Forecast Report: Freeze-Safe Vaccine Carriers

MODELING THE POTENTIAL GLOBAL MARKET

FORECASTING COLD CHAIN EQUIPMENT NEEDS

A FIVE-PART PUBLICATION SERIES

PATH

Contents

All photos: PATH/Doune Porter

Understanding the cold chain landscape

Each issue of this five-part publication series leverages PATH's Installed Base and Forecasting Model to assess the potential global market for a specific cold chain equipment (CCE) innovation that can improve the storage, transportation, and delivery of vaccines in low-resource settings. This first issue focuses on freeze-safe vaccine carriers.

With support from Gavi, the Vaccine Alliance, PATH designed the Installed Base and Forecasting Model to understand and calculate existing and future CCE needs for all 73 Gavi-member countries. A straightforward analytical tool, the model can also assess existing and future CCE needs at regional and global levels.

All vaccines lose potency over time. As the rate of loss is temperature-dependent, the World Health Organization (WHO) recommends vaccine products be transported and stored between 2°C and 8°C. Maintaining this range from the point of manufacture to the point of administration requires a temperature-controlled supply chain or cold chain—a global distribution network of equipment and procedures for sustaining product quality (potency) during transport, storage, and delivery.

The first cold chain and related supply and logistics systems were developed more than 30 years ago as part of the Expanded Programme on Immunization (EPI), a WHO initiative that originally aimed to immunize at least 90 percent of the world's children against six deadly diseases. Since then, the EPI mandate has grown. EPI personnel in low- and middle-income countries are now working to accommodate nearly twice the number of vaccines as well as integrate a variety of essential medicines within their supply chains. Such increases reflect progress in product access and availability but are also straining supply systems.

Investments in CCE and system innovations have helped to facilitate improvements within some developing countries. In addition, multiple tools now exist to help public health program managers record equipment inventories or forecast needs. Yet the ability to understand and assess the global cold chain landscape has been lacking—until now.

The ability to understand and assess the global cold chain landscape has been lacking—until now.

Model and relevant formulas described in this report are available for use under Creative Commons licensing.

Overview of PATH's Installed Base and Forecasting Model

INTRODUCTION

The model uses a simple framework to assess CCE needs. First, it examines available CCE inventories to capture what CCE is currently in use at the national and subnational levels across three primary activities: storage, transportation, and outreach. These inputs establish the installed base portion of the model. Next, the model estimates each country's annual vaccine supply volume needs using information from two sources: the existing routine immunization schedule and planned vaccine introductions for the forecast year. This is the needs portion of the model. Finally, the installed base cold chain capacity is compared with volume needs to identify a surplus or shortage of capacity in the cold chain—generating the forecasting portion of the model. For countries with no data, the model calculates future capacity needs and assumes zero existing capacity. Capacity shortages are then aggregated at the country, regional, or global level and translated into equipment forecasts. To refine assumptions or prioritize specific areas of needs, each forecast can be further segmented by WHO or United Nations Children's Fund (UNICEF) region, Gavi country eligibility, or other filters. See Table 1.

TABLE 1: GOALS AND ACTIVITIES OF PATH'S INSTALLED BASE AND FORECASTING MODEL.

Assessment	Goals	Activities
By country	1. Understand what exists (installed base)	Assess current cold chain capacity across three primary activities: storage, transportation, and outreach.
	2. Calculate needs (annual volume)	Estimate vaccine supply volumes using routine immunization schedules and data on planned vaccine introductions.
	3. Forecast future needs	Compare data from steps 1 and 2 to identify capacity surplus or shortage by cold chain segment activity.
By country, region, or other	4. Calculate a needs-based cold chain equipment forecast	Aggregate capacity shortages across cold chain segments and countries.

SUMMARY OF CALCULATIONS

Derived from formulas commonly used for supply systems and equipment, below are the key formulas employed in the model's calculations of capacity, annual need, and future needs (needs-based forecast).

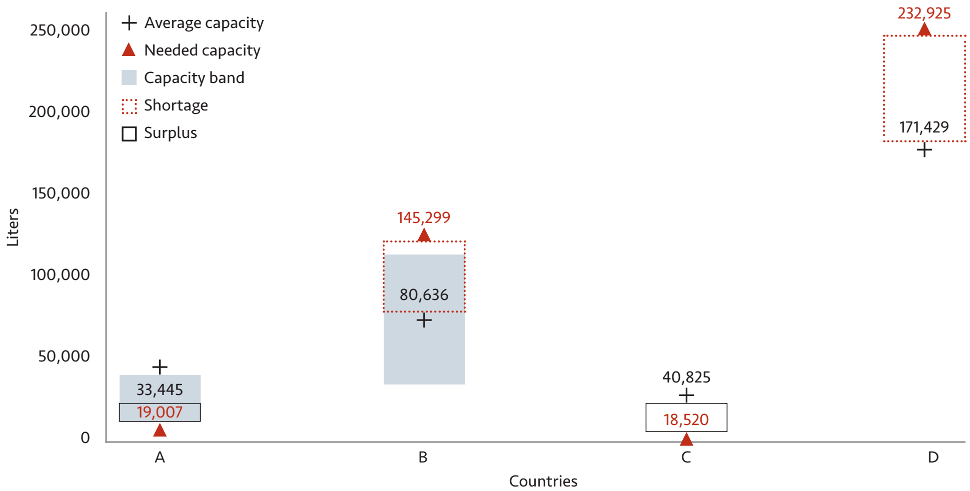
Capacity (installed base)

Leveraging the available CCE data for each country, calculate the country-level storage, transport, and outreach capacity using:

$$\text{Number of units} \times \text{equipment capacity}$$

Calculations for capacity are more accurate when they leverage CCE inventories that provide detailed information on equipment in use. When such information is not available, a range of lower-, average-, and upper-bound capacities (±) is calculated for each country, based on the minimum, average, and maximum capacities of equipment models within a class of technology. When detailed equipment data are not available, the average vaccine storage volume by equipment technology class is the default value. As better information is known about a country's installed base of equipment (e.g., make and model), capacity bands are "tightened" and become more accurate. See Figure 1.

FIGURE 1: STORAGE CAPACITY SHORTAGES AND SURPLUS IN FOUR EXAMPLE COUNTRIES.



Calculations derived using PATH's Installed Base and Forecasting Model are more accurate when model-specific inventory data are shared. When the data are not available, the model calculates capacity ranges, or bands, that can be "tightened" as more information becomes known. In Figure 1, upper- and lower-capacity bands are calculated for countries A and B, whereas countries C and D represent "high-quality data" scenarios that facilitate more accurate calculations. Overall, countries A and C show surplus capacity, and countries B and D show shortages.

Annual need (volume)

Calculate country-level vaccine volume using:

$$\text{Target population} \times \text{number of doses} \times (\text{packed vaccine volume} + \text{packed diluent volume}) \times \text{coverage rate} \times \text{wastage factor} \times \frac{1\text{ L}}{1{,}000\text{ cc}}$$

The target population generally comprises births or surviving infants but may also include a specific target population for a vaccine (e.g., school-aged girls for human papillomavirus). Global annual need is the summation of all country annual vaccine needs.

Future needs (needs-based forecast): by country

Calculate country-level estimates of capacity shortages or surplus across each cold chain segment using:

$$\text{Current capacity} - \text{projected capacity needed in forecast year}$$

Future needs (needs-based forecast): global

Aggregate capacity shortages across countries to generate a global needs-based forecast. In combination, these shortages convert to future equipment needs.

Forecast report: freeze-safe vaccine carriers

Modeling the potential global market for carriers that protect vaccines from the damaging effects of freezing temperatures.

HEALTH NEED

In low- and middle-income countries, temperature-sensitive vaccines are typically transported from subnational-level stores to rural clinics or health outposts in passively cooled cold boxes or vaccine carriers lined with chilled water packs, or conditioned or frozen ice packs, which enable outreach to remote populations but also increase the risk of product exposure to temperature extremes, particularly freezing temperatures (at or below 0°C).

For some vaccines, freezing temperatures are more damaging than heat. Especially vulnerable are liquid vaccines that contain alum adjuvants—an important class of ingredients that boost the immunogenicity of the vaccine antigen but also increase product sensitivity to freezing, particularly freeze-thaw cycles, which can irreversibly damage the adjuvant-antigen particles and compromise vaccine potency.

Studies of cold chain performance show that between 75 and 100 percent of vaccine shipments are exposed to freezing temperatures.[1-3] And the potential for these so-called cold chain "breaks" is highest in low-resource areas where power outages or gas shortages disrupt temperature controls, or when transportation in passively cooled cold boxes or vaccine carriers is required to reach remote populations.[4] When temperature damage is suspected, vaccines are often discarded at great cost to health care programs. When temperature damage and its effect on product potency go unnoticed, immunizations are jeopardized, potentially leaving vaccinated patients unprotected and vulnerable to disease.

GLOBAL POLICY AND PRODUCT GUIDANCE

For conventional carriers, current WHO policy recommends the use of cool water packs rather than frozen ice packs to prevent vaccine exposure to freezing temperatures along vulnerable segments of the cold chain. If ice packs are used, they must be conditioned or allowed to warm to 0°C.[5,6] Yet the conditioning of ice packs is not an exact science. Investigations reveal persistent vaccine exposure to freezing temperatures even when vaccines are stored and transported in a cold box or carrier lined with conditioned ice packs.[4,7,8]

To better protect product potency during transport, PATH developed a technology solution that creates a freeze-safe barrier between the ice packs and vaccines. Its freeze-safe design allows users to place a frozen ice pack, a conditioned ice pack, or a cool water pack within the carrier without risk of vaccine exposure to freezing temperatures. It also does not require additional steps to obtain vaccine freeze protection.

Vaccines—and lives—at risk

Approximately 70 percent of the vaccines procured annually by UNICEF are freeze-sensitive, totaling $70 million per year.[9] Exposure of these freeze-sensitive vaccines to extreme cold could result in a staggering loss of money and effort, and leave vaccinated patients unprotected from vaccine-preventable diseases.

WHO recently established Performance, Quality and Safety (PQS) standards for freeze-safe vaccine carriers. Such standards include product specifications that can help guide the development and manufacture of carriers that maintain appropriate cool life and product potency through the last mile of delivery. However, to maximize the programmatic impact of freeze-safe vaccine carriers, it is important to first understand the market—a precursor to any successful product introduction.

MODELING THE POTENTIAL MARKET

Using PATH's Installed Base and Forecasting Model, we combined the existing number of vaccine carriers (drawn from the installed base data of the 73 Gavi-member countries[†]) with the projected number of freeze-safe carriers needed to meet expanding needs due to projected population growth and/or additional vaccine introductions planned through the year 2020. Since current vaccine carriers do not have freeze-safe capabilities, the replacement of installed base units assumes a 1:1 ratio of conventional carriers to new freeze-safe carriers. The number of additional freeze-safe vaccine carriers needed was calculated using a scenario analysis that leveraged key assumptions on the percentage of routine immunizations administered via outreach activities and the frequency of these outreach activities per supply cycle.

To determine capacity surplus or shortage, PATH applied these same assumptions to each country's vaccine volume needs for the forecasted year's immunization schedule and then compared the assumptions to each country's existing outreach capacity. Our findings are captured in Table 2.

Outreach need formula

To determine outreach needs across countries with dissimilar outreach strategies, we generated scenarios based on outreach percentage and frequency data from several PATH studies (unpublished). We then applied the average volume shortage from the scenarios (see Table 2) to the forecast:

$$\text{Annual need} \times \%\ \text{immunization via outreach} \times \frac{1}{\text{frequency}}$$

TABLE 2: NUMBER OF UNITS NEEDED BASED ON A 1.8 LITER CAPACITY VACCINE CARRIER.

	Lower-bound outreach	Average outreach	Upper-bound outreach
Lower-bound frequency	197,459	455,750	720,795
Average frequency	364,947	825,884	1,310,357
Upper-bound frequency	642,925	2,213,685	2,213,685
Outreach	Percentage of immunizations administered via outreach activities		
	25%	50%	75%
Frequency*	Number of times a device is used between replenishment periods		
	6.75	4	2.48

*Higher frequency of use results in more vaccines transported per carrier.

† Data used in the model are derived from the most recent comprehensive multiyear plans (cMYPs) available, which range from 2005 to 2014 with a majority from 2010. The data will be updated as new cMYPs become available.

TOTAL MARKET FORECAST

We aggregated net outreach capacity shortages to determine outreach capacity needs at the global level. To obtain the forecast, we divided global capacity by the average vaccine carrier size (1.8 liters) to determine the number of freeze-safe carriers needed. See Table 3.

TABLE 3: TOTAL MARKET FORECAST FOR 2020.

Number of freeze-safe vaccine carriers needed	825, 884
Number of non-freeze-safe vaccine carriers in use and needing replacement	+ 1,520,747
Total forecasted market for freeze-safe vaccine carriers	2,346,631

Potential market value for freeze-safe vaccine carriers in 2020	**US$117 million**

To calculate the market potential for all 73 countries by 2020, we applied an anticipated price of US$50 per freeze-safe vaccine carrier to the installed base and forecasted units.

References

1. Matthias DM, Robertson J, Garrison MM, Newland S, Nelson C. Freezing temperatures in the vaccine cold chain: a systematic literature review. *Vaccine*. 2007;25(20):3980–3986.
2. Nelson C, Froes P, Dyck AM, Chavarría J, Boda E, Coca A, Crespo G, Lima H. Monitoring temperatures in the vaccine cold chain in Bolivia. *Vaccine*. 2007;25(3):433–437.
3. Nelson CM, Wibisono H, Purwanto H, Mansyur I, Moniaga V, Widjaya A. Hepatitis B vaccine freezing in the Indonesian cold chain: evidence and solutions. *Bulletin of the World Health Organization*. 2004;82(2):99–105.
4. Murhekar MV, Dutta S, Kapoor AN, et al. Frequent exposure to suboptimal temperatures in vaccine cold-chain system in India: results of temperature monitoring in 10 states. *Bulletin of the World Health Organization*. 2013;91(12):906-913.
5. World Health Organization (WHO). How to use passive containers and coolant-packs for vaccine transport and outreach operations. *In: Vaccine Management Handbook*. Geneva: WHO; 2015:1.
6. WHO. Aide-Memoire for Prevention of Freeze Damage to Vaccines. Geneva: WHO; 2007. Available at: www.unicef.org/supply/files/Total_vaccine_doses_procured_1996-2014.pdf
7. Samant Y, Lanjewar H, Parker L, Block D, Stein B, Tomar G. Relationship between vaccine vial monitors and cold chain infrastructure in a rural district of India. *Rural Remote Health.* 2007;7(1):617.
8. Wirkas T, Toikilik S, Miller N, Morgan C, Clements CJ. A vaccine cold chain freezing study in PNG highlights technology needs for hot climate countries. *Vaccine*. 2007;25(4):691–697.
9. PATH, WHO. Above Zero: Strategies to Prevent Vaccine Freezing [online video]. Seattle: PATH, WHO; 2013. Available at: www.path.org/media/above-zero.php

For more information

PATH's work in vaccine and pharmaceutical technologies extends across three technical focus areas: product formulation and stabilization, delivery devices and packaging, and supply systems and equipment. We advance product and system innovations that reduce costs, ease logistics, improve safety, expand coverage, and maximize public health impact in low-resource settings.

For more information on our work and potential partnering opportunities, please contact us at **vxpharmatech@path.org**.

ABOUT PATH

PATH is a leader in global health innovation. An international nonprofit organization, we save lives and improve health, especially among women and children. We accelerate innovation across five platforms—vaccines, drugs, diagnostics, devices, and system and service innovations—that harness our entrepreneurial insight, scientific and public health expertise, and passion for health equity. By mobilizing partners around the world, we take innovation to scale, working alongside countries primarily in Africa and Asia to tackle their greatest health needs. Together, we deliver measurable results that disrupt the cycle of poor health.

CREATIVE COMMONS LICENSE

Copyright © 2015, PATH. The material in this document may be freely used for educational or noncommercial purposes, provided that the material is accompanied by an acknowledgment. This work is licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view a copy of this license, visit creativecommons.org/licenses/by-nc-nd/4.0/. All other rights reserved.

PATH

November 2015