COLD CHAIN SOLUTIONS FOR VACCINE TRANSPORT:
SELECTING THE RIGHT SOLUTION TO ADDRESS FREEZING IN TRANSPORT

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CLINTON HEALTH ACCESS INITIATIVE

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Objectives and Audience

Objectives:

1) Understand why vaccines freeze during transport and how it can be addressed
2) Enable countries to select the most appropriate freeze-preventive vaccine transport solution(s)

Audience:

- Expanded Programme on Immunization (EPI) decision-makers
- Personnel involved with:
  - ❑ Country immunization strategy development
  - ❑ Cold chain equipment selection, procurement and deployment
  - ❑ Development partners organizations supporting immunization supply chain programs

Note: This document focuses on transport of freeze-sensitive routine immunization vaccines, and does not aim to address transport of non-freeze-sensitive vaccines (such as some of the new COVID-19 vaccines)

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Executive Summary: Overview

Problem Statement

Vaccine transport systems using fully-frozen ice packs without freeze-preventative devices are demonstrated to expose ~20% of vaccines to freezing[1].

- Exposure to freezing temperatures during transport can cause vaccines to be less effective.
- Such exposure is often due to non-compliance in pre-conditioning frozen ice packs prior to packing cold boxes and vaccine carriers.

Solution Evaluation

To address freezing, this document proposes EPI implement one of two solutions per system[2]:

- Freeze-preventative carriers and cold boxes + fully-frozen ice packs
- Conventional carriers and cold boxes + cool water packs

Plan and Implement

Once a solution is chosen, refer to CHAI_Freeze-Preventative Passive CCE Implementation Guide.pptx" for guidance in:

1) Planning for implementation
2) Executing implementation

1) Hanson et al. Is freezing in the vaccine cold chain an ongoing issue? A literature review. *Vaccine*. 2017 Apr 19.
2) "System" is defined as an operational zone within which one of the recommended solutions can be fully executed, i.e., mixing solutions is not desired

Executive Summary: Problem Statement

Exposure to low (below 0°C) and/or high (above 10°C) temperatures impacts vaccine potency and safety.

- Some vaccines are damaged by freezing; others are particularly vulnerable to heat exposure (see Slide 9).
- Freezing causes more immediate damage to freeze-sensitive vaccines.

A system utilizing frozen ice packs without freeze-preventative devices is likely to expose ~20% of vaccines to sub-zero (C^{o}) temperatures during transport.[1]

- Nearly all vaccines are transported using cold boxes (CB)and vaccine carriers (VC) at some point in the cold chain.
- ~20% of vaccines in CB/VC may be at risk of exposure to inadvertent freezing during transport.
- In freezers, ice packs can be frozen to as low as -25^{o}C.

At present, careful handling is needed at all levels of the cold chain to ensure vaccines remain safe and potent.

- These ice packs must be pre-conditioned to 0^{o}C or above before use to avoid freezing risks.
- For multiple and complex reasons, pre-conditioning is not always done properly.

Up to ~$31M worth of vaccines could be damaged if freezing risks are not addressed.

- If frozen vaccines are inadvertently used to vaccinate children, their low potency risks outbreaks of vaccine preventable diseases.

1. Hanson et al. Is freezing in the vaccine cold chain an ongoing issue? A literature review. *Vaccine*. 2017 Apr 19.

Executive Summary: Solutions

Document guides system design with three key principles:

1. Eliminate pre-conditioning of ice packs
   This makes safe handling simple, saves time and effort for HCWs, and drives a key source of variability out of cold chain
2. Eliminate the potential of freezing without requiring user intervention
   If ice packs are fully frozen, they should be combined with freeze-preventative technology; conversely, non-freeze-preventative carriers should only be used with cool water packs
3. Systems ***should not*** rely on using vaccine heat margin and having HCWs monitor VVMs
   Cool water packs are only advisable when ambient conditions and use case reduce hold time requirements

At present, two systems align with these principles:

1. Freeze-Preventative (FP) carriers + fully frozen ice packs
   This system uses thermal barrier technology to prevent freezing while maximizing hold times
2. Conventional carriers + cool water packs
   This system prevents freezing by eliminating ice, but is only advisable for certain ambient temperatures and use cases

Document guidance aims to help EPI teams choose between these two solutions, and to ensure risks are managed during implementation

This guidance acknowledges that solutions will vary based on modes of transport and level of supply chain. This document focuses on the lower levels of supply chain, Sub-national/State/District level to Health Facility and Health Facility to outreach sites, which use cold boxes and vaccine carriers.

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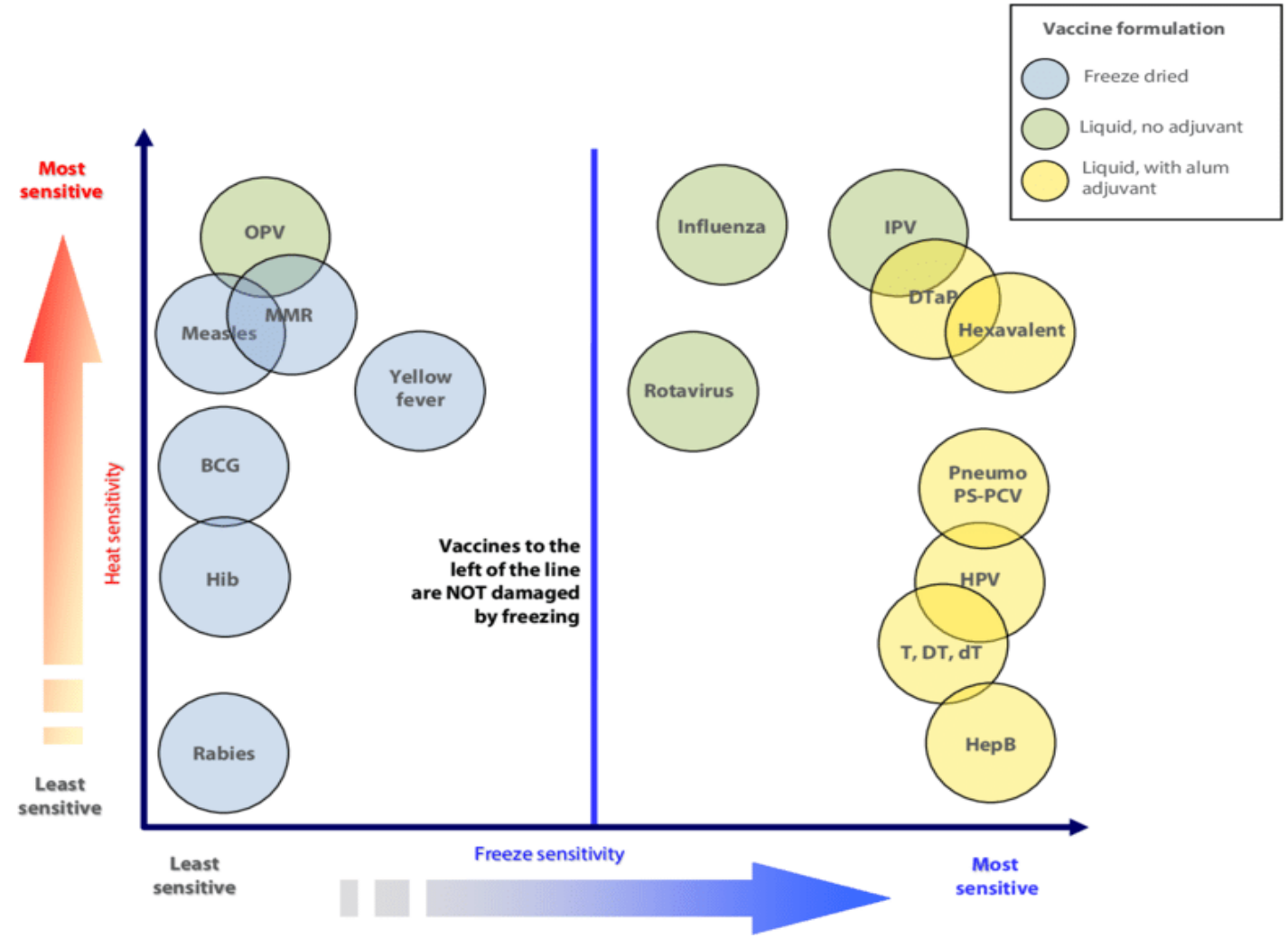
Many vaccines are freeze sensitive and may be damaged and rendered ineffective if exposed to temperatures below 2°C in the cold chain

For most vaccines, lifetime and efficacy are not maximized, and are only guaranteed when stored at the **correct temperature range of 2-8°C.**

Exposure to both high (above 8°C) and low (below 2°C) temperatures impact vaccine potency and safety; however, freezing causes more **immediate damage** to freeze-sensitive vaccines.

When exposed, the **adjuvants contained in freeze-sensitive vaccines clump together** adversely affecting the immunological properties of these vaccines.



Note: the majority of vaccines in routine immunization sessions are freeze-sensitive as illustrated above

Figure source: Meyer, Khosa et al. (2018). Childhood vaccination and the role of the pharmacist. South African pharmaceutical journal 85 (4), pp 26 - 39.

With widespread potential for freezing vaccines, the downstream financial implications could see up to ~$31M worth of vaccines damaged if these risks are not addressed

- Newly introduced vaccines including Penta, IPV, PCV, HPV and Rota are freeze sensitive **and constitute >80% of the total value of vaccines stored.**
- Freezing puts these vaccines, which are often the most expensive, at risk.
- Thus, addressing freezing at scale **holds promise for rapid, high ROI.** See table below for estimate.

The risk of undetected frozen/damaged vaccines is not easy to detect unless the 'Shake Test' is conducted (VVM change is visual sign for heat exposure).

If frozen vaccines are inadvertently used to vaccinate children, their low potency risks outbreaks of vaccine-preventable diseases.

Estimated financial impact from damage to freeze sensitive vaccines in a country with:

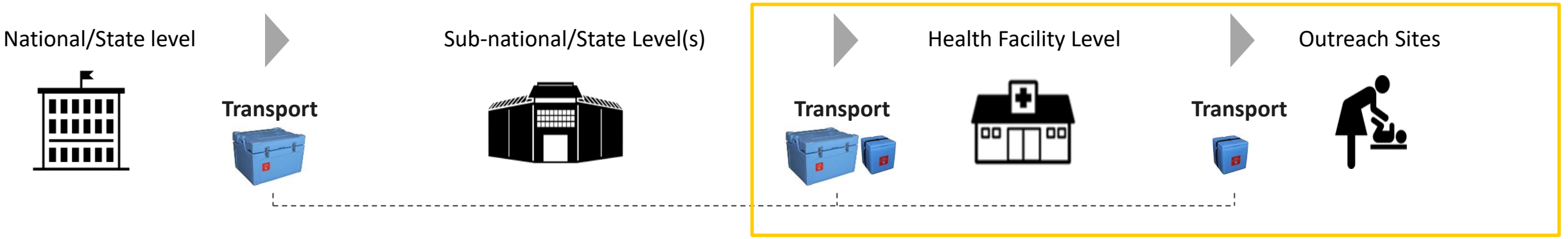
- Birth cohort of ~3.5M
- Immunization schedule of 10 vaccines - BCG, OPV, Measles, OPV, Penta, Rota, IPV, HPV, PCV and Yellow Fever

Scenario	Estimated annual cost implication
Limited freezing in cold chain *~5% of freeze sensitive vaccines are damaged*	USD 3.9M
Medium freezing in cold chain *~20% of freeze sensitive vaccines are damaged*	USD 15.6M
High freezing in cold chain *~40% freeze sensitive vaccines are damaged*	USD 31.3M

Significant vaccine investment is at risk if freezing is not addressed

Investment in CCE systems that address freezing is orders-of-magnitude lower than annual ROI

Nearly all vaccines are transported using cold boxes and vaccine carriers at some point in the cold chain; where ~20% of vaccines in CB/VC may be at risk of exposure to inadvertent freezing during transport



- All vaccines are eventually moved down the cold chain to health facilities and outreach sites.
- At present, this means **nearly all vaccines will be placed in cold boxes or vaccine carriers with pre-conditioned frozen ice packs.**

- To ensure the optimal potency of vaccines, **careful attention is needed in handling practices at all levels of the cold chain.**
- This includes storage and transport of vaccines from the manufacturer through national and sub-national vaccine stores, down to the health facility, and further down to the outreach sites.

At least 1 out of every 5 vaccine shipments are exposed to freezing temperatures

Without proper intervention to minimize freezing risks in transport (cold boxes / vaccine carriers)… currently **freezing puts at risk <u>at least 20%</u> of vaccine shipments** in-country[1]

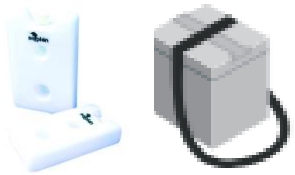
1) Hanson et al. Is freezing in the vaccine cold chain an ongoing issue? A literature review. *Vaccine*. 2017 Apr 19.

The root cause of most inadvertent freezing is improper pre-conditioning of frozen ice packs prior to packing cold boxes and vaccine carriers

Pre-conditioning *frozen ice packs is the* ***status quo policy***[1] *for preparing cold boxes and vaccine carriers prior to use*

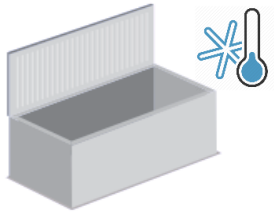
Ice packs are often **fully frozen,** as freezers typically maintain a **-25°C temperature.**

This maximizes hold time for longer transport durations but can **freeze vaccines unless HCWs intervene.**



To avoid freezing risks, frozen ice packs must be **pre-conditioned to 0°C or above** before use in transport.

Pre-conditioning uses HCW time, reduces hold time, and is performed inconsistently across systems



Despite the status quo policy, for multiple and complex reasons, **pre-conditioning is not always done properly**

Monitoring freezing in the field relies on the shake test, which is difficult to conduct and can have inconsistent results. **HCWs cannot simply look at a vaccine and see that it has been inactivated by freeze exposure.**

Vaccines may be at **increased risk temperature exposure if:**

1. **The frozen ice pack is under-conditioned,** e.g., there is insufficient capacity/training to correctly perform the activity
2. **The frozen ice pack is over-conditioned,** e.g., thawed past the point of having sufficient cooling capacity to keep vaccines under 10°C for the duration of the transport
3. **Lack of compliance with conditioning practices:** e.g., health staff face constraints (time, misconceptions about VVM) that prevent them from complying with the ideal practice (i.e., time, VVM misconceptions)

Meta-analysis of research behind this understanding: Hanson et al. Is freezing in the vaccine cold chain an ongoing issue? A literature review. *Vaccine*. 2017 Apr 19.
If you need additional evidence to understand freezing in your cold chain, see Annex slide 23-24 for details about assessment options

1) Status quo is based on prevalence, as of 2023, of conventional (i.e., non-freeze-preventative) coolers and cold boxes

Several challenges with status quo solution of pre-conditioning ice packs places vaccines at risk during transport

1. **Time burden:** Pre-conditioning frozen ice packs can take >1 hour.
2. **Training:** Appropriate staff are not always trained on proper procedures; high turnover reduces knowledge continuity and requires high training frequency.
3. **Misconceptions:** The visual representation of heat exposure in VVM makes heat exposure concerns most prominent and 'freezing' less noticeable. There is also no "VVM for freezing" that allows HCWs to easily spot freezing issues in the field.
4. **Inconsistency:** Pre-conditioning will inherently be done to different levels across HCWs, leading to variability in freeze exposures and hold times.
5. **Reduction of hold time:** Pre-conditioning greatly reduces the cooling capacity of ice packs.

To avoid the challenges with pre-conditioning, **either the type of transport device** (e.g., freeze-preventive passive devices) **or the type of cooling medium** (e.g., cool water packs) **must be changed**

Although thermostable vaccines could become available in future, it is a long-term process and should not delay addressing temperature risks during transport now

- Thermostable vaccines **are more heat- and freeze-stable, meaning they can be stored for extended periods of time above 10 °C.**
- Transitioning to thermostable vaccines is a **long-term process;** we must wait for vaccine manufacturers to do the requisite research and development and move into scaled production.
- Whilst this solution could one day be cost-effective and scalable, the timing to implementation is not yet known, and **likely many years in the future.**
- **At this time, the majority of vaccines still are heat and/or freeze-sensitive**[2]**.** Additionally, new vaccines will almost always need cold chain for the foreseeable future.
- As the timing of scaled, universal introduction of thermostable vaccines is not yet known, and is not within country government control, **this document focuses on the near-term need to address issues associated with temperature sensitivity.**
- In short, **it is not advisable to wait an indefinite period for thermostable vaccines** instead of addressing today's temperature excursion issues in the vaccine cold chain

1) https://www.who.int/immunization/programmes_systems/supply_chain/resources/Controlled-Temperature-Chain-FAQ.pdf?ua=1
2) Tools and approaches to ensure quality of vaccines throughout the cold chain. Umit Kartoglu &Julie Milstien. Pages 843-854 | Published online: 28 May 2014
3) Kristensen DD, Lorenson T, Bartholomew K, Villadiego S. Can thermostable vaccines help address cold-chain challenges? Results from stakeholder interviews in six low- and middle-income countries. *Vaccine*. 2016;34(7):899-904. doi:10.1016/j.vaccine.2016.01.001

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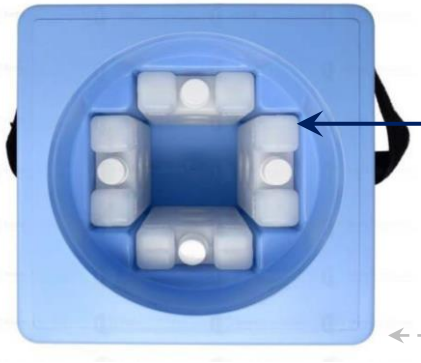
Freeze-preventive (FP) -devices and Cool Water Packs offer numerous advantages over the current status quo to prevent vaccine freezing

Option 1: Cool Water packs in conventional vaccine carriers or passive devices

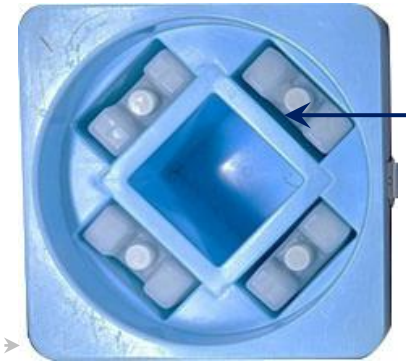


Conventional vaccine carriers keep coolant packs and vaccines in the same chamber (the "vaccine chamber"); cooling packs to around 5 degrees C, prevents freezing of vaccines vis-à-vis frozen or inappropriately conditioned ice packs

Approximately to scale
Each ~1.7L capacity

- **Cool water packs** (CWPs, details on next slide) can be used instead of pre-conditioning frozen ice packs if circumstances are ideal
  - CWP use aligns with low hold time requirements (short-duration use case + low ambient temperatures) and requires a dedicated refrigerator for CWP-cooling
- *Status quo requirement:* **pre-condition frozen ice packs** before use to address freezing issues
  - See slide 11 for details regarding pre-conditioning issues, and slides 22-23 to understand impact

Option 2: Freeze Preventative (FP) devices



FPVCs add a thermal barrier between coolant packs and vaccines; these barriers are built into the carrier body and inaccessible to users

Freeze-Preventative (FP) Devices

- Freeze-preventative technology makes use easy, predictable, and efficient:
  - Fully frozen ice packs are placed in isolated compartments
  - **No pre-conditioning is required by health staff**[1]
  - The **buffer layer controls heat transfer** from frozen ice packs
  - Use of frozen ice packs supports **long hold times, does not rely on a variable process** to address freezing, and **reduces HCWs time burden**
- Second-generation FP technology enables designs that meet or exceed PQS standards for hold time[2], cooldown time[2], and weight[3], **addressing concerns associated with first-generation FP devices**.
- FP vaccine carriers will typically be ~2x the price of similar-size conventional carriers

[1] PATH, Preventing Freezing in Cold Boxes and Vaccine Carriers, https://path.azureedge.net/media/documents/TS_opt_handout_freeze_safe.pdf

[2] WHO PQS 4.2.3, long range: Minimum 30 hours when tested at constant ambient temperatures of +43°C and +15°C (or at a lower test temperature specified by the manufacturer); the cooldown must not exceed 8 hours. Note that "long range" is the standard specification for carriers over ~1.0L.

[3] WHO PQS 4.4.2, long range: The maximum loaded weight of the container, inclusive of the recommended number of coolant-packs, must not exceed 8.0 kg. Note that "long range" is the standard specification for carriers over ~1.0L.

Cool Water Packs (CWP) have numerous advantages over the status quo of frozen ice packs in conventional carriers, but carry some risks

Cool water packs (CWP) are a **cross cold chain solution**, and an alternative use of pre-conditioned ice packs that are typically frozen. The intention is to eliminate freezing risks by only using cooled water conditioned to a temperature of +5°C or less (no less than 0°C)[1]

Conventional vaccine carriers + Cool water packs = **Maximum safety of freeze-sensitive vaccines if conditions are ideal**

Advantages over status quo

1. Assures vaccine potency by eliminating freeze risk
2. Saves HCW time and effort by avoiding the need to condition ice packs
3. Intuitive to use, easy to maintain, and does not require purchase of new devices or ice packs

Performance | Usability | System fit

1. Offers short but reliable cold life during use to ensure optimal vaccine safety[3]
2. User-friendly/user-independent to minimize compliance issues
3. Current guidelines[2] recommend the use of a separate refrigerator for cooling water packs to prevent possible heat degradation of adjacent vaccine vials although some studies suggest that the risk is limited[4]
4. Cool life is shorter than traditional prequalified packs **(a few hours, rather than 24+ hours)**, thus may be suitable for **shorter duration transport or outreach**

Potential risks

1. Health worker confusion over CWP prep protocols, additional trainings needed and inconsistencies of training
2. Heat excursions as duration of /distance to outreach sessions may be longer than the cool-life maintained by CWPs
3. Greater procurement and (Opex) maintenance costs of additional CCE needed for generating CWPs

Mitigation strategies

1. Ensure clear training materials and reinforcement of new SOPs
2. Plan immunization sessions effectively to ensure that the duration sufficiently matches the cold life capabilities of the CWP
3. Incorporate all PPM and curative costs for all additional CCE into the annual maintenance plans

1) WHO Module 2: The vaccine cold chain. https://www.who.int/immunization/documents/IIP2015_Module2.pdf?ua=1
2) WHO Vaccine Management Handbook: How to use passive containers and coolant-packs for vaccine transport and outreach operations. https://www.who.int/publications/i/item/WHO-IVB-15.03
3) Kartoglu U, Ganivet S, Guichard S, 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.
4) Goldwood G, Diesburg S. The effect of cool water pack preparation on vaccine vial temperatures in refrigerators. *Vaccine*. 2018;36(1):128-133. doi:10.1016/j.vaccine.2017.11.024

Freeze-Preventative (FP) devices have also evolved to deliver more reliable safeguards against freezing vaccines during transport

First-generation FP carriers have a characteristic thicker wall between ice packs and vaccine chambers

Second-generation FP carriers have thinner wall between ice packs and vaccine chambers

First-generation FP devices

~1.5L FPVCs are pictured

- First-generation FP devices demonstrated the potential of FP technology but had **disadvantages including high weight and long cooldown times** compared to conventional devices that led to low acceptance.
- First generation FP devices also held risks including **variable performance** (carriers stored at hot temp deplete cooling capacity quickly; carriers stored at low temp may not do so adequately) and **potential for freezing events in ambient temps at or below 15°C.**

Second-generation FP devices

~1.7L FPVCs are pictured

- Second-generation FP devices address the disadvantages of first-generation devices, with **weight and cooldown times approximating same-size conventional devices.**
- Second-generation FP devices also address the risks of first-generation devices: **performance is consistent regardless of initial temperature in ambient conditions from 10°C-43°C.**
- Second-generation FP devices add ~20-30% to the price of first-generation FP devices.

Recommendation

Always choose FP devices demonstrated to have freeze-free performance at 10°C and weight-to-volume ratios consistent with second-generation technology.[1]

Look for the characteristic smaller wall width on the thermal barrier housing as pictured at left.

The 20-30% price increase has significant value-for-money in usability for HCWs and freeze-exposure risk reduction.

This document guidance is written around an assumption of second-generation FP device use; first-generation devices could entail additional tradeoffs.[2]

[1] E.g., ~6Kg loaded for a ~1.7Kg FPVC.

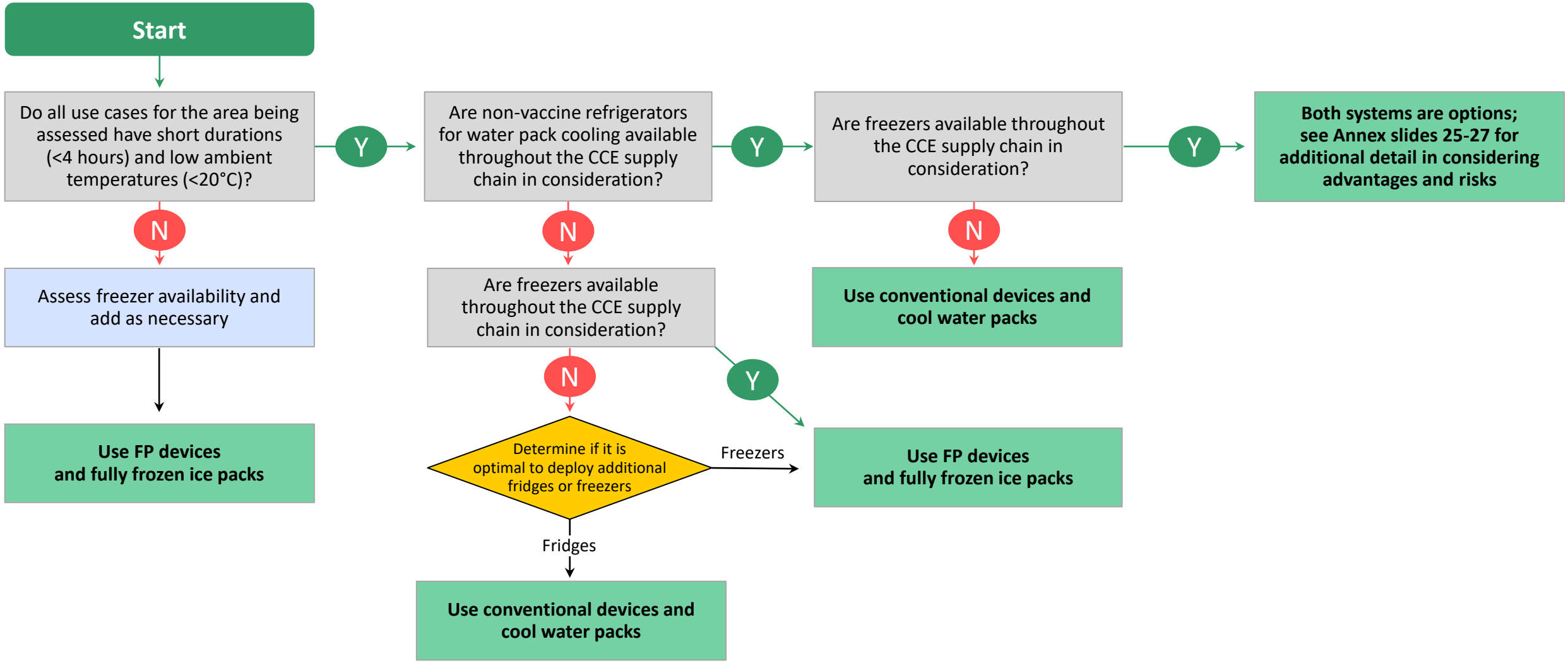
[2] Note PQS weight and thermal performance requirements make first-generation FP carriers or cold boxes >1.7L unfeasible; any device over 1.7L will use second-generation technology.

Matching Transportation Device To Coolant Pack Type

It is critical to match passive transport devices with the correct coolant packs when designing an optimized system

		Coolant pack		
		Fully frozen ice packs	**Pre-conditioned (partially frozen) ice packs**	**Cool water packs**
Device	**Conventional device**	Vaccines are exposed to freezing temperatures	Status quo, but not recommended; see slide 11 for details of challenge and slides 22-23 for details on impact	Workable in low ambient / short-duration use cases when properly implemented
	Second-generation Freeze-preventative device	Optimal performance	Second-generation FP devices will function properly when used with pre-conditioned ice packs; hold time will be a few hours lower vs fully-frozen ice packs	Cool water packs do not have adequate cooling capacity for use in FP devices

Process for Choosing Solution



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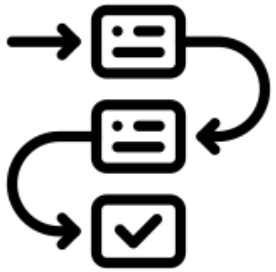
Conclusion

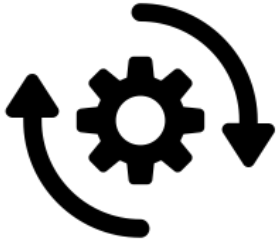
- Recent advances in technology and procedures allow freezing issues in transport to be addressed with minimal disruption to current systems.
- Both freeze-preventative carriers with fully frozen ice packs and conventional carriers with cool water packs are effective in preventing freezing when implemented
- Freeze-preventative carriers with fully frozen ice packs are the recommended solution for most scenarios. For certain combinations of low ambient temperature and short-duration use case, conventional carriers combined with cool water packs may also be an ideal solution, provided systemic oversight to evaluate temperature excursions upon implementation is in place.
- Be sure to engage a robust assessment, selection, planning, and implementation process that is appropriate to your scenario.

Next Steps



Plan for implementation

- Evaluate key solution implementation considerations: operational, financial, current equipment status, and policy planning
- **For FP devices + fully-frozen ice packs:** purchase appropriate freeze-preventative devices, train HCWs, remove conventional devices from the field, ensure attendant freezer-maintenance plan is in place
- **For conventional devices + CWPs:** transition to cool water packs, train HCWs, ensure plans are in place to monitor heat excursions, ensure attendant non-vaccine refrigerator purchase and maintenance plan is in place
- Understand responsibilities of key stakeholders involved in the implementation planning and utilize a process that aligns with these responsibilities



Execute implementation

- Provide useful resources and guidance for monitoring and evaluation post implementation
- Outline the responsibilities of key stakeholders involved in the implementation
- Demonstrate how to monitor and evaluate the effectiveness of the solution; in particular, systems utilizing cool water packs in conventional carriers require follow-up to ensure packs are not too cold or too warm, and associated vaccine temperature excursions are not occurring

For guidance on planning and implementation, please refer to
CHAI_Freeze-Preventative Passive CCE Implementation Guide.pptx

Contents

Conducting Assessments of Freezing If Needed

If a study specific to freezing challenges in your cold chain is needed, different assessments and studies can help*:

Type of assessment	*Process*	*Output*	*SC Level*	*Resources*
EVM assessments	Every 3-4 years, conduct WHO Effective Vaccines Management (EVM) Assessment Tool; obtain assessment report and improvement plan	EVM scores provide snapshot of country capacity to effectively manage its immunization program, including vaccine safety from freezing	National, EVM all levels	EVM Assessment Tool
Temperature studies	Use of temperature monitoring devices to collect temperature data at certain points of the cold chain over a set period	Occurrence of freezing or heat excursions across focus levels of the vaccine cold chain	National, Regional District	WHO/IVB/15.03 WHO, August 2015 TechNet - 2018
Surveying current practices	Field survey and evaluation of vaccine transport packing practices to understand current alignment with SOPs	Understand if vaccines are at risk for freezing due to improper transport packing practices	Regional, District Facility	EVM Model SOP
Shake tests**	Health workers and EPI logisticians shake vaccine vials with suspected freeze exposure, and observe for sediments	Determine whether adsorbed individual vaccine vials have been affected by freezing	Facility	How to conduct the shake test

* Challenge of freezing can vary at subnational level depending on local management capacity and geographic context. Programs should understand and prioritize the appropriate freezing assessment incorporating these factors. Note, different assessments may take various lengths of time which could further delay finding a solution to freezing.

** Please note that shake tests have limitations in convenience and reliability

Conducting Assessments of Freezing: Key Stakeholders' Roles and Responsibilities

If conducting a study specific to freezing challenges in your cold chain, key stakeholders should be engaged:

	Stakeholder	Role in Assessment
	**National / Sub-National EPI Managers and Development Partners**	1. Take global EVM assessment guidance and adapt for country circumstances 2. Provide guidance to the lower levels of the supply chain on type of assessments to be conducted 3. Train EPI managers and HCWs on freeze recognition assessments to recognizing freezing 4. Analyze National and Sub-National-level TMC data and identify of freezing hotspots 5. Evaluate current performance of transport solutions to identify root cause of freezing issues 6. Provide tools and SOPs to allow for freezing recognition 7. Coordinate the conduct of assessments and studies to help understand freezing challenges 8. Supportive supervision and feedback on temperature monitoring control (TMC) practices to the lower level
	**District EPI Managers**	1. Participate in training and assessment for freezing recognition during vaccine transport 2. Collate data from health facilities and share with the higher level for analysis and problem identification 3. Provide hands-on support and feedback to health care workers during supportive supervision 4. Document and report TMC performance trends during transportation of vaccine shipments
	**Health Workers**	1. Document TMC data during transport and storage of vaccine shipments 2. Participate in evaluations to assess freeze occurrence 3. Communicate to EPI any challenges faced with the current vaccine transport practices 4. Ensure data is shared to District, and other upwards levels

Note: Roles and responsibilities of stakeholders may vary based on country context and policies

Selection Detail: Advantages and Risks of the Two Recommended Systems

Both systems offer similar advantages versus *status quo* systems requiring pre-conditioning: they eliminate freeze risk and are intuitive to use and maintain. In selecting a system, it is important to also understand their advantages and risks versus each other.

Conventional + Cool Water Packs

Advantages

1. **Weight / bulk:** conventional carrier designs require less overall space than freeze-free carriers, particularly those using water-bag thermal barriers (first-generation FP technology.)
2. **Carrier cost:** conventional carrier costs are typically 30-50% of same-size freeze-preventative costs.
3. **Freezer cost:** CWP-based systems ***may*** not require freezers for ice production.
4. **Low-ambient performance:** CWP-based systems will not freeze vaccines, even at ~10°C ambient; water-bag-based FP carriers may have freezing events at ambient temperatures <15°C.

Risks

1. **Hold time:** cold life of CWPs will be used up quickly, especially in higher ambient temperatures. Duration of outreach sessions may exceed hold time, leading to vaccine wastage and/or complexity for HCWs.
2. **Use of heat margin:** HCWs may be asked to field-assess impact of heat exposure using VVMs. This creates inconsistency, opportunities for waste, and difficult decisions for HCWs.
3. **Refrigerator cost:** system requires additional refrigerators for cooling of CWPs.
4. **Time and cost of freezers?:** some CWP systems avoid additional refrigerator requirements by cooling CWPs in freezers, then asking HCWs to thaw them completely; this consumes more time than *status quo* pre-conditioning systems

Broad Recommendation

Only implement conventional + CWP systems where use case and ambient temperature is known to be consistently optimal

Freeze-Preventative + Frozen Ice Packs

Advantages

1. **Hold time:** cold life of carriers is maximized by using fully frozen ice packs.
2. **Simplicity:** HCW burden is lowest in this system: no pre-conditioning or thawing-until-liquid of ice packs, no reliance on VVMs in standard scenarios, maximum time to complete outreach sessions
3. **Refrigerator cost:** system does not require additional refrigerators for cooling of CWPs.
4. **Time and cost of freezers?:** some CWP systems avoid additional refrigerator requirements by cooling CWPs in freezers, then asking HCWs to thaw them completely; this consumes more time than *status quo* pre-conditioning systems

Risks

1. **Weight / bulk:** FP carriers have higher weight and bulk vs capacity as compared to conventional carriers – particular FP carriers with first-generation thermal barrier tech
2. **Carrier cost:** FP carriers are typically 2-3x the cost of same-capacity conventional carriers.
3. **Freezer cost:** Freezers need to be maintained well (i.e., fully freeze ice packs) to optimize system performance
4. **Low-ambient performance:** Water-bag-based FP carriers may have freezing events at ambient temperatures <15°C.

Broad Recommendation

In any scenario not aligned with ideal CWP-use conditions, implement FP carriers with weight-to-volume and low-ambient performance aligning with second-generation thermal barrier technology

Selection Detail: Solution Comparisons by Capacity (Vaccine Carrier or Cold Box)

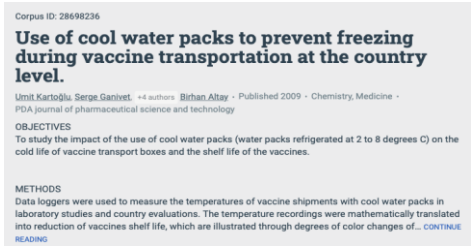
	Last-Mile Solutions		Facility-to-Facility Solutions	
	Freeze-preventive Vaccine Carriers + Frozen Ice Packs	**Conventional Vaccine Carriers + Cool Water Packs**	**Freeze-preventive Cold Boxes + Frozen Ice Packs**	**Conventional Cold Boxes + Cool Water Packs**
Performance and Safety	✓ Provides user-independent freeze protection ✓ Easy to use by health worker × Water-bag FP technology may require several hours to sufficiently cool the vaccine compartment × Water-bag FP technology presents concern about size and weight compared to conventional devices	✓ Provides user-independent freeze protection ✓ For shorter immunization sessions, protects against heat damage × Less suitable for longer duration immunization sessions ✓ Easy to use by health worker	✓ Provides user-independent freeze protection ✓ Meets global PQS standards, and EPI guidance for transport ✓ Easy to use by health worker × Water-bag FP technology presents concern about size, weigh, and cool-down time compared to conventional devices	✓ Provides user-independent freeze protection ✓ For shorter immunization sessions, protects against heat damage × Less suitable for longer duration immunization sessions ✓ Easy to use by health worker
Program Suitability	✓ Suitable for last mile and outreach transportation ✓ Relevant across all vaccine types and presentations	✓ Somewhat scalable across multiple supply chain levels depending on duration of transport leg × Not relevant across all vaccine types and presentations	✓ Scalable for central-level and facility-to-facility transportations ✓ Applicable across all vaccine types and presentations	✓ Somewhat scalable across multiple supply chain levels depending on duration of transport leg × Not relevant across all vaccine types and presentations
Commercial Viability and Scalability	✓ Meets PQS standard, follows EPI guidance ✓ Available in PQS for procurement ✓ Leverages existing freezer and transport vehicle infrastructure × Switchover costs entails purchasing new, more expensive devices	✓ Meets PQS standard, follows EPI guidance ✓ Available in PQS for procurement × Requires separate refrigerator to prepare CWPs × Switchover costs may require purchase of separate refrigerator for preparation	✓ Meets PQS standard, follows EPI guidance ✓ Available in PQS for procurement ✓ Leverages existing freezer and transport vehicle infrastructure × Switchover costs entails purchasing new, more expensive devices; note this is potentially offset by reduced vaccine wastage	✓ Meets PQS standard, follows EPI guidance ✓ Available in PQS for procurement × Requires separate refrigerator to prepare CWPs × Switchover costs may require purchase of separate refrigerator for preparation

Click on solution titles for more details on each solution option

Further Resources to Inform Solution Choice and Implementation

Note, FP studies to date utilize first-generation devices; these demonstrate potential of FP-based systems, while second-generation technology follows up to address HCW concerns with weight and low-ambient performance issues that are not reflected in these studies

Indicator	Data source	Link
Selecting, commissioning and using freeze-preventative vaccine carriers	WHO	https://www.who.int/publications/i/item/WHO-IVB-2021.02Rev.1
Cool Water Pack performance	Journal article: Kartoglu U, Ganivet S, Guichard S, 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.	https://journal.pda.org/content/63/1/11.long
How to use passive containers and coolant-packs for vaccine transport and outreach operations	WHO guidance	https://www.who.int/publications/i/item/WHO-IVB-15.03
Cold life in vaccine carriers with freeze preventive technology	PATH results as illustrated in CHAI poster presentation at Tech Net 21 Conference 2017	https://www.technet-21.org/images/tc2017/Posters/Freeze-Free-Cold-Boxes-and-Vaccine-Carriers_CHAI.pdf
Using long-range freeze-preventive vaccine carriers in Nepal: A study of equipment performance, acceptability, systems fit, and cost	PATH study from Nepal	https://www.sciencedirect.com/science/article/pii/S2590136222000067
Unit costs of vaccine carriers / cold box with freeze preventive technology	PQS Catalogue	https://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/

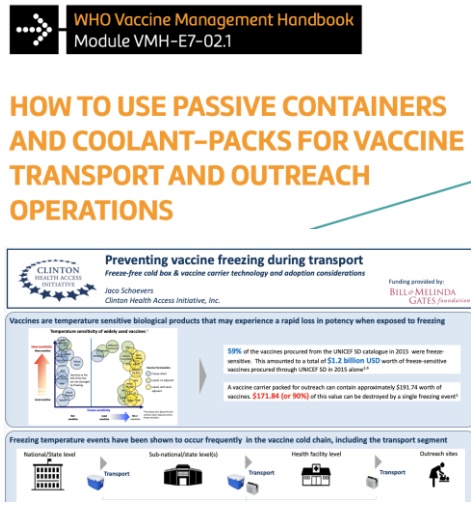

Corpus ID: 28698236

Use of cool water packs to prevent freezing during vaccine transportation at the country level.

Umit Kartoğlu, Serge Ganivet, +4 authors Birhan Altay · Published 2009 · Chemistry, Medicine · PDA journal of pharmaceutical science and technology

OBJECTIVES
To study the impact of the use of cool water packs (water packs refrigerated at 2 to 8 degrees C) on the cold life of vaccine transport boxes and the shelf life of the vaccines.

METHODS
Data loggers were used to measure the temperatures of vaccine shipments with cool water packs in laboratory studies and country evaluations. The temperature recordings were mathematically translated into reduction of vaccines shelf life, which are illustrated through degrees of color changes of... CONTINUE READING



The WHO Performance, Quality and Safety (PQS) process prequalifies products and devices so that member states and UN purchasing agencies are assured of their suitability for use in immunization programs. The PQS process also encourages a wide range of manufacturers to apply for prequalification so that a competitive marketplace develops.

The PQS website provides relevant documents, procedures, and data sheets for all currently prequalified products in the following equipment categories:

- E001: Cold rooms, freezer rooms, and related equipment
- E002: Refrigerated vehicles
- E003: Refrigerators and freezers
- E004: Cold boxes and vaccine carriers
- E005: Coolant-packs
- E006: Temperature monitoring devices
- E007: Cold chain accessories
- E008: Injection devices for immunization
- E010: Waste management equipment
- E013: Injection devices for therapeutic purposes

Active Transport Solutions Overview

- This document focuses on portable CCE systems that utilize passive devices, i.e., unpowered devices that rely on a coolant source such as frozen ice packs or CWPs
- There are also opportunities to deploy active devices, i.e., powered devices that provide their own cooling, also play a role in a robust CCE transport system
- New and upgraded active devices are frequently introduced, as underlying technologies are advanced and incorporated into CCE
- Application of technology depends on specific country use cases; these devices have potential to address critical gaps in CCE supply chains, often with increased expense, complexity, and power/training requirements

Active Transport Solutions: Refrigerated Vehicles

	Refrigerated vehicles
Performance and Safety	✓ When properly fueled, operated and maintained, it protects against freeze and heat exposure ✓ Meets global PQS standards, and EPI guidance for transport × Freeze protection is dependent on proper operation, monitoring and maintenance ✓ Easy to use by trained cold chain logisticians and drivers
Program Suitability	✓ Capable of transporting large volumes of vaccines in a single trip ✓ Applicable across all vaccine types and presentations
Commercial Viability and Scalability	✓ Meets PQS standard, follows EPI guidance × No models currently prequalified by PQS × High upfront purchase costs × Ongoing maintenance needs and associated costs

- Refrigerated trucks and vans are a highly useful solution for transporting **large quantities of vaccine and for distributing over long distances**.
- For **central transport and facility-to-facility distribution** of vaccines, refrigerated vehicles may be the most appropriate solution.
- This option has the **highest purchase price per unit** as well as the **greatest vaccine volume capacity**[1]. Due to the **potential for mechanical breakdowns and risk to large quantities of vaccines**, refrigerated vehicles must undergo routine maintenance.

1) PATH, World Health Organization (WHO). Delivering Vaccines: A Cost Comparison of In-Country Vaccine Transport Container Options. Seattle: PATH, WHO; 2013.
2) Qualification of refrigerated road vehicles Technical supplement to WHO Technical Report Series, No. 961, 2011
3) NS731 Chiodini J (2014) Safe storage and handling of vaccines. Nursing Standard. 28, 25, 45-52. Date of submission: October 13 2013; date of acceptance: December 2 2013.
4) https://www.fiocchetti.it/en/prodotti.asp?id=6

Active Transport Solutions: Transportable Powered Vaccine Systems (TPVS)

	Transportable Powered Vaccine Systems (TPVS)
Performance and Safety	✓ When properly operated and maintained, protects against freeze and heat exposure ✓ Hold promise to create new efficiencies through the cold chain, not just last mile. × HCW adaptation and training may be difficult
Program Suitability	✓ Relevant across vaccine types and presentations × May not be suitable for all types of last mile and outreach transportations
Commercial Viability and Scalability	✓ Meets PQS standard, follows EPI guidance × No models currently prequalified by PQS and available for procurement × Switchover costs entails purchasing new, more expensive devices × Ongoing maintenance needs and associated costs

- As of 2023, TPVS are projected to soon be available in a variety of capacities, weights, and hold times, making them a **suitable solution across different levels of the cold chain**.
- Different TPVS are designed to address different use cases, e.g., last mile delivery, improving supply chain efficiency, temporary PHC refrigeration, mobile clinics, extended drives. **As more devices become available, it is important that decision-makers align device selection with intended use case.**
- TPVS in design work with a variety of power sources (mains, solar, car battery), and are often freeze-preventative.
- Pros: active cooling without need for coolant packs or refrigerants holds potential to address gaps in current supply chain, decrease wastage, and support the Zero Dose Agenda.
- Cons: **relatively more expensive option** for small volume vaccine transport; requires **proper training and operation** to avoid damaging vaccines. Some devices require extended cool down times prior to loading with vaccines. Some devices have concerns about robustness if dropped from a height >1M of more.

1) Qualification of refrigerated road vehicles Technical supplement to WHO Technical Report Series, No. 961, 2011
2) NS731 Chiodini J (2014) Safe storage and handling of vaccines. Nursing Standard. 28, 25, 45-52. Date of submission: October 13 2013; date of acceptance: December 2 2013.
3) https://www.fiocchetti.it/en/prodotti.asp?id=6
4) https://www.janechiodini.co.uk/wp-content/uploads/2017/07/Safe-Storage-and-Handling-of-Vaccines-Nursing-Standard.pdf

Other Last-Mile solutions: Controlled Temperature Chain

Controlled temperature chain (CTC)

Performance and Safety	✓ When properly performed, CTC provides user-independent freeze and heat protection for relevant vaccines × New protocols and processes require strict adherence by health staff
Program Suitability	✓ Suitable for last mile transportation × Not relevant across all vaccine types and presentations
Commercial Viability and Scalability	✓ Meets global standards, EPI guidance, and supporting equipment meets PQS standard ✓ Supporting equipment available in PQS for procurement ✓ Minimal additional costs for country ✓ Minimal infrastructure, equipment needs or changes

- The "Controlled Temperature Chain" (CTC) is an innovative approach to vaccine management that allows vaccines to be **kept at temperatures outside of the traditional cold chain of +2°C to +8°C for a limited period** under monitored and controlled conditions, as appropriate to the stability of the antigen[1].
- This solution is **most appropriate at the last mile** due to being more appropriate for smaller volume of vaccines and inability to scale.
- WHO has established the following programmatic criteria for a vaccine to be labelled for and used in a CTC[1]:
  - The vaccine should be used in a **campaign or special strategy setting**. Not currently recommended for routine immunization service delivery.
  - The vaccine must be able to tolerate ambient temperatures of at least **+40°C for a minimum of 3 days** and should be accompanied by:
    - ✓ A vaccine vial monitor (**VVM**) on each vial, and
    - ✓ A **peak threshold indicator** in each vaccine carrier.
- The vaccine must be **licensed for use in a CTC** by the relevant regulatory authorities, with a label that specifies the conditions.

1) WHO CTC. https://www.who.int/immunization/programmes_systems/supply_chain/ctc/en/
2) Tools and approaches to ensure quality of vaccines throughout the cold chain. Umit Kartoglu &Julie Milstien. Pages 843-854 | Published online: 28 May 2014