Advancing heat-stable vaccines

Vaccine Innovation Prioritisation Strategy (VIPS) consultation on programmatic needs and strategic opportunities in low- and middle-income settings

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unicef for every child
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Cover photo:

Vaccine storage freezer at Kyumbi Community Hospital, a level 3 health facility. Machakos, Kenya. © Gavi/Kelvin Juma

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Photo: *Adan Abdirahman Mohamed carries the portable cooler for vaccines as he and the READO outreach team leave the facility after completing a day of vaccinations in Somalia. © Gavi/Mohamed Abdihakim Ali*

Acronyms

BCG	Bacille Calmette–Guérin vaccine
CHAI	Clinton Health Access Initiative, Inc.
COVID-19	coronavirus disease 2019
CTC	controlled temperature chain
DTP	diphtheria, tetanus and pertussis-containing vaccine
HepB	hepatitis B
Hib	*Haemophilus influenzae* type b
HPV	human papillomavirus
IPV	inactivated polio vaccine
LMIC	low- and middle-income country(ies)
menA	meningococcal serogroup A
MMCV	multivalent meningococcal conjugate vaccine
MR	measles-rubella vaccine
mRNA	messenger RNA
NGO	non-governmental organisation
OCV	oral cholera vaccine
OPV	oral polio vaccine
PPC	preferred product characteristics
TCV	typhoid conjugate vaccine
TPP	target product profiles
UNICEF	United Nations Children's Fund
UCC	ultra-cold chain
VIPS	Vaccine Innovation Prioritisation Strategy
VVM	vaccine vial monitor
VVM2	vaccine vial monitor type 2
VVM14	vaccine vial monitor type 14
VVM30	vaccine vial monitor type 30
VVM250	vaccine vial monitor type 250
WHO	World Health Organization

Executive summary

Context and purpose

The Vaccine Innovation Prioritisation Strategy (VIPS), led by Gavi, the Vaccine Alliance, World Health Organization (WHO), United Nations Children's Fund (UNICEF), Gates Foundation and PATH, identified heat stability and controlled temperature chain (CTC)[1] in 2020 as a key innovation for partner support. Heat stability and CTC have the potential to improve vaccine access for under-served communities; and alleviate cold chain constraints for health workers, thereby directly contributing to addressing equity concerns.

The fundamental requirement to maintain vaccines within specified temperature ranges makes vaccine handling and delivery resource-intensive and potentially subject to risks *(1–3).* This ultimately increases the cost and complexity of managing and delivering vaccines effectively

and could contribute to limitations in reaching un- and under-immunised people due to: (i) restricted outreach and access; (ii) risks of potency loss and wastage; and (iii) increased operational complexity.

While vaccines that can be stored at any ambient temperature are not yet technically feasible, incremental improvements can provide programmatic benefits *(1–5)*. A better understanding of the programmatic needs of low- and middle-income countries (LMIC) and alignment around standardised heat stability profiles can streamline delivery, reduce errors and ease operational pressures. Heat stability is one component of effective vaccine delivery, but remains an important factor shaping feasibility and uptake.

1. Controlled temperature chain (CTC) is defined as a vaccine management approach that allows vaccines to be kept at temperatures not exceeding 40°C for a minimum of three days, just prior to administration, under controlled and monitored conditions.

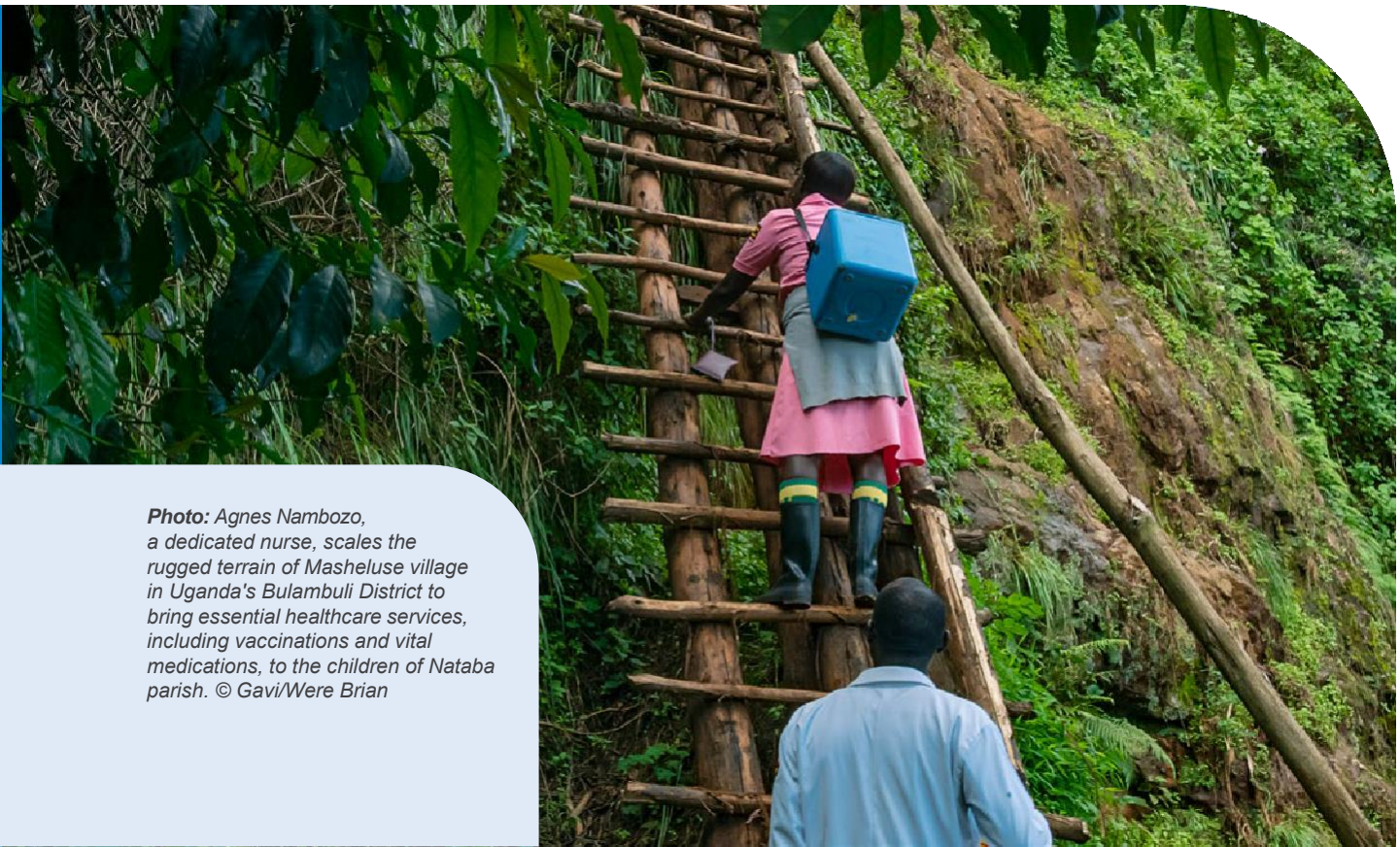


Photo: *Agnes Nambozo, a dedicated nurse, scales the rugged terrain of Masheluse village in Uganda's Bulambuli District to bring essential healthcare services, including vaccinations and vital medications, to the children of Nataba parish. © Gavi/Were Brian*

Key findings

This document draws upon data collected through the 2023–2024 VIPS country consultation on heat stability, including interviews and an online survey, with 33 countries (30 LMIC).[2] The consultation identified challenges caused by varying vaccine heat stability profiles; and clarified the attributes countries seek to enhance programmatic use, and how they view trade-offs.

Country preferences

Countries expressed the preference for all vaccines to be stored at 2–8°C with vaccine vial monitor type 30 (VVM30) and at least 12 months' shelf life remaining upon delivery at the end-user level.

Trade-offs

Improving a vaccine's heat stability is technically complex and often requires trade-offs that affect how a vaccine is used in practice. Countries are willing to accept trade-offs, but only when the benefit is substantial, particularly when it reduces complexity and costs.

- **To gain improvements from ultra-cold chain (UCC) to -20°C or 2–8°C requirements**, respondents indicated a willingness to accept any trade-offs, including shorter shelf life, lyophilised format and moderate price increase.
- **To gain improvements from -20°C to 2–8°C storage requirements**, respondents indicated a willingness to trade off a shorter shelf life, but less willingness to accept changes to a lyophilised format or price increases.
- **To gain improvements from 2–8°C storage with a low VVM to 2–8°C with VVM30**, respondents indicated less willingness to trade off changes to a lyophilised format or price increases.

These insights highlight the importance of aligning product attributes and trade-offs with programmatic needs; and aligning preferred product characteristics (PPC) and target product profiles (TPP) to guide development. As shown by past experience, vaccines with operationally complicated product attributes can hamper programmatic performance by undermining uptake and increasing wastage, and also discouraging further investment and innovation by developers *(2)*.

Recommended actions

Manufacturers should prioritise heat stability during product development, targeting 2–8°C storage (including a VVM30); and have at least 12 months' shelf life remaining upon delivery at the end-user level.

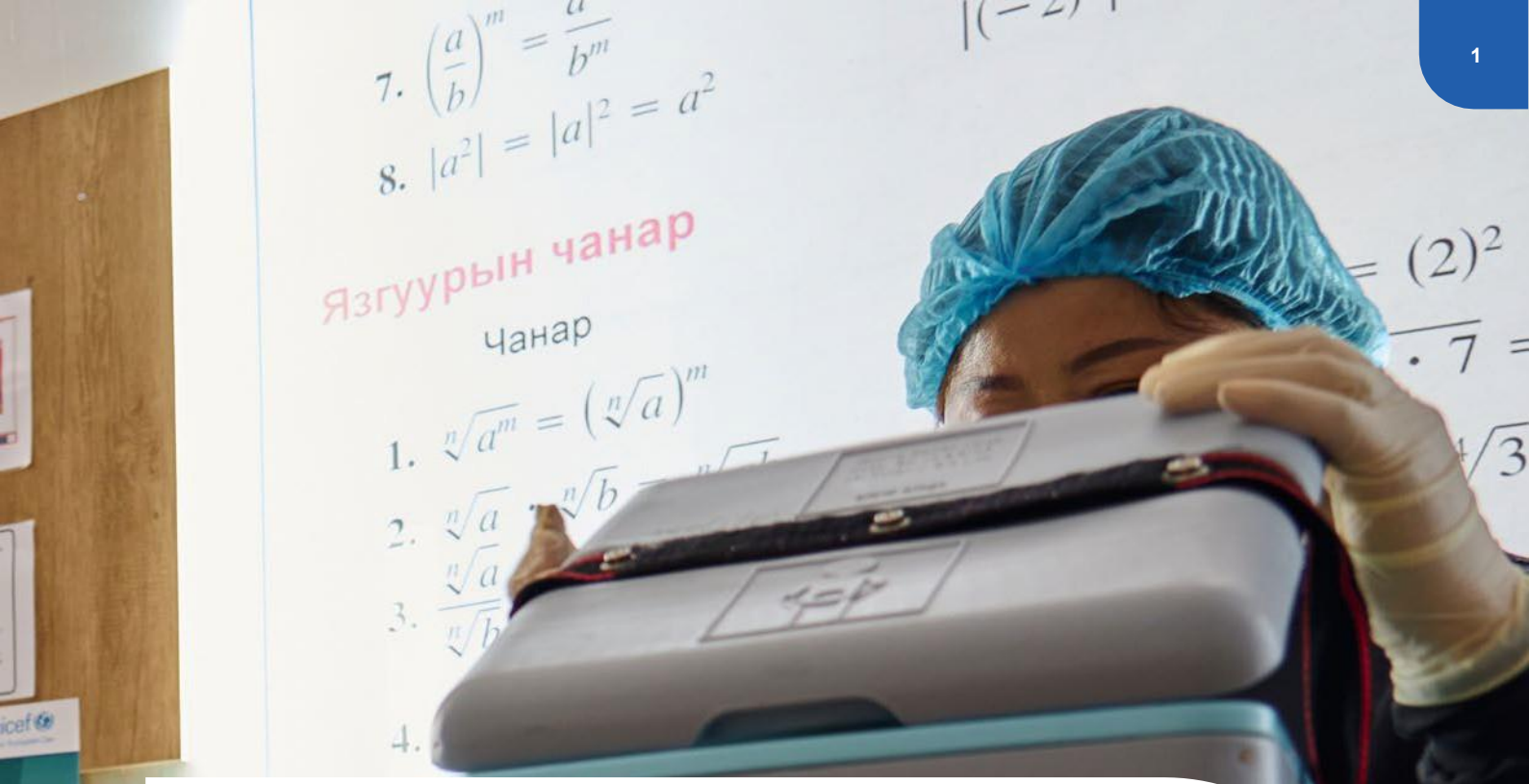
Funders should incentivise heat stability improvements or targets through market shaping approaches and continued support for research and development.

Policymakers and implementers should continue to collect data on, document, and communicate country experiences and preferences clearly and strengthen cold chain systems to consistently support safe and effective delivery.

By advancing these actions, stakeholders can reduce avoidable cold chain burdens and increase operational efficiencies, which ultimately contribute to closing immunisation gaps.

2. Three high-income countries also responded to the online survey.

Photo: *HPV vaccination at school in Altanbulag, Mongolia.*
© Gavi/Khasar Sandag



Introduction

The Vaccine Innovation Prioritisation Strategy (VIPS), a collaboration of Gavi, the Vaccine Alliance, World Health Organization (WHO), United Nations Children's Fund (UNICEF), the Gates Foundation and PATH, undertook a two-phase process (2018–2020) to prioritise vaccine product innovations with the greatest potential to address country-reported delivery barriers to vaccination and immunisation coverage. Using an assessment framework focused on coverage and equity, health impact and safety, delivery economics, feasibility and breadth of use, VIPS first evaluated 24 candidate innovations and shortlisted nine for deeper analysis. This process identified three priorities: microarray patches, barcodes on vaccine primary and secondary packaging and heat-stable and controlled temperature chain (CTC).[3] Heat stability and CTC were prioritised for their potential to directly address equity concerns through improving access to hard-to-reach populations and easing cold chain constraints for health workers.

In 2023–2024, to close critical knowledge gaps around country needs for heat stability, VIPS:

- **consulted immunisation experts in 33 countries, including 30 low- and middle-income countries (LMICs)**, through surveys and in-depth interviews, to identify operational challenges, delivery barriers, programmatic needs and acceptable trade-offs for improved heat stability product attributes; and
- **engaged partners and manufacturers** to understand challenges in developing more heat-stable vaccines.

This document draws upon data collected through this work and aims to share country insights on desired heat stability characteristics. It represents the culmination of VIPS's work on heat stability to date.

This document is intended for funders, developers and manufacturers. **It aims to clarify country-level needs and programmatic trade-offs associated with different heat stability profiles that can aid product design, development and costing.**

3. Controlled temperature chain (CTC) is defined as a vaccine management approach that allows vaccines to be kept at temperatures not exceeding 40°C for a minimum of three days, just prior to administration, under controlled and monitored conditions.

Background

Heat stability contributes to equitable, efficient and resilient vaccine delivery. Vaccines that can be stored at higher temperatures for longer times reduce dependence on cold chain infrastructure, simplify logistics for reaching un- and under-immunised children and populations, including those in fragile or emergency settings, and decrease both system costs and environmental impact.

Heat stability versus thermostability

Heat stability refers to a vaccine's ability to retain potency after exposure to elevated temperatures for a defined period of time.

Thermostability describes a vaccine's overall resilience to temperature stress, including both heat and freeze exposure.

What are vaccine vial monitors?

They are small temperature-sensitive indicators on vaccine vials that change colour to show how much heat the vaccine has been cumulatively exposed to over time. They help health workers decide if the vaccine is still acceptable to use, or needs to be discarded. Vaccine vial monitors (VVMs) are based on heat stability profile data assigned to vaccines as part of the WHO prequalification process.

VVMs exist for different heat stability profiles. The manufacturer and WHO select the correct VVM type based on the specific heat stability of each vaccine. For example, a VVM30 means that cumulative heat exposures outside normal conditions up to 37°C for 30 days do not impact on vaccine potency. When exposed to temperatures above 37°C, the VVM will reach the discard point faster.

- VVM2: up to 2 days
- VVM7: up to 7 days
- VVM14: up to 14 days
- VVM30: up to 30 days
- VVM250: up to 250 days

If the inner square is lighter than the outer circle, the vaccine can be used.

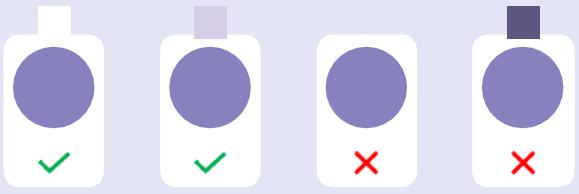


Photo: *Close-up of a health worker holding a polio vaccine during a door-to-door campaign in Pakistan.*
© Gavi/Asad Zaidi

In this document, we refer to the following heat stability profiles, considering cold chain needs at national, secondary and tertiary facilities and outreach activities, as well as VVM type (Table 1).

Table 1: Heat stability profiles

Category		Ultra-cold chain (UCC) vaccines stored at -90ºC to -50ºC	Vaccines stored at -20ºC	Vaccines stored at 2–8ºC with lower stability	Vaccines stored at 2–8ºC with higher stability	Vaccines stored at 2–8°C with a higher stability and CTC-approved[4]
Cold chain need	National	UCC freezer	-20ºC freezers	2–8ºC refrigerators	2–8ºC refrigerators	2–8ºC refrigerators
	Secondary facilities					
	Tertiary facilities	2–8ºC refrigerators	2–8ºC refrigerators			
	Outreach	Vaccine carriers with conditioned ice packs	Vaccine carriers with conditioned ice packs	Vaccine carriers with conditioned ice packs	Vaccine carriers with conditioned ice packs	Transported in vaccine carriers without ice packs for at least 3 days, provided temperatures do not exceed 40°C[5]
VVM type		None currently on marketed UCC vaccines*	VVM2, VVM7, or VVM14	VVM7, or VVM14	VVM30	VVM30
Examples		COVID-19 mRNA, Ebola	OPV	DTP-hepB-Hib, HPV, IPV, MR, measles, hexavalent, malaria, rotavirus	HPV, menA, MMCV, OCV, pneumococcal conjugate, TCV	HPV, menA, MMCV, TCV

*Some vaccines are initially labelled for storage at UCC due to limited stability data. As additional data becomes available, these vaccines can be stored at higher temperatures (e.g. -20°C or 2–8°C) for defined periods.

4. CTC is defined as a vaccine management approach that allows vaccines to be kept at temperatures not exceeding 40° C for a minimum of three days, just prior to administration, under controlled and monitored conditions.
5. Typbar typhoid conjugate vaccine can withstand ambient temperatures of up to 55° C.

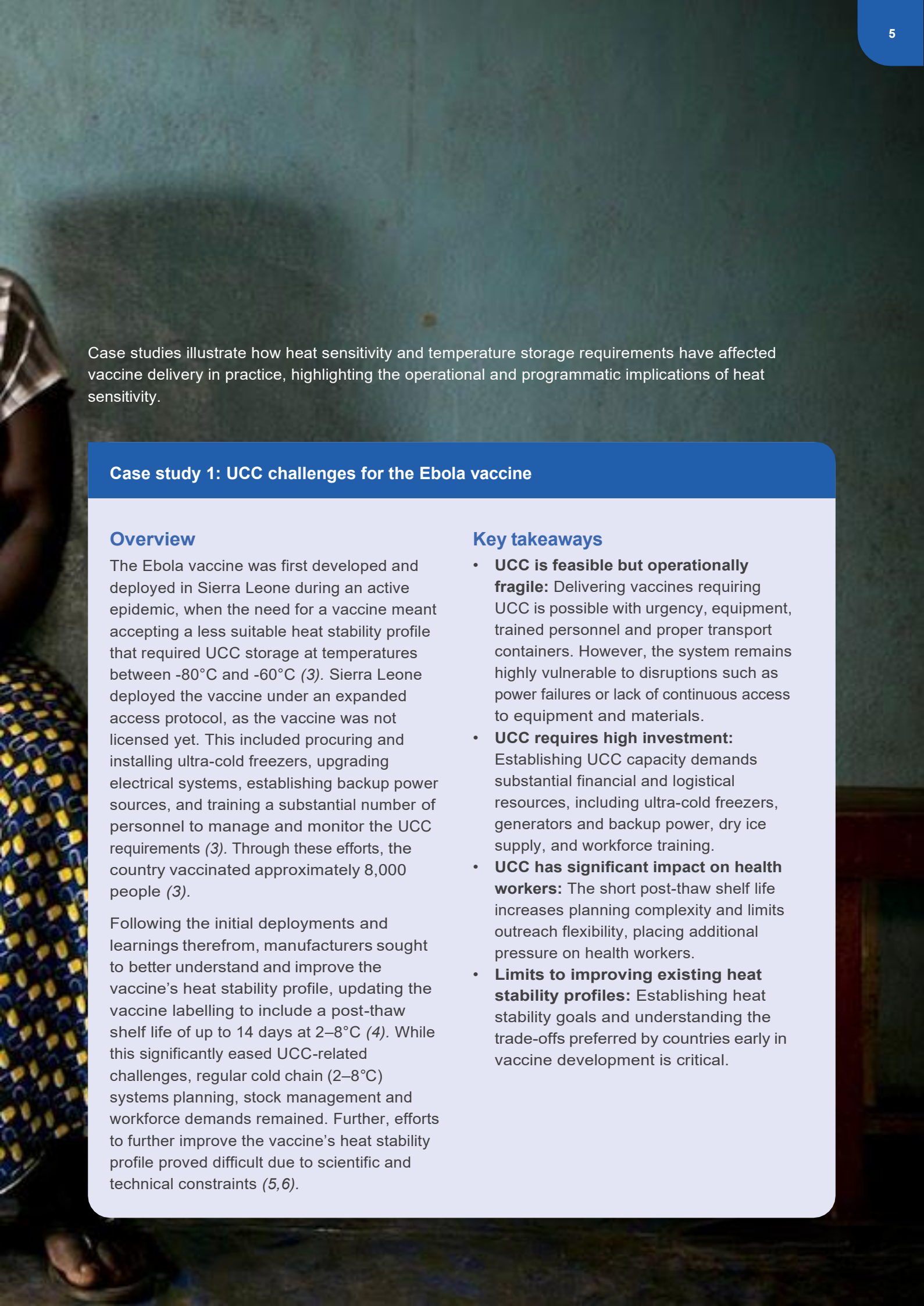
Problem statement

Despite significant investments in cold chain infrastructure, the fundamental reliance on maintaining vaccines within specified temperature ranges at refrigerated or colder temperatures makes vaccine delivery complex and resource-intensive. Country stakeholders indicate that this ultimately contributes to the challenges in reaching un- and under-immunised people and increasing the cost of vaccination.

Vaccine temperature control requirements will continue to be a barrier to equitable and efficient vaccine delivery in LMICs in three principal ways:

- Restricts last-mile access, especially for non-fixed services: dependence on cold chain infrastructure and the energy to power the infrastructure limits the ability to reach the last mile (fixed, outreach and mobile service delivery points). This is worse for remote, fragile or hard-to-reach populations.
- Risk of increased wastage or reduced protection: exposure to temperatures outside of expected ranges (e.g. due to power outages or transport delays) can compromise vaccine potency reducing protection if administered, or drive wastage if compromised vaccines are discarded.
- Increased operational complexity: diverse storage and handling requirements across products increase training needs, error risks and logistical burdens, particularly during outreach.

Photo: *Isatu Fornah, then aged 40, poses with her vaccination certificate in Magburaka, Sierra Leone, in February 2016, after receiving the Ebola vaccine alongside her six children as part of a ring vaccination campaign. © Gavi/Kate Holt*



Case studies illustrate how heat sensitivity and temperature storage requirements have affected vaccine delivery in practice, highlighting the operational and programmatic implications of heat sensitivity.

Case study 1: UCC challenges for the Ebola vaccine

Overview

The Ebola vaccine was first developed and deployed in Sierra Leone during an active epidemic, when the need for a vaccine meant accepting a less suitable heat stability profile that required UCC storage at temperatures between -80°C and -60°C *(3)*. Sierra Leone deployed the vaccine under an expanded access protocol, as the vaccine was not licensed yet. This included procuring and installing ultra-cold freezers, upgrading electrical systems, establishing backup power sources, and training a substantial number of personnel to manage and monitor the UCC requirements *(3)*. Through these efforts, the country vaccinated approximately 8,000 people *(3)*.

Following the initial deployments and learnings therefrom, manufacturers sought to better understand and improve the vaccine's heat stability profile, updating the vaccine labelling to include a post-thaw shelf life of up to 14 days at 2–8°C *(4)*. While this significantly eased UCC-related challenges, regular cold chain (2–8°C) systems planning, stock management and workforce demands remained. Further, efforts to further improve the vaccine's heat stability profile proved difficult due to scientific and technical constraints *(5,6)*.

Key takeaways

- **UCC is feasible but operationally fragile:** Delivering vaccines requiring UCC is possible with urgency, equipment, trained personnel and proper transport containers. However, the system remains highly vulnerable to disruptions such as power failures or lack of continuous access to equipment and materials.
- **UCC requires high investment:** Establishing UCC capacity demands substantial financial and logistical resources, including ultra-cold freezers, generators and backup power, dry ice supply, and workforce training.
- **UCC has significant impact on health workers:** The short post-thaw shelf life increases planning complexity and limits outreach flexibility, placing additional pressure on health workers.
- **Limits to improving existing heat stability profiles:** Establishing heat stability goals and understanding the trade-offs preferred by countries early in vaccine development is critical.

Photo: *A health worker administering polio vaccine drops to a child during the door-to-door polio vaccination campaign in Khalid town, Pakistan. © Gavi/Asad Zaidi*

Case study 2: Challenges of oral polio vaccines and VVM2

Overview

Oral polio vaccine (OPV) requires careful temperature management. Long-term storage is at -20°C, followed by storage for up to six months at 2–8°C. OPV carries the most restrictive vaccine vial monitor (VVM2); and laboratory studies show that OPV can lose up to 34% of its potency per day at 37°C, and even more when exposed to temperatures exceeding 45°C *(7,8)*.

Because OPV is central to global polio eradication efforts, countries must maintain robust cold chain systems, including installing and sustaining freezers and ensuring reliable electricity. Cold chain failures, particularly in hot climates, can cause vaccine degradation, resulting in up to 49% wastage. High wastage rates are often due to session-end losses and VVM endpoint expiration during campaigns *(9–12)*.

Many health facilities cannot maintain the strict cold chain requirements, so OPV vials are often stored at higher-level facilities with reliable freezers and power. From there, vials must be transported long distances to health facilities as well as being managed via carriers for hard-to-reach communities. These practices increase vaccine management and handling complexity; and create additional operational pressures for health workers *(13)*.

Key takeaways

- **Heat sensitivity drives operational complexity:** Vaccines that rapidly lose potency when exposed to elevated temperatures require careful monitoring and handling.
- **High wastage and programmatic burden:** Losses from VVM endpoint expiry and session-end wastage increase costs and complicate vaccine management.
- **Infrastructure and human resource demands:** Limited cold chain capacity necessitates central storage, complex transport and trained personnel, which ultimately increases workload and operational strain.
- **Access and equity considerations:** Reliance on central storage and long transport can slow vaccine delivery to remote areas, affecting coverage.

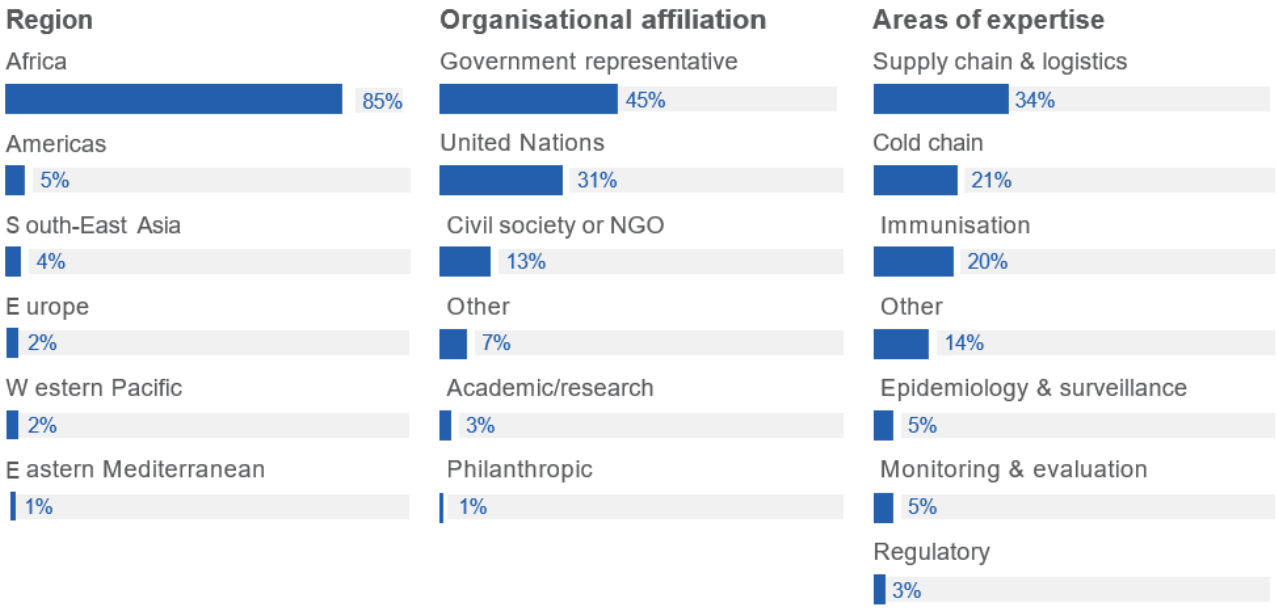
Country consultation results

Demographics

To better understand operational challenges and the relevance of vaccine heat stability, VIPS conducted a two-pronged consultation in 2023–2024, consisting of an online survey and stakeholder interviews with respondents across 33 countries. For additional details on the methodology, see Annex 1.

The consultation included 82 survey responses[6] and 14 in-depth interviews with key stakeholders in LMICs involved in national immunisation systems. The majority of the respondents were in 22 countries across the African region (85%), representing government agencies or departments (44%) or a UN agency (31%). The respondents were largely experts in immunisation supply chain and cold chain (63%). Figure 1 provides an overview of respondents' demographics.

Figure 1: Overview of demographics



6. Includes partial responses.

Key challenges related to heat stability and their consequences

Respondents reported moderate or significant challenges related to managing vaccines requiring UCC (61%), vaccines with -20°C requirements (50%), vaccines stored at 2–8°C (36%) and CTC (33%). The primary challenges reported included infrastructure and logistical issues, short and variable shelf life, and the impact on health workers' time management and workload, which ultimately contribute to reducing the ability to reach un- and under-immunised populations (Figure 2).

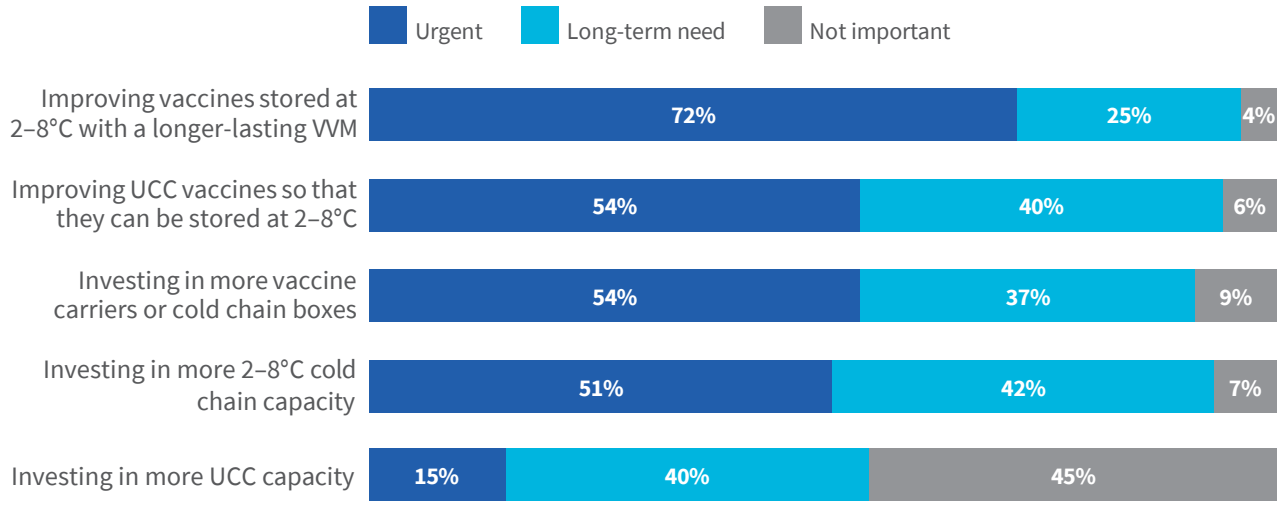
Figure 2: Key challenges identified and their potential consequences

		Potential consequences			
	Challenges	Unreliable vaccine availability	High discard rates from exposure or expiry	Increase in errors	Reduced coverage and equity
Health worker	Difficulty ensuring training and refresher training of health workers is completed		X	X	X
	Complexity in managing different temperature requirements across vaccines at national and sub-national levels		X	X	X
	Significant time requirements to manage cold chain logistics and excursions	X	X	X	X
Logistical	Insufficient supply of cold boxes and carriers	X	X		
	Delays in transportation (e.g. custom delays)		X		X
Product characteristic	Short and variable shelf life of vaccines	X	X		X
Infrastructure	Infrastructure vulnerabilities (e.g. power outages/fluctuations, insufficient power backup)	X	X		
	High maintenance cost for cold chain equipment	X			
	Inadequate cold capacity at various levels	X	X		X

Priority improvements for existing vaccines

When asked to prioritise improvements needed to address challenges, countries highlighted that **their most urgent need was for vaccines stored at 2–8° C** (the temperature at which most vaccines are stored) to have **longer-lasting VVMs**. This was closely followed by improving UCC vaccines to 2–8°C and investing in more cold chain equipment, including vaccine carriers and 2–8°C storage capacity (Figure 3). Because relatively few vaccines are stored under UCC conditions, respondents may have emphasised the need for 2–8°C with longer-lasting VVMs, which they viewed as offering greater overall benefit to their programmes.

Figure 3: Areas for improvements or investments to address identified challenges[7]



Potential trade-offs

The consultation also explored trade-offs that decision-makers might accept to obtain vaccines with improved heat stability. Respondents were asked to choose between: (i) an existing stability profile (e.g. UCC, -20°C, or 2–8°C with VVM2 to VVM14); and (ii) an improved stability profile with an associated trade-off (e.g. change from a liquid to a lyophilised format, 20% price increase or shorter shelf life).

Trade-offs for UCC-stored vaccines

Respondents showed a clear preference to eliminate UCC requirements. Eighty-seven percent preferred a 2–8°C vaccine with a six-month shelf life over a vaccine requiring UCC storage. The majority favoured moving away from UCC, even when the trade-off involved changing from a liquid to a lyophilised format (73%) or a 20% price increase (65%). Respondents indicated high energy demands, limited UCC infrastructure and poor integration with existing vaccine logistics as reasons for this preference.

7. The analysis prioritises UCC and 2–8°C storage, which account for the bulk of vaccine volumes and cold chain needs. Storage at -20°C is excluded given minimal demand and no material capacity gaps observed.

***Photo:** Temperature-controlled storage in Dakar, Senegal. © Gavi/Ollivier Girard*

By contrast, respondents were less willing to accept trade-offs for vaccines compatible with existing cold chain systems.

Trade-offs for vaccines stored at -20°C

Sixty-eight percent accepted a trade-off of shorter shelf life to remove the -20°C requirement; however, slightly fewer than half (49%) accepted a change in vaccine format from liquid to lyophilised or a 20% increase in the price (48%).

Trade-offs for vaccines stored at 2–8°C with VVM types 2–14

For a vaccine stored at 2–8°C with VVM 2–14 that could be changed to VVM30, 56% accepted the trade-off of changing from a liquid to a lyophilised format; and 54% accepted the trade-off of an increase in price to obtain VVM30.

Key takeaways on trade-offs

Overall, respondents were willing to accept trade-offs to eliminate UCC requirements because the perceived operational benefits were high. However, for -20°C and 2–8°C vaccines, respondents were less likely to accept trade-offs involving a price increase or more complex handling created by lyophilisation (Table 2).

Table 2: Acceptability of trade-offs for improved heat stability

Existing profile → improvement	Perceived operational benefit	Typical trade-offs tested	Approx. acceptance level	Conclusion
UCC → -20°C or 2–8°C[8]	Eliminates UCC infrastructure, power and logistics burden	Shorter shelf life	87%	Respondents are willing to accept trade-offs to remove UCC requirements.
		Lyophilisation	73%	
		20% price increase	65%	
-20°C → 2–8°C	Reduces freezer reliance; simplifies supply chain	Shorter shelf life	68%	Respondents are willing to accept a trade-off of shorter shelf life, but not trade-offs related to increasing complexity or cost.
		Lyophilisation	49%	
		20% price increase	48%	
2–8°C (VVM 2–14) → VVM 30	Extends usability but no major system change	Lyophilisation	56%	Respondents are less willing to accept trade-offs for a change in VVM type.
		20% price increase	54%	

8. The consultation did not explicitly provide information on the trade-off at -20°C; however, this information has been included considering discussions with countries and the VIPS partners.

Trade-offs explained

While improvements in vaccine heat stability are always important, achieving alignment on which trade-offs are acceptable to decision-makers and frontline implementers are critical.

At national levels, if heat stability improvements are introduced with unacceptable product attribute compromises, uptake and programme impact can suffer. Additionally, trade-offs that reduce health worker confidence, such as short shelf life, or low or restrictive VVMs, can lead to lower coverage, particularly among un- or under-immunised populations.

At global levels, poorly understood trade-offs can result in a misalignment of expectations regarding demand and supply. The implications for funders and manufacturers include: opportunity costs; and the inability to recoup research and development costs that can deter further investments, and weaken confidence in vaccine innovation.

Despite the good intentions of product developers, misaligned product attribute trade-offs may result in vaccines that have greater heat stability but do not achieve their intended benefits.

Case study 3: Rotavirus vaccine with VVM250

Overview

This case illustrates how vaccines with improved heat stability may not be widely adopted if they are more complex to manage than existing alternatives *(14–16).*

A lyophilised, heat-stable rotavirus vaccine with a VVM250 was developed to allow storage at 25°C for up to 30 days, providing flexibility outside the traditional cold chain.

Despite its strong safety, efficacy and stability profile, the vaccine differed from existing rotavirus vaccines and other routine vaccines administered in the same vaccination session, which are liquid vaccines. The heat-stable rotavirus vaccine was supplied in a lyophilised format, meaning it had to be reconstituted with a diluent and used within six hours of reconstitution. This added preparation time, and required careful and aseptic handling. Many LMIC settings often have ambient temperatures exceeding 25°C; thus, taking advantage of the heat stable characteristics (e.g. removing the vaccine from the cold chain and 2–8°C) would still require a separate cooling system. Health workers also required additional retraining to manage the dual-component storage and reconstitution process.

Consequently, the complex preparation, additional monitoring, specialised storage and retraining requirements limited the uptake of the vaccine *(17).* This experience highlights that improved heat stability alone does not guarantee successful implementation. Heat stability must be considered alongside programmatic trade-offs and the requirements of other available vaccines.

Key takeaways

Complexity limits adoption: Vaccines that are harder to manage may not be widely used, even if more heat-stable.

Dual-component handling increases workload: Reconstitution and specialised storage require extra training and supervision, and can offset any heat stability benefits.

Programmatic fit is critical: Vaccines must align with existing immunisation activities. Vaccines that have different handling or storage requirements can reduce uptake.

Conclusions

Greater heat stability in vaccines can help countries close immunisation gaps and achieve more equitable coverage. The consultation conducted by the VIPS partnership in 2023–2024 confirms that temperature-sensitive vaccines continue to impose constraints on vaccine access at the last mile, impacting outreach, logistics and health-worker capacity, particularly in fragile settings where cold chain reliability is lowest. Addressing these barriers requires designing vaccines with LMIC programmatic realities at the forefront, and with clear alignment between country needs and developers' and funders' priorities on desirable and achievable heat stability profiles.

Across countries, there is a consistent preference for future vaccines to achieve **2–8°C storage, VVM30 and at least 12 months' shelf life remaining upon delivery at the end-user level**, as these characteristics simplify logistics, reduce wastage, and support more flexible outreach to un- and under-immunised populations. While incremental improvements for existing products are valuable, countries' willingness to accept trade-offs varies.

Country acceptable trade-offs

- Countries are strongly motivated to eliminate UCC storage, even when this entails shorter shelf life, lyophilisation or higher cost.
- For -20°C vaccines, shorter shelf life is acceptable to move to 2–8°C, but countries were less willing to accept lyophilisation or price increases.
- For vaccines already stored at 2–8°C with VVM2–14, countries were less willing to accept lyophilisation or higher cost solely to obtain VVM30.

These findings highlight that **technical improvements must be paired with acceptable programmatic trade-offs** to achieve impact. Prioritising the attributes countries value most, and incorporating these preferences into preferred product characteristics and target product profiles, will help ensure that future investments translate into vaccines that are feasible to deliver, widely adopted and capable of advancing equitable access.

Photo: *Various vaccines inside temperature-controlled storage in Dakar, Senegal. © Gavi/Ollivier Girard*

Recommended actions

Stakeholders can use this overview of country challenges and preferences related to heat stability to more effectively develop and implement vaccines with improved heat stability:

For funders of vaccine development

- Ensure that LMIC-identified heat stability needs and acceptable trade-offs are incorporated in early stages of funded development.
- Continue funding evidence-generation on the impact and cost-effectiveness of heat-stable formulations.

For vaccine manufacturers

- Systematically integrate heat-stable characteristics and trade-offs important for LMICs early in product design.
- Where technically feasible, prioritise development of vaccines with 2–8°C storage, VVM30 and at least 12 months' shelf life.
- Avoid lyophilised formats unless they offer more programmatic or clinical advantages that justify the added complexity.

For policymakers and implementers

- Provide clear, consistent articulation of country heat stability needs and trade-offs through PPC and TPP.
- Ensure that cold chain infrastructure and maintenance systems are sufficient to support consistent 2–8°C storage, minimise temperature-related interruptions, and continue to document and share experiences and preferences from country programmes.

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Annex 1: Methodology for country consultations

This document draws upon data collected through the 2023–2024 VIPS country consultations on heat stability, which identified the key programmatic requirements for heat stability of vaccines from the perspective of LMICs.

To better understand the programmatic challenges caused by low vaccine heat stability and to identify priorities for improvement of existing vaccines, VIPS, through the Clinton Health Access Initiative, Inc. (CHAI) and PATH, conducted mixed-method consultations across 33 countries.

- **Survey:** An online survey was disseminated in English and French to national immunisation and logistics personnel, UN partners and technical advisers, and published on the TechNet 21 forum. Questions covered cold chain bottlenecks, perceived value of incremental thermostability improvements, acceptable trade-offs (e.g. cost, format, shelf life) and priority vaccines for heat stability improvement. Basic demographic information was also collected but not linked to individual responses.
- **Interviews:** In-depth interviews with country experts using a semi-structured interview guide were conducted to capture qualitative insights into operational realities and contextual nuances. Interviews explored vaccine handling, outreach logistics and the perceived impact of different levels of thermostability improvement.

Qualitative data was analysed thematically to identify recurring patterns, while quantitative survey data was analysed descriptively through the calculation of frequencies, percentages and mean values to summarise response distributions.