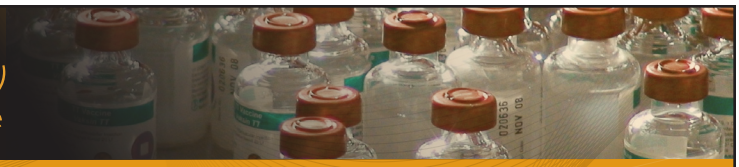
OP • TI • MIZE *(transitive v.)*
To make as effective or functional as possible



Issue 8, April 2011

Contents

Dear Colleagues,

In continuation of our thematic exploration of the essential characteristics of future immunization supply systems, this newsletter focuses primarily on tenet 3 of the draft global vision: "*The environmental impact of energy, materials, and processes used in vaccine distribution systems at the national and international levels is monitored and minimized.*"

As readers will see, much work around environmental impact dovetails nicely with other tenets that call for efficiency and effectiveness of supply chain solutions.

Today's growing global concerns around environmental issues and the increasing cost of air and road transport and fuels make it imperative that these aspects be carefully considered throughout immunization programs and their supply systems.

As usual, we invite your comments and questions and encourage you to share information on the work that you are doing in these areas. We also encourage you to reach out directly to authors to learn more about their work.

Sincerely,
Michel Zaffran
Director, Project Optimize

Labeling vaccines to reflect their true heat stability

by Simona Zipursky, PATH; Christoph Conrad, WHO/Quality, Safety & Standards; Tony Richardson, CDC/ Vaccine Supply & Assurance Branch

Photo: Bill & Melinda Gates Foundation

Horsemen carry rotavirus vaccine to remote health posts in Nicaragua.

They call it the Decade of Vaccines for a reason. More new vaccines will become available between 2010 and 2020 than all previous decades combined. Not only that, these vaccines will reach new target groups at different stages of life and in more remote geographic areas. While still among the most cost-effective of all public health interventions, these newer vaccines are more expensive and better suited to single-dose presentations, both to avoid waste and minimize the need to reformulate with preservatives. The requirement to store these vaccines between 2°C to 8°C means that low-resource countries, which stand to benefit enormously from increased access to lifesaving vaccines, must stretch limited financial, human, and capital resources to safely manage the distribution of these vaccines—including dealing with tropical temperatures, impassable roads, long foot trails, and unreliable electricity.

Historically, it has been prudent to maintain a single global policy regarding temperature management of vaccines. Until very recently, every country in the world has been instructed to keep all vaccines between 2°C and 8°C at all stages of the supply chain past the central level. But maintaining such a narrow temperature range is difficult. Vaccines are often damaged through accidental freezing, requiring health workers to discard vaccines that are exposed to temperatures below 0°C. In reality, however, many vaccines are or could be highly stable at temperatures up to 37°C, and laboratory tests have shown that some remain stable at this temperature for as long as six months without a significant impact on potency.

Supporting countries to safely transport specific, heat-stable vaccines at higher temperatures for limited excursions will not only prevent accidental damage by freezing, but enable health workers to reach the most remote communities, even when electricity or ice packs are not available. Several countries have demonstrated the feasibility of such an approach. Indonesia, for example, has demonstrated how to reach infants with a birth dose of hepatitis B vaccine by allowing midwives to carry vaccines the last few miles of the last few days of the supply chain without ice packs. Studies like these are promising but are still just that—small-scale studies and pilot projects. Global policy change will not occur unless manufacturers are willing to work collaboratively with the public sector to label vaccines to reflect their true heat and freeze stability.

Developing countries are not alone in their need for more flexible vaccine temperature requirements for heat-stable vaccines. Despite comparatively less extreme environmental conditions, industrialized countries are also interested in a controlled-temperature supply chain. The US Centers for Disease Control and Prevention (CDC) has formed an international vaccine stability working group to discuss

the possibility of expanding temperature control guidelines with manufacturers. At the request of the provincial health authorities, vaccine manufacturers have submitted to Health Canada changes to product inserts for some vaccines so that labels include information regarding higher-temperature storage. This review has led to changes in the labels of certain vaccines, such as VAQTA®, a vaccine that protects against hepatitis A, manufactured by Merck Frosst. While VAQTA®'s label in most countries, such as the United States, stipulates that it must always be stored between 2° to 8°C, it reads differently in Canada:

> Store vaccine at 2° to 8°C (36° to 46°F).
> **Do not freeze (below 0°C) since freezing destroys potency.**
> VAQTA® can be administered provided total (cumulative multiple excursion) time out of refrigeration (at temperatures between 8°C and 25°C) does not exceed 72 hours. Cumulative multiple excursions between 0°C and 2°C are also permitted, as long as the total time between 0°C and 2°C does not exceed 72 hours. These are not, however, recommendations for storage.

WHO's quality, safety and standards team, which is responsible for reviewing and prequalifying all vaccines procured through the United Nations system, is currently also reviewing the data available on the true stability of the vaccines in its system that have revised labels in Canada. This review aims to see how the true stability of vaccines and guidance on cold chain excursions can best be supported in developing countries, building on the learning and work of Health Canada. These changes to the product inserts are a step in the right direction but as of yet do not endorse what developing countries are hoping for—the ability to store vaccines out of the cold chain for limited periods of time.

Last year, the CDC's International Vaccine Stability Work Group created a subgroup on stability data and temperature control guidelines to discuss the issue with manufacturers. Representatives from Health Canada, the CDC, the US Food and Drug Administration, PATH, and the World Health Organization had a preliminary discussion in October 2010. A second meeting has been scheduled for November 2011 to share more about the risks and opportunities of new labeling standards.

As part of this work, we are seeking input from countries and partners on their experiences of using vaccines in a controlled temperature chain. We are also interested in thoughts and experiences with the controlled temperature chain approach including how and where it can be used for maximum impact.

Solutions to the waste management conundrum

by Yves Chartier, WHO, and Olga Popova, Crucell

Worldwide immunization programs have had an enormously positive impact on health and health care since 1974 when the World Health Assembly launched the Expanded Programme on Immunization. However, like all great achievements the effort has unveiled new challenges. One of the most serious has been the re-use of syringes without adequate sterilization. As this issue came to light in the 1950s, disposable syringes were developed to resolve the problem. Unfortunately, they did not, and the rise of HIV/AIDS and hepatitis B and C transmission raised the issue into an even greater sphere of concern. The late 1980s brought the successful development and deployment of autodisable syringes, which are now in widespread use in immunization programs. And while autodisable syringes have considerably reduced re-use and contamination issues—at least within the relatively narrow confines of immunization programs—their use has given rise to an associated concern, how to manage injection-related waste.

Improper management of injection-related waste can have both direct and indirect health consequences

for health personnel, community members, and the environment. Direct consequences of improper waste management arise when disposable materials (especially syringes) are intentionally re-used. The transmission of hepatitis B and C and HIV represent the main disease burden caused by inadequate management of injection-related waste. Unintentional injuries may also occur when people mishandle or are exposed to inadequately disposed waste, for example through scavenging on waste sites.

Indirect health effects can arise from environmental pollution in the form of toxic emissions from inadequate burning of medical waste or in the sheer volume of waste generated in a short period of time. For instance, a countrywide mass immunization campaign will produce millions of used syringes in a period of three to four weeks. This requires appropriate options and a well-prepared strategy defined months before the campaign starts.

A variety of technologies have been developed to aid in the safe storage, collection, treatment, and disposal of health care wastes. Several types of treatment and disposal processes, such as incineration, microwave or chemical treatment, and melting have been applied in health care settings with varying degrees of safety, cost, and impact on the environment. However most are geared toward industrialized country settings. None of the available low-cost treatment devices (i.e., below US$500) on the market are both safe and environmentally friendly. In developing countries, a trade-off has to be made between direct health risks resulting from the absence of a waste management strategy, and indirect health risks created by environmental pollution (e.g., by production of dioxins from inadequate incineration).

Despite the difficult tradeoffs in waste management approaches, countries are better off with a waste management strategy than without one. Some countries have made significant improvements by adopting purchasing policies that consider the waste stream and/or by isolating and treating the most harmful segments of the waste.

Photo: Crucell

This prototype packaging configuration from Crucell would hold ten prefilled Unijects in a single pouch.

At the global level, vaccine manufacturers and injection equipment suppliers are also seeking solutions. Crucell, for example, is adopting a holistic approach to its pentavalent vaccine, looking for solutions that can meet the needs of complex, developing-country environments. First, it changed its formulation from lyophilized to liquid, thus reducing opportunities for reconstitution errors, eliminating multiple procedural steps, shortening the vaccination session, shrinking storage needs, and minimizing waste. Next, it offered the vaccine in single-dose vials, thus reducing vaccine wastage, eliminating the need for preservatives, and minimizing the possibility of contamination. Recently it has begun to explore the feasibility of offering liquid pentavalent vaccine in the Uniject™[1] injection system, a plastic, compact, prefilled, autodisable system. Belying its big name, Uniject is nothing more than a small bubble of plastic attached to a needle. It is precisely prefilled with a single dose by manufacturers, thus eliminating vaccine wastage or improper dosing. It is so easy to use that health workers need a scant two hours of training before successfully using it. From a waste-management perspective, Uniject cannot be reused, thus minimizing the threat of disease transmission. It contains only about 35 percent of the plastic of a standard disposable syringe, and the type of plastic used in Uniject can be incinerated without generating toxic fumes (unlike those produced by syringes with a rubber piston).

1. Uniject is a trademark of BD.

By testing and seeking solutions such as these, pharmaceutical companies like Crucell can ameliorate some of the health care waste management problem countries face. Ultimately, the waste management conundrum must be addressed at all levels, from upstream technology development to downstream waste minimization and management, to ensure that health care can be delivered without side effects on health care workers, communities, or the environment.

Solar is getting hotter

by Steve McCarney and Joanie Robertson, PATH

Many health facilities in remote areas operate without grid electricity, have unreliable electricity, or find that using electricity is too costly. In these settings, solar energy is a promising solution for powering the storage and transportation needs of vaccines and heat-sensitive drugs at controlled temperatures. Project Optimize has been collaborating with public and private partners on several solar technologies tailored to local electrical power conditions: unavailable or unreliable power, intermittent power, and reliable power.

Unreliable power

When electricity is available less than four to eight hours on average per day, it becomes very difficult to rely on electric refrigerators for vaccine storage. While kerosene- or gas-fueled absorption refrigerators are one option, they are difficult to maintain at proper temperatures, require significant maintenance, are not energy efficient, contribute to global warming, and the fuel is often diverted to other uses.

An alternative option that has been in use for over 30 years is solar-powered vaccine refrigerators. Until recently, the refrigerators available in this class were essentially first-generation design, using photovoltaic (solar) modules that recharge a high quality, industrial battery system to store solar energy for use during night and poor solar weather conditions. While successful solar refrigeration projects of over ten years have been reported, many have suffered from battery system failures. If battery replacement is not anticipated or funding is unavailable, then the entire vaccine refrigeration system fails. Optimize has been encouraging companies to improve the reliability and life of solar-powered vaccine refrigeration.

Lifetime battery refrigerators in Vietnam

A “lifetime battery” is a battery that can outlast the 10- to 20-year lifetime of the refrigerator or the 20+ year lifetime of the solar module. New battery technologies (e.g., lithium) developed for the growing electric and hybrid vehicle market appear promising in solar refrigeration applications. This innovation decreases battery maintenance and disposal burden for health centers while hopefully eliminating battery replacement entirely. Vietnam is currently piloting the use of lifetime batteries in refrigerators at two government health centers on Cat Ba and Cat Hai. This PATH Health Innovations Portfolio project is principally funded by the Bill & Melinda Gates Foundation with support from Optimize and collaboration with Hai Phong Medical University.

Solar direct-drive vaccine refrigerators in Vietnam and Senegal

The latest generation of solar refrigerators has solved the problems of the external battery by doing away with it all together, connecting solar panels directly to the compressor driving the refrigeration cycle. In 2010, the first solar direct-drive vaccine refrigerator was prequalified by WHO, meeting a new set of Performance, Quality and Safety (PQS) standards for solar direct-drive refrigerators. Instead of storing electrical energy in a battery, these direct-drive refrigerators use cool storage (i.e., an “ice battery”) hidden in the refrigerator cabinet to maintain vaccine temperatures between the required +2º to +8ºC.

At night or during prolonged cloudy, rainy weather, the well-insulated cool storage maintains acceptable temperatures for many days.

Senegal and Vietnam are conducting demonstration projects of solar direct-drive battery-free refrigerators

Photo: (Left & far right) Vestfrost (Denmark) SolarChill direct-drive refrigerator. (Center) PATH/Carib Nelson

A small solar array of 180 watts can power this solar direct-drive vaccine refrigerator.

in health facilities. Field demonstration of 15 WHO PQS prequalified solar refrigerators is taking place at health posts in Senegal's Podor and Pete districts. In Vietnam, a solar direct-drive refrigerator is being tested at a health center in Thanh Phu district (Ben Tre province) in the south of Vietnam and the Thanh Ba district (Phu Tho province) in the north.

Intermittent power

With intermittent power conditions, electricity shortages result in frequent interruptions and sudden reestablishments of power. In places where grid electricity is not reliable, diesel back-up generators are needed to ensure an energy supply to refrigerators. However, generators are costly to operate, difficult to maintain and repair, create air and noise pollution, and the fuel supply is subject to disruptions and may be diverted for other uses.

Photo: True Energy (UK) long-life ice-lined refrigerator

In Senegal, grid electricity is being used for super long-life ice-lined refrigerators while solar energy provides backup for other essential needs during grid power outages.

Hybrid solar and electric refrigeration in Senegal

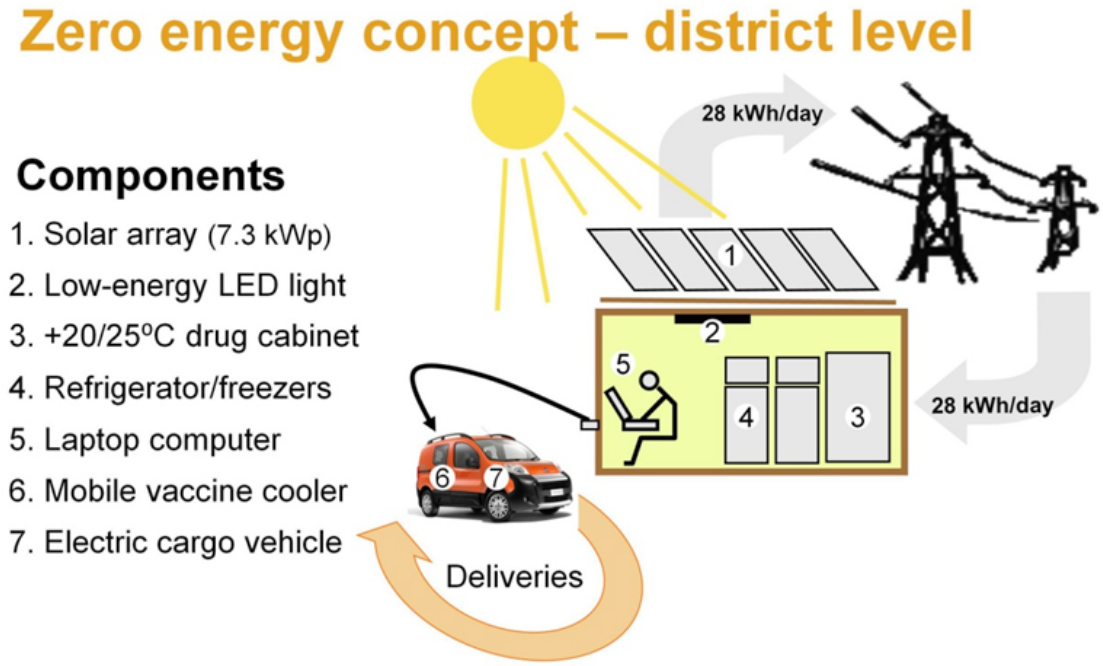
Senegal benefits from excellent solar radiation, but solar energy is not exploited because of the high initial equipment costs. Meanwhile, grid electrical power outages are common in Senegal. Fortunately, solar power system costs

are decreasing, making a solar and electric grid hybrid system an attractive alternative where diesel-fueled back-up generators traditionally have been used.

The Senegal Department of Preventive Medicine is working with project Optimize to explore ways to improve reliability, acceptability, and efficiency of solar energy in powering the cold chain at regional and peripheral levels. The team is installing a hybrid solar and grid electric power system at the Regional Supply Pharmacy in St. Louis. In addition, new ice-lined refrigerators have become WHO PQS prequalified, demonstrating over ten days of sustained vaccine temperature control without any power, even in the hot climate of Senegal. Grid power will be used for these super long-life ice-lined refrigerators while solar electricity backs up other critical loads like freezers, lights, and computers.

Reliable power

Locations with reliable energy are often dependent on jet fuels, diesel vehicles, and electric refrigeration for vaccine distribution and storage. Some countries, like Tunisia, are using limited sea transport for vaccines shipped from Europe, which is an energy-saving solution because boats are more efficient and pollute less than air freight. However, there are several additional opportunities for energy efficiency in the transportation and storage of vaccines and heat-sensitive drugs even in places with reliable power.



Energy use reduction followed by renewable energy production can attain "net zero energy" for local cold chain storage and transport.

Toward net-zero energy in Tunisia

The Tunisian Ministry of Health is working with project Optimize to demonstrate the benefits of a "net-zero energy" supply chain. Over the course of a year, four health facilities are being designed to produce as much on-site renewable energy (e.g., wind or solar) as is consumed by on-site cold chain storage and transport. Rather than operating diesel-fueled vehicles, the team is introducing electric vehicles that can be powered by solar energy collected on site.

In addition, energy-intensive equipment such as refrigerators, computers, and lights are being made more efficient through low- or no-cost management decisions. In some cases, the contents of two refrigerators can be consolidated into one, cutting energy use roughly in half. Older, less-efficient refrigerators and desktop computers can be replaced with new, higher-efficiency refrigerators and laptops.

The Tunisia team (as well as the Senegal team) has started using light emitting diode (LED) lights in place of traditional incandescent lights. This reduces energy without sacrificing lighting levels and ultimately cuts operating costs. And because LED lights run cool, this reduces unwanted heat from less-efficient lights, decreasing the need for cooling energy. LED lights also last up to 25 times longer than incandescents and are mercury free which minimizes pollution. Through measures like these, the anticipated benefits of the net-zero supply chain include reductions in electricity costs, fuel costs, maintenance, and environmental impacts.

Cool innovations for vaccine transportation and storage

by Steve McCarney, John Lloyd, and Joanie Robertson, PATH

A group of public- and private-sector partners are collaborating with project Optimize to evaluate a range of innovative transportation and storage containers for heat-sensitive drugs and vaccines that operate in environments with or without access to reliable power. The following is a brief description of each technology, the niche it was designed to fill, and the context in which it will be tested.

Photos: SAVSU (USA) Nano-Q cooling device

Small-volume passive cooling devices with a thermal battery that can store a small number of vaccines for at least a week and up to a month are being tested in Vietnam.

Stationary passive coolers

Commune-level passive cooling in Vietnam

Currently in Vietnam, not all commune health centers have the capacity to provide vaccine cold storage for a full month. Vaccines are generally brought in for one- or two-day immunization sessions as part of the monthly national immunization strategy. However, it is important for certain vaccines (such as hepatitis B) to be available throughout the month so that babies can receive necessary vaccinations at birth.

With support from Optimize, the National Expanded Programme on Immunization is evaluating the appropriateness of new small-volume (about 3 to 4 liters) passive cooling devices, creating capacity to store a small number of vaccines all month at the communes. These devices provide approximately one to four weeks of cooling on one “charge” of ice. In this way cooling can be provided with no requirement for a refrigerator or even an on-site energy supply.

It is anticipated that these coolers will improve on-time delivery of hepatitis B birth dose while also decreasing closed-vial wastage. The intervention would not increase cooling energy use at the commune, would be compatible with intermittent power conditions, and would not disrupt the current monthly immunization-day system which is working very well.

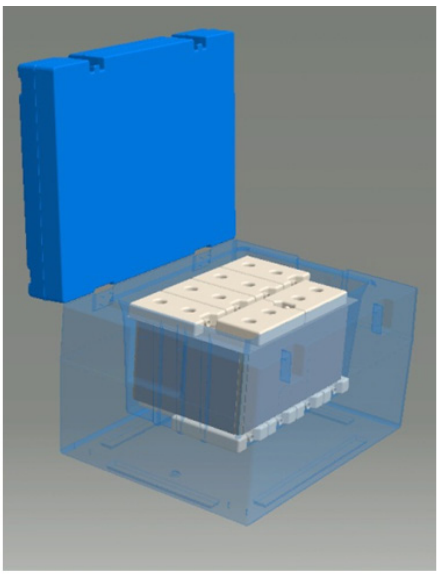


Photo: Dometic (Luxembourg) RCW 4/30 27-liter vaccine transport cold box

Solidly frozen PCMs can freeze at a vaccine-safe temperature (e.g., +5°C) and have direct contact with freeze-sensitive vaccines.

Mobile passive coolers

Passive cooling for vaccine transport in Tunisia

To safely transport new vaccines, Tunisia’s EPI program is working with Optimize to evaluate phase change material (PCM) packs as a possible passive cooling storage alternative to ice packs. Similar to ice, solidly frozen PCMs hold more cooling power than when in the melted or liquid phase. PCMs are ideal because they can freeze at a vaccine-safe temperature (e.g., +5°C) and can have direct contact with freeze-sensitive vaccines, allowing the entire box area to be used for vaccine. Traditional cold boxes can substitute PCM packs for ice packs and provide adequate cooling for up to 15 hours in the heat of the Sahara.

Photo: AirContainer (Sweden) Big Box polypropen container

Optimize hopes to help improve vaccine supply chain efficiency by introducing large insulated containers with PCM coolants on moving warehouses. Together, these innovations can decrease delivery time, improve stock management, and ensure vaccine quality and access at the point of consumption.

Insulated containers on Senegal's moving warehouses

The Ministry of Health in Senegal is piloting a "moving warehouse" approach. Rather than requiring health-post staff to pick up vaccines, antiretrovirals, malaria, and tuberculosis medications, along with associated supplies from a district center, two trucks serve as moving warehouses and distribute supplies from the regional level to health posts in all five districts of the Saint-Louis Medical Region.

Integral to the moving warehouse concept is the use of large rolling insulated containers to transport necessary drugs and vaccines. These containers can be rolled by workers or handled by forklift. With a capacity of 161 liters, the volume of one rolling container is equivalent to eight long-range traditional cold boxes, which saves space in transit and makes it easier to handle larger volumes of bulkier single-dose vaccines. The containers are cooled by PCMs that have been chilled in a refrigerator at safe temperatures for a specified time. The PCM panels are placed in the container, and vaccine can be loaded in direct contact with all inside surfaces of the rolling container. Currently, trucks equipped with these containers are able to keep vaccines at proper temperatures for as long as six days while on the road. And in areas where roads are poor, moving warehouses equipped with passive containers have a lower maintenance burden and higher reliability compared to insulated trucks with active refrigeration.

Active refrigeration

Ice-lined refrigerators in Senegal

Power problems that occur throughout the developing world, including in Senegal, make it challenging to cool vaccines and heat-sensitive drugs with electric refrigerators. In this type of intermittent power setting, conventional practices often rely on diesel generators to back up unreliable grid electricity. However, generators are costly, difficult to maintain, create noise and air pollution, and are subject to fuel supply disruptions and diversions.

In Senegal's St. Louis region, a more reliable and energy-efficient solution for vaccine storage is being demonstrated: the super long-life ice-lined refrigerator (ILR). ILRs provide stability in intermittent power conditions, and their cost is minimal in contrast with absorption-type refrigerators powered by electricity, bottled gas, or kerosene. The use of ILRs with longer-than-average holdover times can eliminate the need for back-up generators if grid electricity provides at least eight hours of power on average per day. The best-in-class ILR can operate with just four hours of electricity and provide over ten days of holdover to maintain acceptable vaccine temperatures, even in warmer climates. Particularly in settings where electricity is unreliable, the ILR is a safer, more reliable choice for vaccine storage than domestic refrigerators.

Domestic fridge study in Tunisia

Many countries, including the United States, are using untested, unmonitored, domestic-style refrigerators for storing vaccine and reporting significant losses due to poor temperature control. The WHO Performance, Quality and Safety (PQS) program has established equipment standards and testing protocols for vaccine refrigerators including electric, ILRs, gas/kerosene, and solar-powered refrigerators. Using these PQS prequalified refrigerators is the recommended approach for purchasing vaccine storage refrigerators.

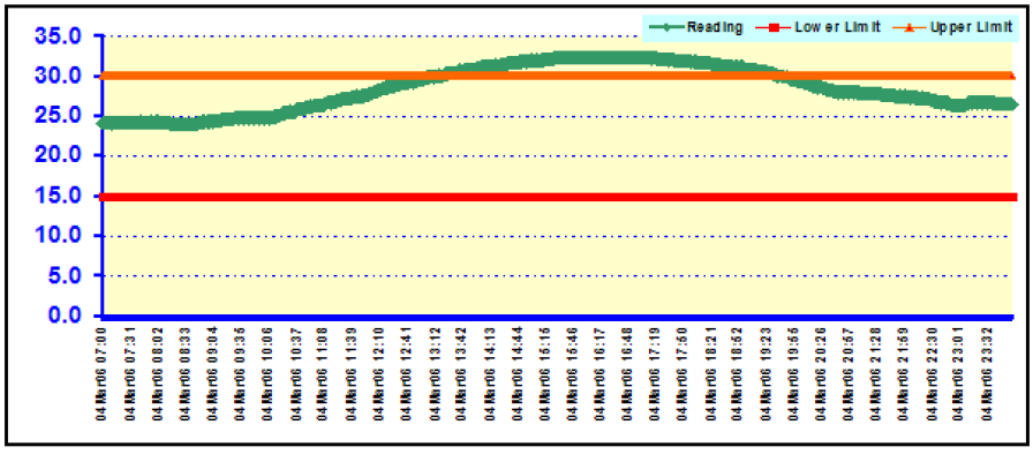
However, many countries elect to purchase locally available refrigerators because these are usually less expensive, quickly available, employ front opening doors, and are familiar to local service technicians. Unfortunately, few of these domestic-type refrigerators are sufficiently monitored to ensure safe vaccine temperatures.

Monitoring has shown that domestic refrigerators have widely varying temperature performance and can expose the vaccine to freezing temperatures and rapid warm-up after power cuts. The widespread practice of domestic refrigerator use warrants better temperature monitoring to find and isolate problem refrigerators before they damage vaccines.

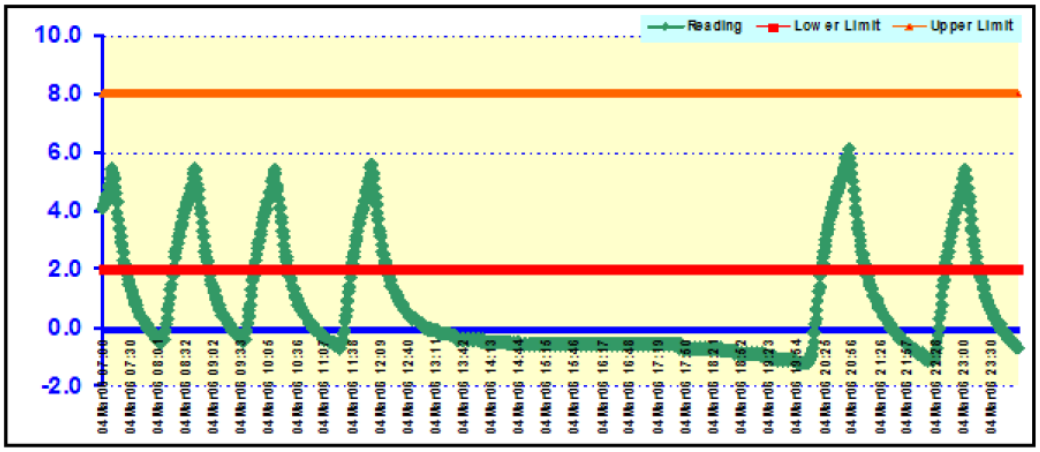
In Tunisia, Optimize is working with Centre Technique des Industries Mécaniques et Electriques (CETIME), a government-sponsored laboratory, to use WHO PQS protocols to test typical domestic refrigerators that have been used for vaccine storage or are being considered for future purchases.

Domestic refrigerators already in use are also being monitored, and their performance will be evaluated. Evaluation results will help Tunisian decision-makers assess the risk of using domestic refrigerators, and laboratory testing of new models will identify potential risks as well as help to inform solutions for maintaining acceptable temperature control. If no suitable refrigerator or solutions can be identified, decision-makers have evidence to make the case to develop improved models in country or to purchase WHO PQS prequalified refrigerators. The demonstration in Tunisia is intended to convey to all countries using domestic refrigerators that first, they should all be continuously monitored in use; second, they should be tested and their performance confirmed before procurement; and third, they should meet the global WHO/PQS norms for vaccine storage.

Cyclic Defrost Fridge



Ambient (room) temperature rises above 30°C.



Graphs: E2E IT Solutions Pty. Ltd.

Effect of ambient temperature changes on refrigerator temperature (exposed evaporator fins at rear of refrigerator).

These graphs show the effects of ambient temperature changes on a typical domestic refrigerator.

Seeking VVM stories

Optimize is seeking real-life stories of how vaccine vial monitors are being used in the field. Share your story here.

Meetings

People that Deliver: Meeting tomorrow's health challenges through workforce excellence in supply chain management. This project, led by the Reproductive Health Supplies Coalition, USAID, WHO, and Bioforce Institute, will be convening a global positioning and harmonization conference on June 28–29, 2011, at WHO headquarters in Geneva. The meeting is co-hosted by the Departments of Reproductive Health and Research (RHR) and Immunization, Vaccines and Biologicals (IVB).

Announcements

Shake test publication awarded Ludwig Rajchman prize

- Download the article or the video-article.
- View an accompanying educational video on how to do a shake test.

Three studies awarded IQPC Europe Cold Chain Excellence Award

- Validation of the shake test for detecting freeze damage to adsorbed vaccines. Read full article.
- Use of cool water packs to prevent freezing during vaccine transportation at the country level. Read full article.
- WHO-PDA Pharmaceutical Cold Chain "Management on Wheels" learning event. Watch video.

"Moving warehouse" up and running in Senegal

- Read full article.

Resources

Always Cola, Rarely Essential Medicines

- This article, published by the INSEAD Social Innovation Centre, compares medicine and consumer product supply chains in the developing world, highlighting best practices from Coke that can be applied to medical supply chains.

Intradermal delivery of vaccines: potential benefits and current challenges

- Published in the *Bulletin of the World Health Organization*, this article examines the knowledge gaps, operational challenges, and potential benefits of intradermal vaccine delivery.

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