Freeze-preventive vaccine carrier

Frequently asked questions

WHY IS FREEZING AN ISSUE?

All vaccines lose potency over time, and the rate of loss is temperature dependent,[1] which is why a cold chain is necessary for vaccine storage and transport. For some vaccines, freezing temperatures are even more damaging than heat. Especially vulnerable are liquid vaccines that contain aluminum salt adjuvants, which increase the freeze sensitivity of the vaccine. Many of the newer Expanded Programme on Immunization (EPI) vaccines being introduced into low-resource settings are freeze sensitive and much more expensive than traditional vaccines. A handful of other vaccines are also freeze sensitive, including inactivated poliovirus vaccine and some inactivated influenza vaccines.[2] For these types of vaccines, freezing can irreversibly compromise vaccine potency,[3] and when a vaccine loses potency, it is less likely to protect against disease. Vaccines with reduced potency can leave a vaccinated child unprotected and jeopardize the reputation of the vaccination program.

Studies of cold chain performance have shown that exposure of vaccines to freezing temperatures occurs frequently in developing and developed countries.[4,5] In some countries, up to 100 percent of vaccine shipments were exposed to freezing temperatures at least once during distribution.[4] Very low ambient temperatures can also result in the freezing of vaccines during transport.

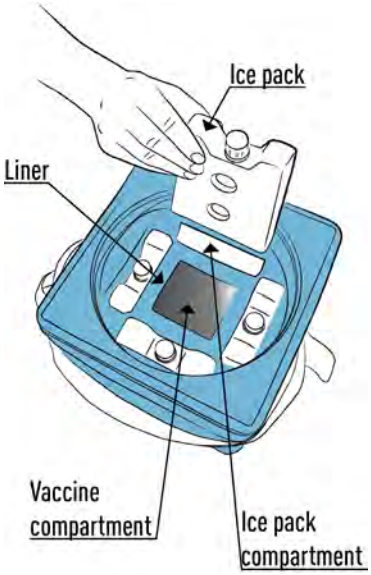
HOW CAN VACCINE FREEZING BE PREVENTED?

Preventing freezing in the vaccine supply chain requires a comprehensive approach. Each country has a different set of needs, and each solution has its advantages. A few common approaches include better monitoring of the cold chain for freezing temperatures, developing thermostable vaccine formulations, and providing health worker training.

One new approach is investing in freeze-preventive equipment. Freeze-preventive vaccine carriers have shown promising results in laboratory settings and meet World Health Organization (WHO) requirements for Grade A user-independent freeze prevention.* The Grade A designation is given to technologies that mitigate the risk that freezing will occur from user noncompliance by requiring no extra actions by the user to prevent freezing temperatures in the equipment.

HOW DO FREEZE-PREVENTIVE VACCINE CARRIERS ADDRESS FREEZING?

Several promising freeze-preventive vaccine carrier designs contain a liner that acts as a buffer, physically and thermally separating the vaccine storage compartment's contents from the ice packs on all sides.

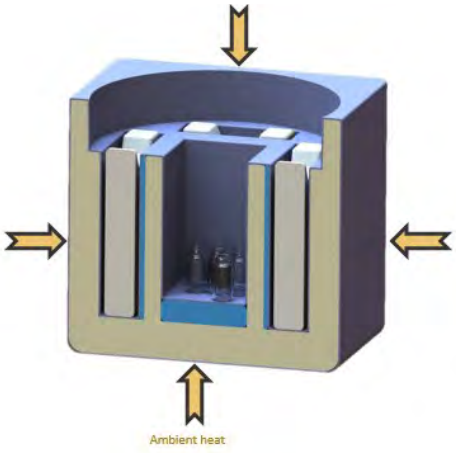


When the ice packs gradually warm from -25°C to 0°C, heat is drawn from ambient surroundings and from the liner.

A thin layer of water inside the liner functions as a phase-change material. As the water layer cools, it maintains a temperature inside the vaccine compartment of greater than 0°C as the water changes to ice. A layer of foam insulation provides additional protection against freezing.

For a comprehensive understanding of how traditional carriers differ from freeze-preventive carriers, the E004 section on WHO's Performance, Quality and Safety (PQS) website contains detailed specifications for both traditional vaccine carriers and freeze-preventive vaccine carriers.

* **Grade A.** Requires no user intervention. **Grade B.** Requires one user intervention. **Grade C.** Requires more than one user intervention. For example, a vaccine compartment that the user needs to place in the carrier to prevent freezing is a user intervention.



WHAT ARE THE BENEFITS OF A FREEZE-PREVENTIVE CARRIER?

Freeze-preventive carriers:

- **Protect vaccines from freezing.** Health workers often find it difficult to tell whether vaccine has been exposed to freezing temperatures, which can result in vaccines with reduced potency being delivered.[6,7] After placement in the carrier's vaccine compartment, freeze-sensitive vaccines are no longer at risk of freezing even when frozen ice packs are used, helping to protect the vaccine's potency.
- **Simplify preparation and reduce health worker burden.** Freeze-preventive vaccine carriers allow the use of fully frozen ice packs, eliminating the time-consuming step of conditioning the ice packs. The use of conditioned ice packs (in which the ice is "slushy" and the ice cores are able to move freely inside the packs when shaken) has long been recommended by WHO to avoid freezing vaccines. However, the entire process of conditioning ice packs can take 30 to 60 minutes and has proven difficult to implement. Cold chain surveys have shown that this practice is frequently not enforced. During immunization training sessions, explaining how to properly condition ice packs takes time. Freeze-preventive carriers simplify the process, as conditioning of ice packs is unnecessary.

WHAT IS THE TEMPERATURE RANGE MAINTAINED BY FREEZE-PREVENTIVE VACCINE CARRIERS

According to WHO PQS specifications, vaccine carriers, like all other passively cooled vaccine storage devices, must maintain temperatures exceeding 0°C up to less than 10°C. To achieve this, traditional carriers require ice packs to be conditioned to bring temperatures to within that range. Freeze-preventive carriers stay within the required range without the need to condition ice packs.

HOW IS PATH INVOLVED WITH THIS TECHNOLOGY?

PATH has a long history of inventing, adapting, testing, and validating emerging concepts to improve global health and advancing promising designs to ensure product effectiveness and impact. For freeze-preventive carriers, we:

- **Raised global awareness.** Drafted the original WHO protocol for temperature monitoring of vaccine cold chains to assess risks, and raised global awareness of vaccine freeze-exposure issues.
- **Advanced the product category.** Developed a freeze-preventive vaccine carrier prototype and ensured the concept was open access and available to all carrier manufacturers.
- **Conduct objective and independent evaluations.** To maximize health impact and maintain objectivity, our mission is to advance the product category of "freeze-preventive carriers," not individual products. Using our in-house laboratory facilities and country expertise, we provide manufacturers and developers with thorough, unbiased evaluations of new freeze-preventive design concepts and feedback for improvement.
- **Provide commercialization expertise.** Using our analytic skills, we provide tools and support for countries to make informed decisions on equipment selection. Simultaneously, we support suppliers with market intelligence and demand estimates.

WHAT TESTS HAVE BEEN DONE TO VALIDATE FREEZE-PREVENTIVE CARRIERS?

Several carriers are being tested and validated in the PATH laboratory, following standard WHO PQS test protocols. Manufacturers will be required to pass independent laboratory verification by a WHO-certified laboratory before they will be prequalified. Independent field evaluations will also need to be conducted before the products are fully prequalified and listed in the WHO PQS catalog. Many studies have already proven the negative effects of freezing on vaccine potency;[3] therefore, vaccine potency studies will not be conducted as part of this testing.

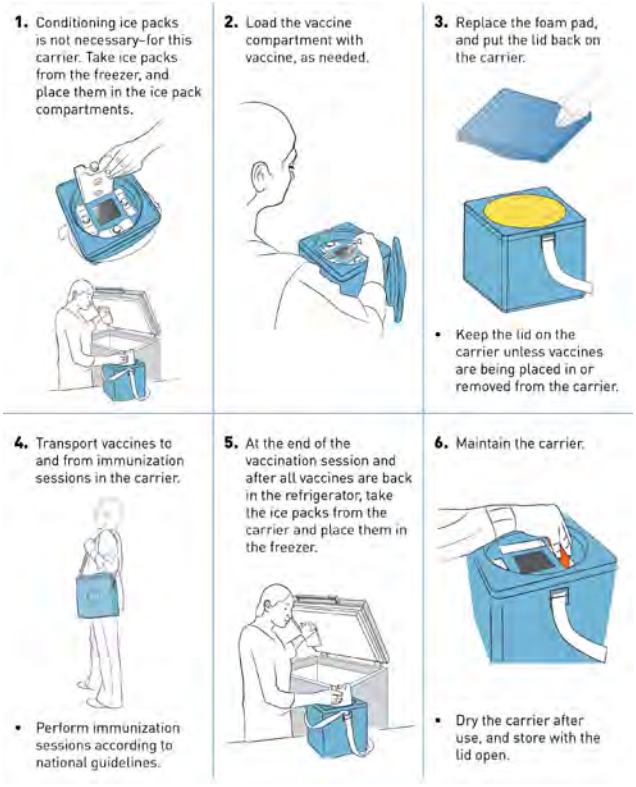
SHOULD ICE PACKS BE CONDITIONED FOR FREEZE-PREVENTIVE CARRIERS?

Health care workers should still condition ice packs when using traditional carriers, but this step is not needed when using freeze-preventive carriers. When tested in PATH's laboratory, conditioned ice packs in freeze preventive carriers had only slightly decreased holdover. The effects on holdover were minimal and unlikely to cause additional vaccine wastage. However, for maximum holdover, we recommend using frozen ice packs.

It is recommended that decision-makers introduce freeze-preventive equipment in a stepwise fashion, replacing all carriers in a particular region at once so that health care workers do not have a mix of traditional and freeze-preventive carriers. National guidelines should be followed when introducing freeze-preventive vaccine carriers.

HOW IS THIS NEW CARRIER USED?

To use the freeze-preventive vaccine carrier:



CAN TRADITIONAL VACCINE CARRIERS STILL BE USED ONCE FREEZE-PREVENTIVE CARRIERS HAVE BEEN INTRODUCED?

Ideally, countries will introduce freeze-preventive vaccine carriers nationwide to avoid any confusion regarding the need to condition ice packs. However, if this is not feasible, these new carriers should be introduced throughout one region where all standard carriers can be replaced with freeze-preventive carriers, to ensure consistent practice.

IS THE PROCESS FOR CLEANING AND MAINTAINING CARRIERS THE SAME?

The procedure for cleaning freeze-preventive vaccine carriers remains unchanged. However, freeze-preventive carriers have separate compartments (ice pack compartments and vaccine compartment) that need to be cleaned and dried at the end of each immunization session.

ARE FREEZE-PREVENTIVE CARRIERS HEAVIER OR LARGER?

Freeze-preventive vaccine carriers are slightly larger and heavier than traditional carriers, while still meeting the WHO PQS specification of weighing less than 8 kg, fully loaded. The additional weight and size accommodates the freeze-preventive liner while still allowing for a minimum 1.5 liter vaccine storage capacity.

DO FREEZE-PREVENTIVE CARRIERS HOLD AS MANY VACCINES AS A TRADITIONAL VACCINE CARRIER?

The vaccine storage compartment of current freeze-preventive carriers can hold 1.5 liters of vaccines, sufficient for most outreach needs. Anecdotal evidence suggests that vaccine carriers are most often used for immunization outreach sessions that last up to ten hours and require transportation of ten or more individual vials. Field testing feedback on capacity will help inform sizing of future freeze-preventive vaccine carriers.

WHY SHOULD A COUNTRY SWITCH FROM A TRADITIONAL CARRIER TO A FREEZE-PREVENTIVE CARRIER?

By protecting the quality of all vaccines, but particularly the more expensive, freeze-sensitive ones, these new carriers are expected to result in cost savings to health systems that will outweigh the somewhat higher purchase costs. According to a PATH analysis,** six standard EPI vaccines (pentavalent, rotavirus, inactivated poliovirus, pneumococcal conjugate, bacillus Calmette-Guérin, and measles-rubella) for ten children have a value of approximately $95, 91% ($86) of which are freeze sensitive. This example highlights the considerable investment each vaccine carrier load represents, in actual dollar value.

By eliminating the need to condition ice packs, time will be freed up for already burdened health workers. Protecting vaccine quality and safety also protects the reputation of immunization programs.

** Calculations were made using 2016 pricing from Gavi, the Vaccine Alliance.

WHAT ARE THE NEXT STEPS FOR THIS TECHNOLOGY?

Freeze-preventive carriers are now commercially available and have passed WHO PQS testing. Field trials began in February 2018 to ensure freeze-preventive carriers perform as expected.

WHAT IS THE UNIT COST OF A FREEZE-PREVENTIVE CARRIER?

Costs may be influenced by a variety of market factors. Please check the manufacturer's website or the United Nations Children's Fund (UNICEF) Supply Division catalog for pricing.

HOW DO I PURCHASE A FREEZE-PREVENTIVE CARRIER?

Freeze-preventive carriers may be ordered directly from the manufacturers or via the UNICEF Supply Division.

The WHO PQS catalog lists prequalified freeze-preventive vaccine carriers and includes the link for each manufacturer: apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/categorypage.aspx?id_cat=18.

WHERE DO I FIND MORE INFORMATION?

For more information on freeze-preventive vaccine carriers, please visit WHO's PQS catalog: apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/index.aspx.

REFERENCES

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3 PATH. *Effects of Freezing on Vaccine Potency: Literature Review*. Seattle: PATH; 2003. Available at: www.path.org/publications/files/TS_cc_effects.pdf.

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STREET ADDRESS
2201 Westlake Avenue
Suite 200
Seattle, WA 98121 USA

MAILING ADDRESS
PO Box 900922
Seattle, WA 98109 USA

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