Annex 8

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

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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 the Interagency Pharmaceutical Coordination group (IPC) representatives, it was decided to initiate a project to establish a document on remaining shelf-life for procurement and supply of medical products.

The concept and project to establish such a document was also discussed during the meeting of the Fifty-third Expert Committee on Specifications for Pharmaceutical Products (ECSPP) 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 not cover only finished pharmaceutical products but should be extended to also cover other products, including, but not limited to, 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 IPC members, as well as 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; and

- 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.

As "kits" are made up of different products, and owing to certain specifics related to the shelf-life of kits, these are not included in the scope of this guideline. The principles contained in this guideline may, however, be used in considering the remaining shelf-life of items in a kit, as the expiry date of the kit can be short because of a specific product in the kit.

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(s), 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 (FPP). A product that has undergone all stages of production, including packaging in its final container and labelling. An FPP 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.

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, and includes details of packaging, labelling and shelf-life.

manufacturer (IVD). 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 his or her name, whether or not such an IVD product is designed and/or manufactured by that person him- or herself or on his or her behalf by (an)other person(s).

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.

medical product. Products including, but not limited to, 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 and/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. Defined as the period remaining, from the date upon 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 the medical product is delivered as specified, e.g. 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 will 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 the availability of quality medical products within their remaining shelf-life reaching the end-user. 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 standalone document. It should be read with other documents, guides and guidelines, including, but not limited to, WHO guidelines such as *Stability testing of active pharmaceutical ingredients and finished pharmaceutical products* (*2*), *Good storage and distribution practices* (*3*), *Guidelines for medicines donations* (*1*), *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 (*6*).

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 on page 195. It should be defined and be based on relevant factors, including but not limited to the category and type of product; inventory level; manufacturing and transit lead time; local release lead time; storage condition; 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* (*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 (*7*).

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, e.g. 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 allow for 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; and

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

Risk assessment to ensure that the parameters listed above are met should be done, 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 the remaining shelf-life at delivery time can be estimated;
- compliance with WHO guidelines on *Good storage and distribution practices* (3);
- delivery time to storage facility;
- storage conditions;
- stock rotation;
- delivery time from storage to end-user;
- frequency of stock replenishment – 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 the 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 life-saving medical products will be received on time; and that the needs will be covered if there is an increased demand.;
- the logistic setup: the location of the premises, the number of means/types of transportation and the number of e.g. vehicles, and its adaptability will have an impact on the speed of the delivery and, hence, on the confidence that products will be used before their expiry date;
- the activity specificities: similarly, whether the medical products will be used by the national programme, or are managed directly by the importer, outside of a national programme, will make a difference in terms of speed of delivery to the end-user; and

- the 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, e.g. 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.

References

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6. The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (https://www.ich.org/, accessed 18 November 2019).

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Further reading

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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 the product quality is maintained.

Table A8.1
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		