swissmedic

Guidance document

Details required regarding manufacturers of herbal active substances

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List of contents

1 Terms, definitions, abbreviations

1.1 Definitions

Herbal active substances are *herbal substances* or *herbal preparations*.

Herbal substances encompass all whole, shredded or cut plants, parts of plants, algae, fungi and lichens in their unprocessed state, whether dried or fresh. Certain exudates, which will not be further processed, are also considered to be herbal substances.

Herbal preparations are those manufactured by means of a process to extract, distil, press, fractionate, clean, concentrate or ferment herbal substances. This definition includes crushed or pulverised herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates**.**

Essential oils are products, without any additives, obtained exclusively from distillation with water or steam, mechanical processing, or dry distillation from herbal drugs.

Vegetable fats and oils are primarily liquid or solid triglycerides of fatty acids. They may contain small quantities of other lipids, such as waxes, free fatty acids, partial glycerides or unsaponifiable fractions. Vegetable fats and oils are obtained from the seeds, fruit or drupes of various plants by means of pressing and/or extraction with solvents, after which they can be refined or hydrogenated. A suitable antioxidant can be added if necessary.

Powders are crushed, ground or pulverised herbal substances**.**

Purified substances that are obtained from herbal medicines or preparations of herbal medicines obtained by enrichment or cleansing processes, are not considered to be herbal substances (e.g. Cineol, Levomenthol). These substances are considered comparable to synthetic active substances.

2 Introduction

This guidance document describes the requirements regarding the data on the manufacturers of herbal active substances stated in the form *Manufacturer information HMV4*.

3 Objective

Since this guidance document is aimed at administrative bodies, it does not directly specify the rights and obligations of private individuals. Swissmedic uses this guidance document first and foremost as a resource for applying the legal provisions on authorisation in a uniform and equitable manner. The publication of the Instruction is designed to make it clear to third parties what requirements must be fulfilled according to the practice of Swissmedic.

4 Scope

The present guidance document is intended for applicants and authorisation holders of products with herbal active substances who are required to submit the form *Manufacturer information HMV4* within the context of an application.

5 Description

5.1 Details required regarding manufacturers of active substances

The same requirements to be fulfilled regarding manufacturers of active substances apply to all manufacturers, whether the active substances are obtained from a manufacturer in Switzerland or abroad. A difference nevertheless exists with regard to the level regulation of the manufacturer by the relevant authorities. While it is mandatory for manufacturers of active substances in Switzerland to have a licence and to be regularly inspected by the authorities with regard to compliance with the rules of Good Manufacturing Practice (GMP), this is not the case elsewhere. Art. 7, para. 3 of the *Ordinance on Establishment Licences* (AMBV; SR 812.212.1) stipulates that the authorisation holder must ensure that each batch of a medicinal product complies with the authorisation documents in terms of composition, manufacturing process, specifications and quality requirements and is manufactured in accordance with GMP rules. This constitutes a guarantee that the active substance also corresponds to the quality standards defined in the licence. It is therefore the responsibility of the authorisation holder to demonstrate, when applying for authorisation, how the required standards have been achieved and will be maintained in the future.

Swissmedic must be provided with details of the manufacturer of the active substance in the context of an application for marketing authorisation of a medicinal product or a variation to the manufacturer of an active substance.

The aforementioned form *Manufacturer information HMV4* to be completed is among the documentation to be submitted [Art. 3, para. 1, part b) in connection with Art. 3, para. 3 of the *Ordinance on the Authorisation of Medicinal Products* (AMZV, SR 812.212.22)]. Even if the *Manufacturer information HMV4* form is submitted in the context of other applications, the data on the active substance manufacturer must comply with the specifications given here.

5.2 Details to be provided in the form *Manufacturer Information HMV4* with regard to manufacturers of herbal active substances

Details of all companies and establishments involved in the manufacturing (including, if applicable, the *test laboratory* and the *batch release point)* must be included on the form for the authorisation of medicinal products containing herbal active substances. The table below gives an overview of the details required for the various categories of herbal active substances used and demonstrates that the information to be provided is in alignment with the GMP mandatory regulations.

Category	Herbal active substances	Company / establishment	Mandatory in GMP rules	To be included on the form
I	Herbal substances	Manufacturer *(e.g. cultivator)*	No	No
		Test laboratory	Yes	Yes
		Batch release point	Yes	Yes
II	Herbal preparations (with the exception of essential oils, vegetable fats and oils, and powders)	Manufacturer (e.g. manufacturer of extract)	Yes	Yes
		Test laboratory	Yes	Yes
		Batch release point	Yes	Yes
III	Essential oils, vegetable fats and oils, and powders	Manufacturer (e.g. mill)	No	No
		Test laboratory	Yes	Yes
		Batch release point	Yes	Yes

Manufacturers

In general, the GMP requirements for manufacturers of herbal active substances (herbal extracts used as API[1]) are the same as the provisions set out in the *PIC/S GMP Guide for Active Pharmaceutical Ingredients* (PE 007-2). In accordance with document PE 007-2, Swissmedic considers that full compliance with GMP requirements for manufacturers of i) herbal substances (Category I) and ii) essential oils, vegetable fats and oils, and powders (Category III), is compulsory only for the manufacturing steps associated with testing and batch release, as the manufacturers concerned do not usually serve the pharmaceutical market alone, but also supply herbal substances to other markets such as the food, flavourings and cosmetics markets. In this regard, Swissmedic is of the opinion that the authorisation holder or manufacturer of the medicinal product must remain flexible with regard to the purchasing of these products, and will only able to adequately verify the quality of the herbal substance after carrying out the appropriate analytical tests.

[1] Table 1 in *PIC/S GMP Guide for Active Pharmaceutical Ingredients* (PE 007-2)

It is essential that the company responsible does not release a medicinal product for the market which contains herbal active substances, which have been released without a GMP compliant quality control performed under the terms of an appropriate licence.

For manufacturers of *herbal preparations* (Category II), however, the products are generally the result of manufacturing processes of varying degrees of complexity, and mostly manufactured specifically for the pharmaceutical market. Since the entire manufacturing process influences the profile of the ingredients, it is possible, for example, that a (minor) variation to the extraction conditions has a significant impact on the profile that is not identified during the release analysis. Consequently, the manufacture of these products requires a manufacturing licence and compliance with the requirements set out in Art. 3-10 MPLO. For this reason, the details must be entered on the form. Each time such a manufacturer changes, a new application must be submitted (Form *Variations and extensions HMV4*).

Test laboratory and batch release point

In accordance with Art. 4, para. 1 c) TPA, quality controls and batch release fall within the definition of manufacturing and, for that reason, must be carried out in accordance with the requirements for manufacturing medicinal products and complementary medicines, and respect GMP requirements (Art. 4, paras. 2 and 3, MPLO). The quality controls must be carried out *either* directly by the manufacturer of the active substance *or* by a test laboratory with an appropriate establishment licence.

The laboratory carrying out the quality controls (for identity, impurities or other quality parameters) of herbal substances (Category I) or of essential oils, vegetable fats and oils, or powders (Category III) ensures that a specific batch of active substance corresponds to the specified quality standards. The quality controls ensure that the herbal substances transition from a non-GMP environment to a GMP-regulated one. As a result, all manufacturers performing testing in the context of the quality controls must be included on the form *Manufacturer information HMV4*. The release of the herbal active substances can only take place after the required quality controls have been performed.

It is essential that the information given regarding the manufacturer indicates the company or establishment responsible for releasing the herbal active substance and which therefore guarantees that the specified quality standards are respected.

Change history

Version	Change	sig
1.2	New layout, no content adjustments to the previous version.	dei
1.1	Formal adjustments to the header and footer No content adjustments to the previous version.	dei
1.0	Implementation of TPO4	rin