HMA
Heads of Medicines Agencies

HOMEOPATHIC MEDICINAL PRODUCT WORKING GROUP

(HMPWG)

POINTS TO CONSIDER ON STABILITY TESTING OF HOMEOPATHIC MEDICINAL PRODUCTS

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1. Introduction

In principle, stability testing of homeopathic medicinal products must be regulated according to the same requirements that are applied to other medicinal products. The general principles are laid down in the "Guideline on Stability Testing: Stability Testing of Existing Active Substances and Related Finished Products" (CPMP/QWP/122/02, rev 1 corr)[1].
Because of the particularities of homeopathic preparations and the content of Annex 1 of the Directive 2001/83/EC, justified deviations within the scope of the Guideline on Stability Testing can be accepted.

2. Scope

These points to consider are intended to promote harmonisation of stability testing with respect to homeopathic medicinal products[2] subject to procedures according to Art. 14, 15 and 16, Directive 2001/83/EC.

3. Special requirements for stability testing of homeopathic medicinal products

Justified deviations from the Guideline on Stability Testing to demonstrate stability of homeopathic medicinal products may be acceptable.

3.1 Homeopathic stock[3]

The following options a) and b) are acceptable:

a) Stability testing on the homeopathic stock[4] should include all stability relevant parameters of the relevant monograph (Ph. Eur., in the absence thereof, an official pharmacopoeia of a Member State or in the absence thereof, an in-house-monograph equivalent to a pharmacopoeia monograph).

   According to Annex I of Directive 2001/83/EC stability data from homeopathic stocks are generally transferable to dilutions / triturations obtained thereof. The expiry date of the dilutions / triturations may not exceed that of the homeopathic stock[4].

[1] in the following referred to as 'Guideline on Stability Testing'
[2] as defined in Art. 1(5) of Directive 2001/83/EC
[3] as defined in the Ph. Eur.
[4] or the first possible homeopathic preparation according to the monograph, if required

The absence of an assay should be justified.

b) If the homeopathic stock[4] is tested for compliance with the monograph immediately before further processing to the finished product no stability tests on the homeopathic stock[4] are required. The time between the production of the homeopathic stock[4] and further processing to the finished product should be defined.

The absence of an assay should be justified.

3.2 Finished product

Stability tests on the finished product should refer to the general and particular stability relevant properties of the finished product and should be based on the Ph. Eur. monograph for the relevant dosage forms as well as on the monographs (Ph. Eur., in the absence thereof, an official pharmacopoeia of a Member State or in the absence thereof, an in-house-monograph) of the homeopathic stocks.

Whether substance-related stability testing and assaying should take place depends on the degree of dilution of the homeopathic stock (active substance) and / or its content in the finished product.

The proposed shelf-life should be documented by test results of each individual homeopathic medicinal product. However, in view of the particularities of homeopathic products deviations from this requirement are possible where justified (see 3.2.3).

Homeopathic medicinal products can be divided into two groups depending on whether the active substance can be identified (or identified and quantified) or cannot be identified.

3.2.1 Homeopathic medicinal products in which the active substance(s) can be identified (or identified and quantified)

These homeopathic medicinal products are characterised by active substance-specific characteristics of identity and possibly of assay according to monographs of the homeopathic stocks (Ph. Eur., in the absence thereof, an official pharmacopoeia of a Member State or in the absence thereof, an in-house-monograph) unless otherwise justified.
Therefore, stability testing includes both general stability properties of the dosage form and the substance-specific stability specifications (e.g. chromatographic fingerprints) as well as the active substance assay, where appropriate.

3.2.2 Homeopathic medicinal products in which the active substance(s) cannot be identified

In homeopathic finished medicinal products containing active substances in higher degrees of dilution and / or in a low content, the testing of the general stability-relevant properties of the dosage form of the finished product may be considered.

The identification and assay on active substances in a calculated value smaller than / equal to one part in 10.000 of the raw material in the finished product may be omitted. Omission of identification and assay of active substances in a calculated value greater than one part in 10.000 of the raw material in the finished product should be justified with appropriate documentation.

3.2.3 Transferability of stability data of homeopathic medicinal products

Under certain conditions the shelf-life of a homeopathic finished medicinal product as defined under 3.2.2 can be specified by reference to stability results for comparable products.

Comparability of the homeopathic medicinal products may be expected if among others the following conditions apply:

- reference products have the same dosage form
- reference products have the same specifications
- reference products are of comparable* composition in respect of other excipients (e.g. isotonicity agent), if contained
- comparable* manufacturing procedure, comparable* vehicle and type of starting material (e.g. herbal)
- same primary packaging material (complying with Ph. Eur.)
- manufacture of the products of the same applicant under comparable* manufacturing conditions

* has to be scientifically justified

- compliance with storage conditions and testing frequencies according to the Guideline on Stability Testing

- data from two pilot batches or two production batches from an appropriate number of reference products

If transferability of data is claimed, extrapolation of stability data according to Annex II of the Guideline on Stability Testing is not possible, unless otherwise justified (e.g. in case of same excipients).

4. In-use stability

As a rule, in-use stability data obtained according to the "Note for Guidance on In-Use-Stability Testing of Human Medicinal Products"[5] should be presented in the case of homeopathic finished medicinal products in multidose containers.

Where appropriate, the requirements of 3.2.3 of this Points to Consider document can be applied.

Information on in-use shelf life and in-use storage recommendations should be provided in the labelling of the finished product, where necessary.

[5] Note for Guidance on In-Use Stability Testing of Human Medicinal Products (CPMP/QWP/2934/99)