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Optimizing presentation and packaging for HPV vaccines

by Debbie Kristensen and D. Scott LaMontagne, PATH

Working in collaboration with the [Vaccine Presentation and Packaging Advisory Group \(VPPAG\)](#), representatives from the public health community have initiated a series of studies to guide presentation and packaging decisions for future iterations of human papillomavirus (HPV) vaccines destined for low-income countries. Presentation and packaging decisions, such as the number of doses per container, type of container, and recommended storage temperatures greatly impact the way vaccines are handled, the quantity of vaccine doses wasted, and the ability of health workers to get the vaccines to remote, low-resource settings. By influencing these decisions early in the development process, public health officials can make sure that the specific needs of developing countries are considered.

HPV vaccines present unique characteristics that differentiate them from current World Health Organization (WHO)-prequalified infant vaccines. HPV vaccines target an older, gender-specific population; are currently available at higher prices than most existing WHO-prequalified vaccines; offer promising heat-stability profiles; and similar to pneumococcal vaccines, are currently available only as liquid formulations, in one- and two-dose vials, without preservative.

The following are a list of studies recently initiated to gather data from users, procurement specialists, and economists to better understand needs and constraints regarding HPV vaccines:

- A retrospective, cross-sectional analysis of data on vaccination session size from three HPV vaccine demonstration projects in Uganda, Peru, and Vietnam.
- A small-scale, time-and-motion study to assess the time and ease of vaccine delivery across different HPV vaccine presentations.



Adolescent girls in Uganda await vaccination with HPV vaccines.

PATH/ Robin Biellik

- Documentation of ambient temperatures experienced during the final stages of HPV vaccine distribution and use in Vietnam and Uganda to assess the feasibility of controlled ambient temperature storage and transport.
- Surveys with immunization program managers and health workers in Vietnam involved in the HPV vaccine demonstration project to sample preferences for HPV vaccine presentation, packaging, and logistics. (Note: similar surveys may also be conducted in Uganda and Peru).
- Breakeven analysis of potential price, wastage, and cold chain costs for various HPV vaccine presentations using the [Vaccine Presentation Assessment Tool](#).
- Analysis of qualitative data from questionnaires that assess individual experiences of those involved in HPV vaccine demonstration project activities in Uganda, Peru, and Vietnam.

The VPPAG will compile the results of these studies and additional data available from industry into a preferred product profile for HPV vaccines describing characteristics, including optimal vial size, presentation, and storage temperature requirements, for future HPV vaccines for use in developing countries.

Increasing the acceptable temperature range for certain vaccines

by Michel Zaffran, WHO; Julie Milstien, consultant; and Modibo Dicko, WHO

It has long been known that [certain vaccines](#) are stable for long periods of time at temperatures outside the standard cold chain protocol of 2° to 8°C. However, until recently, there have been few reasons to consider changing the relatively simple, blanket policy that all vaccines need to be stored between 2° and 8°C. The only exceptions have been occasional “off-label” [use of some vaccines](#) for immunizing hard-to-reach populations, such as “out-of-cold-chain” use of hepatitis B vaccine birth dose; use of tetanus toxoid in pregnancy, just before delivery; and the use of oral polio vaccine with or without cool water packs during campaigns.

A change in the vaccine storage temperature policy is not easy. It requires a great deal of evidence gathering, licensing and regulatory changes, and careful consideration of the programmatic impact of the change for countries. Depending on the country, such a change may merit new equipment, training, and monitoring to ensure that the new policy is followed correctly and consistently for all applicable vaccines.

However, despite the challenges in doing so, a policy change is becoming increasingly necessary for the following reasons:

- Temporarily removing vaccines from the traditional cold chain is often the only way to provide on-time immunizations to those who are hardest to reach.
- A large amount of relatively costly vaccines are currently being exposed to freezing temperatures that can damage them.
- Newer vaccines are much bulkier and much more costly than traditional Expanded Programme on Immunization vaccines. Under the current policy the only way to accommodate new vaccines is to build new cold rooms, buy bigger coolers, and require health workers to carry heavier cold boxes.

Because several vaccines are quite stable at temperatures above 40°C for months at a time, refrigerating these vaccines at all times is unnecessary, potentially harmful (due to accidental freezing), and a waste of precious resources.

The World Health Organization (WHO) and PATH, through project Optimize, are collaborating with manufacturers, regulatory bodies, countries, and a programmatic working group to take steps toward new policies that allow for vaccines to be handled in a “[controlled temperature chain](#)” where certain heat-stable vaccines can be stored at controlled temperatures that are outside of the traditional 2° to 8°C cold chain. To achieve this change, work is ongoing in three streams:

1. Define the regulatory pathway. The process begins by gathering evidence to understand precisely how higher temperatures may impact vaccine potency and delivery in real-world situations for each heat-stable vaccine. A study of this nature is currently underway with the hepatitis B vaccine. This particular vaccine was chosen for its well-known stability to heat and for the need to reach infants as soon as possible after birth. Positive results from this study will facilitate relabeling the vaccine for its true heat-stability profile, thus giving countries the option to implement new outreach strategies by using the vaccine within a broader, yet controlled temperature range.

2. Gather more country-level evidence. Country-level evidence can further confirm vaccine temperature stability in real-world settings, thus contributing to the evidence base upon which regulatory issues are decided. It will also generate critical data that will help inform and develop implementation strategies.

3. Provide programmatic guidance. A programmatic working group has been convened to discuss and develop programmatic guidelines for countries to follow should they consider adopting new temperature policies for specific vaccines.

When the licensing, regulatory, and programmatic requirements are met, then WHO will be in a better position to consider changes to the blanket temperature storage policy to accommodate different handling requirements for heat-stable vaccines under controlled temperatures.

When is a new policy likely to be developed? The hepatitis B study, which will help define the regulatory pathway for a policy change, is ongoing. Results of the laboratory testing are expected by early 2010. If the results are positive, a change in the regulatory license for relevant hepatitis B vaccines could be proposed to allow storage and transport beyond the traditional 2° to 8°C range. However, this is only a first step. Ideally, all vaccines would be licensed to their true stability. While some vaccines will need to remain in the 2° to 8°C range, others will be able to be handled in a broader controlled temperature range, giving countries increased flexibility to deal with an increasing number of vaccines.

Albania explores computerized immunization registries

by Jan Grevendonk, PATH; and Olivier Ronveaux, WHO

In early 2009, the Albanian Institute for Public Health (IPH) asked Optimize, a WHO-PATH collaboration, to develop a strategy for a computerized national immunization registry and vaccine ordering system.

Working with IPH and other large stakeholder groups, Optimize assessed the existing paper-

based system this summer and developed a strategy for implementing a small-scale pilot under IPH management in one district (Skodra).

In Albania, health workers are expected to record vaccinations for children in their catchment area on five different paper records. In order to determine vaccine orders, these records are compiled at the end of each month into two different reports that are aggregated at the district and national levels. The existing system, while functional, places a tremendous administrative burden on health workers and does not provide enough detail about populations that could be falling through the system's cracks.

The benefits of an online centralized registry linked to vaccine ordering are potentially enormous. Most importantly, a central registry would allow health workers to accurately track each child's vaccinations even if that child moves between catchment areas. The system could also facilitate more accurate forecasting and improved inventory records of the vaccines needed in each area of the country.

The success of the pilot will be measured by how well it can:

- Improve the quality of the monitoring system for immunization coverage by providing access to more accurate and more relevant disaggregated data at the central level in a more timely fashion.
- Increase ordering accuracy—using the information collected through the immunization registry, vaccine inventory and wastage can be better assessed enabling the right quantity of vaccines, diluents, syringes, and safety boxes to be available at each level of the system. This could possibly reduce the need for buffer stocks.
- Decrease the administrative burden on health workers.

The proposed system will integrate the immunization registry with the functionality of the basic logistics management information system. In the future, the two functions can be integrated further and expanded to accommodate other applications such as disease and adverse events following immunization surveillance.

Albania, like many lower-resource settings, has varying levels of access to consistent electricity, internet access, and mobile-phone service. The pilot will therefore use a combination of three modes of communication: internet access with personal computers at the national and district levels as well as in large health centers; mobile phone access in other health centers and village outposts; and paper-based access in areas without access to mobile technology.

The pilot system will roll out in mid-2010 with the goal of expanding the program nationally after evaluating and revising the pilot system.

Fee-based immunization in Vietnam—what can we learn?

by Dai Hozumi; PATH, and Nguyen Van Cuong, NIHE

While most people in Vietnam receive traditional Expanded Programme on Immunization vaccines free from government-run clinics and health centers, many others elect to receive these and other immunizations for a fee from private and public medical providers. Understanding the extent and quality

of these fee-based services and the reasons families prefer them can help the government improve regulatory oversight of private providers and perhaps improve both public and private provision of immunization services by sharing information between them.

Working with the Vietnam National Institute for Hygiene and Epidemiology (NIHE), Optimize is launching a fee-based immunization services assessment to (1) understand the extent of fee-based immunization service delivery practices and related vaccine supply practices; (2) document government policies, regulations, guidelines, and enforcement mechanisms related to fee-based immunization services; and (3) identify potential mechanisms and interventions to improve regulatory processes and capability of fee-based immunization services.

The assessment will include a literature and document review, key informant interviews at the national level, provider surveys, interviews with patients, and a mapping exercise of the private-sector vaccine supply chain. When analysis is complete in early 2010, Optimize and NIHE will develop a set of recommendations for the government.

This assessment, combined with the country's first effective vaccine management assessment launched in September, will help the government identify areas of strength and weakness in its vaccination services and point toward areas where further investment and capacity building are needed.

Managing cold chain equipment is getting easier

by Sophie Newland, David Lubinski, and John Lloyd, PATH

Introducing newer, bulkier vaccines into a national immunization schedule can be a tricky job for logisticians. Is there enough space? Is there enough equipment? Is it in the right location? Is the equipment functioning properly? All immunization programs depend on reliable and sufficient refrigeration equipment to cool vaccines during transport and storage, but managing that information can be a daunting task.

In an effort to help countries more accurately establish and maintain cold chain equipment inventories and forecast future equipment needs, PATH and the United Nations Children's Fund (UNICEF) collaborated in 2008 to create a software tool called [Cold Chain Equipment Manager \(CCEM\)](#). CCEM is a free, fast, accurate and easy-to-use Microsoft Access-based package designed to help countries create a comprehensive inventory of cold chain equipment and forecast future cold chain equipment needs according to planned changes in vaccines, schedules, and the target population.

A new version of the CCEM software tool, developed by PATH, is scheduled for release in January 2010.

The focus of the latest development is to make the application even easier to use and speed the process of creating reports and forecasts. To update the tool PATH partnered with iLink Systems, a professional software engineering firm, to apply best practices in user-driven software design.

Critical priorities addressed in version 2.1 will allow users to:

- **View key performance indicators** across geographic regions and drill down for deeper analysis.
- **Forecast future equipment needs** for each year of a [multiyear plan](#), considering changes in vaccines and vaccine schedules, growth in target populations, and removal and allocation of equipment according to national policies.

- **Easy comparison of overall capital and running costs** of different forecast scenarios according to different assumptions on the future plans.

The goal of the CCEM tool remains the same: to help managers quickly and accurately forecast costs of equipment needed for multiyear national immunization plans. As more vaccines become available and affordable to low- and middle-income countries, the need to accurately plan, manage, and track cold chain equipment is increasingly critical. This tool helps countries anticipate needs and monitor performance with minimal effort.

The new version of the CCEM tool and related documents are scheduled to be tested in Kenya in January 2010 and will be available soon thereafter for download in English, French, and Spanish from the PATH website at www.path.org/projects/cold-chain-ccem.php. To obtain a CD containing all CCEM materials, please email publications@path.org.

What's your vision for vaccine logistics?

On November 19 and 20, 2009, two panel discussions at the [GAVI Partner's Forum](#) in Hanoi will discuss, "What does it take to design an innovative supply system?" We invite and encourage you to participate in this session at the forum. Afterward, we will post a [summary of the session](#).

What's in a name?

Thanks to your feedback the term "controlled temperature supply chain" is now being used to describe storing and transporting vaccines beyond the 2° to 8°C temperature range. A summary of the decision-making process is available in the [TechNet library](#).

Literature review of vaccines used in a controlled temperature supply chain

A growing body of research is available to help policymakers evaluate the possibility of storing and transporting heat-stable vaccines in a controlled temperature supply chain. This [literature review](#) identifies research available as well as gaps in research needed to advance a policy for storing and transporting hepatitis B vaccine in a wider controlled temperature environment.

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Batiment Avant Centre, 13 chemin du Levant
Ferney Voltaire 01210 FRANCE
+33 450 28 43 75 | technet21.org
who.int/immunization_delivery | path.org/vaccine-delivery.php



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