swissmedic

Information sheet
Preparation for blinded dispensing

Identification number:	BW101_10_817
Version:	1.0
Valid from:	01.11.2024

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1 Background

Manufacture of a blinded investigational medicinal product always involves a change to the medicinal product and is therefore not permissible under Category A. However, "preparation for blinded dispensing" of an otherwise unchanged investigational medicinal product is permissible under category A (see Art. 19 para. 1 let. b Clinical Trials Ordinance (ClinO)). In this case, the investigational medicinal product is not manufactured as ablinded batch, but prepared on the spot immediately prior to dispensing under blinded conditions. More specifically, this means the provision of a single dispensing/administration/dosage unit of an investigational medicinal product (test/reference product or placebo) authorised in Switzerland and which is prepared and blinded in a single work step. This must be done by a designated individual with no associations with the trial, who prepares a single dispensing/administration/dosage unit for a single patient immediately prior to administration (e.g. swallowing a tablet, injecting a solution) in accordance with the Information for healthcare professionals and then applies the appropriate trial-specific label or another form of masking for the purpose of blinding. After that, the single dispensing/administration/dosage unit of blinded investigational medicinal product is handed over to the trial team for application to the trial participant..

2 Definitions

2.1 Licence to manufacture medicinal products and investigational medicinal products

The legal requirements for companies that manufacture medicinal products for the market are set out in Eudralex Volume 4. The documents in Annex 13 of Eudralex Volume 4 set out the provisions governing the manufacture of investigational medicinal products.

Any pharmacy/hospital pharmacy that manufactures investigational medicinal products in accordance with Art. 4 para. 1 let. c of the Federal Act on Medicinal Products and Medical Devices (Therapeutic Products Act, TPA) requires an establishment licence for this purpose from Swissmedic (Art. 5 para. 1 let. a TPA).

2.2 Preparation and reconstitution

In many cases, however, hospital pharmacies' involvement in clinical trials in terms of preparation does not extend beyond the reconstitution of the investigational medicinal product. Annex 13 describes the reconstitution of investigational medicinal products in detail and distinguishes it from the manufacture of investigational medicinal products.

Reconstitution is defined as:

A defined activity with the investigational medicinal product

I. Dissolving or dispersing the investigational medicinal product for administration
II. Diluting or mixing the investigational medicinal product with some other substance used as a vehicle for the purposes of administering it.

The investigational medicinal product must exist before a process can be defined as reconstitution. Reconstitution has to be undertaken as soon as practicable before administration.

Reconstitution is not:

The mixing of several ingredients, including the active substance, to produce the investigational medicinal product.

3 Clarification

Once the process of manufacturing the investigational medicinal product has been completed, the medicinal product is ready to dispense for use. In certain cases, the investigational medicinal product may have to be prepared for administration or use.

3.1 Preparing investigational medicinal products

If preparation for dispensing, including preparation for blinded dispensing to a trial participant, meets the definition of reconstitution and no additional manufacturing step, such as batch blinding, is introduced, this activity is not regarded as manufacture and does not require a manufacturing licence from Swissmedic.

3.2 Batch blinding

Batch blinding is intended for a group of trial participants and is done on a stock creation basis. This complex, error-prone process is regarded as manufacturing and ends when the batch is blind-packed and blind-labelled. The validity of the data from a double-blind trial is directly dependent on correct blinding.

3.3 Preparation for blinded dispensing

Preparation for blinded dispensing is intended for single trial participants and must be done sequentially (i.e. one trial participant after the other). Trial participants are first allocated a particular treatment from a selection of treatments or placebo using a randomisation sequence prescribed by

the sponsor (as a document or by interactive exchangeable (i.e. voice or web) response system (IXRS)). This is followed by the actual process of preparation/reconstitution. After preparation, the investigational medicinal product is blinded as part of the same work procedure by labelling it in such a way that there is no way of identifying what choice of treatment was made when it is dispensed. The entire process must be described in a working instruction and traceability must be guaranteed. This working instruction must be submitted to the relevant authorities with the Clinical Trial Application (CTA) dossier regardless of whether the trial falls into Category A, B or C.

3.4 Swissmedic manufacturing licence

Since the process of preparation or patient-specific preparation for blinded dispensing follows manufacture and is not identical to manufacture as defined in Art. 4 para. 1 let. c TPA, the legal requirements of the Therapeutic Products Act for manufacture do not apply in this case. Since, under the provisions of the TPA, a Swissmedic licence is mandatory only for manufacture, it can be inferred that preparation does not require a manufacturing licence.

It follows from this:

No Swissmedic manufacturing licence is required for the preparation or patient-specific preparation of investigational medicinal products for blinded dispensing.

3.5 Categorisation

The category is assigned on the basis of Art. 19 ClinO. Trials in Category A must only use unchanged medicinal products that have been authorised in Switzerland and may only use them in their authorised indication. Since manufacture of a blinded investigational medicinal product batch always involves a change to the medicinal product, it is therefore not permissible under Category A. However, "preparation for blinded dispensing" of an otherwise unchanged investigational medicinal product (see Art. 19 para 1 let. b ClinO) is permissible under category A according to Art. 19 para. 1 ClinO.

3.6 Clinical Trial Application (CTA) dossiers

1. No documents on cantonal legislation have to be submitted to the authorities with applications for approval of new clinical trials.
   It is the responsibility of the sponsor to evaluate pharmacies and the responsibility of medical staff/pharmacists to act in accordance with cantonal legislative requirements and authorisations (e.g. provision of oncologicals, sterile medicinal products, etc.)
   The compliance of the process for sequential preparation for blind dispensing with this information sheet can be verified during GCP inspections.
2. The working instruction containing the process description must be described in the Pharmacy Manual of the CTA dossier or exist as a separate document so that the authority reviewing the dossier can easily recognise that preparation is patient-specific for blinded dispensing.
3. It is the responsibility of the sponsor to ensure guaranteed traceability of blinded treatments (this would also be the case for preparation on its own).
4. The procedure applies to authorised and non-authorised investigational medicinal products and thus to Category A, B and C trials.

5. It is the sponsor's responsibility to ensure that marking (labelling) is done correctly during preparation and, if necessary, that blinding is maintained. These labels do not have to be submitted (see CTA guideline).

4 References

1. EudraLex - Volume 4 - Good Manufacturing Practice (GMP) Guidelines
2. 812.21 Bundesgesetz über Arzneimittel und Medizinprodukte (Heilmittelgesetz, HMG)
3. 810.305 Verordnung über klinische Versuche mit Ausnahme klinischer Versuche mit Medizinprodukten (Verordnung über klinische Versuche, KlinV)
4. CTA Guideline (BW101_10_006e_AA Guideline Clinical Trial Application Dossier)
5. Teilrevision des Ausführungsrechts zum Bundesgesetz über die Forschung am Menschen (HFG), Erläuternder Bericht (07.06.2024)

Change history

Version	Change	sig
1.0	New information sheet	gav