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MCA Technical Working Group

Guideline for In-Use Stability Testing of Human Medicines

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This is a new guideline.

Comments should be provided by using the template (MCA-F-021/03) for Submission of Comments and sent to info@mca.gm

Keywords	in-use stability, stability study, test design, storage condition, batch

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Guideline for In-Use Stability Testing of Human Medicines

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Executive summary

This guideline has been developed by using the adoption approach based on the work-plan agreed in March 2023 by the Joint Technical Working Group for Guidelines in Marketing Authorization (TWG-MAG). The TWG-MAG consists of two representatives each of the national medicines regulatory authorities (NMRA) of Liberia (LMHRA, Liberia Medicines and Health Products Regulatory Authority), Sierra Leone (PBSL, Pharmacy Board of Sierra Leone), The Gambia (MCA, Medicines Control Agency), and Ghana (FDA, Food and Drugs Authority) and is facilitated by the GHPP PharmTrain2 Project team of the Federal Institute for Drugs and Medical Devices (BfArM, Germany).

Version 1 of the Guideline on In-Use Stability Testing of Human Medicinal Products for the National Medicines Regulatory Authorities of Ghana, Liberia, Sierra Leone, and The Gambia was finalised on 20 December 2023 for annotation in the MCA guideline.

This document should be read in conjunction with relevant sections of the MCA *Guideline for Marketing Authorisation (Registration) of Medicines* and other applicable guidance.

Information on the parent guideline

Title: Note For Guidance On In-Use Stability Testing Of Human Medicinal Products

Author(s): European Medicines Agency (EMA) - Committee For Proprietary Medicinal Products (CPMP),

Document No: CPMP/QWP/2934/99

Version No: (Not applicable)

Date of issue: 1 March 2001

Source (e.g. website link):
https://www.ema.europa.eu/en/documents/scientific-guideline/note-guidance-use-stability-testing-human-medicinal-products_en.pdf
(Accessed October 2025)

Document History

DISCUSSION IN THE QUALITY WORKING PARTY (QWP)	January/October 1999
TRANSMISSION TO THE CPMP	December 1999
RELEASE FOR CONSULTATION	December 1999
DEADLINE FOR COMMENTS	June 2000
ADOPTION BY CPMP	February 2001
DATE FOR COMING INTO OPERATION	September 2001

1 General aspects and terms deviating from parent guideline

1.1. For the purpose of consistency with other MCA guidelines, the terms of the parent guideline (left column) shall read as synonymous to the following terms (right column):

Parent guideline term	**Synonymous term**
Medicinal product	Medicine
SPC	SmPC
Leaflet	PIL

1.2. For the purpose of consistency with other guidelines, the following definitions apply:

Medicine
Any substance or combination of substances prepared, sold or presented for use in the diagnosis, treatment, mitigation or prevention of disease, disorder of abnormal physical state or the symptoms of it or restoring, correcting or modifying organic functions in human beings This includes finished pharmaceutical products, biotherapeutics, and vaccines. Not included are medical devices, in-vitro diagnostics, blood products, and animal products.

Container
The material employed in the packaging of a pharmaceutical product. Containers include primary, secondary and transportation containers. Containers are referred to as primary if they are intended to be in direct contact with the product. Secondary containers are not intended to be in direct contact with the product.

2 Text of Parent Guideline with MCA's annotations

Objective

The purpose of in-use stability testing is to establish - where applicable - a period of time during which a multidose product can be used whilst retaining quality within an accepted specification once the container is opened.

Scope

This guideline refers to medicinal products in multidose containers which - by nature of their physical form and chemical composition - due to repeated opening and closing, may pose a risk to its content with regard to microbiological contamination, proliferation and/or physico- chemical degradation once the closure system has been breached.

Introduction

The continued integrity of products in multidose containers after the first opening is an important quality issue. While this principle is acknowledged in the Ph. Eur. and EU Guidelines, no specific guidance is available on defining test design and conduct of studies to be undertaken to define in use shelf life in a uniform fashion. Therefore, this document attempts to define a framework for selection of batches, test design, test storage conditions, test parameters, test procedures etc., taking into consideration the broad range of products concerned.

Nevertheless, should this Note for guidance also be read in connection with the Notes for guidance on Development pharmaceutics (CPMP/QWP/155/96), Stability testing of existing active substances and related finished products (CPMP/QWP/556/96) and Stability testing of new drug substances and products (CPMP/ICH/2736/99).

The registration dossier for a multi-dose product should include either the in-use stability data on which the in-use shelf life is based or a justification why no in-use shelf life is established. This justification can also be based on experimental results.

MCA's Annotation: The following part needs to be rephrased: "While this principle is acknowledged in the Ph. Eur. and EU Guidelines, no specific guidance is available on defining test design and conduct of studies to be undertaken to define in-use shelf life in a uniform fashion."
by: "While this principle is acknowledged in some recognised pharmacopoeias and guidelines, no specific guidance is available on defining test design and conduct of studies to be undertaken to define in use shelf life in a uniform fashion."

Rationale: Other recognised pharmacopoeias and guidelines can be applied by to widen the scope. It is not restricted to Ph. Eur. and EU-Guidelines.

MCA's Annotation: The following documents need to be replaced: "Nevertheless should this Note for guidance also be read in connection with the Notes for guidance on Development pharmaceutics (CPMP/QWP/155/96), Stability testing of existing active substances and related finished products (CPMP/QWP/556/96) and Stability testing of new drug substances and products (CPMP/ICH/2736/99)."
by the following documents: "Nevertheless, should this Note for guidance also be read in connection with the MCA Guideline for Pharmaceutical Development, MCA Guideline for Stability Testing of Active Pharmaceutical Ingredients and Finished Pharmaceutical Products, and Stability testing of new drug substances and products (CPMP/ICH/2736/99)."

Rationale: These guidelines are applied by the MCA instead of the guidelines stated in the parent guideline.

Selection of batches

A minimum of two batches, at least pilot scale batches, should be subjected to the test. At least one of the batches should be chosen towards the end of its shelf life. If such results are not available, one batch should be tested at the final point of the submitted stability studies. The batch number,

date of manufacture and size of each batch should be stated. The container and closure of the product and, if present, the medicinal device should be equivalent to that proposed for marketing.

If the product is to be supplied in more than one container size or in different strengths, the in-use stability test should be applied to the product which presents the greatest susceptibility to change. The choice of the tested product should always be justified.

Test design

As far as possible the test should be designed to simulate the use of the product in practice taking into consideration the filling volume of the container and any dilution/reconstitution before use. At intervals comparable to those which occur in practice appropriate quantities should be removed by the withdrawal methods normally used and described in the product literature. Sampling should take place under normal environmental conditions of use.

The appropriate physical, chemical and microbial properties of the product susceptible to change during storage should be determined over the period of the proposed in-use shelf life. If possible, testing should be performed at intermediate time points and at the end of the proposed in-use shelf life on the final remaining amount of the product in the container.

Test storage conditions

The product should be stored under the conditions as recommended in the product literature (SPC and PIL) throughout the in-use stability test period.

Any other storage conditions should be justified.

Test parameters

The appropriate physical, chemical and microbial properties of the product susceptible to change during use should be monitored. The tests used must be appropriate to individual dosage forms, however, examples of parameter types which may need to be studied are given below:

Physical:	colour, clarity, closure integrity, particulate matter, particle size
Chemical content(s):	active substance assay(s), antimicrobial preservative and antioxidant degradation product level(s), pH
Microbial:	Total viable count, sterility

Analytical procedures

The analytical procedures used in the study should be described and fully validated. Stability indicating assays should be employed.

Presentation of the results

The results should be summarized and tabulated.

If relevant, the results should be presented graphically.

Evaluation

Conclusions reached based on the data provided should be stated. In the case of anomalous results these should be explained.

Where applicable and justified an in-use shelf life specification should be given.

In-use stability data should be used to determine whether or not a declaration of an in-use shelf life and additional storage conditions are necessary.

Labelling of the primary container

The in-use shelf life should be stated on the label. In addition (if space allows) there should be a space for the user to write the date of opening or the "use-by" date.

SPC, leaflet and labelling of the secondary container

The in-use shelf life and in-use storage recommendations- if applicable- should be included in SPC, leaflet and outer carton text.

3 Annotations to aspects not included in parent guideline

MCA's Annotation: The legal basis should be included as follows: This guideline has to be read in conjunction with the Medicines and Related Product Act, 2014. This guideline is coherent with national/regional frameworks and policies. The usage of this guideline by MCA is supported/embedded in the Act.

Rationale: Legal basis has to be followed by MCA therefore reference is made.

References used for this guideline adoption approach

- MCA Guideline on Pharmaceutical Development (MCA-GL-131)
- MCA Guideline on Stability Testing of Active Pharmaceutical Ingredients and Finished Pharmaceutical Products (MCA-GL-123)
- WHO - Quality Assurance of Medicines Terminology Database - List of Terms and related guideline, 13 October 2025 https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/mqa-terminology-sept-2020.pdf?sfvrsn=48461cfc_14&download=true (Accessed October 2025)

[When this document will be published, delete the section below before converting to PDF file.]

Prepared by:

Name: ..... Job Title: .....

Signature: ..... Date .....

Executive Director: ....
Signature Date