

Annex 8

Points to consider for setting the remaining shelf-life of medical products upon delivery

Edit and republication of *Points to consider for setting the remaining shelf-life of medical products upon delivery*, WHO Technical Report Series No. 1025, Annex 8, with a new Appendix 2.

Background

Following the publication of *Points to consider for setting the remaining shelf-life of medical products upon delivery* in 2020, a group from international agencies and humanitarian organizations procuring health kits (including the International Committee of the Red Cross, Médecins Sans Frontières, Save the Children, United Nations Children’s Fund, United Nations Population Fund and the World Health Organization) submitted a draft proposal for an amendment to include emergency health kits used as part of the humanitarian response as an additional example for consideration. During the fifth-sixth WHO Expert Committee on Specifications for Pharmaceutical Preparations, the *Points to consider for setting the remaining shelf-life of medical products upon delivery* guideline with a new Appendix 2 (*Example of minimum remaining shelf-life of emergency health kits used as part of the humanitarian response*) was adopted.

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1. Introduction

Following discussions relating to establishing a document for the remaining shelf-life of medical products upon delivery, and considering the discussion between representatives of the Interagency Pharmaceutical Coordination Group, it was decided to initiate a project to prepare a document on remaining shelf-life for procurement and supply of medical products.

The concept and project to prepare such a document was also discussed during the meeting of the fifty-third Expert Committee on Specifications for Pharmaceutical Products in October 2018. It was noted that some guidance documents were available from different procurement agencies. It was agreed that the World Health Organization (WHO) would initiate the discussion and preparation of a document, while following the WHO process for the establishment of such a paper.

Information and policy on remaining shelf-life was collected from different agencies and interested parties and a first draft document was prepared after an informal discussion meeting in Geneva, Switzerland, in January 2019.

It was then agreed that the document should cover not only finished pharmaceutical products but should be extended to cover other products, including medical devices, vaccines and in vitro diagnostics (IVD) products. (These products are collectively referred to as “medical products” hereafter.)

A draft document was prepared and circulated to members of the Interagency Pharmaceutical Coordination Group and other interested parties, inviting comments. The comments received were reviewed during an informal discussion meeting in June 2019 and the draft document was updated.

The aims of this document are:

- to facilitate the national authorization of importation of medical products, where applicable;
- to promote and support the efficient processing of medical products in the supply chain at all levels and thus prevent wastage because of delays;
- to assist in ensuring that there is sufficient stock of medical products, with acceptable remaining shelf-life, in-country;
- to prevent dumping of medical products;
- to ensure that barriers to access and supply of medical products are addressed;
- to prevent out-of-stock situations;
- to prevent receipt of donations of medical products that are not in accordance with this guideline;
- to prevent having expired stock of medical products.

The document is intended to provide guidance on setting the remaining shelf-life of medical products upon delivery and should be considered by all stakeholders in the supply chain of medical products. It is also recommended that the recommendations herein should be considered for inclusion in the national policy of countries.

2. Scope

The principles contained in this document should be applied to medical products in the supply chain. This includes donated products (1).

This document focuses on remaining shelf-life and does not address details contained in other guidelines, guides and agreements between different parties in the supply chain.

While the principles contained in this guideline apply to humanitarian emergency health kits, “kits” are made up of different products, owing to certain specifics related to the shelf-life of kits. These considerations are outlined in Appendix 2.

All stakeholders, including national regulatory authorities, manufacturers, suppliers, donors and recipients, should consider the recommendations on remaining shelf-life contained in this document.

3. Glossary

The definitions given below are taken from existing WHO guidelines, where available, or alternatively from other recognized guidelines.

batch. A defined quantity of starting material, packaging material or product, processed in a single process or series of processes, so that it is expected to be homogeneous. It may sometimes be necessary to divide a batch into a number of sub-batches, which are later brought together to form a final homogeneous batch. In the case of terminal sterilization, the batch size is determined by the capacity of the autoclave. In continuous manufacture, the batch must correspond to a defined fraction of the production, characterized by its intended homogeneity. The batch size can be defined either as a fixed quantity or as the amount produced in a fixed time interval.

consignment (or delivery). The quantity of a medical product or products, made by one manufacturer and supplied at one time in response to a particular request or order. A consignment may comprise one or more packages or containers and may include material belonging to more than one batch.

expiry date (or expiration date). The date placed on the container or labels of a medical product designating the time during which it is expected to remain within established shelf-life specifications if stored under defined conditions, and after which it should not be used.

finished pharmaceutical product. A product that has undergone all stages of production, including packaging in its final container and labelling. A finished pharmaceutical product may contain one or more active pharmaceutical ingredients.

install-by date. The date by which an instrument, device or other has to be installed.

manufacture. All operations of purchase of materials and products, production, quality control, release, storage and distribution of medical products, and the related controls.

manufacturer. A company that carries out operations such as production, packaging, repackaging, labelling and relabelling of medical products.

manufacturer (in vitro diagnostics). Any natural or legal person with responsibility for design and/or manufacture of an IVD product with the intention of making it available for use under their name, whether or not such a product is designed and/or manufactured by that person or on their behalf.

manufacturing date. The date of production of a batch is defined as the date that the first step is performed involving combination of the active ingredient with other ingredients. Where there are no other ingredients than an active ingredient, the date of the start of the processing or filling operation is considered as the date of production.

marketing authorization (product licence, registration certificate). A legal document issued by the competent medicines regulatory authority that establishes the detailed composition and formulation of the product and the pharmacopoeial or other recognized specifications of its ingredients and of the final product itself, including details of packaging, labelling and shelf-life.

medical product. Medical products include a wide range of manufactured items, such as finished pharmaceutical products, medical devices, vaccines and IVD products.

pharmaceutical product. Any material or product intended for human or veterinary use presented in its finished dosage form, or as a starting material for use in such a dosage form, that is subject to control by pharmaceutical legislation in the exporting state or the importing state.

production. All operations involved in the preparation of a product, from receipt of materials, through processing, packaging and repackaging, labelling and relabelling, to completion of the finished product.

remaining shelf-life. The period remaining from the date of delivery to the expiry date, retest date, install-by date or other use-before date established by the manufacturer.

retest date. The date when a material should be re-examined to ensure that it is still suitable for use.

shelf-life. The period of time, from the date of manufacture, that a product is expected to remain within its approved product specification while handled and stored under defined conditions.

upon delivery. The date a medical product is delivered as specified, for example at the port, at the point in-country after customs clearance, or at the end user, and as defined in the agreement between relevant parties.

4. The need for recommendations

As there was no harmonized approach on remaining shelf-life for medical products amongst procurers, donors and recipient countries, it was agreed that it would be beneficial to have a harmonized approach when considering remaining shelf-life. This will assist national regulatory authorities (NRAs), suppliers, donors, procurers, importers and distributors to manage medical products throughout the supply chain, thus ensuring that quality medical products reach the end user within their remaining shelf-life. The authorization of importation of medical products by NRAs sometimes delays access to medical products. A harmonized approach among countries may facilitate authorization and release of medical products in the supply chain in a timely manner.

This is not a stand-alone document. It should be read with other documents, guides and guidelines, including WHO guidelines such as *Guidelines for medicines donations* (1), *Stability testing of active pharmaceutical ingredients and finished pharmaceutical products* (2), *Good storage and distribution practices for medical products* (3), *Model quality assurance system for procurement agencies* (4), *The International Pharmacopoeia* (5) and guidelines of the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

5. Remaining shelf-life

Note: The manufacturing date of a medical product should be defined by the manufacturer and be provided, if requested.

5.1 Principles

Decisions on remaining shelf-life for medical products should be defined realistically, contextualized and adapted to each importer, following a thorough risk assessment taking into account the criteria below (at the end of this subsection). Remaining shelf-life should be defined based on relevant factors, including the category and type of product, inventory level, manufacturing and transit lead time, local release lead time, storage conditions, delivery chain, and resources in the recipient country or region.

There should be agreements between suppliers, purchasers and recipients covering the relevant responsibilities of each party, including remaining shelf-life or expiry date.

Products should be transported, received, stored and distributed in accordance with WHO *Good storage and distribution practices for medical products* (3). Special attention should be given to temperature-, light- and moisture-sensitive products.

Products supplied by the manufacturer or supplier should meet the policy of national government and the recommendations in terms of remaining shelf-life prescribed in this document.

Products should be appropriately labelled. The label should include the expiry, retest or install-by date, as appropriate. Products with an install-by date should be installed prior to the date specified by the supplier.

Products received should be scrutinized in an attempt to identify possible substandard and falsified products. It should be ensured that, for example, the expiry date is not falsified (6).

Where different periods for remaining shelf-life have been defined for products, recipients should ensure that the products meet the remaining shelf-life requirement for the intended destination, such as central warehouse, regional warehouse, testing site or user point.

National authorization for importation, where required, should be obtained based on the available information, including the expiry date of the product, to enable calculation of the remaining shelf-life and to assist in expediting approval.

Where so justified, suppliers, recipients and national authorities may negotiate deviations from the policy for remaining shelf-life, provided that:

- where the remaining shelf-life is shorter than stipulated in the policy, it is ensured that the stock will be consumed prior to expiry;

- the medical product reaches end users with adequate remaining shelf-life to permit confidence that there is time to consume it before expiry.

Risk assessment should be carried out to ensure that the parameters listed above are met, taking into account the following considerations:

- assessment of need;
- type of product: different criticality for the safety of the patient between pharmaceutical products, vaccines, medical devices and IVD products;
- expiry date: with this information, the remaining shelf-life at delivery time can be estimated;
- compliance with WHO guidelines on *Good storage and distribution practices for medical products* (3);
- delivery time to storage facility;
- storage conditions;
- stock rotation;
- delivery time from storage to end user;
- frequency of stock replenishment or order frequency (based on consumption): recipients and end users should regularly verify that medical products in stock are rotated or used within their remaining shelf-life, and adjust the quantities ordered to make sure that the medical products will be used during their remaining shelf-life;
- assessment of real needs, to ensure that the medical products can be used within their shelf-life;
- emergencies: during an emergency situation, the remaining shelf-life policy should be well balanced to ensure that lifesaving medical products will be received on time, and that the needs will be covered if there is an increased demand;
- logistic set-up: the location of the premises, the number of means or types of transportation (for example, the number of vehicles), and its adaptability will have an impact on the speed of delivery and, hence, on the confidence that products will be used before their expiry date;
- activity specificities: similarly, whether the medical products will be used by the national programme, or are managed directly by the importer outside a national programme, will make a difference in terms of speed of delivery to the end user;

- point of delivery: national warehouses or importer or end user facilities will also have an impact on the speed of delivery.

5.2 Expiry date

Products, such as pharmaceutical products, should have an expiry date allocated by the manufacturer. The expiry date should be established based on the results of stability testing obtained in the relevant packaging (primary and secondary packaging, where appropriate) and required stability conditions (2).

5.3 Retesting

Where a manufacturer or supplier has obtained approval from an NRA for a new or extended shelf-life, this may be applied.

Products with an expiry date should not be subjected to retesting by the purchaser or recipient for the purpose of extension of shelf-life. Only in exceptional cases, such as product shortages, should a recipient consider extending the expiry date of received batches, subject to certain conditions, such as availability of scientific data, the application of risk management principles, and NRA approval. The new expiry date should be reflected on the packaging.

Products with a retest date allocated by a manufacturer, such as chemicals and reagents, may be retested and used if the quality parameters are met.

An illustrative example of recommended remaining shelf-life of products is given in Appendix 1 for bulk medical products and Appendix 2 for the emergency health kits used in humanitarian response.

References

1. Interagency guidelines. Guidelines for medicines donations, third edition. Geneva: World Health Organization; 2011.
2. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-second report. WHO Technical Report Series No. 1010, Annex 10. Geneva: World Health Organization; 2018.
3. Good storage and distribution practices for medical products. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-fourth report. WHO Technical Report Series No. 1025, Annex 7. Geneva: World Health Organization; 2020.
4. Model quality assurance system for procurement agencies. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-eighth report. WHO Technical Report Series No. 986, Annex 3. Geneva: World Health Organization; 2014.
5. The International Pharmacopoeia, ninth edition. Geneva: World Health Organization; 2019.
6. WHO guidance on testing of “suspect” falsified medicines. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty-second report. WHO Technical Report Series No. 1010, Annex 5. Geneva: World Health Organization; 2018.

Further reading

- WHO guidelines for sampling of pharmaceutical products and related materials. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-ninth report. WHO Technical Report Series No. 929, Annex 4. Geneva: World Health Organization; 2005.
- WHO good practices for pharmaceutical quality control laboratories. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-fourth report. WHO Technical Report Series No. 957, Annex 1. Geneva: World Health Organization; 2010.
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- Guidance for procurement of in vitro diagnostics and related laboratory items and equipment. Geneva: World Health Organization; 2017.
- Establishing stability of in vitro diagnostic medical devices. Technical Guidance Series (TGS) for WHO Prequalification: Diagnostic Assessment (TGS2): In: WHO Expert Committee on Biological Standardization: sixty-eighth report. WHO Technical Report Series No. 1011, Annex 5. Geneva: World Health Organization; 2018.
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- ISO 23640:2011. In vitro diagnostic medical devices: evaluation of stability of in vitro diagnostic reagents. International Organization for Standardization.
- EP25-A: Evaluation of stability of in vitro diagnostic reagents: approved guideline. Wayne (PA): Clinical and Laboratory Standards Institute; 2009.

Appendix 1

Example of minimum remaining shelf-life of medical products

Note: The total shelf-life of a product is based on results from testing during stability (and, where relevant, sterility) studies under specified conditions. The storage and transport conditions stipulated by the manufacturer should be followed to ensure that the product quality is maintained.

Table 1

Example of the minimum remaining shelf-life (RSL), at the time of dispatch and upon delivery, of medical products, based on the outcome of risk assessment

Total shelf-life (TSL)	RSL at time of dispatch from manufacturer's premises	RSL at time of delivery at port of entry of country	RSL at time of delivery at end user level
48 months < TSL ≤ 60 months	40 months	30 months	12 months
36 months < TSL ≤ 48 months	30 months	24 months	12 months
24 months < TSL ≤ 36 months	20 months	15 months	6 months
12 < TSL ≤ 24 months	9 months	7 months	3 months
TSL ≤ 12 months	Special arrangements and conditions apply		

Appendix 2

Example of minimum remaining shelf-life for emergency health kits for use as part of humanitarian response

Emergency health kits are designed to facilitate the provision of priority health services in humanitarian emergencies to affected populations without access to medical facilities or where medical facilities are disrupted during a crisis. Depending on the type of emergency health kit, they contain a mix of essential medicines, health supplies and equipment designed to be used for a limited period of time and for a specific number of people.

Many different international and national organizations will be providing these emergency health kits in an acute or post-acute humanitarian response. Some examples of these organizations include:

- International Committee of the Red Cross (ICRC)
- Médecins Sans Frontières (MSF)
- Save the Children
- United Nations Children’s Fund (UNICEF)
- United Nations Population Fund (UNFPA)
- World Health Organization (WHO).

Examples of these kits include interagency emergency health kits, interagency emergency reproductive health kits, MSF emergency health kits, cholera kits, and ICRC surgical team kits. “Kits” manufactured and validated as such are not considered in the amendment (such as in vitro diagnostic kits, laboratory reagent kits or polymerase chain reaction (PCR) kits) and are not intended to be covered by this annex.

Background clarifications

Expiry date of an emergency health kit. Each emergency health kit should have a manufacturing date, defined as an “assembly date”, and an expiry date, defined as the “first item to be expired in the kit”, allocated by the supplier or the manufacturer assembling the kit.

The shelf-life of an emergency health kit is defined by the “first item to be expired in the kit”. In other words, the item in the kit with the shortest expiry date will define the expiry date of the entire kit. This implies that all the other items composing the emergency health kit have the same or a longer shelf-life.

The expiry date of the “first item to be expired in the kit” should follow the principles described in the document. Products, such as pharmaceutical products, should have an expiry date allocated by the manufacturer. The expiry date should be established based on the stability testing results obtained on the relevant packaging (primary and secondary packaging, where appropriate) and the required stability conditions. These are presented in the number of years, based on the calculation from the date of manufacture.

Remaining shelf-life of an emergency health kit. The remaining shelf-life is calculated based on the expiry date, storage conditions and risks. The remaining shelf-life of an emergency health kit should consider the expiry date of the entire kit (see definition of expiry date of an emergency health kit above) as the end date of possible use of the kit.

Criteria that influence the recommended remaining shelf-life are the purpose of the emergency kit (immediate response or prepositioning) and the phase of the emergency – acute or post-acute (protracted or recovery). Emergency health kit prepositioning requires that careful attention be paid to stock rotation in order to ensure that expiry dates do not arrive before use.

Examples of remaining shelf-life (RSL) at the different point of delivery for the shelf-life, up to the total shelf-life (TSL), are laid out in Table 2.

Table 2

Example of the minimum remaining shelf-life (RSL), at the time of dispatch and upon delivery, of emergency health kits, based on the outcome of risk assessment

Expiry date (as defined above)	RSL at time of dispatch from supplier's premises	RSL at time of delivery at port of entry of country	RSL at time of delivery at end user level
Acute emergency response^a			
Greater than 48 months	24 months	12 months	6 months
36 months < TSL ≤ 48 months	20 months	12 months	6 months
24 months < TSL ≤ 36 months	16 months	12 months	6 months
15 months < TSL ≤ 24 months	12 months	7 months	3 months
15 months or less	Special arrangements and conditions apply ^b		
Prepositioning in preparedness or post-acute emergency response^c			
Greater than 48 months	40 months	30 months	12 months
36 months < TSL ≤ 48 months	30 months	24 months	12 months

Table 2 *continued*

Expiry date (as defined above)	RSL at time of dispatch from supplier's premises	RSL at time of delivery at port of entry of country	RSL at time of delivery at end user level
24 months < TSL ≤ 36 months	18 months	15 months	6 months
15 months < TSL ≤ 24 months	14 months	12 months	3 months
15 months or less	Special arrangements and conditions apply ^b		

^a An acute emergency refers to a period of time when there are sudden, often unpredicted, humanitarian needs due to a natural or human-induced crisis, where the complexities of the crisis setting lead to added complexities in the delivery of humanitarian response, or where the scale of humanitarian needs exceeds the capacity of local or national actors; this may or may not refer to an official or unofficial scale-up of a coordinated interagency response.

^b There are some items that will never have more than 12 months of total shelf-life.

^c A post-acute emergency refers to a period of time when there are significant humanitarian needs due to a natural or human-induced crisis, where the complexities of the crisis setting have remained stable for a significant period of time (protracted) or where the crisis has begun to subside, with an implied gradual return to stability (recovery).

It should be kept in mind that when an emergency health kit has expired, many of the items in the kit will still be viable for use. The expired items should be disposed of and replaced in a manner that maintains the integrity and quality of the kit. In cases where these cannot be replaced, the remaining items can be used as bulk individual items and integrated into the health system, provided these individual components of the kits have been manufactured for dedicated use as a “single product” and stored and repackaged according to the approved stability and packaging conditions.