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Change history

Version	Valid and binding as of:	Modified without version change	Description, comments (by author)	Author's initials
02	**25.07.16**		**Adaptation following the introduction of a template for RP Declaration.** **Details of the documents to be submitted.**	**gme**
		18.05.15	New change history inserted in the document. The remaining content of the documents was not reviewed and is unchanged.	wis
01	02.08.10		First registry in the Swissmedic Quality Management System	zim

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1 Objective

The objective of this information sheet is to clarify which documents should be submitted within the framework of an authorisation application (new application) or a variation requiring notification / approval for a product that has already been authorised, in order to demonstrate that the responsible person (see section “3 Duties of the responsible person (RP)” below) has verified compliance with Good Manufacturing Practice (GMP) rules on the part of foreign manufacturers of active pharmaceutical ingredients and / or ready-to-use medicinal products, in accordance with Art. 7, para. 1, part i Medicinal Products Licensing Ordinance (MPLO).

2 Scope

This information sheet is intended for authorisation holders or applicants for the authorisation of ready-to-use medicines that are manufactured abroad and / or those manufactured in Switzerland, and that contain active pharmaceutical ingredients produced by foreign manufacturers.

3 Other valid documents

Document ID
ZL000_00_002e_FO Manufacturer information
ZL000_00_025e_FO Responsible Person Declaration
BW105_00_002e_VZ_List_of_Countries_with_recognised_GMP_control_systems
ZL000_00_001e_WL Formal requirements
ZL000_00_002e_VZ Overview documents to submitted

4 Duties of the responsible person (RP)

It is the duty of the responsible person (RP) to ensure that ready-to-use medicinal products to be released to the market have been manufactured in compliance with the GMP rules. The RP must also ensure that the active pharmaceutical ingredients contained therein are also manufactured in compliance with the GMP rules (MPLO Art. 5, para. 1 and Art. 10, para. 3, part b).

5 Verification of GMP compliance by the responsible person

The verification of GMP compliance by foreign manufacturers must be carried out regularly, under the responsibility of the RP. Documents such as GMP certificates, audit reports, inspection reports and Site Master Files, etc. that are taken into consideration for this verification may be requested by Swissmedic at any time and / or examined within the framework of inspections.

6 Proof that GMP compliance has been verified

Form *Declaration by the Responsible Person* (RP Declaration) and the documents described in section 6.1 must always be submitted with applications for authorisation (new applications) or variations requiring notification / approval for authorised preparations. In the RP Declaration, the RP confirms the manufacturer's GMP conformity on the basis of an audit conducted by the authorisation holder or by a third party commissioned by the authorisation holder and on the basis of existing official documents and documentation from the foreign manufacturer (see point 5 above).
One form per manufacturer and per active pharmaceutical ingredient (if a preparation contains several active pharmaceutical ingredients) must be submitted for the finished preparation.
For non-ready-to-use medicinal products (active substances), the RP Declaration and the other documents only need to be submitted for the manufacturer that carries out the last manufacturing step (incl. release) and guarantees the GMP-compliant manufacture of the product. The RP is responsible for ensuring that possible intermediate steps outsourced to third parties (incl. QC) were also carried out in accordance with GMP. The FVP must ensure that the active substance manufacturer has

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fulfilled its responsibilities. If a clear responsibility cascade as described above does not exist, the RP Declaration must be submitted for all individual manufacturers.
Instead of an RP Declaration, only those documents mentioned in section 6.1 need to be submitted for the steps of packing, quality control or batch release of ready-to-use medicinal products.

6.1 Manufacturers from a country whose GMP control system is considered by Switzerland to be equivalent

The following documents at least must be enclosed with the RP Declaration:

6.1.1 Manufacturers of ready-to-use medicinal products

- A GMP certificate based on an inspection within the past 3 years

or

- an official document confirming that the manufacturer satisfies the PIC/S GMP requirements and has been inspected accordingly by the authority (date of inspection within the past 3 years) (e.g.: inspection report with a definitive assessment of the GMP status)

6.1.2 Manufacturers of medicinal products that are not ready-to-use (active pharmaceutical ingredients)

- A GMP certificate based on an inspection within the past 3 years

or

- an official document confirming that the manufacturer satisfies the PIC/S GMP requirements and has been inspected accordingly by the authority (date of inspection within the past 3 years) (e.g.: inspection report with a definitive assessment of the GMP status)

or

- Copy of an audit report, no more than 3 years old.

6.2 Manufacturers from a country whose GMP control system is not considered by Switzerland to be equivalent.

The following documents at least must be enclosed with the RP Declaration:

6.2.1 Manufacturers of ready-to-use medicinal products

- A GMP certificate based on an inspection within the past 3 years and issued by a foreign regulatory authority whose GMP control system is recognised by Switzerland

or

- an official document issued by a foreign regulatory authority whose GMP control system is considered by Switzerland to be equivalent and confirming that the manufacturer satisfies the PIC/S GMP requirements and has been inspected accordingly by the authority (date of inspection within the past 3 years) (e.g.: inspection report with a definitive assessment of the GMP status)

or

- Copy of an audit report, no more than 3 years old

and

- Copy of a GMP certificate issued by the authority of the country in which the manufacturer is located, no more than 3 years old

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6.2.2 Manufacturers of medicinal products that are not ready-to-use (active pharmaceutical ingredients)

- A GMP certificate based on an inspection within the past 3 years and issued by a foreign regulatory authority whose GMP control system is considered by Switzerland to be equivalent.

or

- an official document issued by a foreign regulatory authority whose GMP control system is considered by Switzerland to be equivalent and confirming that the manufacturer satisfies the PIC/S GMP requirements and has been inspected accordingly by the authority (date of inspection within the past 3 years) (e.g.: inspection report with a definitive assessment of the GMP status)

or

- Copy of an audit report, no more than 3 years old

and

- copy of a GMP certificate issued by the authorities of the manufacturer's country, no older than 3 years, unless it can be proved that the local authorities do not issue such certificates

6.3 Exemption clause for so-called "atypical active pharmaceutical ingredients"

If no proof of GMP compliance exists for an ingredient because the ingredient in question is not manufactured as a pharmaceutical ingredient but, for example, for food products or cosmetics, the RP of the authorisation holder / applicant must carry out an assessment of the manufacturing of the "atypical active pharmaceutical ingredient". The assessment must address the extent to which the GMP rules for active pharmaceutical ingredients have been taken into consideration. On the basis of this assessment, the lack of proof of GMP compliance must be justified on a risk basis. This risk-based justification must be signed and dated by the RP of the authorisation holder / applicant and enclosed with the RP Declaration.

6.4 Authorisation by means of the notification procedure in accordance with Art. 39 TPLO – exceptions

For authorisation of veterinary medicinal products by means of the notification procedure in accordance with Art. 39 TPLO or – if relevant – for variations to such preparations, it is sufficient to submit just one copy of the GMP certificate or manufacturing licence per foreign manufacturer. Neither the form *Manufacturer information* nor the form *Responsible Person Declaration* (RP Declaration) have to be submitted.

6.5 Age of the documents

The term "No more than 3 years old" means that the inspection or audit to which the document refers must have taken place no more than three years ago.

7 Audit report

A GMP audit on the product or product class must be carried out by qualified auditors, either internal or external. . The audit report must cover all relevant GMP aspects (see e.g. questions 9 and 10 under Q & A EU GMP guide part II: Basic requirements for active substances used as starting materials: GMP compliance for active substances http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000027.jsp&mid=WC0b01ac05800296ca#section11).
An audit carried out by the authorisation holder or the manufacturer must be carried out within the framework of their quality assurance system (i.e. in accordance with GMP rules such as SOPs and documentation). If an audit is outsourced, the requirements of Chapter 7, part I, GMP must also be taken into consideration.

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8 Languages used for the documents

All documents listed under point 6 (with the exception of inspection and audit reports) may be written in the following languages: German, English, French, Italian or Spanish. Documents in other languages must be submitted together with an accompanying certified English translation.
Audit reports and inspection reports may be written in German, Italian, French or English. Reports in other languages must be submitted together with an accompanying certified English translation.

9 Countries with recognised GMP control system that is considered by Switzerland to be equivalent

For a list of those countries whose GMP control system is recognised by Switzerland or considered to be equivalent to the Swiss system, please refer to the Directory *List of Countries with recognised GMP control systems*.

10 Inspections by Swissmedic

Swissmedic reserves the right to inspect, at the expense of the Swiss authorisation holder/applicant, manufacturers from countries whose regulatory authority does not have a GMP control system recognised by Switzerland (Art. 42 para. 2 of the Medicinal Products Licensing Ordinance – MBLO). Art. 8 MBLO (reanalysis) also applies.

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