COLD CHAIN TECHNOLOGY BRIEF

VACCINES
The United Nations Environment Programme (UNEP) is the leading global environmental authority that sets the global environmental agenda, promotes the coherent implementation of the environmental dimension of sustainable development within the United Nations system, and serves as an authoritative advocate for the global environment. UNEP’s mission is to provide leadership and encourage partnership in caring for the environment by inspiring, informing, and enabling nations and peoples to improve their quality of life without compromising that of future generations.

UN Environment Programme is an Implementing Agency of the Multilateral Fund of the Montreal Protocol on Substances that Deplete the Ozone Layer. OzonAction strengthens the capacity of governments – particularly the operational focal points known as National Ozone Units – and industry in developing countries to elaborate and enforce the policies required to implement the Protocol and to make informed decisions about alternative technologies. OzonAction’s overall goal is to enable those countries to meet and sustain their compliance obligations under the treaty.

The International Institute of Refrigeration (IIR) is an independent intergovernmental organisation. It is the only one in the world to gather scientific and technical knowledge in every sector of refrigeration. Founded in 1908, the IIR has a worldwide network of 59 member countries, more than 300 experts divided into 10 commissions, and over 950 private and corporate members. The Institute is committed to disseminating knowledge of refrigeration to improve the quality of life for all, while respecting the environment and taking into account economic imperatives.

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Introduction

Since the start of the COVID-19 vaccination campaigns at the end of 2020, the world has become aware of the importance of refrigeration and, in particular, of the cold chain, which is essential for the organisation of a global vaccination campaign against the SARS-COV-II virus. The use of very low storage temperatures for the first vaccines has raised the public’s awareness about the importance of the cold chain for vaccine preservation and mobilised all those involved in temperature-controlled logistics.

Vaccines, which appeared more than two centuries ago in the United Kingdom have been stored under controlled temperatures for a very long time. In 1920, Professor d’Arsonval\(^1\) proposed using vacuum freeze-drying at -80°C to replace the iceboxes and antiseptics commonly used for transporting and preserving vaccine pulps. A vaccine cold chain has been developed for many years, particularly under the aegis of the World Health Organization (WHO)\(^2\). Prior to COVID-19, more than 4.7 billion doses of vaccine were injected worldwide each year, representing a market of more than US$40 billion (2019), which is expected to reach US$80 billion by 2025\(^3\). The COVID-19 vaccination campaign has revolutionised the vaccine cold chain, with volumes almost twice as high as usual\(^4\), but also because of the new storage and transport temperature ranges that require new equipment, new solutions and new organisations. To date, more than 7 billion COVID-19 vaccines have already been pre-ordered worldwide\(^5\), with storage temperatures ranging from -90°C to +8°C\(^6\).

This note provides an overview of the vaccine cold chain in general and COVID-19 in particular, its requirements and challenges. First, the effects of temperature on these vaccines, old and new, and their storage and transport requirements should be known. Second, the temperature-controlled logistics of vaccines in general and COVID-19 vaccines in particular, and the equipment and solutions used for their cold chain, must be analysed. Finally, if refrigeration is essential for our health as well as for our food, it must be sustainable, and it is therefore necessary to analyse the challenges to be met so that the cold chain for vaccines disrupted by COVID-19, is sustainable in the short, medium, and long term.

\(^4\)L’économie du médicament. Quel est le poids de l’industrie du vaccin ?. June 2012.
Vaccines are among the many health products that are heat-sensitive. Failure to comply with the maximum or minimum storage temperature has consequences of varying nature and severity. They can lead to immediate or progressive deterioration of the vaccine, its active ingredient or its excipients. Each vaccine is subject to stability studies and the World Health Organisation has established a summary of these studies7.

Vaccine storage conditions are established through standardised stability studies based on tests performed according to International Council on Harmonisation (ICH) methods. The stability tests for Biological/Biotechnological products ICH Q5_C make it possible to evaluate the impact of exceeding the maximum authorised temperatures on the degradation of the active ingredients. These effects are taken into account to define the shelf life established by these same stability studies.

The data from the stability studies are used to establish a specific stability budget for each product. This stability budget, or time-temperature capital, makes it possible in certain studies to define a maximum temperature excursion time beyond the authorised storage temperature for the vaccine. This authorised excursion time is generally called ToR (Time out of Refrigeration) or ToS (Time out of Storage). The pharmaceutical company is the sole owner of these data, covering all stages from production to distribution and through administration of the product.

1.1. The effects of temperature on traditional vaccines

The majority of vaccines, consisting of vaccine antigens, adjuvant and stabiliser, should be stored and transported at +5°C ±3°C (+2°C/-8°C). This is the case for vaccines made from inactivated or attenuated viruses, such as polio, pertussis, measles or influenza vaccines, or vaccines with sub-parts – inactivated proteins or toxins for example – such as tetanus, hepatitis B or meningococcal meningitis vaccines. Some COVID-19 vaccines are of this type and should be stored at these temperatures.

When subjected to higher temperatures, above +8°C, the harmful effects of heat on vaccines are cumulative. They depend on the duration and amplitude of the temperature excursion and gradually lead to the destruction of the active ingredient. It is a cumulative and exponentially progressive effect.

Most vaccines, however, tolerate a few days at room temperature for manufacture, distribution and handling during dispensing and injection, but the higher the temperature, the faster the degradation.

7 WHO. Vaccine supply and quality; surveillance of adverse events following immunization. Weekly Epidemiological Record. Vol 71, 32. 9 August 1996.
When subjected to lower temperatures, harmful effects of refrigeration are mainly related to the risk of freezing. For freeze-sensitive vaccines (see graph above), a single exposure to sub-zero temperature is usually sufficient to accidentally freeze vaccine doses and make some vaccines ineffective. Other physical phenomena such as precipitation of vaccine components during thawing (e.g. adjuvant or stabiliser), may also occur. Freezing can also simply weaken the glass of the primary container, which can lead to the bulbs shattering.

Therefore, if vaccines were to be refrigerated until now, they should never be frozen, so it is important to store them in the refrigerator and avoid storing them against the walls or near the freezing compartment. These instructions are very often recalled in the leaflets and summaries of product characteristics validated by health authorities.

It may therefore have come as a surprise to hear that some COVID-19 vaccines have to be stored at sub-zero or ultra-low temperatures.

1.2. Vaccines stored at very low temperatures

More recently, some vaccines have emerged that need to be stored at very low temperatures. This is particularly the case for viral vector vaccines such as the Ebola vaccine coming on the market in 2019 and vaccines using genetic and nucleic acid techniques with fragments of the virus’ DNA or RNA. While trials had been conducted until now, prior to COVID-19, none of these vaccines had gone through the full approval process for human use.

The rapid development of these vaccines has left little time to optimise their formulation and assess their stability. As the components of these new vaccines are very fragile and much less stable, new storage and transport temperature ranges are required, in particular two ranges: -75°C ±15°C which equates to -90°C to -60°C and -20°C ±5°C which equates to -25°C/-15°C.

Summaries of product characteristics (SPCs) for COVID-19 mRNA vaccines available to date indicate shelf lives of 6 months at -90°C to -60°C for BioNTech Pfizer’s Comirnaty vaccine and 7 months at -25°C to -15°C for Moderna’s vaccine, for example.

While some health products were already stored at these temperatures, such as certain labile blood products at -20°C or frozen plasma at -70°C, these temperatures were rarely used for vaccine storage, which implies adapting the logistics chains for storage, transport and dispensing.

1.3. Vaccine storage temperatures from laboratory to patient

Vaccine doses contain only a few millilitres of liquid and even a vial of 5 or 6 doses of vaccine has a very small volume and therefore little thermal inertia. Any exposure of the container to a temperature higher than the maximum tolerated temperature will therefore very quickly lead to a significant and sudden rise in temperature of the vaccine itself.

The handling of vaccines for the distribution of vials, for example, must therefore be very rapid. For frozen vaccines stored at sub-zero temperatures, the tolerance is less than 3 minutes for example. Any vial exposed to room temperature for more than 3 minutes is considered thawed and cannot be refrozen. It should be used under the following conditions.

A box of 195 vials of 5 doses of vaccine stored at -75°C may take 3 hours to thaw at +2/+8°C. Thereafter, the vaccines can be stored at +2°C to +8°C, like conventional vaccines, but for a limited period of time (a few days).\(^8\)

\(^8\) AFF. Note de compréhension de certains phénomènes applicables à la maîtrise de la chaîne du froid des vaccins. Note d’information « Chaîne du froid du vaccin Covid-19 » n° 2021-003. p. 4.
From the pharmaceutical laboratory to the patient, the COVID-19 vaccine cold chain links many different actors.
2.1. The stakeholders in the vaccine cold chain

Pharmaceutical companies

The first actors in the vaccine cold chain are the pharmaceutical companies that produce them. During the vaccine development phase, once the final formulation of the vaccine is defined, they perform vaccine stability studies to define the acceptance limits of temperature excursions and the storage temperatures of the vaccine from production to injection. These information are included in the regulatory file of the vaccine, in its marketing authorisation, but also on its packaging and instruction leaflet. The pharmaceutical laboratory will ensure the traceability of the vaccines throughout the cold chain until injection. The laboratory will determine what to do if the product’s temperature is outside the authorised range.

As soon as it is produced, the vaccine will be stored under controlled temperatures. Before marketing, vaccines are stored in dedicated warehouses managed by the laboratory itself. The batches of vaccines to be distributed are released by batch after verification of their conformity by the qualified person representing the laboratory.

Once the batch of vaccine has been released for marketing, the Responsible Person (RP) will need to ensure that the safety, quality and efficacy of the vaccine are maintained within the sales and distribution operations, in accordance to local guidelines enforced by the country or region. Example with the EU Guide to Good Distribution Practice (EU GDP 2013/C343/01).

The distribution chain for vaccines can be complex. Some vaccines are delivered directly by the laboratory to hospital pharmacies or vaccination centres during public vaccination campaigns. This is the case, for example, for COVID-19 vaccines in many countries, especially messenger RNA vaccines stored at -75°C or -20°C. But for traditional vaccine flows, the distribution network of pharmaceutical distributors also supplies hospital pharmacies, retail pharmacies and, more generally, all health establishments authorised to dispense vaccines. While the +5°C cold chain is well developed in the networks of pharmaceutical distributors, this is not the case for the -20°C or -70°C cold chains required for mRNA-based viral vector vaccines.

Vaccination centres

Many countries have set up vaccination centres dedicated to vaccination against Covid-19. These centres can vaccinate up to several thousand patients per day, such as the one in Saint Quentin en Yvelines, France, which has carried out more than 150,000 vaccinations, with a record of more than 3,200 vaccinations in one day\(^9\). These centres have their own vaccine cold chain and dedicated teams of up to several hundred people.

Hospital and retail pharmacies

Vaccines are also dispensed in health institutions’ pharmacies or in retail pharmacies for vaccines intended for doctors, pharmacists, nurses or directly for patients. These pharmacies handle temperature-sensitive products and must therefore be equipped to store vaccines at the right temperature.

Patients

Although most vaccines in the world are injected in vaccination centres run by health professionals, the patient can also obtain the vaccine from a pharmacy and have it injected by the pharmacist, a nurse or their doctor. The patient then becomes a link in the vaccine cold chain and must be informed and made aware of good practices for the transport and storage of their vaccines. The patient remains the weak link in the cold chain.

The EVM initiative has helped countries to address the gaps identified in the vaccine management assessments, and subsequently to develop EVM improvement plans.

Through the comprehensive framework for EVM, the continuous cycle of EVM improvement, supply chain optimisation and innovation will result in supply chains that are:

- Designed to maximise efficiency, performance, flexibility and responsiveness to meet the needs of today’s and tomorrow’s immunisation programmes;
- Robust enough to continuously adapt and comply with recommended practices and WHO/UNICEF minimum standards and policies;
- Able to adopt systemic and technological solutions that are known to be cost-effective, supporting improvements in immunization coverage and equity goals;
- Operated by skilled health workers, managing the supply chain using performance indicators;
- Adequately financed by mobilizing available health systems strengthening resources.

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2.2. Vaccine cold chain equipment

Cold rooms and warehouses

The cold chain for vaccines normally begins in cold rooms or warehouses dedicated to vaccine storage. Until the recent development of vaccines stored at -70°C or -20°C, these cold rooms were designed for temperatures of +5°C ±3°C. Designed conventionally, they are usually refrigerated by vapour compression refrigeration units. The temperature requirements of health care products imply a higher degree of homogeneity and temperature stability than is commonly required in the food cold chain for example. Storage areas for heat-sensitive health products are clearly defined and identified, and air circulation and temperature monitoring and recording are generally continuous. Initial and regular qualification ensures this performance.

Isothermal and refrigerated packaging

Isothermal or refrigerated packaging is commonly used for transporting vaccines, both for local distribution and for long-distance transport, particularly by air. The useful volumes of the packages vary from a few litres for the smallest to more than a cubic metre. The first quality of a vaccine transport package is its good insulation. Packaging generally uses insulating foams made of polyurethane or extruded polystyrene for their insulating properties. For shorter transports or for pouches, polyethylene has also been used. While other insulations may be used, high thermal resistance insulations such as vacuum insulated panels (VIPs)\textsuperscript{11} or aerogels embedded in insulating matrices have emerged more recently.

Isothermal and refrigerated packaging is used for periods ranging from a few minutes for the administration of vaccines in hospitals or medical practices to several days for long-distance transport. Cooling losses through the walls must be compensated by a cold source. Cooling packaging commonly uses eutectic plates filled with a solution designed to have a melting point close to the target temperature of the products. Water with or without added salts or gellants is commonly used, but paraffins with melting temperatures above 0°C are also used. These passive cooling solutions require the packaging to be sized for each type of use, taking into account the external temperatures encountered by the packaging along its journey. For lower temperatures, dry ice is also used. It allows temperatures as low as -78.5°C.

Temperature-controlled transport equipment

While some may have opposed transport via refrigerated packaging and transport by refrigerated truck or active temperature-controlled containers, the two are totally complementary. Indeed, the refrigerated truck keeps the packaging in a controlled environment and thus reduces the risks of temperature excursions due to the limited time regulation capacity of the packaging’s passive cooling. Passive packaging, on the other hand, prevents temperature excursions at the interfaces during loading and unloading of the truck, which is exposed to outside temperatures. Vans, trucks, semi-trailers, swap bodies, sea containers and air containers are all essential components of the cold chain. Consisting of isothermal walls, usually made of polyurethane sandwich panels, isothermal cells are equipped with a cold source. Vapour compression refrigerating units dominate the market, with a predominance of ventilated evaporator units, but also eutectic plate units and mixed units. They still almost exclusively use high global warming potential (GWP) hydrofluorocarbons (HFCs) as refrigerants. Specific versions of temperature-controlled transport equipment have been designed by manufacturers to meet pharmaceutical requirements for homogeneity and temperature stability. Continuous ventilation, for example, but also the marking of loading areas are mandatory for this type of equipment.

\textsuperscript{11} A. Kacimi, G. Labranque. Vacuum insulated panels (VIP) in insulated packaging. 21 August 2011.
Refrigerated cabinets and refrigerators

At the end of the chain in the hospital, vaccination centre or pharmacy, before dispensing, vaccines must be stored in dedicated refrigerators or cold storage cabinets. Hospitals are equipped with numerous refrigerated cabinets for the storage of various health products including vaccines.

It is essential to use dedicated equipment, specifically designed for the storage of vaccines. This equipment must also keep the vaccines in a stable and homogeneous temperature environment that is not sensitive to the openings necessary for the dispensing of vaccines, which can be very frequent in certain circumstances. At vaccination sites, electrical power is not always available or continuous. Solar or gas refrigerators have been developed to overcome these problems.

With the advent of vaccines to be stored at -75°C or -20°C, specific equipment has had to be developed or adapted. They typically use vapour compression refrigerating units, but they still often use fluids with high GWP and their coefficients of performance deteriorate sharply below -50°C. Hydrocarbons (HCs) have emerged in this equipment as alternatives to hydrofluorocarbons (HFCs), albeit with new safety issues.

Temperature metrology

An efficient cold chain cannot be achieved without temperature traceability. Thermometers, indicators, integrators and temperature recorders are the guardians of the cold chain for vaccines as for any other heat-sensitive or perishable product.

The thermometer allows a one-off measurement of temperature, but the measurement of the temperature of a vaccine is difficult, particularly at interfaces where the ambient temperature can vary significantly and rapidly. For products with a low thermal inertia such as vaccines, measuring the environment and its stability using a temperature recorder is therefore the best solution. It allows the evolution of temperatures throughout the chain to be known and validated, either retrospectively or in real time. The use of temperature integrators or indicators is also common in vaccine logistics. It enables alerts to be detected and tracked and is therefore a useful complement to temperature recording. Their generally lower cost makes it possible to track the temperature as close as possible to the vaccines, at the secondary packaging level, and to limit recording to the transport or storage volume.
2.3. Good practices for the cold chain of vaccines

Even the best equipment in the world gives poor results if it is not used correctly. The dissemination and application of good practice are therefore essential.

**Equipment qualification**

Good practice begins with equipment qualification, from design qualification (DQ) to performance qualification (PQ) and maintenance qualification (MQ), including installation qualification (IQ) and operational qualification (OQ). They ensure that the equipment functions properly and meets pharmaceutical requirements from the design stage through to use in real-life situations.

For the vaccine cold chain, the World Health Organisation has had a Quality Safety Programme (QSP) in place for forty years to qualify equipment for the health product cold chain, from packaging to refrigeration, including semi-trailers and temperature recorders.

The certification of equipment, type or product, makes it possible to meet most of these requirements.

**Good operating practices and operator training**

The use of cold chain equipment requires knowing the rules. Operators should respect the loading areas in the equipment and the maximum duration and number of door openings. Cold chain equipment for vaccines should not, of course, be used for other products such as staff food or drinks. Temperatures should be checked regularly. The maintenance and servicing of the equipment also contributes to its performance, and health professionals should be familiar with the fundamentals.

This information should be widely disseminated to vaccine cold chain operators. Training of professionals is essential: logisticians, transporters, stockists, pharmacists and their teams must be familiar with good cold chain practices for health products, particularly vaccines. Guides have been developed for this purpose, such as the “Practical guide to the cold chain for health products”, published by IIR, AFF and SFSTP in 2008 in French and in 2010 in English, as well as the WHO practical guides for temperature traceability or the establishment of the cold chain. Other national initiatives complement these guides, in the form of information sheets or recommendations, for example.

**Patient awareness**

The patient, the last link in the chain, is always the weak link. When dispensing vaccines, patients should be made aware of how to transport and store vaccines in their refrigerator while waiting for their injection. The pharmacist’s dispensing advice is of prime importance in this context.

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3.1. The challenge of continuity and ubiquity

Delivering all the vaccines needed for human or animal vaccination campaigns anywhere, any time and on time remains a challenge in the 21st century. The global COVID-19 vaccination campaign, which requires enhanced cold chain for many vaccines or vaccine candidates, increases these difficulties. Vaccinating millions of people in well-equipped areas is not easy, and is a real challenge in areas where the cold chain and infrastructure are almost non-existent.

The challenge of temperature stability of vaccines

The pressure to develop vaccines as quickly as possible and to make vaccine doses available to save lives has been strong. The time available to develop stability profiles that meet the capability of the distribution network is often too short and results in a fragile distribution chain that can put the delivery of vaccines to patients at risk. Stability studies should be conducted to take into account the risks of temperature excursions encountered during the production, distribution and administration of the vaccine. For example, WHO has set criteria for a “temperature controlled chain”, or TCC, which is an innovative approach to vaccine management that allows vaccines to be stored at temperatures other than the usual +2°C to +8°C range used in the cold chain, for a limited period of time, under controlled and monitored conditions, and depending on the stability of the antigen. TCC generally involves a single release of the vaccine at ambient temperatures not exceeding +40°C for a specified number of days, immediately prior to administration.

The challenge of cold chain continuity

Continuity of the vaccine cold chain can never be taken for granted, as demonstrated by an incident in December 2020, which resulted in the destruction of thousands of doses of COVID-19 vaccines due to a cold chain break. Similarly, in 2019, a cold chain break resulted in the revaccination of several thousand people. More generally, the WHO estimates that a significant proportion of the vaccines injected each year worldwide is subject to temperature excursions between the laboratory and the patient. The effectiveness of vaccination campaigns depends on the continuity of the cold chain, the implementation of effective traceability and reinforced risk management.

The challenge of traceability and reliability

The success of vaccination campaigns depends of course on their logistical organisation, but also in many parts of the world on the population's approval and trust. The latter is based on confidence in the product and its effectiveness, but also in the vaccination system and its cold chain. Indeed, if until now patients were not necessarily informed, they are now aware of the crucial role of refrigeration in the preservation of vaccines. This confidence in the vaccine cold chain is based on the ability of professionals to demonstrate its effectiveness through impeccable traceability. Cold chain metrology and temperature recording, but above all their link with the products, are essential. Proving that 7 billion doses of vaccines are well preserved in a few weeks is a real challenge in terms of measuring, recording and managing data. The challenge of traceability also involves the digitalisation of temperature traceability and the modernisation of its metrology.

The challenge of competence

The deployment of this cold chain everywhere requires competent and trained people in all regions of the world. Training refrigeration professionals in the specific features of health care is as essential as training health care professionals in the specific features of refrigeration and its continuous chain from the laboratory to the patient. This means that tens of thousands of people must be trained throughout the world.

The challenge of equipment and solution performance

For healthcare professionals, the performance of cold chain equipment and solutions is also a real challenge. They are not cold chain professionals and do not intend to become so, but they must be able to trust the solutions and equipment they use. This requires their qualification by a third party, from their design to their maintenance, including installation and use, but also the certification of equipment and solutions. The development of globally recognised labels drawn up by the various players in the chain is essential17.

3.2. The environmental challenge

Although the respect of the vaccine cold chain remains the primary objective, its environmental, energy and economic efficiency must be optimal. Those involved in the chain must constantly strive to maximise its efficiency. The vaccine cold chain, by reducing vaccine wastage and saving several million lives each year, is a clear environmental benefit, but its energy consumption and direct impact on the greenhouse effect through direct emissions of high-GWP refrigerants constitute an environmental cost. The environmental balance of the vaccine cold chain can and should definitely tip in favour of sustainability.

The energy challenge

The energy consumption of the vaccine cold chain is not always optimal. The correct dimensioning of the cold sources in the packaging, their cooling to the right temperature, the volume of dry ice used, all contribute to overconsumption of energy. However, refrigeration systems from the warehouse to the dispensary cabinet can also be optimised. This is especially true of the -20°C and -80°C climate chambers for COVID-19 vaccines. Their direct installation in working environments with an ambient temperature of around +20°C increases energy consumption considerably. The installation of airlocks limiting temperature variations during openings would be preferable. Using top-opening freezers for sub-zero temperatures would also be a plus to limit cooling loss when opening. For these temperatures below -50°C, the choice of more efficient refrigeration systems should be studied, such as open air cycles18, whose energy yields are interesting in addition to the use of air as a refrigerant. Maintaining energy performance also requires good maintenance and servicing of installations, both in terms of insulation and cold production and distribution. Without maintenance and servicing, performance deteriorates very quickly.


The challenges of the vaccine cold chain

The refrigerant challenge

Temperature-controlled logistics is still the most neglected link in the cold chain in terms of refrigerants, especially for transport and for ultra-low temperatures. The use of very high GWP fluids below -50°C remains a challenge for refrigeration professionals, as does the replacement of high GWP HFCs, mainly R404A and R452A, in transport refrigeration units. Replacing R23 with hydrocarbons for temperatures below -50°C is an interesting alternative, but it should not overshadow energy performance and safety.

In application of environmental regulations on fluorinated fluids and more particularly on refrigerants controlled by the Kigali Amendment to the Montreal Protocol, vaccine cold chain professionals must look for alternatives to HFCs with high GWP. Natural fluids (CO₂), hydrocarbons (HC), but also air are good candidates. The table below shows the environmental impact and level of hazard of the various refrigerants currently in use and their alternatives.

<table>
<thead>
<tr>
<th>Refrigerant</th>
<th>Chemical Name</th>
<th>Formula</th>
<th>Chemical Type</th>
<th>GWP (100 years)</th>
<th>Safety Class</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>R22</td>
<td>Chlorodifluoromethane</td>
<td>CHClF₂</td>
<td>HCFC</td>
<td>1 780</td>
<td>A1</td>
<td>-20°C</td>
</tr>
<tr>
<td>R23</td>
<td>Fluoroform</td>
<td>CH₃F₃</td>
<td>HFC</td>
<td>12 690</td>
<td>A1</td>
<td>-70°C</td>
</tr>
<tr>
<td>R134a</td>
<td>1,1,1,2-Tetrafluoroethane</td>
<td>C₂H₂F₄</td>
<td>HFC</td>
<td>1 360</td>
<td>A1</td>
<td>0°C</td>
</tr>
<tr>
<td>R170</td>
<td>Ethane</td>
<td>C₂H₆</td>
<td>HC</td>
<td>1.4</td>
<td>A3</td>
<td>-70°C</td>
</tr>
<tr>
<td>R290</td>
<td>Propane</td>
<td>C₃H₈</td>
<td>HC</td>
<td>&lt;1</td>
<td>A3</td>
<td>-70°C</td>
</tr>
<tr>
<td>R404A</td>
<td>R125/R143a/R134a (44/52/4)</td>
<td>HFC</td>
<td></td>
<td>4 200</td>
<td>A1</td>
<td>-20°C</td>
</tr>
<tr>
<td>R410A</td>
<td>R32/R125 (50/50)</td>
<td>HFC</td>
<td></td>
<td>2 100</td>
<td>A1</td>
<td>-20°C</td>
</tr>
<tr>
<td>R600</td>
<td>Butane</td>
<td>CH₃CH₂CH₂CH₃</td>
<td>HC</td>
<td>&lt;1</td>
<td>A3</td>
<td>-20°C</td>
</tr>
<tr>
<td>R717</td>
<td>Ammonia</td>
<td>NH₃</td>
<td></td>
<td>-</td>
<td>B2</td>
<td>-20°C</td>
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<tr>
<td>R718</td>
<td>Water</td>
<td>H₂O</td>
<td></td>
<td>-</td>
<td>A1</td>
<td>0°C</td>
</tr>
<tr>
<td>R744</td>
<td>Carbon dioxide</td>
<td>CO₂</td>
<td></td>
<td>1</td>
<td>A1</td>
<td>-20°C</td>
</tr>
<tr>
<td>Air</td>
<td></td>
<td>N₂, O₂, ...</td>
<td></td>
<td>-</td>
<td>A1</td>
<td>-70°C</td>
</tr>
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</table>


Conclusion

The vaccine cold chain is more critical than ever to the success and performance of vaccination campaigns around the world. The COVID-19 pandemic has highlighted the major role of the cold chain and more than doubled the needed capacity by adding new temperature ranges.

Refrigeration and health professionals must work together to meet this unprecedented challenge of primary importance to humanity: controlling and curbing the first major global pandemic in human history.

This will of course require technical solutions, but above all it will require the men and women in the refrigeration and health sectors to implement new solutions on a daily basis and to continue this effort for many years to come!

The waste challenge

The vaccine cold chain generates a lot of waste, particularly with single-use refrigerated packaging. While their return is not always possible for quality and safety reasons, but also because of the cost of reverse logistics, their reuse for other applications at destination is possible, particularly in the food cold chain or building insulation.

The disposal or reuse of cold sources is also a challenge. Dry ice must be disposed of safely outside closed rooms and without contact with people who are not aware of its dangers. Eutectic plates can be easily recycled or reused.

Time-temperature indicators or integrators (TTIs) and temperature recorders should be reused or recycled. Many of these are designed for single-use only, so their electronic circuitry must be recycled, but the reverse logistics are simpler than those for packaging and should be considered wherever possible.

The challenge of digitisation

The digitisation of refrigeration using machine learning, process optimisation, preventive and above all predictive maintenance, but also real-time monitoring of the E2E temperature (from the laboratory to the injection) and alert management will also help reduce losses and improve environmental performance. In the future, the ideal would be to be able to check with a mobile phone just before dispensing that the vaccine has been stored and distributed in accordance with the temperature stability specifications of the product.

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