

Temperature-sensitive health products in the Expanded Programme on Immunization cold chain

A WHO-UNICEF joint statement encouraging greater health commodity supply chain integration for temperature-sensitive pharmaceuticals where appropriate

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Introduction

After officially declaring COVID-19 a public health emergency of international concern, the World Health Organization (WHO) and the Global Polio Eradication Initiative (GPEI) have released interim guidance on both routine and supplemental immunization activities. The pandemic and countries' response strain cold chain systems due to the surge capacity needed to store temperature-sensitive COVID-19 diagnostic and therapeutic products. This requires flexibility of the existing cold chain system to manage surplus vaccine and other essential health commodities and to ensure continuity of the delivery of comprehensive health care service.

The WHO and United Nations Children's Fund (UNICEF), reiterate the value of safe, feasible and cost-effective integration of temperature-sensitive health products into the Expanded Programme on Immunization (EPI) cold chain system.

This joint statement highlights integration as a practical solution and provides reference to planning tools and other existing mechanisms to design and implement a safe and efficient integrated cold chain system.

Ensuring safety requires recognition of risks associated with an integrated cold chain approach and ensuring sufficient capacities and mechanisms are in place to mitigate these risks.

Background

On 11 March 2020, WHO declared COVID-19 a public health emergency of international concern (1). Since then, many countries have adopted strict measures to control the spread of the disease in communities. On 24 March 2020, GPEI and, specifically, the Polio Oversight Board recommended suspending all polio campaigns whilst the COVID-19 pandemic is still active (2).

Some countries have also set up subnational laboratories to support testing for COVID-19. The test kits, reagents and other laboratory supplies that require cold storage may likely use the existing national and subnational cold chain facilities and equipment to accommodate the surge. The disrupted delivery schedules and the need to store other heat-sensitive health commodities, including COVID-19 diagnostic and therapeutic products, significantly challenge the existing cold chain capacity and alter the supply and stock balances.

Overview

The "cold chain" is a system of storing and transporting temperature-sensitive products at recommended temperatures from the point of manufacture to the point of use (3). Effective management of the cold chain is key to maintaining the safety and potency of vaccines and temperature-sensitive pharmaceuticals during storage, transport and service delivery (4).

Challenges in maintaining this cold chain can damage or diminish access to life-saving medicines and contribute to high wastage rates. To ensure efficacy and quality of care, health systems must find ways to ensure all cold chain medical products are properly managed from the manufacturer, through the entire supply chain, to the point of use.

In May 2015, WHO and UNICEF published a joint statement permitting the integration of other health commodities into the vaccine cold chain system if feasible and accomplished in a safe and efficient manner (5).

This statement remains valid and is updated to cover additional health commodities, including but not limited to medicines, laboratory reagents and test kits used for COVID-19, provided full adherence to best storage, handling and labelling practices to always clearly distinguish non-vaccine products from vaccines and diluents. Countries need to ensure that their cold chain system is sufficiently flexible to manage fluctuations due to logistical restrictions caused by health emergencies, such as the COVID-19 pandemic, and the additional demands placed on cold chain storage capacity from COVID-19 therapeutics and diagnostics and catch up of routine immunization/ supplemental immunization activities, in addition to other cold chain items utilized to deliver essential health services.

The strategy of integrating vaccine and non-vaccine essential health commodities in the cold chain contributes to achieving universal health coverage and equity. Some of the benefits of this approach includes allowing safe storage and availability of quality vaccine, therapeutic and diagnostic products, ensuring continuous delivery of essential health care services and achieving cost-efficiencies in storage, handling, management and transportation (6).

A cold chain integration strategy is not risk free. While some risk may occur during storage and delivery, the main concern is the risk of adverse events following immunization (AEFI) due to immunization-related errors. Improper segregation and labelling of products in the cold chain can easily lead to picking and administering the wrong product, which can lead to AEFI. A serious incident of AEFI can jeopardize public trust and confidence in the immunization programme. In the context of medicines, wrong product administration could put patient health and life at risk due to failure to receive appropriate treatment. These risks can be mitigated with proper training, monitoring and supervision, and full compliance of the health workers with the standards for medicine/vaccine administration and effective management of the cold chain and supply chain systems (6).

This new joint statement provides further guidance on how countries could mitigate the risks and maximize the benefits of an integrated cold chain strategy.

WHO and UNICEF guidance

The WHO and UNICEF guidance materials have included broad language suggesting that, if key provisions are met, other products may be safely stored in the vaccine cold chain (5).

These provisions include:

1. Maintaining good storage practices in accordance to the WHO guidance on storage and transport of time- and temperature-sensitive pharmaceutical products (7); and
2. Clear labelling and physical separation of non-vaccine products from vaccines and diluents at all times.

In April 2014, the WHO Strategic Advisory Group of Experts (SAGE) on Immunization (8) endorsed the recommendation of the WHO's Immunization Practices Advisory Committee (IPAC) to increase efforts toward the convergence and integration of health commodity supply chains, including cold chains (9). The 2015 WHO Immunization in Practice manual (10) also provides specific examples on how to safely apply integration of other heat-sensitive health commodities in vaccine refrigerators at health centres. Further, the WHO guidance on storage and transport of time- and temperature-sensitive pharmaceutical products can be found in the WHO Technical Report Series, No. 961, 2011, Annex 9 (7).

In the context of the COVID-19 pandemic, the guidance is further expanded to integrate the storage and transport of temperature-sensitive COVID-19 therapeutics, laboratory reagents and test kits in the vaccine cold chain system. However, **EPI refrigerators and vaccine carriers should NEVER be used for the storage of COVID-19 laboratory specimens or samples – to prevent contamination of vaccines and other pharmaceutical and laboratory products (11)**. Regardless of the demand for COVID-19 confirmatory testing, which may entail temporary storage of specimens in a cold chain prior to transport for testing in reference laboratories, it is critical that this recommendation is respected.

WHO and UNICEF Joint Statement on safe integration

As greater demands are placed on cold chain systems in countries, it is necessary to re-emphasize that:

1. It is permissible to use the EPI/vaccine cold chain system for the storage and transport of appropriate temperature-sensitive pharmaceuticals provided that labelling and separation to distinguish vaccine and non-vaccine products is consistently adhered to.

2. The WHO and UNICEF guidance on safe integration must be followed to ensure the quality and potency of all health products in the shared storage space.
3. The decision to integrate should be guided by a risk-benefit analysis, cold chain capacity assessment and an integration plan.

To that end, WHO and UNICEF recommend:

1. Careful evaluation of country-context benefits and risks of cold chain integration and use of this information to guide decision and policy-making, strengthen the capacity for surveillance and response to AEFI, and build health workers' capacity to safely implement the integration, especially at service-delivery points.
2. Safe integration of temperature-sensitive pharmaceuticals (including but not limited to COVID-19 diagnostics and therapeutics, oxytocin, insulin and HIV diagnostic kits and treatments requiring refrigeration) with vaccine products in the cold chain system require adoption of best storage and handling practices, including proper labelling and segregation to clearly distinguish non-vaccine products from vaccines and diluents and compliance with the standards for safe medication practices (12) (e.g. five "rights" of medicine/vaccine administration), especially at service-delivery points.
3. Comprehensive assessment of existing cold chain capacity, supply chain system design, policies and vaccine stock inventory prior to integration of non-vaccine products in the vaccine cold chain system to guide planning, including development of appropriate standard operating procedures (SOPs), information management system, training materials and job aids.

In particular, WHO and UNICEF recommend the following:

1. Safety considerations

- Where a variety of cold chain equipment is available, vaccines and diluents should be stored separately from other temperature-sensitive health products.
- Before a country integrates non-vaccine products into the EPI supply chain, all staff handling products in the supply chain need to be trained on the updated SOPs and safety guidelines to ensure effective integration and mitigate against products being mistaken for one another.
- For any new staff designated to manage the vaccine and health supply chain, including staff repurposed for COVID-19 surge capacity, countries are advised to use available innovative learning materials to ensure that staff responsible for managing the cold chain gain basic knowledge on supply chain management and the management of temperature-sensitive health products.
- To keep non-vaccine products and vaccines and diluents safely separated, each product should be allocated with a dedicated, labelled space within the shared cold chain equipment.
- If allotting dedicated space for each product is not feasible due to limited storage capacity, leaders and health care workers must adopt solutions to quickly and clearly distinguish vaccines from other products, such as placing clear and unambiguous visual cues on the external packaging.
- During storage and transport, ensure that pharmaceuticals and vaccines are kept in the original secondary packaging provided by the manufacturers.
- Countries should consider modifying receipt and distribution schedules for vaccines and relevant pharmaceutical products where and when required to avoid excess burden on the cold chain.
- Sustained facility-level monitoring and supervision should be in place to ensure consistent adherence to the five "rights" of medicine/vaccine administration (e.g. right product, right dose, right person, right route and right time) at the service delivery points.

2. Cold chain capacity assessment and forecasting

- When planning for future expansion of cold chain capacity, countries are advised to consider including an additional 25% to 30% storage space – depending on the usual forecast and planned supply chain interval – for surge capacity in times of emergency. This should be clearly reflected and aligned with the cold chain contingency plan and health emergency preparedness plan.
- Countries should maintain an updated list of all potential facilities (public and/or private) with functional cold chain equipment to ensure surge capacity and maintain updated cold chain inventories, particularly in the context of COVID-19 pandemic.
- Countries are encouraged to use data from latest assessments, such as the WHO-UNICEF Effective Vaccine Management (EVM) (13), Cold Chain Equipment Optimization Platform (CCEOP) (14), applicable system design analysis or cold chain mapping exercises, to determine their existing cold chain capacity and the feasibility of integrating storage of vaccines and appropriate non-vaccine products in the EPI cold chain system. In the absence of these, a rapid assessment should be conducted to ensure capacity is enough and compliant with the required storage temperature.
- To understand the total storage volume required, countries can use the existing WHO-UNICEF EPI Logistic Forecasting Tool (15) and WHO COVID-19 Essential Supplies Forecasting Tool (ESFT) (16).
- If the existing capacity is not sufficient to accommodate all appropriate temperature-sensitive health products or if the required storage temperatures are outside the usual ranges used for storing vaccines, countries are advised to explore options to manage surplus stock, such as:
 - planning storage allocation for each health product with consideration to need, delivery strategy, heat-sensitivity, packed volume, etc.;
 - adjusting distribution frequency based on cold chain capacity and utilization rate;
 - using any available and functional WHO prequalified cold chain equipment (17); and
 - commissioning of private cold chain facility where the temperature can be maintained to safely store the products.

3. Integration and documentation

- Countries should consider integrating temperature-sensitive health products, including but not limited to COVID-19 diagnostics and therapeutics, oxytocin, insulin and HIV diagnostic kits and treatments requiring refrigeration, into the national EPI cold chain system (including storage and transportation), where safe and feasible.
- Integration should not be limited to physical storage but should extend to recording, reporting, and monitoring of all supplies using the same cold chain equipment/ facility to ensure proper management.
- Countries should involve all personnel managing health programmes and health supply chain system in the process of developing/updating relevant guidelines, policies and SOPs in accordance to the global guidance.
- Countries are encouraged to strengthen their AEFI surveillance and response system (18) as part of risk management.
- Countries are advised to allow sufficient transition period or gradual implementation of the cold chain integration to ensure efficiency and safety. Temperature-sensitive products that are commonly used in primary health care settings, including but not limited to HIV test kits, some maternal health products such as oxytocin and insulin, could be useful starting points to explore integration with vaccines (6).
- Ensure that systems for supervising staff, monitoring temperatures and maintaining cold chain equipment are in place given the increased value (both monetary and breadth of health needs being met) of health products being stored jointly, especially with the possible stockpiling of vaccines and pharmaceuticals due to disrupted service delivery and programme activities.
- Closely monitor the implementation of cold chain integration at all levels and use collected data to draw lessons for corrective action and re-planning.

- Countries using cold chain as part of implementing clinical trials for new vaccines or health products are advised to conscientiously follow the handling, storage and transport protocol specific to the new product being tested.
 - Monitoring and recording temperatures of cold chain equipment used in clinical trials is done meticulously. Any fluctuation in the temperature must be recorded and reported per protocol. Therefore, it is recommended to designate a cold chain equipment with a continuous temperature monitoring device to accurately record the storage temperature of the tested product.
 - Any newly developed temperature-sensitive health products undergoing clinical trial must be properly labelled and physically separated from vaccines and pharmaceuticals in the cold chain system.
- Countries are encouraged to document experiences and best practices as evidence for future policies and guidance.

4. Communication and coordination

- Countries should consider developing a communication strategy to ensure all stakeholders and implementing parties are well informed about the relevant policies, guidelines and SOPs for the integrated cold chain strategy.
- Appropriate communication and orientation materials, including job aids and standard labels, should be made available for all concerned staff, especially at the lower level stores and service delivery points.
- Each officer responsible for managing the integrated cold chain and supply chain systems should have written and clearly defined roles and responsibilities.
- Establish a coordination mechanism to ensure timely notification and response to incidents of AEFI.

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WHO and UNICEF continue to monitor the situation closely for any changes that may affect this joint statement. Should any factors change, WHO and UNICEF will issue a further update. Otherwise, this joint statement will expire 5 years after the date of publication.

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