Notice to applicant

Central Administration of Pharmaceutical Products
General Administration For Stability

Requirement for post approval stability studies submission (Shelf-Life Extension /Change In-Use Study/Change in Stability Storage Conditions /change in short term excursion outside the label storage conditions)

Year 2025

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Purpose:

This guidance for submission document is intended to provide applicant on technical and other general data requirements to support stability studies post market approval submission in case of

shelf-life extension /change In-use study /change in Stability Storage Conditions without variation approval for locally and imported manufactured pharmaceutical product

• Scope:

This document is applicable to Human, herbal preparations, and veterinary products locally Pharmaceuticals Variation

Definition:

Short term excursion outside the label storage conditions: Supportive stability studies Ancillary stability studies that are conducted (as applicable) to support the practical use of the product (including label claims) or a re-test period or a shelf life photostability, in-use, short-term studies and studies to support excursions or modelling). Data to support short-term storage conditions, where relevant, may be provided as part of the primary stability studies.

• Documentation and Requirement for stability studies submission:

1-Change in the shelf-life of the FPP (as packaged for sale)

2-Change in the in-use period of the FPP (after first opening or after reconstitution or dilution)

3-Change in the labelled storage conditions of the finished pharmaceutical product (as packaged for sale), the product during the in-use period or the product after reconstitution or dilution

4- Change in short term excursion study outside the label storage conditions such as might occur during shipping or handling.

Description of change	Conditions to be fulfilled	Documentation required
Change in the shelf-life of the FPP (as packaged for sale) involving		
Extension	1-2	1-3-6-7
Change in the in-use period of the FPP (after first opening or after reconstitution or dilution):		
Extension	Non	1-2-6-7
Change in the labelled storage conditions of the FPP (as packaged for sale), the product during the in-use period or the product after reconstitution or dilution		
Extension:	3	4-5-6-7-8-10
change in short term excursion study outside the label storage conditions such as might occur during shipping or handling:		

Extension/Addition	4	9-10

Conditions to be fulfilled:

1. No change to the primary packaging type in direct contact with the FPP and to the recommended conditions of storage.

2. Stability data were generated in accordance with the currently accepted stability protocol.

3. The change is not necessitated by failure to meet specifications resulting from unexpected events arising during manufacture, or because of stability concerns

4-for drug products intended for storage in refrigerator and freezer

Documentation required:

1. Copy of the currently accepted shelf-life specifications and when applicable specification after dilution or reconstitution.

2. Proposed shelf-life, summary of long-term stability testing according to currently accepted protocol and test results for a minimum of two pilot- or production-scale batches for a period sufficient to support the proposed shelf-life.

3. Updated post-acceptance stability protocol and stability commitment and justification of change

4.Proposed in-use period, for 2 pilot batches or production (as required in EMA guidelines for in use) test results and justification of change. (at least one of these batches should be chosen towards end of its shelf life

5-if applicable, stability and/or compatibility test results to support the change to the storage conditions.

6- Commitment from stability testing site that method of analysis submitted for assay/ related/anti-oxidant/preservative is the same method of analysis submitted and validated in CADC (last updated guidelines for file assessment for pharmaceutical products for human use). (annex 1)

7- In case of change method, justification is required and full validation data and comparative results between previous and new method.

8-full validation data and chromatograms after dilution and reconstitution should be submitted.

9-One batch tested for the proposed excursion period at the accelerated conditions (30°C ± 2°C/65% RH ± 5% RH / 30°C ± 2°C/75% RH ± 5% RH. for FPP stored at 2-8 °C, for product stored at freezer, one batch study at 5°C ± 3°C or 25°C ± 2°C

10-Testing interval for in use and excursion studies should include time points and at the end of proposed in use shelf life /excursion studies (at least 3 points).

Notes:

1)As far as possible the in-use stability testing protocol should be designed to simulate the use of the FPP in practice, taking into consideration the filling volume of the container and any dilution or reconstitution before use.

2)Climatic zone the zones into which the world is divided based on the prevailing annual climatic conditions.

Climatic zone	Definition	Long term testing
IV a	Hot/humid climate	30C / 65% RH
IV b	Hot/very humid climate	30C / 75% RH

3)N. B: Egypt is categorized in climatic zone IVa, however studies performed at 250C / 60% RH would be accepted by submitting commitment for taking the responsibility of protecting the product under this condition

4)For full requirement for Stability study dossier please refer to "EDA Guidance for File Content of Stability Study Dossier"

https://www.edaegypt.gov.eg/media/qaeji1s5/note-to-applicant-guidance-for-file-content-of-stability-study.pdf

References:

1. **WHO** guidelines on variations to a prequalified product TRS 981 annex 3-2013
2. **EDA** Guidelines for Human Pharmaceuticals Variations, Updated Version
3. **EMA** Note for Guidance on In-use Stability Testing of Human Medicinal Products 2001
4. **ICH** -Q1A(R2) Stability Testing of New Drug Substances and Products
5. **ICH**-Q1E evaluation for stability data
6. **TRS** 1010 ANNEX 10 ,2018 WHO guidelines on stability testing of active pharmaceutical ingredients and finished pharmaceutical products
7. **VICH** –GL3 Stability testing of new veterinary drug substances and medicinal products - Scientific guideline
8. **EMA** Stability testing of herbal medicinal products and traditional herbal medicinal products - Scientific guideline
9. EDA frequently Q & A of in use stability.

Annex 1

Commitment

We, [Company Name], the owner of the product/ site of stability study

[Product Name],

History of Change:

Versions (Effective Date)	Updated Sections	Summary of changes
1/8/2025	Documentation and fulfilment requirements	Adding section for: short term excursion study outside the label storage conditions such as might occur during shipping or handling