POLICY ON REMAINING SHELF-LIFE OF MEDICAL PRODUCTS UPON DELIVERY*

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DRAFT FOR COMMENTS

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*Explanatory note : « delivery » could mean delivery at different stages of the supply chain

POLICY ON REMAINING SHELF-LIFE OF MEDICAL PRODUCTS UPON DELIVERY

1. INTRODUCTION

Following discussions relating to establishing policy for remaining shelf-life (RSL) of medical products upon delivery, and considering the discussion between the Interagency Pharmaceutical Coordination (IPC) group representatives, it was decided to initiate a project to establish a policy on remaining shelf-life for procurement and supply of medical products.

The concept and project to establish such a policy 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 policy whilst following the WHO process for the establishment of such a policy 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 policy 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 (IVDs). (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 policy document are:

- to ensure that there is a balance between enforcing the remaining shelf-life policy and ensuring availability of medical products;
- 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 stock-outs;
- to prevent receiving donations of medical products that are not in accordance with this guideline; and
- to prevent having expired stock of medical products.

The policy contained in this document is intended to provide guidance on remaining shelf-life of medical products upon delivery and should be implemented by all stakeholders in the supply chain of medical products. It is also recommended that the policy be considered 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. (*See WHO Guidelines on Donations*).

This document presents policy on 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 due 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 kits.

All stakeholders, including manufacturers, suppliers, donors and recipients should implement the shelf-life policy contained in this document.

3. GLOSSARY

*(**Note:** the definitions below are taken from existing WHO guidelines where available, or alternatively, from other recognised 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 pharmaceutical or pharmaceuticals, 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 an API designating the time during which the API 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 APIs.

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 (QC), release, storage and distribution of pharmaceutical products, and the related controls.

Manufacturer
A company that carries out operations such as production, packaging, repackaging, labelling and relabelling of pharmaceuticals.

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)
Means any natural or legal person with responsibility for design and/or manufacture of an IVD with the intention of making the IVD available for use, under his or her name, whether or not such an IVD 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 the combining 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. (*Adapted from EU*.)

Medical product
Products including, but not limited to, finished pharmaceutical products, medical devices, vaccines and in vitro diagnostics (IVDs).

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 pharmaceutical 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 supplier

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

Shelf-life
Shelf-life is 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
Means 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 POLICY

As there was no harmonized policy 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 on policy for remaining shelf-life. This will assist national regulatory authorities (NRAs), suppliers, donors, procurers, importers and distributers to manage medical products throughout the supply chain, thus ensuring the availability of quality medical products within the 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 policy document 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, Good Storage and Distribution Practices, Donations, Model Quality Assurance System for Procurement Agencies (MQAS), Pharmacopoeia and International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines.

5. POLICY ON REMAINING SHELF-LIFE

Note: *The manufacturing date of a medical product should be defined by the manufacturer and be provided upon request, e.g. when this is not on the packaging.*

Principles

Policy on remaining shelf-life should be realistic. It should be defined for medical products and be based on factors such as, but not limited to, the category and type of product, inventory level, storage condition and resources in-country.

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

Products should be transported, received, stored and distributed in accordance with WHO Good Storage and Distribution Practices (GSDP). 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 guideline. Compliance with this requirement may be verified by an appropriate means, such as a pre-shipment inspection or other.

Products should be appropriately labelled. The label should include the expiry, re-test 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 scrutinised in an attempt to identify possible substandard and falsified products. It should be ensured that, for example, the expiry date is not falsified. (*See Guidelines on Substandard and Falsified Products, WHO Guidance on Testing of "suspect" falsified medicines.*)

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 shelf-life or expiry date of the product as well as the remaining shelf-life (where possible), to assist in expediting approval.

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

(a) the medical product quality will be assured;
(b) where the shelf-life is shorter than stipulated in the policy, it is ensured that the stock will be consumed prior to expiry;
(c) the medical product should reach end-users with adequate remaining shelf-life to show confidence on the quality of the medical product and time to consume it before expiry.

Risk assessment to ensure that the parameters are met should be done, taking into account at least the following criteria:

- type of product: different criticality for the safety of the patient between pharmaceutical products, vaccines, medical devices and IVDs;
- existing shelf-life: with this the remaining shelf-life at delivery time can be estimated;
- compliance with WHO GSDP guidelines;
- order frequency (based on consumption): recipients and end-user 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;
- emergency: during an emergency situation, the remaining shelf-life policy should be well balanced to ensure that patients will receive the medical products in time;
- the logistic set-up: the premises location, number of transportation means and its agility will have an impact on the speed of the delivery and, hence, have the products being used before their expiry date;
- the activity specificities: similarly, whether the medical products will be used by the national programme, or at own driven activities managed directly by the importer, will make a difference in terms of speed of delivery to the end-user;
- the point of delivery: national warehouses, importer or end-user facilities will also have an impact on the speed of delivery.

Expiry date

Products, such as pharmaceutical products, should have an expiry date allocated by the manufacturer. The expiry date should be established based on stability testing results obtained in the relevant packaging (primary, and secondary packaging, where appropriate) and required stability conditions. (*See WHO Guideline: Stability Testing of Active Pharmaceutical Ingredients and Finished Pharmaceutical Products. WHO Technical Report Series, No. 1010, Annex 10, 2018.*)

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 to extend 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 or supplier should have at least one year of shelf-life remaining (from the date of delivery to the enduser, to the labelled retest date). 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.

Examples of considerations and recommended remaining shelf-life of products are given in the Annexure.

References

[Note from the Secretariat: The references will be completed in the final text.]

Further Reading

1. WHO Good Manufacturing Practices for Pharmaceutical Products: Main Principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
Short name: WHO TRS No. 986, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

2. WHO Guidelines for Sampling of Pharmaceutical Products and Related Materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4.
Short name: WHO TRS No. 929, Annex 4
http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

3. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1).
Short name: WHO TRS No. 961, 957), Annex 1
http://www.who.int/medicines/publications/44threport/en/

4. Model Guidance for the Storage and Transport of Time-and Temperature-Sensitive Pharmaceutical Products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report. Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9.
Short name: WHO TRS No. 961, Annex 9
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

5. WHO Guidelines on Quality Risk Management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report. Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
Short name: WHO TRS No. 981, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

6. WHO Technical Supplements to Model Guidance for Storage and Transport of Time – and Temperature–Sensitive Pharmaceutical Products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report. Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5.
Short name: WHO TRS No. 992, Annex 5
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHOTRS_992_web.pdf

7. WHO Good Manufacturing Practices for Biological Products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report. Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 3.
Short name: WHO TRS No. 996, Annex 3
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex03.pdf

8. WHO Guidance on Procurement of IVDs and Related Laboratory Items.
https://apps.who.int/iris/bitstream/handle/10665/255577/9789241512558-eng.pdf?sequence=1

9. WHO TGS-2 on Establishing Stability of In Vitro Diagnostic Medical Devices.
https://apps.who.int/iris/bitstream/handle/10665/259742/WHO-BS-2017.2304-eng.pdf?ua=1

10. Annex to TGS-2 Establishing Component Stability for In Vitro Diagnostic Medical Devices. https://apps.who.int/iris/bitstream/handle/10665/311345/WHO-MVP-EMP-RHT-PQT-2019.03-eng.pdf?ua=1

11. International Standards Organization. ISO 23640: 2011. In Vitro Diagnostic Medical Devices -Evaluation of Stability of In Vitro Diagnostic Reagents.

12. Clinical and Laboratory Standards Institute. CLSI EP25-A Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline, 2009.

13. Model Quality Assurance System for Procurement agencies. WHO Technical Report 937, 2006, Annex 6.

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