Notifications according to Article 41, MPLO

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Approval

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1 Purpose and scope

Article 41 of the Medicinal Products Licensing Ordinance (MPLO; SR 812.212.1) defines that all major changes on installations, equipment or processes should be submitted for approval or notified to Swissmedic by the establishment license holder. This Technical Interpretation describes the interpretation of paragraph 2 of this article by the Swiss inspectorates. It can also be used by companies as a basis for assessing, whether a change is major according to article 41, paragraph 2 of the MPLO and if and how it should be submitted.

This document applies to the Swiss inspectorates, which conduct inspections under the jurisdiction of Swissmedic (i.e. the Swissmedic Inspectorate and the inspectorates of the cantons according to art. 60 TPA), subsequently referred to as inspectorates.

2 Basics

- Therapeutic Products Act (TPA; SR 812.21), Article 69
- Medicinal Products Licensing Ordinance (MPLO; SR 812.212.1)
- Ordinance on Fees Levied by the Swiss Agency for Therapeutic Products (FeeO-Swissmedic; SR 812.214.5)
- Explanatory notes for pharmaceutical manufacturers on the preparation of a site master file (PIC/S PE 008-4)

3 Definitions and abbreviations

MPLO Medicinal Products Licensing Ordinance (SR 812.212.1)

4 Interpretation

Major changes according to article 41, paragraph 2 of the MPLO are listed in table 1 and should be notified to Swissmedic in written form before implementation. It is the responsibility of the license holder to verify if a change needs to be submitted following Article 41 paragraph 1, or if it should be notified according to Article 41, paragraph r 2. The following listing applies mainly to manufacturing license holders. The changes marked with a * do also apply to distribution activities.

Table 1: Major changes (art. 41, para. 2 MPLO) to be notified to Swissmedic

Area	Change
Buildings	Construction or revamping of clean rooms (room class A-D), incl. HVAC
	Construction of new room(s) for processing open products during manufacturing of non-sterile medicinal product or active substance
	Construction or extension of temperature controlled storage area (e.g. climate chamber / room, (stand-alone equipment excluded), high rack storage area for medicinal products and active substances (packaging material and excipients are excluded)*
	Construction of rooms for collecting and processing of blood donations
	Relocation of quality control activities
Equipment	Installation of new major processing equipment for sterile products manufacturing (e.g. filling line, RABS, isolator, freeze dryer, compounding and sterilization filter units)

Area	Change
	Installation of major equipment for sterilization of terminally sterilized products (e.g. autoclave)
	Installation of new isolator(s) for sterility testing
	Introduction of new major computerized system for process and data management, in particular switch from paper-based to electronic system (e.g. documentation management, batch record, enterprise resource planning (ERP))*
	Introduction of new technology(ies) in production or quality control (e.g. continuous manufacturing, new type of major manufacturing equipment, new approach for container closure integrity testing or visual control of parenterals, change of packaging process from manual to automated, introduction of rapid microbiological methods)
	Installation of new major equipment, revamping of existing one and/or process change in relation with the manufacturing of product(s) which present(s) a high cross-contamination risk
	Move of equipment and related process activity into a room with a lower classification
	Major change in control strategy (e.g. introduction of real time release testing)
Plant	New plant for the production, storage and distribution of water for injection (WFI), purified water (PW) and clean steam
Product	Manufacturing of a new dosage form of a class already produced at the site (e.g. introduction of capsules at a site producing tablets)[1]
	Change from a dedicated to multi-product manufacturing line/facility

The notifications, including the relevant documentation, should be submitted in electronic form only using the “licences – major changes” eGov service. This will guarantee secure data communication between companies and Swissmedic.

To be able to use the “licences – major changes” eGov service, the following conditions must be fulfilled:

- Companies must have an establishment license issued under the legislation valid from 1 January 2019;
- Companies must have access to the eGov portal.

More information is available on the Swissmedic Webpage https://www.swissmedic.ch/swissmedic/de/home/services/egov-services/licences-major-changes.html.

The planned changes should be briefly summarized and, where appropriate, supplemented with supporting documents (e.g. change control, layout, project plan, time lines and/or qualification documentation). These documents, together with the form for the notification of major changes, are submitted via eGov services as pdf format.

The documentation will be assessed and the company will be informed whether additional information or time is required or if an inspection needs to take place before approval of the change. Any objections will be communicated in written form within 30 days after receipt of the notification. Fees are charged at cost.

[1] Depending on the license, this change may require a request for a change of the establishment license (art. 41, para.1 MPLO) instead of a notification according to art. 41, para. 2 MPLO

Changes that have an impact on the establishment license (art. 41, para. 1 MPLO) should be submitted only as a change request of the establishment license.

Changes that underlay also the variation of the market authorisation should additionally be submitted as such according to the usual procedure.

5 Changes to the previous version

- Chapter 4: change to electronic submission of notifications