

Retention samples

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1. Purpose and scope

Article 12 paragraph 1.b of the Medicinal Products Licensing Ordinance (MPLO) requires that for each batch of ready to use medicinal product (the finished product), which is to be released for the (Swiss) market, a retention sample must be available.

In its definition of retention samples (see 3. hereunder), Annex 19 of the Guide to GMP stipulates that “there may be exceptional circumstances where this requirement can be met without retention of duplicate samples e.g. where small amounts of a batch are packaged for different markets or in the production of very expensive medicinal products”.

This technical interpretation defines the circumstances where the requirement of keeping retention samples for finished products (including investigational medicinal products) may be fulfilled with other means and describes such other means.

This technical interpretation does apply to the requirements for the Marketing Authorisation Holder only.

2. Basis

- Article 12 Paragraphs 1.a and 1.b MPLO (Medicinal Products Licensing Ordinance, SR 812.212.1)
- Annex 19 of the Guide to Good Manufacturing Practice (PIC/S PE 009 respectively Eudralex Volume 4)

3. Definitions and abbreviations

MAH: Marketing Authorization Holder

Reference sample: A sample of a batch of starting material, packaging material, bulk product, semi-finished product or finished product which is stored for the purpose of being **analysed** should the need arise during the shelf life of the batch concerned. Where stability permits, reference samples from critical intermediate stages (e.g. those requiring analytical testing and release) or intermediates that are transported outside of the manufacturer’s control should be kept.
(Echantillon d’analyse/ Analysenmuster)

Retention sample: A sample of a fully packaged unit from a batch of finished product. It is stored for **identification** purposes. For example, presentation, packaging, labelling, patient information leaflet, batch number, expiry date should the need arise during the shelf life of the batch concerned.
(Échantillon-témoin/ Ansichtsmuster)

Finished Product Product in its final pack which is ready to be released to the market.

4. Interpretation

4.1 Standard situation

4.1.1 Conditions

Retaining retention samples of finished products in normal circumstances (majority of cases) should be done under the following conditions:

Duration of storage: at least one year after the expiry date of the batch.

Size of samples: at least one sample from each individual batch of finished product.

Storage conditions: no special requirements related to temperature, humidity, light (since they are not kept for analytical purposes). However the readability of packaging materials should be ensured during the whole storage duration. It must also be considered, that temperature and humidity might influence the adhesive characteristics of labels.

If stored in accordance with the Marketing Authorisation, retention samples may be interchangeable with reference samples. If such interchangeable sample has been used for analytical purposes, empty primary and secondary packaging material together with leaflet for patients should not be discarded but kept like any unopened retention sample until the end of the period of storage.

Place of storage: preferably at the site where the responsible person of the MAH releasing the batch for the Swiss market is located. Retention samples may be kept at a contract acceptor, if available for the MAH within a few hours (i.e. during any inspection by a competent authority).

4.2 Exceptional cases

In some exceptional cases other means than retention samples of the finished product can be accepted. Any proposed exception to this should be justified to, and agreed with the relevant competent inspectorate.

The responsible person of the MAH is responsible that the criteria and requirements for exceptional cases, the possible alternatives to replace retention samples and the conditions as listed below, are fulfilled.

4.2.1 Criteria for exceptional cases

Exceptions should generally be granted case by case. Following criteria may be used, alone or in combination (e.g. A with B), in order to justify exceptional cases:

- A. Size of a batch (amount of units packaged per batch): 30 to 50 units are given as a guiding value. Investigational medicinal products (IMP) do not fall into this category despite that IMP batches are mostly small.
- B. The retail price for the sample exceeds 600.- Sfr.
- C. Medicinal products with short shelf life (less than 12 months).
- D. Size of one packaged unit (e.g. some medicated feeds or medicated pre-mixes,) or of some large (hospital) packages (e.g. 12 x 0.5 litre bags of solutions for infusion).

4.2.2 Possible alternatives to replace retention samples

The following alternatives to a retention sample of a finished product may be accepted if the criteria of an exceptional case are fulfilled:

- A. Storage of batch specific primary and secondary packaging materials. This material must include all variable data. This means that (the labelling of) the primary packaging material and the folding box (secondary packaging material), the leaflet for patients and the dosing aids are available for a full visual check.
- B. Colour photographs or photocopies of batch specific primary and secondary packaging material, i.e. labelling of primary packaging material, folding box (secondary packaging material) and leaflet for patients. Thus photographs can be accepted if they are easily readable and if all relevant aspects for a full visual check are covered (i.e. including lot number and version of the secondary packaging material and any markings or texts directly applied on primary packaging, e.g. ampoules).

The retention of colour photographs or photocopies must allow the identification of a hologram, of specially coloured glue, information given in braille, information on dosing aids or of

other special secondary packaging markings which may be used in order to facilitate the distinction between an original and a counterfeit product.

The whole process, including unpacking and repacking of the samples, must be described in an SOP. The company does need an establishment license for this activity (this does not have to be a manufacturing license).

4.2.3 Conditions

Duration of storage: at least one year after the expiry date of the batch.

Size of samples: at least one sample of packaging material from each batch of finished product.

Storage conditions: no special requirement related to temperature, humidity, light. However the readability of materials replacing retention samples should be ensured during the whole storage duration.

Place of storage: preferably at the site where the responsible person of the MAH releasing the batch for the Swiss market is located. Retention samples may be kept at a contract acceptor, if available for the MAH within a few hours (i.e. during any inspection).

Traceability of samples: The traceability in such exceptional cases should also be ensured and documented, e.g. through batch records or the responsible person of the Swiss MAH may state that the packaging material or the photographs of the packaging material and of the leaflet for patients is/are identical with those of the released batch of medicinal product.

5. Changes to the previous version

- Update of the references due to the revision of the MPLO (valid from January 1st, 2019)

6. Appendixes

- None