very cold, typically between  $-20^{\circ}\text{C}$  and  $-25^{\circ}\text{C}$ . As Figure 2 shows, when frozen ice-packs are placed in a passive container, the container temperature immediately drops to well below  $0^{\circ}\text{C}$  and stays there for a period of up to several hours. For this reason, even though they ensure a long cold life, they **MUST NEVER** be used to transport freeze-sensitive vaccines.
- **Conditioned ice-packs** are ice-packs that have been removed from the freezer and left at room temperature until they begin to melt. At this point, they contain a mixture of ice and water at a temperature of about  $0^{\circ}\text{C}$ . As shown in Figure 2, conditioning eliminates the initial freezing risk without much reduction in cold life. The problem with using conditioned ice-packs is that compliance with correct conditioning practice is a challenge. **Annex 3** describes the correct ice-pack conditioning procedure.
- **Cool water-packs** contain liquid water at an initial temperature of between  $+2^{\circ}\text{C}$  and  $+8^{\circ}\text{C}$ . Cool water-packs eliminate the freezing risk, but cold water lacks the cooling performance of ice and protects vaccines for a much shorter period of time. It is important to note that the experimental work of validating the use of cool water-packs is based on the argument that it is safe to expose vaccines other than oral poliovirus vaccine (OPV) to temperatures of up to  $+20^{\circ}\text{C}$  for short time periods,<sup>8</sup> **BUT ONLY IF THE VACCINES HAVE VVMs**. **Annex 4** describes how cool water-packs should be prepared using a dedicated refrigerator.
- **Warm water-packs** contain water, initially at about  $+18^{\circ}\text{C}$  (with an allowable maximum of  $+24^{\circ}\text{C}$ ). Warm water-packs can be used to protect vaccines against freeze damage during transport in very cold climates. Cool water-packs can be used for the same purpose but offer a shorter period of protection.

**Note:** A sub-zero temperature drop always occurs when frozen ice-packs are placed in a passive container immediately after they have been removed from a freezer. Because of this drop, freeze-sensitive vaccines must **NEVER** be placed in a container with frozen ice-packs, **UNLESS** they have been correctly conditioned as described in **Annex 3**.

There is a widely held belief that wrapping freeze-sensitive vaccines prevents the vaccine from freezing in containers lined with frozen ice-packs. WHO does not recommend this practice because it is ineffective and does not protect vaccines from freeze damage.<sup>9</sup>

## 2.3 Coolant-packs

The choice of **coolant-pack** type depends on the type[s] of vaccine being transported and the ambient temperatures to which the passive container will be exposed. In order to ensure consistent performance, it is also important that packs are the correct size and type for the passive container being used.

### 2.3.1 Prequalified water-packs

WHO currently recommends the use of water-filled **coolant-packs**. Drinking water is safe for such use and is generally available; this makes it the most practical substance for filling **coolant-packs** because both water and ice can effectively control the temperature of the vaccine load, when correctly used.

WHO recommends the use of prequalified water-packs; these products are laboratory tested to ensure that they are robust enough to survive repeated use. A limited range of four different sizes of water-packs is currently prequalified [see Table 1]. This ensures that packs from different manufacturers can be used interchangeably across a range of passive container models. Dimensions, construction and performance standards are described in the relevant WHO performance, quality and safety (PQS) specification.<sup>10</sup>

<sup>8</sup> Kartoglu U, Ganiuet S, Guichard S, Aiger V, Bollen P, Maire D et al. Use of cool water packs to prevent freezing during vaccine transportation at the country level. *PDA J Pharm Sci Technol.* 2009;63(1):11–26.

<sup>9</sup> Immunization in practice: A practical guide for health staff. Geneva: World Health Organization; 2004 (<http://www.who.int/immunization/documents/training/en/>, accessed 30 March 2015).

<sup>10</sup> See: PQS catalogue – prequalified devices and equipment [online database]. Geneva, World Health Organization; 2015 ([http://apps.who.int/immunization\\_standards/vaccine\\_quality/pqs\\_catalogue/categorylist.aspx?cat\\_type=device](http://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/categorylist.aspx?cat_type=device), accessed 30 March 2015).

**Table 1. Dimensions of prequalified water-packs**

Type	Nominal size (litres)	Water content (litres)	Length (mm)	Width (mm)	Thickness (mm)
1	0.3	0.25 to 0.35	173	120	26
2	0.3	0.25 to 0.30	163	90	34
3	0.4	0.35 to 0.40	163	94	34
4	0.6	0.55 to 0.60	190	120	34

### 2.3.2 Other types of coolant-pack

Other **coolant-pack** technologies are widely used in pharmaceutical cold chains. WHO continues to keep these technologies under review but remains in favour of countries using standard water-filled **coolant-packs**, for both operational and economic reasons.

**Gel-packs:** These contain a mixture of water and thickening additives of various kinds. Gel-packs are widely available commercially and are typically supplied in a prefilled, sealed, flexible plastic bag or in a rectangular plastic container. WHO does not recommend using gel-packs because their thermal properties may not be the same as water-packs of the same volume. For example, the freezing point of some gel-packs can be significantly below 0°C. In addition, the flexible pouch type is unlikely to survive long-term use.

**Phase-change material packs (PCM-packs):** These contain phase-change materials that are generally not water based. Fill materials include various types of paraffin wax or vegetable-sourced substances. The great advantage of PCMs is that they can be designed to change phase at temperatures within the +2°C to +8°C range recommended for vaccine storage and transport. This overcomes the vaccine freezing risk associated with frozen water. However, PCM-packs have a significantly lower cooling performance than ice on a weight-for-weight and volume-for-volume basis; they are also more expensive. Finally, in order to trigger the freezing process, PCM-packs

generally have to be frozen in a freezer and then conditioned for up to 24 hours in a refrigerator before use. This two-stage procedure reintroduces the compliance problems associated with conditioning ice-packs.

**Coolant-packs recovered from international shipping containers:** Vaccine manufacturers ship products by air using **coolant-packs** of various types and sizes containing various fill materials, including water, gel and PCM. These packs do not necessarily perform in the same way as the standard-sized prequalified water-packs. In addition, they are not designed for repeated use and may not be dimensionally compatible with the prequalified passive containers used for the in-country supply chain.

**Note:** For the reasons described above, WHO recommends the use of water-filled **coolant-packs** for in-country transport. WHO discourages countries from using **coolant-packs** that have been recovered from international vaccine shipping containers for in-country vaccine transport. After vaccine arrival, these packs should be removed from the receiving vaccine store. They should be recycled or disposed of according to the vaccine manufacturer's recommendations and/or national waste management policies.

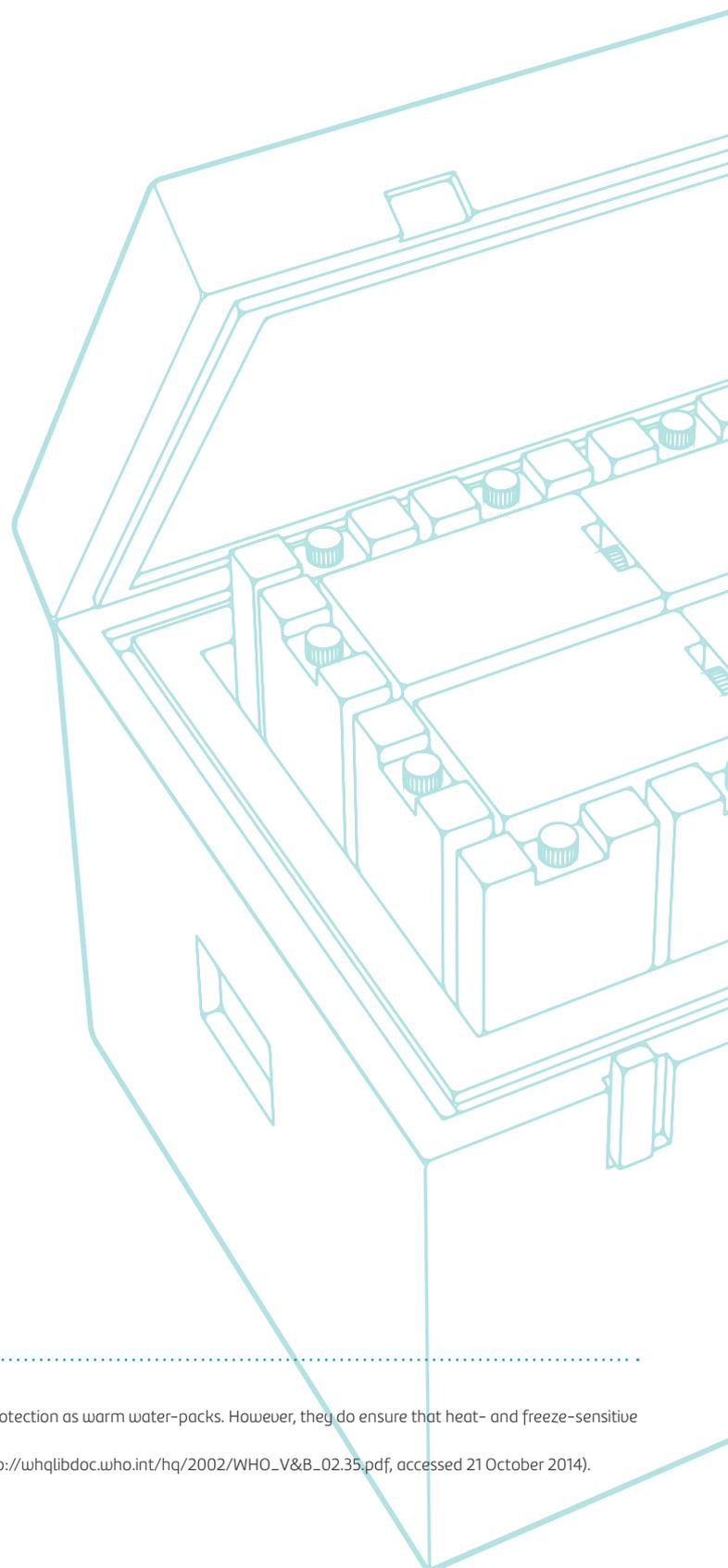
## 3. Choosing the right type of coolant-pack

The basic rules for using water-packs for transporting vaccines, with and without VVMs, are as follows:

- **Frozen ice-packs:** This option can be used to transport all lyophilized vaccines, or any liquid vaccine that is NOT freeze sensitive, such as OPV. Frozen ice-packs must NEVER be used to transport a freeze-sensitive vaccine or a lyophilized vaccine that is packaged (bundled) with its diluent.
- **Conditioned ice-packs:** This option can be used to transport any vaccine, including lyophilized vaccines with bundled diluent. However, the ice-packs MUST be conditioned correctly, as described in **Annex 3**.
- **Cool water-packs:** If the vaccine has a VVM, this option can be used for transport between the primary store and the health facility for any vaccine EXCEPT those with a VVM 2 or VVM 7; this includes OPV, some brands of inactivated poliovirus vaccine (IPV) and varicella vaccine. For outreach purposes, cool water-packs can be used for ALL vaccines that carry a VVM.
- **Cool water-packs for sub-zero protection in unheated vehicles:**<sup>11</sup> For short journeys in sub-zero temperatures, cool water-packs will protect both liquid freeze-sensitive vaccines and vaccine diluents against the risk of freezing.<sup>12</sup> They can safely be used for this purpose even when the vaccine does not have a VVM.
- **Warm water-packs for sub-zero protection in unheated vehicles:** For long journeys in sub-zero temperatures, warm water-packs are needed to prevent most liquid freeze-sensitive vaccines and vaccine diluents from freezing, provided the vaccines have VVMs. However, warm water-packs should NEVER be used to transport OPV, IPV with VVM 7, varicella or any other highly heat-sensitive vaccine. They should also NEVER be used for any vaccine without a VVM because there is no way to monitor the effect of exposure to temperatures above the labelled storage range of +2°C to +8°C.

### 3.1 Water-pack options for vaccines with VVMs

VVMs provide operational flexibility because the effect of exposure to temperatures above +8°C can be monitored by checking the status of the indicator.<sup>13</sup> Table 2 covers the transport of vaccines with VVMs from the primary store down to the health facility level, and during outreach.



<sup>11</sup> This includes unheated aircraft holds, even in hot climates.

<sup>12</sup> Note that cool water-packs, used in this way, do not provide as long a period of freeze protection as warm water-packs. However, they do ensure that heat- and freeze-sensitive vaccines are not exposed to temperatures above +8°C.

<sup>13</sup> Getting started with vaccine vial monitors. Geneva: World Health Organization; 2002 ([http://whqlibdoc.who.int/hq/2002/WHO\\_V&B\\_02.35.pdf](http://whqlibdoc.who.int/hq/2002/WHO_V&B_02.35.pdf), accessed 21 October 2014).

**Table 2. Safe coolant-pack options for vaccines with VVMs**

Product	Frozen ice-packs	Conditioned ice-packs	Cool water-packs	Warm water-packs
Transport from primary store to health facility				
Liquid vaccines: freeze sensitive		✓	✓ [at sub-zero ambient]	✓ [at sub-zero ambient]
Liquid vaccines: NOT freeze sensitive	✓	✓	✓ [for greater than VVM 7]	
Lyophilized vaccines: separate diluent	✓	✓	✓ [for greater than VVM 7]	
Lyophilized vaccines: packed with diluent		✓	✓ [for greater than VVM 7]	✓ [at sub-zero ambient]
Diluent packaged alone		✓	✓	✓ [at sub-zero ambient]
Transport to outreach sessions				
Liquid vaccines: freeze sensitive		✓	✓	
Liquid vaccines: NOT freeze sensitive	✓ [for campaigns]	✓	✓	
Lyophilized vaccines with diluent		✓	✓	

**Note:** During outreach sessions, opened vials of unpreserved liquid vaccine and reconstituted vials of lyophilized vaccine must always be kept at a temperature between +2°C and +8°C. If cool water-packs are used for transport, one or more ice-packs must also be taken to the session, unless there is ice-making capacity at the outreach site.

Except under exceptionally harsh cold weather conditions, with long transport periods in unheated vehicles, it is unlikely that warm water-packs will be needed for outreach operations. If circumstances do require the use of warm water-packs, a country-specific protocol should be developed and validated as part of the overall transport plan.

### 3.2 Transporting vaccines without VVMs

Table 3 covers transport and outreach operations for vaccines that are NOT supplied with VVMs. In this situation, the operational choices are more limited because there is no means of monitoring cumulative exposure to temperatures above +8°C over the course of multiple transport legs.

**Table 3. Safe coolant-pack options for vaccines without VVMs**

Product	Frozen ice-packs	Conditioned ice-packs	Cool water-packs	Warm water-packs
Transport from primary store to health facility				
Liquid vaccines: freeze sensitive		✓	✓ [at sub-zero ambient only]	
Liquid vaccines: NOT freeze sensitive	✓	✓		
Lyophilized vaccines: separate diluent	✓	✓		
Lyophilized vaccines: packed with diluent		✓	✓ [at sub-zero ambient only]	
Diluent packaged alone		✓	✓	✓ [at sub-zero ambient]
Transport to outreach sessions				
Liquid vaccines: freeze sensitive		✓	✓ [except for RotaTeq®]	
Liquid vaccines: NOT freeze sensitive	✓	✓	✓	
Lyophilized vaccines with diluent		✓	✓	

**Note:** During outreach sessions, opened vials of unpreserved liquid vaccine and reconstituted vials of lyophilized vaccine must always be kept at a temperature between +2°C and +8°C. If cool water-packs are used for transport, one or more ice-packs must also be taken to the session, unless there is ice-making capacity at the outreach site.

For vaccines NOT supplied with VVMs, the following principles for choosing **coolant-packs** apply:

- In warm and hot climates, cool water-packs should NOT be used for routine vaccine transport because cumulative heat exposure to temperatures above +8°C cannot be monitored adequately.
- In cold climates, use cool water-packs to protect freeze-sensitive vaccines or lyophilized vaccines bundled with diluent from exposure to sub-zero conditions. Warm water-packs should NEVER be used for this purpose because of the risk of prolonged exposure to temperatures above +8°C.
- RotaTeq® should only be transported using conditioned ice-packs; its freeze-sensitivity status is not fully established<sup>14</sup> and a suitable VVM is not available for this vaccine. In addition, its maximum allowable exposure time at temperatures above +8°C is only 48 hours at +9°C to +25°C. It is highly likely that temperatures above +8°C will occur when cool water-packs are used in hot climates. Since there are usually two or three transport legs between the national store and the health facility, it is possible that this 48-hour exposure period could be exceeded, unless all the journey times are very short.

Outreach recommendations are the same as for vaccines with VVMs because of the relatively short transport times involved.

### 3.3 Transporting separate diluents

Separately packed diluents are generally supplied in ampoules and do not have VVMs. Ampoules can break if the contents are frozen. In addition, if it contains an active ingredient, the diluent itself may be damaged by freezing.

- In general, separately packed diluents can be transported down to the health facility level at ambient temperature, although exposure to temperatures above those recommended by the manufacturer should be avoided.<sup>15</sup> When diluents arrive at the health facility, they should be placed in the refrigerator, unless the vaccine manufacturer specifically states that the vaccine can be reconstituted with diluent kept at room temperature.
- In climates with sub-zero temperatures, diluents MUST be protected from freezing. In this case, the diluents should be packed in insulated containers with warm water-packs or cool water-packs, unless the cartons that are not insulated can be transported in a heated vehicle.

<sup>14</sup> The package insert states: *If RotaTeq® is inadvertently exposed to temperatures below 0°C, limited data suggest that the potency of the vaccine is maintained.*

<sup>15</sup> Some vaccine manufacturers give the recommended temperature range for diluent storage in the package insert.

## 4. Choosing and using passive containers

The following general recommendations apply in all situations in which passive containers are used and ambient temperatures along the route do not generally exceed **+43°C**:

- All passive containers and water-packs should be WHO prequalified or have been laboratory tested to establish thermal performance in accordance with the relevant PQS verification protocol.<sup>16</sup>
- The correct number and size of water-packs must be used, exactly as specified by the container manufacturer; otherwise, cold life, cool life or warm life will be affected.
- Packed containers must be transported in a covered vehicle to avoid exposure to direct sunlight, which will reduce cold life or cool life.
- Avoid parking loaded vehicles in the sun and avoid parking outside for extended periods in cold climates.

If any of the recommendations in this section, including the following subsections, cannot be observed, follow the *transport route profiling* approach introduced in section 5.

### 4.1 Passive containers with frozen ice-packs

When frozen ice-packs are the correct choice, observe the following rules:

- Use containers with a published cold life **at least as long** as that required for the longest planned transport leg, measured from the time of packing the container in the supplying store to the time of unpacking in the receiving store. It is important to provide a good safety margin to cover unexpected events such as transport delays.
- If vaccines have VVMs, record VVM status of each vaccine batch upon dispatch and arrival.

### 4.2 Passive containers with conditioned ice-packs

When conditioned ice-packs are used, observe the following rules:

- Use passive containers with a published cold life **at least as long** as that required for the longest planned transport leg, measured from the time of packing the container in the supplying store to the time of unpacking in the receiving store. It is important to understand that some cold life is lost during the conditioning process, so make sure that a good safety margin is allowed to cover eventualities such as transport delays and variations in the extent to which conditioned ice-packs have melted at the time of packing.
- Confirm that the minimum ambient temperature during transport does not drop below +5°C. If ambient temperatures along the route are close to or below 0°C, there is a risk that freezing episodes will occur. Under these circumstances, it may be safer to use cool water-packs.

If freeze-sensitive vaccines are being transported, pack an

electronic freeze indicator with the vaccine load. When vaccine is being delivered to a lower-level store or health facility, check and record the freeze indicator status at the receiving facility. Report if the device has triggered an alarm. If an alarm is triggered, carry out a shake test on each type of freeze-sensitive vaccine in the load. If only a small number of vaccine vials are in this load, it may be impractical to implement the shake test.<sup>17</sup> In this case, the freeze-sensitive vaccines in the load should be quarantined and the shipment should be replaced.

- If vaccines have VVMs, ALWAYS check and record the VVM status of each vaccine batch upon dispatch and arrival.

During outreach operations, check the VVM and freeze indicator status at the point of arrival, before the session starts. If the freeze indicator shows an alarm, the health worker should NOT administer any freeze-sensitive vaccines and should contact a supervisor because the vaccines may have been damaged. In the interim, the affected vials must be clearly marked and separated from the others in the vaccine carrier by placing them in a plastic bag inside the vaccine carrier.

### 4.3 Passive containers with cool water-packs

In situations in which the use of cool water-packs is appropriate, observe the following rules:

- Use passive containers with a published cool life **at least as long** as that required for the longest planned transport leg, measured from the time of packing the container in the supplying store to the time of unpacking in the receiving store. It is important to allow a good safety margin to cover unexpected events such as transport delays and variations in cool water-pack temperature.
- Store passive containers in the coolest available place, such as an air-conditioned room, for 24 hours before they are loaded. This helps to extend cool life. Ideally, if a cold room is available, place the containers themselves in the cold room for a few hours before packing.
- Prepare cool water-packs as described in **Annex 4**. Set the thermostat of the dedicated cool water-pack refrigerator as low as possible to ensure that the water-packs are at a temperature of no more than +5°C at the time of packing.
- Record the VVM status of each vaccine batch before dispatch and upon arrival.

Countries may want to check that vaccines have not been exposed to temperatures above the cool water-pack test threshold of +20°C. A stem thermometer can be used for this purpose. It should be packed with the vaccine and read upon arrival. Provided the ambient temperature is generally higher than the load temperature throughout the journey, the temperature of the load will gradually rise and the arrival temperature will be the highest experienced during the trip. However, a stem thermometer will not give an accurate peak temperature reading if the ambient temperature drops significantly below

<sup>16</sup> WHO/PQS/E004/CB01.3 for cold boxes and WHO/PQS/E004/VC01.2 for vaccine carriers. In: Category documentation [website]. Geneva: World Health Organization; 2015 ([http://apps.who.int/immunization\\_standards/vaccine\\_quality/pqs\\_catalogue/catdocumentation.aspx?id\\_cat=18](http://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/catdocumentation.aspx?id_cat=18), accessed 30 March 2015).

<sup>17</sup> Details on the "Validation of the shake test for detecting freeze damage to adsorbed vaccines" are available at: <http://www.who.int/bulletin/volumes/88/8/08-056879/en/>

the load temperature toward the end of the journey, because the container will start to cool down again. This situation can occur if the journey starts in the heat of the day and finishes at night, or if the route rises from a hot lowland area to a cool highland zone.

#### 4.4 Passive containers with warm water-packs

Warm water-packs are used to protect freeze-sensitive vaccines in countries where temperatures are frequently below 0°C and heated vehicles are not available. Their use is essential on long journeys.

- Passive containers should have a rated warm life **at least as long** as that required for the longest planned transport leg, measured from the time of packing the container in the supplying store to the time of unpacking in the receiving store.<sup>18</sup> Once again, it is important to ensure a good safety margin to cover eventualities such as transport delays and variations in warm water-pack temperature at the time of packing.
- At the time of packing, warm water-packs should be at room temperature [between +18°C and a maximum of +24°C].
- Pack an electronic freeze indicator with the vaccine load.
- Record the freeze indicator status upon arrival. Report if the device has triggered an alarm. If an alarm has been triggered, carry out a shake test on each of the freeze-sensitive vaccines in the load. If only a small number of vaccine vials are in this load, it may be impractical to implement the shake test. In this case, the freeze-sensitive vaccines in the load should be quarantined and the shipment should be replaced.
- Record the VVM status of each vaccine batch before dispatch and upon arrival.

**Note:** If heat-sensitive vaccines have no VVMs, and warm water-packs are used repeatedly on multiple transport legs, there is no way to monitor the effect of cumulative heat exposure above +8°C. It is therefore safer to use cool water-packs. However, cool water-packs are likely to provide less than 50% of the published warm life of the container, so they can only provide protection during short journeys.

#### 4.5 Packing passive containers

Passive containers must be packed correctly and the packing arrangements should be planned in advance and ideally documented in an SOP that staff can access as they prepare vaccine shipments.<sup>19</sup> In addition to protecting vaccines from temperature excursions, correct packing arrangements are necessary to prevent vial breakage. Improper packing is the main cause of vial breakage. This is often due to the fact that vials or even secondary cartons are free inside the box. Empty space inside the container should be filled with bubble wrap or any other suitable materials to protect vials from banging around. Correct packing makes efficient use of the available storage volume, reduces the number of containers and **coolant-packs** required for a shipment and minimizes the likelihood that vaccine will be damaged during transport.

##### 4.5.1 Estimating usable storage capacity in cold boxes

Secondary vaccine cartons come in a wide range of sizes. When cold boxes are used to transport secondary cartons, there will always be some wasted space. For each cold box model, the percentage of the published vaccine storage capacity that can actually be used – the utilization percentage – will vary between vaccine products. This variability should be taken into account as part of the transport planning process.

User-friendly software tools<sup>20</sup> are now available that automatically optimize packing arrangements if the dimensions of the container and the dimensions of the secondary cartons are known. These tools produce a three-dimensional diagram of the packing layout, which can be printed and used in an SOP or work instruction. If the packing layout and the percentage utilization is known in advance, it is much easier to estimate the number of cold boxes and **coolant-packs** required for a given shipment.

Figure 4 shows an example of a utilization percentage calculation for a specific vaccine packed in a specific cold box.

<sup>18</sup> For the current range of prequalified products, this gives allowable journey times from 11 to 35 hours for cold boxes and from 3 to 13 hours for vaccine carriers – see Annex 2.

<sup>19</sup> Packing vaccine and diluents for transport, using cold boxes (EVM-SOP-E7-02), and Packing vaccine and diluents in vaccine carriers (EVM-SOP-E7-03). In: Effective Vaccine Management (EVM) Initiative Model Standard Operating Procedures. Geneva: World Health Organization, 2011 ([http://www.who.int/immunization/programmes\\_systems/supply\\_chain/eum/en/index2.html](http://www.who.int/immunization/programmes_systems/supply_chain/eum/en/index2.html), accessed 30 March 2015).

<sup>20</sup> Calculation carried out using PLMPack StackBuilder. This freeware programme is available at: <http://stackbuilder.codeplex.com/>. Other, similar tools are available; for example, see:

<http://www.capesystems.com/index.html>

<http://www.topseng.com/index.html>

<http://www.koona.com/qpm/>

<http://www.magiclogic.com/>

<http://www.logensolutions.com/default.html>

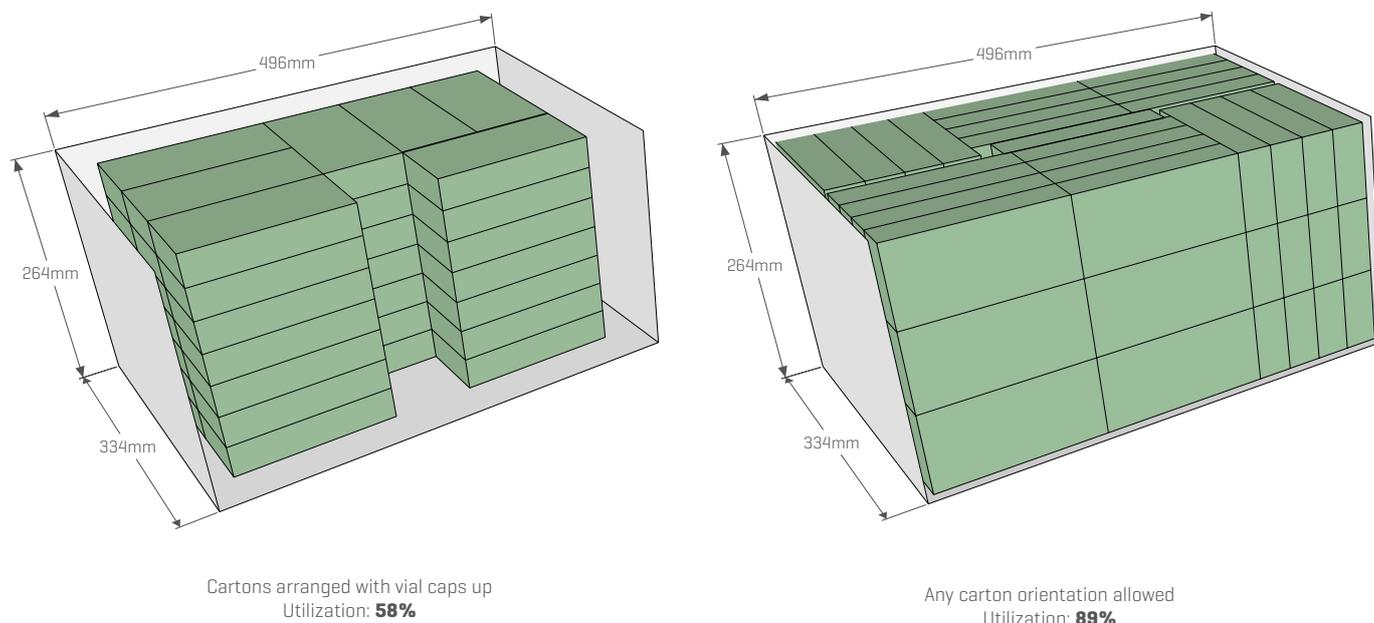
<http://www.iris-it.com/en/products/robotics/palletization-software.html>

<http://www.cubemaster.net/Subscription/home.asp>

Internal dimensions of WHO-prequalified cold boxes and vaccine carriers are published in the PQS catalogue. Carton dimensions for individual vaccines can be obtained from the United Nations Children's Fund Supply Division (by direct enquiry), from the WHO vaccine database (some vaccines), from the vaccine manufacturer, or by physical measurement.

Figure 4. Example of a utilization percentage calculation

### Cartons of pentavalent vaccine packed in a prequalified cold box



The dimensions shown in the two diagrams are for the vaccine storage compartment, measured inside the **coolant-pack** lining. The left-hand image shows an arrangement with 49 cartons stacked vial cap upward, giving a utilization of 58%. The arrangement on the right-hand side shows cartons oriented in the most space-efficient way; this allows 75 cartons to be packed in the same volume and a utilization of 89%. Organizing boxes of unopened vials in any orientation is a perfectly acceptable practice during transport operations because long-term vaccine stability studies are conducted with vials inverted.

#### 4.5.2 Estimating usable storage capacity in vaccine carriers

It is more difficult to estimate vaccine carrier capacity because vaccines are generally transported as primary containers and these come in a wide variety of shapes and sizes. Estimation is best carried out on an empirical basis.

#### 4.5.3 Ensuring correct **coolant-pack** temperatures

**Coolant-packs** must be prepared correctly. If conditioned ice-packs are not properly conditioned, freeze-sensitive vaccines will be exposed to sub-zero temperatures and may be damaged. If **coolant-packs** are not adequately cooled, the cool life of the container will be reduced and vaccines may be exposed to excessive heat. Refer to **Annex 3** and **Annex 4**.

#### 4.5.4 Loading **coolant-packs** correctly

The correct size and number of **coolant-packs** must be used; for prequalified products, this information is shown on the inside of the container lid. Uncontrolled use of different-sized water-packs is strongly discouraged because consistent thermal performance cannot be achieved under these circumstances.

**Coolant-packs** must be arranged exactly as shown in the manufacturer's instructions. If this is not done, the vaccine may be exposed to the unprotected inner surface of the container. Compliance failures of this type can also occur if a section of the **coolant-pack** lining is removed in order to fit extra vaccine cartons. This is another reason why packing arrangements should be designed in advance.

## 5. Developing a vaccine transport strategy

This section describes some basic rules for developing a passive container transport strategy. These rules are designed to cover both in-country vaccine transport and outreach operations. Regardless of the mode of transport, there should be sufficient written evidence to demonstrate that vaccines have not been exposed to conditions that may compromise their quality and integrity.<sup>21</sup>

WHO strongly recommends that a country's transport strategy be validated by carrying out systematic *transport route profiling exercises*; these exercises should cover a representative sample of the transport routes in the country. Optimum use of equipment and the ensuring of vaccine safety can only be achieved if transport route validation has been carried out. See the technical supplement: *Transport route profiling qualification*.<sup>21</sup>

The strategy must be designed to suit local conditions. The following tasks need to be completed and documented:

- Determine the heat and freeze sensitivity of every vaccine being transported (see **Annex 1**).
- Identify the existing risks to which vaccines are currently exposed during transport. An important step in this process is to carry out a temperature monitoring study based on the WHO study protocol.<sup>22</sup> The results of the study may reveal weaknesses in existing cold chain equipment performance and operational practices and procedures.
- Determine transport durations and distances, geographical and natural hazards and other risks along all intended routes.
- Determine day-night and seasonal temperature extremes along each route.<sup>23</sup>
- Agree on the transport modes<sup>24</sup> and vehicle types that are to be used on each route.
- Define a policy for labelling passive containers (e.g. content, storage and transport conditions, and destination).
- Record the published storage capacities of the passive containers currently used, and their laboratory-tested performance (cold life, cool life and, if relevant, warm life).
- Establish whether current passive containers are fit for purpose and define a policy for future procurement and/or replacement of this equipment.
- Evaluate the risks and benefits associated with the four different types of water-packs (frozen, conditioned, cool and warm) in the local context.

- For each route, establish the following for all transport operations, both routine and supplementary:
  - supply period;
  - maximum transport volume;
  - the number of passive containers required, taking into account the expected utilization factor for the containers used [see section 4.5.1];
  - the quantity of **coolant-packs** needed; and
  - the freezing or cooling capacity required to meet these needs.
- Define procedures for investigating and handling temperature excursions, training, record-keeping and supervision.

If the vaccine transport strategy design is to be successful, it is important to take into account local challenges and opportunities and to consult those responsible for transport operations at all levels. In situations in which all or part of the transport operation is outsourced, this will include the third-party supplier. Once the strategy has been finalized, key staff must be fully informed so that they know how to implement it correctly.

Finally, before the vaccine transport strategy is rolled out, it is essential that SOPs are in place that cover all key aspects of transport management, including passive container use, **coolant-pack** preparation and use, transport contingencies and maintenance of vehicles and equipment. All responsible staff should receive regular training based on these SOPs.

Below is a list of relevant model SOPs. These can be found on the WHO Effective Vaccine Management (EVM) Initiative website.<sup>25</sup> Word versions can be downloaded in English or French and adapted to suit country needs:

- VMH-E7-02.2: How to monitor and control storage temperatures in the vaccine supply chain
- EVM-SOP-E7-01: Monitoring temperature exposure during vaccine transport
- EVM-SOP-E7-02: Packing vaccine and diluents for transport, using cold boxes
- EVM-SOP-E7-03: Packing vaccine and diluents in vaccine carriers
- EVM-SOP-E7-04: Conditioning frozen icepacks
- EVM-SOP-E7-06: Responding to emergencies during vaccine transport operations
- EVM-SOP-E8-02: Using Vaccine Vial Monitors.

<sup>21</sup> Available at: [http://www.who.int/medicines/areas/quality\\_safety/quality\\_assurance/en/](http://www.who.int/medicines/areas/quality_safety/quality_assurance/en/), accessed 31 March 2015).

<sup>22</sup> Study protocol for temperature monitoring in the vaccine cold chain. Geneva: World Health Organization; 2011 ([http://whqlibdoc.who.int/hq/2011/WHO\\_IVB\\_05.01\\_Rev1\\_eng.pdf](http://whqlibdoc.who.int/hq/2011/WHO_IVB_05.01_Rev1_eng.pdf), accessed 30 March 2015).

<sup>23</sup> Comprehensive seasonal climate data are available at [www.weatherbase.com](http://www.weatherbase.com) and [www.wolframalpha.com](http://www.wolframalpha.com). Local meteorological data may also be available.

<sup>24</sup> If air transport is used, it is important to establish the hold temperature. In smaller aircraft with unheated holds, this will be far below the ambient temperatures at ground level and this may place freeze-sensitive vaccines at risk.

<sup>25</sup> Effective Vaccine Management (EVM) Initiative Model Standard Operating Procedures. Geneva: World Health Organization; 2011. ([http://www.who.int/immunization/programmes\\_systems/supply\\_chain/eum/en/index2.html](http://www.who.int/immunization/programmes_systems/supply_chain/eum/en/index2.html), accessed 30 March 2015).

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- WHO effective vaccine management standard operating procedures (SOPs) can be downloaded from the WHO Effective Vaccine Management (EVM) Initiative website [[http://www.who.int/immunization/programmes\\_systems/supply\\_chain/evm/en/index2.html](http://www.who.int/immunization/programmes_systems/supply_chain/evm/en/index2.html), accessed 31 March 2015]. Model SOPs relevant to this module are:
  - VMH-E7-02.2: How to monitor and control storage temperatures in the vaccine supply chain
  - EVM-SOP-E7-01: Monitoring temperature exposure during vaccine transport
  - EVM-SOP-E7-02: Packing vaccine and diluents for transport, using cold boxes
  - EVM-SOP-E7-03: Packing vaccine and diluents in vaccine carriers
  - EVM-SOP-E7-04: Conditioning frozen icepacks
  - EVM-SOP-E7-06: Responding to emergencies during vaccine transport operations
  - EVM-SOP-E8-02: Using Vaccine Vial Monitors.
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  - Calibration of temperature control and monitoring devices
  - Qualification of temperature-controlled storage areas
  - Temperature mapping of storage areas
  - Temperature monitoring of storage areas
  - Temperature-controlled transport operations
  - Temperature and humidity monitoring systems for transport operations
  - Transport route profiling qualification
  - Qualification of temperature-controlled road vehicles

# Annex 1. Temperature sensitivity of vaccines

The World Health Organization hosts a database of prequalified vaccines, and the package inserts for these products can be viewed online in order to check recommended storage conditions and the type of vaccine vial monitor used for each product.<sup>26</sup>

## A1.1 Freezing

Vaccines that are damaged by freezing should never be exposed to temperatures below 0°C. Table A1.1 shows which vaccines are damaged by freezing and which are not. Freeze-dried vaccines are shown in **bold** type. Within each of the groups, the vaccines are arranged in alphabetical order, NOT in order of sensitivity to freezing. However, all the vaccines in the top group are more freeze sensitive than those in the second group.

**Table A1.1. Freeze sensitivity of current vaccines**

All these vaccines are damaged by freezing	<b>Vaccine</b> DTaP DTaP-hepatitis B-Hib-IPV (hexavalent) DTwP DTwP-hepatitis B-Hib (pentavalent) Hepatitis A Hepatitis B Human papillomavirus Meningitis C [polysaccharide-protein conjugate] Pneumococcal [polysaccharide-protein conjugate] TT, DT, Td
	Cholera [inactivated] Influenza [inactivated, split] Hib [liquid] Inactivated poliovirus Typhoid polysaccharide
These vaccines are not damaged by freezing	<b>Meningitis A (polysaccharide-protein conjugate)*</b> Rotavirus [liquid and freeze dried] Yellow fever
	<b>Bacillus Calmette-Guérin</b> <b>Hib (freeze dried)</b> <b>Japanese encephalitis (live and inactivated)</b> <b>Measles</b> <b>Measles, mumps, rubella</b> Oral poliovirus <b>Rabies</b> <b>Rubella</b> <b>Varicella-zoster virus</b>

DT = diphtheria and tetanus toxoid vaccine; DTaP = diphtheria, tetanus, and [acellular] pertussis vaccine; DTwP = diphtheria and tetanus toxoid (whole cell) and pertussis vaccine; Hib = *Haemophilus influenzae* type b vaccine; IPV = inactivated poliovirus vaccine; Td = children's dose of diphtheria and tetanus toxoid; TT = tetanus toxoid.

**Note:** Freeze-dried vaccines are shown in bold.

\* The diluent for meningitis A vaccine is damaged by freezing.

Diluents should NEVER be frozen. This applies equally to pharmacologically active diluents and to those that contain water for injection or inorganic salt solutions.

## A1.2 Heat damage

The labelled recommendation for vaccine transport is generally +2°C to +8°C. However, most vaccines can tolerate brief temperature excursions up to +37°C.<sup>27</sup> In Table A1.2, freeze-dried vaccines are shown in **bold** type. The right-hand column shows the relative heat sensitivity of each of six groups of vaccine, divided by horizontal lines. Within each of these groups, the vaccines are arranged in alphabetical order, NOT in order of sensitivity to heat. However, all the vaccines in each group are more heat sensitive than those in the group immediately below in the table.

**Table A1.2. Relative heat sensitivity of current vaccines**

Heat sensitivity Most-sensitive group  Least-sensitive group	<b>Vaccine</b> Oral poliovirus <b>Varicella-zoster virus</b>
	Influenza [inactivated, split]
	Inactivated poliovirus <b>Japanese encephalitis (live)</b> <b>Measles, mumps, rubella</b>
	Cholera [inactivated] DTaP DTwP DTaP-hepatitis B-Hib-IPV (hexavalent) DTwP-hepatitis B-Hib (pentavalent) Hib [liquid] <b>Measles</b> Rotavirus [liquid and <b>freeze dried</b> ] <b>Rubella</b> <b>Yellow fever</b>
	<b>Bacillus Calmette-Guérin</b> Human papillomavirus <b>Japanese encephalitis (inactivated)</b> TT, DT, Td
	Hepatitis A Hepatitis B <b>Hib (freeze dried)</b> <b>Meningitis A (polysaccharide-protein conjugate)</b> Meningitis C [polysaccharide-protein conjugate] Pneumococcal [polysaccharide-protein conjugate] <b>Rabies</b> Typhoid polysaccharide

DT = diphtheria and tetanus toxoid vaccine; DTaP = diphtheria, tetanus, and [acellular] pertussis vaccine; DTwP = diphtheria and tetanus toxoid (whole cell) and pertussis vaccine; Hib = *Haemophilus influenzae* type b vaccine; IPV = inactivated poliovirus vaccine; Td = children's dose of diphtheria and tetanus toxoid; TT = tetanus.

**Note:** Freeze-dried vaccines are shown in bold.

<sup>26</sup> WHO prequalified vaccines [online database]. Geneva: World Health Organization; 2014 ([http://www.who.int/immunization\\_standards/vaccine\\_quality/PQ\\_vaccine\\_list\\_en/en/index.html](http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html), accessed 31 March 2015).

<sup>27</sup> The MenAfriVac™ meningitis A vaccine can be exposed to temperatures up to +40°C during campaign operations using a controlled temperature chain. See: Use of MenAfriVac™ (meningitis A vaccine) in a controlled temperature chain (CTC) during campaigns. In: WHO Immunization, Vaccines and Biologicals [website] ([http://www.who.int/immunization/documents/WHO\\_IVB\\_13.04\\_5\\_6/en/](http://www.who.int/immunization/documents/WHO_IVB_13.04_5_6/en/), accessed 31 March 2015).

## Annex 2. Cold box and vaccine carrier performance

Table A2.1 shows the performance range of World Health Organization-prequalified cold boxes and vaccine carriers in the July 2014 catalogue.<sup>28</sup> The table clearly shows that the cool life and warm life figures are substantially shorter than the cold life.

**Note:** Cold life with conditioned ice-packs is NOT currently measured under the performance, quality and safety (PQS) test procedure. Cold life in Table A2.1 is measured with frozen ice-packs at -20°C.

<sup>28</sup> Performance of the latest products can be checked by consulting the E004 section on the PQS website. See: World Health Organization PQS Catalogue – Prequalified Devices and Equipment [online database]. Geneva, World Health Organization; 2015 ([http://apps.who.int/immunization\\_standards/vaccine\\_quality/pqs\\_catalogue/categorylist.aspx?cat\\_type=device](http://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/categorylist.aspx?cat_type=device), accessed 31 March 2015).

**Table A2.1. Performance of prequalified passive containers**

Product type		Cold life [hours]	Cool life [hours]	Warm life [hours]
Minimum PQS standard for cold boxes	Long range	96.0	No standard set	No standard set
	Short range	48.0	No standard set	No standard set
Large cold box [≥15 litres]	MAX	156.0	51.3	53.1
	MIN	53.6	18.7	16.4
Small cold box [<15 litres]	MAX	132.3	30.0	48.7
	MIN	57.9	12.0	21.6
Minimum PQS standard for vaccine carriers	Long range	30.0	No standard set	No standard set
	Short range	15.0	No standard set	No standard set
Large vaccine carrier [≥1 litre]	MAX	50.2	18.0	19.0
	MIN	30.3	6.0	7.0
Small vaccine carrier [<1 litre]	MAX	21.5	4.5	8.0
	MIN	17.8	3.0	4.4

**Note:** The maximum and minimum figures for each category do not necessarily apply to any individual product.

## Annex 3. Conditioning ice-packs

Safe and effective use of conditioned icepacks is critically dependent on compliance with the conditioning practice described below, and workers must be properly trained to carry out the procedure. Poor compliance is frequently observed in the field and is a major cause of vaccine freezing.

- a. Determine how many packs are required for the vaccine consignment. The underside of the lid of each prequalified cold box or vaccine carrier has a diagram showing the number and type of pack required for that type of box or carrier.
- b. Lay the required number of frozen ice-packs on a designated table or work surface in a single layer, leaving gaps of about 5 cm between packs.
- c. Wait until ALL packs are properly conditioned – there must be liquid water inside every pack and the ice cores should be able to move freely inside the packs when shaken. This will take at least 30 to 45 minutes in hot weather and will take much longer in cool conditions – from 90 to 120 minutes at +20°C.
- d. Arrange the conditioned ice-packs in the cold boxes and/or vaccine carriers according to the manufacturer's instructions.

- e. Pack the vaccine.

For more details, refer to EVM-SOP-E7-04: Conditioning frozen icepacks, and EVM-SOP-E7-02: Packing vaccine and diluents for transport, using cold boxes.

**Note:** It is safer to over-condition ice-packs than it is to under-condition them. If the rules set out in section 4.2 governing the ratio between container cold life and journey time are followed, there will still be a good safety margin, even if the ice core is partly melted.

## Annex 4. Preparing cool water-packs

Cool water-packs should be prepared in a dedicated refrigerator or in a cold room that is set between +2°C and +8°C. If the refrigerator has an adjustable thermostat, the water-packs should be cooled to a temperature of between 0°C and +5°C, to achieve optimum cool life. In order to minimize the cooling time needed, unused water-packs should be stored in a cool place and in the shade.

### **A4.1 Using a refrigerator to prepare cool water-packs**

- a. Use a dedicated refrigerator for water-pack cooling. NEVER place cool water-packs in a refrigerator that contains vaccine. Introducing a large volume of warm water risks exposing the vaccine to temperatures above +8°C. Note that compression-cycle refrigerators are preferred to absorption-cycle refrigerators for cooling water-packs because they are much more efficient.
- b. If the refrigerator has an adjustable thermostat, set it as low as possible because cool life will be improved if the temperature of the water-pack is below +5°C. Place a thermometer or 30-day temperature recorder in the refrigerator. Check the refrigerator temperature before loading the water-packs.
- c. Determine how many packs are needed for the vaccine consignment. The underside of the lid of each prequalified cold box or vaccine carrier has a diagram showing the number and type required for that type of box or carrier.
- d. Leave the water-packs to cool in the refrigerator for a minimum of 12 hours. If there are regular power cuts, or there is a large load of water-packs, a longer period may be required. Check the temperature of the refrigerator before removing the packs; if the temperature is above +8°C the water-packs are not cold enough.

### **A4.2 Using a cold room to prepare cool water-packs**

- a. Unless very large quantities of water-packs are being prepared, it is generally safe to cool water-packs in a cold room that contains vaccine.
- b. Do not place the water-packs on shelves with vaccine. It is preferable to place them in boxes on the floor in the middle of the room. Storing them near floor level ensures that they are in the coolest part of the room. Place a thermometer or 30-day temperature recorder in the area where the packs are placed.
- c. Determine how many packs are needed for the vaccine consignment. The underside of the lid of each prequalified cold box or vaccine carrier has a diagram showing the number and type required for that type of box or carrier.
- d. In order to minimize the risk of temperature excursions, monitor the temperature of the room using the room's continuous temperature monitoring equipment. Establish the maximum quantity of water-packs that can safely be introduced without exposing the vaccine to temperatures above +8°C.
- e. Leave the water-packs to cool in the cold room for a minimum of 12 hours. Most cold rooms are connected to a standby generator, so power cuts should not generally affect the preparation time. Check the thermometer or 30-day temperature recorder before removing the packs; if the temperature is above +8°C, the water-packs are not cold enough.

For more details, refer to EVM-SQP-E7-02: Packing vaccine and diluents for transport, using cold boxes.



