Putting vaccines to use with an ultra-cold chain (UCC) system

A briefing for country and programme focal points

January 2021

1. Introduction

Across the globe, the COVID-19 pandemic is causing unprecedented human and economic costs. The solution to saving lives, ending the pandemic and preventing future epidemics likely lies in the development and administration of a safe and effective vaccine against the COVID-19 virus.

More than a hundred COVID-19 vaccine candidates are in the research and development pipeline. Some of them—especially the messenger ribonucleic acid (mRNA) vaccine types—may need to be kept at ultra-low temperatures (ULTs) to maintain their potency. This poses additional challenges to cold chain storage and transport, especially in areas without major transport links, refrigeration facilities or stable power supplies.

Depending on stability data, mRNA vaccines may have different requirements for ULT storage and post-storage management. This makes it particularly important to pay attention to vaccine-specific recommendations when handling and delivering different types of COVID-19 vaccine.

Only a few low- and middle-income countries (LMICs) that have used Ebola vaccines have any experience in using ULT equipment and managing ultra-cold chain (UCC) systems. Putting the new mRNA COVID-19 vaccines to use in most LMICs will require countries to overcome logistical challenges in three key areas of UCC system management: equipment, transport and deployment.

COVID-19 mRNA vaccine BNT162b2: storage requirements

On 31 December 2020, WHO listed the first COVID-19 vaccine for emergency use. The COVID-19 mRNA vaccine BNT162b2, funded by Pfizer and BioNTech, is one of the vaccines that will require ultra-cold storage and transport to maintain potency.

It must be kept at ULTs (<-60°C). Once thawed, undiluted COVID-19 mRNA vaccine BNT162b2 can only be stored for five days at 2°C to 8°C (or two hours at 30°C) before use.

2. Equipment

The equipment challenge

UCC systems require special equipment to create and maintain the ULTs needed to store ultra-cold vaccines and to produce effective coolants for storage and transport. Ensuring staff can effectively manage this equipment further requires standard operating procedures and training.

UCC systems comprise two types of equipment: active and passive devices.

2.1. Active devices

Given a secure power supply, active devices produce ULTs indefinitely. ULT freezers, for example, can produce temperatures ranging from -86°C to -60°C. They come in two sizes:

- Large: 500–1 000 L, up to 30 000 vials loading capacity.
- Small: 70–200 L, up to 9 000 vials loading capacity.

Figure 1. ULT freezer

At both sizes, it is worth noting for cold chain sizing purposes that only about 50% of the storage capacity can actually be used. So, for a ULT freezer of 700 L, only about 350 L would be used.

ULT freezers are typically used to maintain the temperature-controlled environment needed to store central supplies of ultra-cold vaccines. They can also be important in enabling temporary storage and transport as they are also used to freeze ULT phase change materials (PCMs) (see Section 2.3 below).

When using Aktek device with PCM for transport and distribution, countries will need at least two separate ULT freezers at the main storage site: one to store vaccines and one to pre-freeze PCMs or store dry ice (frozen carbon dioxide) (see Section 4.1 below).

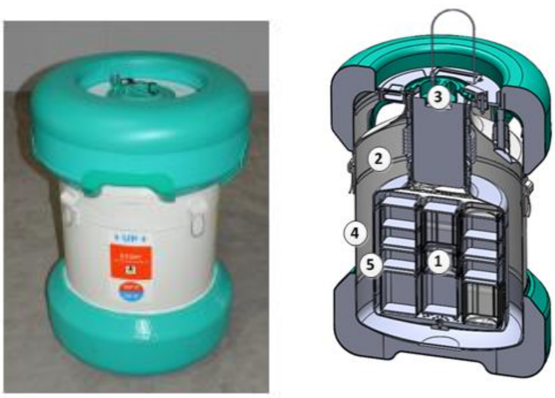
2.2. Passive devices

Passive insulated containers are designed to maintain ULTs in the short term (typically up to five days). This makes them critical to transporting and storing ultra-cold vaccines at the facility level. There are two main types of insulated container available for passive freezing of ultra-cold vaccines.

Arktek long-duration passive ultra cooler

The Arktek (YBC -5) is a super-insulated, double-walled large bottle-like container that uses multi-layer insulation technology and eight PCM packs (1L each) to keep vaccines at ULTs (-80°C to -60°C) in remote storage and vaccination sites for up to five days without any powered refrigeration or extra coolant. It comes with a vial rack system and has a storage capacity of 7.9 litres. Each unit is built to withstand a lot of use in the field; and each one is equipped with a built-in temperature data logger capable of monitoring and reporting ULTs.

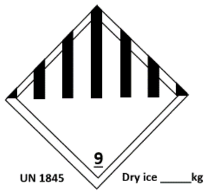
Figure 2. Arktek



Arktek parts:
1. Vaccine cup stacks
2. Insulative vacuum space
3. Removable assess cap
4. Protective outer shell
5. Inner shell

Thermal shippers

As their name suggests, thermal shippers are usually used by manufacturers to ship vaccines abroad. Like the Arktek, they do not need an external power supply but instead use a combination of insulation technology and coolants (for example, dry ice) to keep vaccines at ULTs (-80 °C to -60 °C) over the short term. They also typically have an impact-resistant outer layer for durability in the field. Thermal shippers come in a range of sizes: the manufacturer's information will give the precise storage capacity of any individual product.



Use only thermal shipper labeled for dangerous goods/ dry ice use, e.g. with 'UN 1845' marking.

When fully loaded with dry ice and opened only twice a day for less than five minutes per opening, the thermal shipper can maintain ULT conditions for at least 5 days, depending on ambient temperature. With frequent opening, this cold life will drop to few hours. Either way, thermal shippers should never be depleted of dry ice when used as vaccine storage. This means checking the level of dry ice regularly and refilling it as necessary. Note that you will need to secure a consistent supply of dry ice when using thermal shippers, for example through advance orders from a reliable local supplier.

Thermal shippers can also be reused for longer if the dry ice is regularly replenished and there are no signs of wear and tear.

Figure 3. Thermal shippers

Tests are currently underway to establish whether WHO prequalified cold boxes that use dry ice can be used to effectively store ultra-cold vaccines. Once these tests are finished and their data are available, relevant guidance will be developed and distributed.

Generally, when choosing passive devices it is important to consider the storage temperature and duration of storage required. The passive device you choose to use should have:

- the **right insulation** to guarantee the cold life you need;
- **enough capacity** to meet your storage requirements;
- a regular supply of appropriate **coolants**; and
- a **temperature monitoring device** capable of showing alerts for any temperature fluctuation in transit.

COVID-19 mRNA vaccine BNT162b2: thermal shippers

The new Pfizer/BioNTech vaccine comes with a specially-designed thermal shipper that has:

- a foam lid;
- and built-in temperature logger;
- a box that holds vial trays;
- vial trays; and
- a dry ice pod.

Find out more at: www.cvdvaccine-us.com/product-storage-and-dry-ice

2.3. Considering storage levels

The choice of ULT equipment will vary depending on where it needs to be used (store levels). Central, long-term storage facilities have different requirements, infrastructure and operating conditions to short-term stores. So the best equipment to use at each will differ. Similarly, the best equipment to move ultra-cold vaccines from storage to storage will differ from that needed to move them from storage to session site (see Table 1).

In general, central stores require ULT freezers or thermal shippers (following manufacturer's instructions for use with ultra-cold vaccines); while remote stores require Arkteks or thermal shippers (with relevant coolant materials).

Table 1. Equipment requirements at different storage levels

STORAGE LEVEL	ULT EQUIPMENT NEEDS
Central storage	• Large ULT -86°C freezers (500-1000L, up to 20,000 vials loading capacity). • Small ULT -86°C freezers (70-200L) up to 9,000 vials, for back up and PCM pack storage. • Small ULT -20°C freezers (70-200L) for pre-freezing PCM packs.
Remote storage	• Small ULT -86°C freezers (70L) for nearby sub-national or district stores. • Arktek and PCMs (-80°C) or thermal shipper and dry ice for remote stores and vaccination sites.
Storage-to-storage transport	• Thermal shippers (or equivalent) and dry ice, or • Arktek and PCMs (-80°C)
Storage-to-session transport	• Arktek and PCMs (-80°C) or thermal shippers and dry ice to transport and store frozen vaccine for later use at vaccination sites. • High density vaccine-carriers with conditioned ice-packs for thawed vaccine vials at 2°C to 8°C for immediate use at vaccination sites.

3. Transport

The transport challenge

UCC systems require the means to maintain vaccines in ULTs away from central storage points, most notably during transport and service delivery. In some countries, this often means maintaining ULTs in remote areas with little infrastructure.

Planning for ultra-cold vaccine transport and delivery with passive freezing equipment includes a consideration of the coolants required to provide thermal control. In traditional cold chain systems (2°C to 8 °C), water/ice packs are used to keep vaccines cool during transit and service delivery. But for ultra-cold vaccines, ice packs are not sufficient and other coolants, with lower phase change temperatures, are required.

For example, thermal shippers often use dry ice; and the Arktek uses PCMs that have extremely low melting points and can store energy during their transition from solid to liquid. While the precise temperature at which PCMs melt (the phase change temperature) varies widely across different PCMs, each PCM maintains a constant temperature during transition. In other words, as the PCM melts it absorbs heat without increasing in temperature until it has all turned into liquid. This helps keep the vaccines within their optimum temperature range throughout the PCM transition. The amount of energy required to melt a PCM (latent heat) combined with the effectiveness of the insulation container (the heat leak at any given ambient temperature) determines the cold life.

Figure 4. Packing dry ice

Figure 5. PCMs used in the Arktek

Different coolants have different characteristics; they are produced in different ways and are used in different devices (see Table 2).

Table 2. Characteristics of different coolants

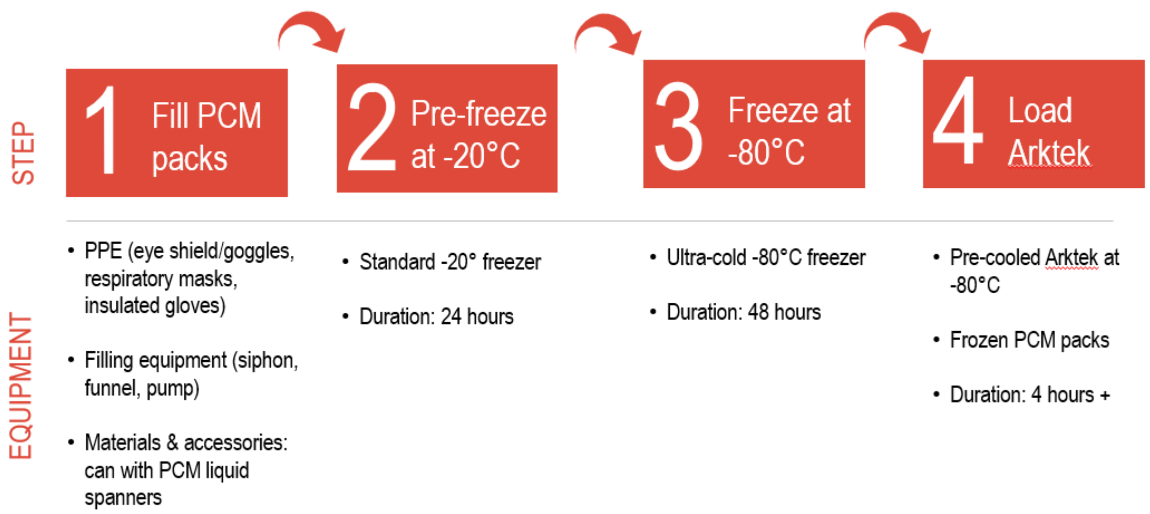
CHARACTERISTICS	COOLANT	
	DRY ICE	SPECIAL ULT PCMS
Phase change temperature	-78.5°C	-78°C to -65°C
Latent heat of phase change	571 kJ/kg	115 kJ/kg (for Pulse E-75)
Personal protective equipment	Eye shield/goggles, cryogenic/insulated waterproof gloves	Eye shield/goggles, cryogenic/insulated waterproof gloves
Method of preparation	Produce it using small units; or procure it from local sources	Fill cooling packs, pre-freeze (at -20°C) then complete freezing (at -80°C) for at least 24 hours

Uses	Packing vaccines for transport and temporary storage	Packing vaccines for transport and temporary storage
Relevant container	Thermal shipper/ Arktek	Arktek
Safety considerations	Work in open, well-ventilated area to prevent risk of suffocation from carbon dioxide emissions	Avoid direct contact with eyes/skin to prevent irritation

3.1. PCM preparation

While dry ice can be produced or procured ready for use, the special PCM packs for long-range storage devices like the Arktek must go through a four-step preparation process before they can be used. At each step, a selection of special equipment is needed (see Figure 6).

Figure 6. PCM pack preparation



4. Deployment

The deployment challenge

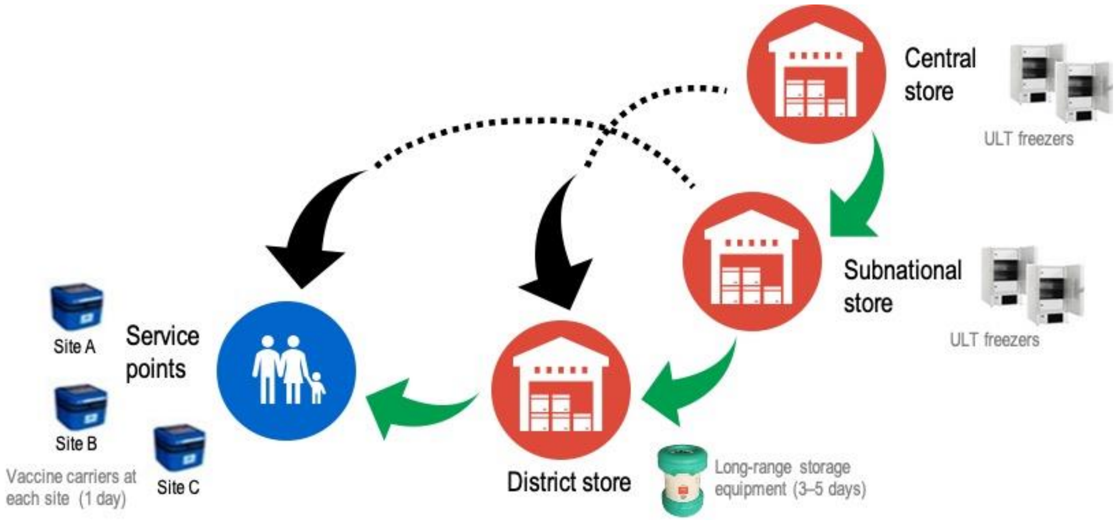
ULT equipment requires careful management at national, sub-national and local levels as vaccines are deployed for use to minimize wastage and ensure the continued availability of safe and effective vaccines.

One of the keys to overcoming the deployment challenge is to develop an effective deployment strategy, that uses appropriate equipment at different levels of deployment, based on local contexts and capacities.

4.1. Cascade deployment

As its name suggests, cascade deployment works by cascading storage points at different levels from central storage to service delivery (see Figure 7). This strategy is best suited to countries with vaccination points that are more than one day's travel away from the central store. It is primarily driven by active cooling devices and requires careful inventory management and robust temperature tracking.

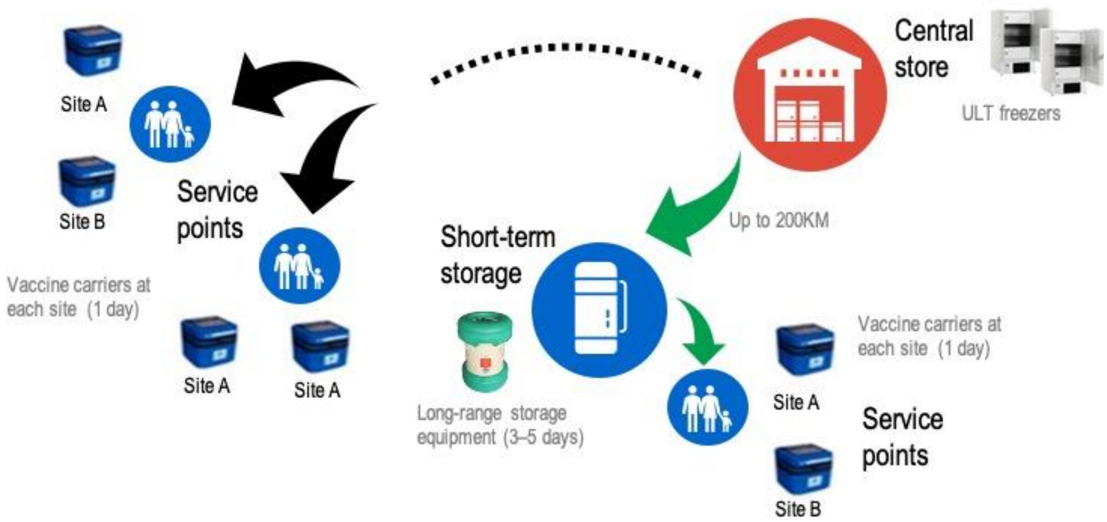
Figure 7. Cascade deployment strategy and equipment needs.



4.2. Rapid deployment

Rapid deployment strategies move vaccines directly from the central store to vaccination points with or without limited intermediate, short-term storage (see Figure 8). This strategy is best suited to countries where service delivery happens near to the central store (within a day's travel). It is primarily driven by passive cooling devices, including high-density vaccine carriers for storing vaccines that will be used within a single day (so there is no need to renew ice packs)

Figure 8. Rapid deployment strategy



Experience with implementing UCC systems to support Ebola vaccines suggests that the rapid deployment strategy can work well to distribute vaccines quickly and efficiently, thereby maximizing vaccine potency and impact on outbreak control. Considering the high cost of ULT equipment and the potentially limited use of ultra-cold vaccines, many countries may choose rapid deployment because it is simply not practical or cost-effective to install ULT freezers at all levels of the vaccine store. In these cases, efficiently deploying ultra-cold vaccines means taking the vaccines from the central store directly to short-term storage points, closer to service delivery, and by-passing intermediary stores.

4.3. Common requirements

Regardless of whether countries choose to use rapid or cascade deployment, they will require:

- **Strong hub teams** to manage storage, PCM pack freezing and dispatch from national or sub-national stores.
- **Cold chain expertise**, including at least one cold chain technician and two assistants (one for vaccines and one for PCM freezing or dry ice preparation).
- **ULT equipment**, including some ULT freezers to match vaccine volumes, Arktek devices + PCM or thermal shippers + dry ice, and standard vaccine carriers with conditioned ice packs for storing opened vaccine vials at service points.

5. Structural support

Generally, countries will only be able to overcome the equipment, transport and deployment challenges and implement UCC systems if they have:

- **Adequate infrastructure**, including a robust and reliable power supply, with back-up generator, to power ULT freezers (a 700L ULT freezer consumes as much energy as a $20m^3$ walk-in cold room). ULT freezers also require stringent operating conditions (with a controlled ambient temperature under -27°C and no more than 50% humidity).
- **Technical support**, including updated standard operating procedures and training for responsible staff.
- **Protective equipment** for staff, including for example cryogenic/insulated gloves and eye shield/googles.

Find out more

For more information on UCC system requirements and guidance, see:

- COVID-19 vaccination, country readiness and delivery: Supply and logistics guidance. Geneva: UNICEF & World Health Organization; 2020 (working document). https://www.technet-21.org/en/library/main/6717-covid-19-vaccination,-country-readiness-and-delivery:-supply-and-logistics-guidance
- Pfizer-BioNTech COVID-19 Vaccine. [website] New York: Pfizer; 2021. https://www.cvdvaccine-us.com/product-storage-and-dry-ice