# Market release and distribution in cooperation with a pre-wholesaler

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## 1. Purpose and scope

Marketing Authorisation Holders are bound to follow comprehensively valid requirements, especially the Therapeutic Products Act (TPA; SR 812.21) and the Medicinal Products Licensing Ordinance (MPLO; SR 812.212.1). Essential elements of these requirements are the release of a batch of a ready-to-use medicinal product for the Swiss market according to Article 13 MPLO and the GDP compliant distribution following the market release (cf. Article 15 Paragraph 2 MPLO). This document highlights aspects of special importance in situations where the Marketing Authorisation Holder has fully or partially contracted out storage facilities and/ or related physical operations to another company (e.g. storage, retention sample storage, delivery).

## 2. Basics

- Article 13 MPLO
- Article 15 Paragraph 2 MPLO
- Article 18 Paragraph 2 MPLO
- Chapter 7 of the Guide to Good Manufacturing Practice (GMP; i.e. PIC/S Document PE 009 or Eudralex Volume 4, respectively)
- EU Guidelines 2013/C 343/01 on Good Distribution Practice of medicinal products for human use (Human GDP)
- EU Regulation 2021/1248 on Good Distribution Practice for veterinary medicinal products (Vet GDP), Article 59 TPA

## 3. Definitions and abbreviations

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| Batch certificate | A document summarising and certifying the quality relevant information on a batch of a ready-to-use medicinal product according to the Internationally Harmonised Requirements for Batch Certification as given by the European Medicines Agency EMA (document EMA/INS/MRA/387218/2011 Rev 5). |
| MAH | Marketing Authorisation Holder |
| RP | Responsible Person, designated by the MAH: Should carry out their duties in such a way as to ensure GDP compliance and that public service and legal obligations are met |
| Pre-wholesaler | Authorised wholesaler to whom a MAH who does not maintain own storage facilities has contracted out the physical operations of market release and distribution (e.g. receipt, visual check of received goods, storage, delivery) |

## 4. Interpretation

### 4.1 General remarks on market release and distribution

With the market release, the MAH takes over the responsibility for the released medicinal product and confirms that the batch corresponds to the marketing authorisation with regard to composition, manufacturing process, specifications and quality demands (including type of container and package presentation) and that it is manufactured in accordance with the rules of GMP (cf. Article 13 MPLO).

The market release must therefore be based on the complete knowledge and unambiguous documentation of the full history of a batch through all manufacturing stages (including the transport to the stock where the batch to be released is stored).

In order to maintain full traceability of the decision on the market release, the MAH needs to guarantee the availability of general documentation and batch documents on the manufacture and testing of a medicinal product (cf. Article 12 Paragraph 1 Letter c MPLO).

As for the distribution following the market release, the MAH needs to guarantee that unambiguous documentation (on paper or electronically) is available for the purchase and sale of the distributed medicinal products. This documentation must be easily accessible and allow a fast and complete notification of the recipients of a medicinal product in case of product recalls (cf. chapters 1, 2, 4, 5, and 6 of the EU Guideline on Human GDP as well as chapters II, III, V, VI and VII of the EU Regulation on Vet GDP). It must be defined how the legitimacy of customers receiving the medicinal product is checked (cf. chapter 2 of the EU Guideline on Human GDP as well as chapter III of the EU Regulation on Vet GDP). Further on, the MAH has to guarantee that distributed medicinal products are stored and delivered in compliance with the necessary conditions (chapters 3, 5 and 9 of the EU Guideline on Human GDP as well as chapters IV, VI and X of the EU Regulation on Vet GDP).

## 4.2 Market release and distribution in cooperation with a pre-wholesaler

The MAH is allowed to contract out the physical operations of market release and distribution (e.g. receipt, visual check of received goods, storage, delivery) to another company (i.e. the pre-wholesaler) provided that:

- all requirements for market release are met as described in Article 11, Article 12 and Article 13 MPLO (under consideration of the remarks in chapter 4.1 of this document);
- the distribution following the market release is performed in compliance with the EU Guideline on GDP (human and vet as applicable);
- a technical contract between the MAH and the pre-wholesaler is established and continuously updated and meets the guidance given in Chapter 7 of the Guide to GMP;
- the pre-wholesaler has the required establishment licence for the performed activities: at least an establishment licence for wholesale without market release and if applicable, for importation without market release.

The following aspects are of special importance and need to be considered:

- the MAH must be in possession of a establishment licence including marked release;
- the MAH must make all arrangements which enable him to perform the market release and to take over the responsibility for the released batch;
- the technical contract must assign clear responsibilities and define clearly which procedures apply;
- the final decision on the market release and the taking over of the final responsibility for the released batch (including a possible decision on batch recall) cannot be delegated/outsourced by the MAH; Remark: This is the reason for the high requirements for a technically responsible person of MAHs, as it is required in Article 18 Paragraph 2 MPLO;
- the MAH is expected to store in any case at his own site all information which is requested to be included in a batch certificate (cf. chapter 3 of this document);
- some of the relevant documentation on market release and distribution as well as retention samples (“Ansichtsmuster” / “Echatillons-témoin”) may be stored at contract acceptors, provided that the documents or copies thereof as well as retention samples or appropriate alternatives if justified (as defined in I-SMI.TI 03) can be accessed by the MAH within short notice (i.e. several hours). The contract giver should periodically check this accessibility;

- the MAH's overall responsibility for the marketed medicinal products includes the responsibility for establishing a system for market surveillance (including pharmacovigilance) and for reporting conclusions resulting from market surveillance to the competent authority, e.g. decisions on batch recalls (cf. Article 59 TPA);
- there must be a written contract between the contract giver and the contract acceptor. The compliance of delegated activities must be regularly assessed, based on risk depending on the nature of outsourced activities, and whenever there has been a change to the outsourced activities. Audits should be permitted at any time by the MAH in terms of compliance with legal requirements and compliance with the technical contract. The contract acceptor should not pass to a third party any of the work entrusted to him under the contract without the contract giver's prior evaluation and approval (cf. chapter 7 of the EU Guideline on Human GDP as well as chapter VIII of the EU Regulation on Vet GDP);
- whereas it might be possible to refer for general compliance with legal requirements to an establishment licence or certificate and to inspections performed by the competent authorities, the concrete compliance with the contract needs to be assessed in form of regular audits;
- the assessment procedure should be described and include a risk-based definition of the type (e.g. reference to establishment licence or certificate, performance of audits), length, depth and frequency of the assessments. A documented justification for the defined procedure should be available.

## 5. Changes to the previous version

- Chapter 1: precisions about scope added: a MAH can fully or partially contract out storage facilities and/or related physical operations to another company independently of his own storage facilities
- Chapter 2: Introduction of the EU GDP Regulation for veterinary medicinal products
- Chapter 4: Introduction of references to the chapters of the EU GDP Regulation for veterinary medicinal products
- Chapter: 4.2: precision about the needed establishment licence for the pre-wholesaler and for the MAH; Addition of the reference to I-SMI.TI.03

## 6. Annexes

- None