swissmedic

Guidance document
Guidance Article 13 TPA final

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1 List of Abbreviations

CTD	Common Technical Document
DMF	Drug Master File
eCTD	Electronic submission as Common Technical Document
KPA	Complementary and Herbal Medicines
LoQ	List of Questions
NeeS	Non-eCTD electronic submission
NTA	Notice to Applicants
STF	Study Tagging Files
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
WL	Wegleitung = guidance document Authorisation human medicinal product under Art. 13 TPA
XML	Extensible Markup Language

2 Glossary

Term	Definition
Reference country	The country in which the product, that is to be evaluated, has been approved. Swissmedic takes into account the evaluation of the health authority of this country.
Reference dossier	The dossier submitted in the reference country.
Reference authority	The health authority which has already approved the product that is to be evaluated by Swissmedic and to which the applicant refers in the Swiss submission.

3 Legal Basis and Guidances

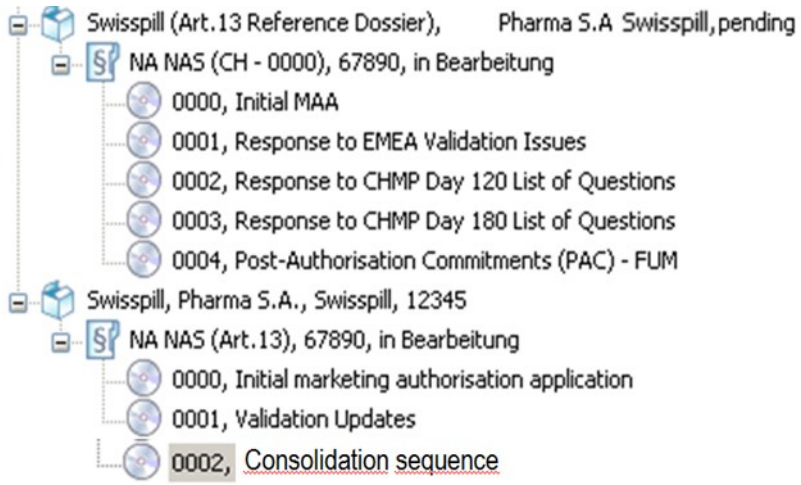
- Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21), Art. 13:
- Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21), Art. 16-19
- Guidance document Authorisation human medicinal product under Art. 13 TPA
- Swiss Module 1 Specification for eCTD
- Guidance for Industry on Providing Regulatory Information in eCTD Format
- Questions & Answers of Swissmedic eCTD Implementation
- Swiss eCTD Validation Criteria

4 Basic principles

This guidance deals only with the eCTD specific aspects of Article 13 TPA and should be read in conjunction with the *Guidance document Authorisation human medicinal product under Art. 13 TPA*.

1. The initial submission of an application under Article 13 TPA consists of two distinct parts:
   A. a Swiss eCTD containing module 1 only (no modules 2-5)
   B. a reference dossier, i.e., the entire documentation (modules 1-5) as approved by the reference authority.
2. The initial Swiss eCTD sequence and the reference dossier have to be submitted simultaneously.
3. The Swiss eCTD must meet the current Swiss eCTD Validation Criteria.
4. A consolidation sequence with modules 2-5 of the reference dossier, including approved variations, will be provided during the process at the request of Swissmedic.
5. The medicinal product approved in the reference country and the product for which an authorisation is applied for in Switzerland must be identical.

Illustration 1: Designed example of an application according to Article 13 TPA



5 Reference dossier

- The reference dossier consists of modules 1-5 as approved by the reference authority and should be in CTD format: either eCTD, NeeS or paper dossiers are accepted.
- Reference dossiers originally submitted to the reference authority in NTA format (e.g., Complementary and Herbal Medicinal Products / KPA) should be converted into CTD format before submission to Swissmedic.
- If the reference dossier is in eCTD format, it must contain all sequences submitted to the reference authority.
- If the reference dossier is a NeeS or is in paper format, the approved version must be submitted including answers to questions and all changes as well as additional information added to the dossier.
- If there have been updates to the product (e.g. variations) after approval in the reference country the corresponding documentation must be submitted to Swissmedic
    - If the basis was an eCTD, all sequences regarding the variations must be submitted.
    - If the basis was a NeeS or a paper dossier, the variation(s) which led to approval of the updates must be submitted.
    - If the updates are already included in the dossier, changes need to be specified as well as status (approved, pending). This information must be included in the tracking table as described in chapter 7.
- The reference dossier from the reference country will not undergo detailed technical validation at Swissmedic.
- The reference dossier may contain Study Tagging Files (STF), although STFs are not accepted by Swissmedic in regular Swiss submissions.
- Swissmedic does not accept unsorted files in the Zip file for the portal delivery. All files must be filed in an appropriate folder structure. Please see also the *MB Swissmedic eGov Portal – Standard functions* guidance document.
- No Zip files are allowed nested into the Reference Dossier Zip file itself.

6 Swiss eCTD

6.1 General structure

The documents submitted in Modul 1 of the initial Swiss eCTD sequence (0000) must fulfill the requirements of the currently valid version of the *Swiss module 1 Specification for eCTD*, the

Guidance document Formal Requirements, the *Guidance document Authorisation human medicinal product under Art. 13 TPA*, and the *Directory Overview of documents to be submitted*. Even though some documents may already be included in the reference dossier, they must be submitted in the Swiss module 1 as well.
For information about working documents please refer to the latest version of the *Guidance for Industry on Providing Regulatory Information in eCTD Format*. In the Swiss module 1 hyperlinks are not required.

6.2 Section 1.7.6 Article 13 TPA additional documentation

The requirements for additional documentation depending on the reference country and underlying procedure are described in the *Guidance document Authorisation human medicinal product under Art. 13 TPA*.

A tracking table must be integrated in module 1.7.6 Article 13 Additional Documentation. The table must include a chronological list of submissions in the reference country with a description of all changes made in the life cycle of the product since the initial Marketing Authorisation Application in the reference country and before submission to Swissmedic. This will provide Swissmedic with a historical overview of the Marketing Authorisation process in the reference country.→ Example (for a NeeS or paper without sequence numbers):

Table 2

Date submitted	EU Seq.	CH-Mod. 1	Approval Date	Description
15 January 2021	0000	n.a.		Initial submission of the application dossier for marketing authorisation Procedure number . – RMS: AT, CMSs: DE, ES, IT, FR
13 April 2021	0001	1.7.1		Validation phase - RMS: AT, CMSs: DE, ES, IT, FR • Responses
27 April 2021	n.a.	n.a.		Start of the procedure for .
06 July 2021	n.a.	1.7.2		RMS Day 70 Preliminary Assessment Report for • Quality • Non-Clinical • Clinical • Overview and LoQ • Labelling, PIL, SmPC • ASMF Assessment Report • ASMF Assessment Report
05 August 2021	n.a.	1.7.2		CMS Day 100 Comments – ES
11 January 2023	0002	1.7.1		Submission of day 106 response - RMS: AT, CMSs: DE, ES, IT, FR • Response Quality / Non-Clinical / Clinical / Module 1 • Response Labelling / PIL / SmpC • Response • Response
16 February 2023	n.a.	1.7.2		RMS Day 120 Draft Assessment Report for / • Quality • Overview

6.3 How to maintain the lifecycle after approval?

Line extensions and variations that can be submitted in accordance with Art 13 TPA are described exhaustively in the relevant Guidance.

7 Consolidation sequence

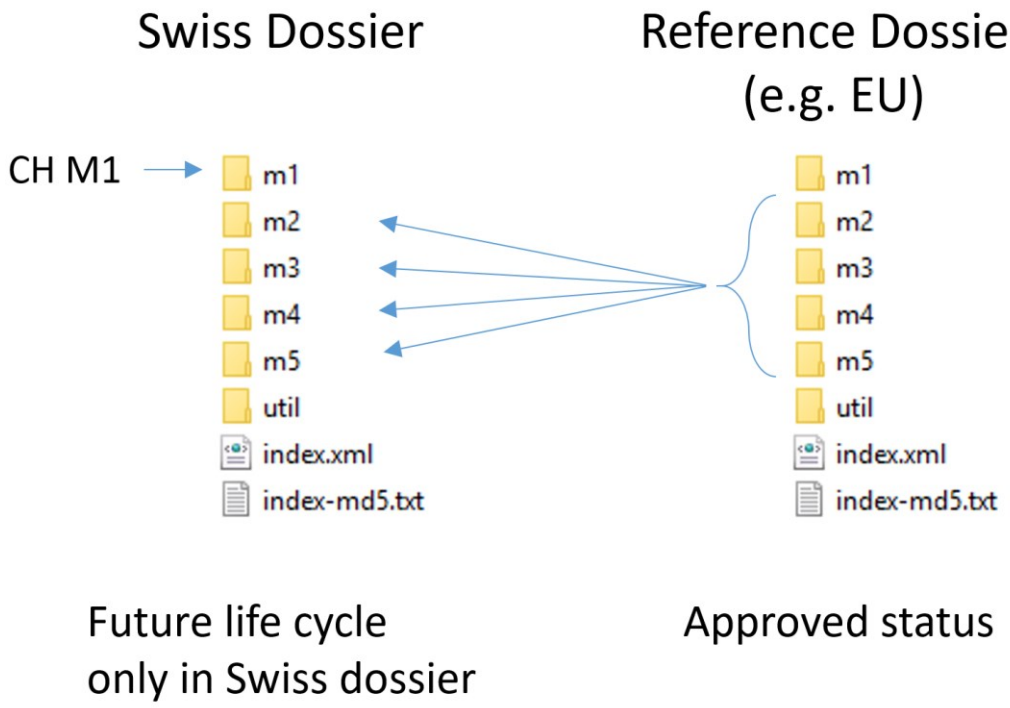
7.1 Marketing authorization application

If Swissmedic has accepted a procedure under article 13 TPA, the applicant is required to provide a consolidation sequence, at the latest with the response to the preliminary decision, as two consecutive, separate sequences.
For this purpose, modules 2-5 of the reference dossier (original, approved variations, STF) have to be incorporated into the Swiss eCTD. Hypertext linking is only necessary if there are still open points to discuss.
The module 1 of the reference country is not required in the consolidation sequence.
This new eCTD sequence is a prerequisite for approval of the application.

A signed declaration must be submitted as an annex to the cover letter, e.g.: *We confirm that the content/data of the submitted consolidation sequence reflects the status of the reference dossier currently approved by the reference country and that there have been no changes to the dossier content as a result of the provision of this consolidation sequence.*

If clarification is required before a preliminary decision can be issued and a LoQ is communicated to the marketing authorisation holder, the consolidation sequence has to be provided with the response to the LoQ, as two consecutive, separate sequences. For detailed requirements regarding hypertext linking from the response document to the documentation, please refer to the *Guidance for Industry on Providing Regulatory Information in eCTD Format.*

Illustration 2: Incorporating the reference Modules 2-5 life cycle into the Swiss eCTD



7.2 Extensions and variations

Variation applications and applications for line extensions in eCTD format must always be submitted in consolidated form. If an application for an extension is newly submitted in eCTD format, it is not necessary to create an electronic baseline file for the previously submitted paper documentation according to the *Guidance document Authorisation human medicinal product under Art. 13 TPA*.

8 Deviations from the reference product

Possible deviations between the product applied for in Switzerland and the one approved by the reference authority are described exhaustively in the *Guidance document Authorisation human medicinal product under Art. 13 TPA*.

The deviations that are not applied for must not be removed from the consolidation sequence.

Change history

Version	Change	sig
1.6	General update and corrections due to inconsistencies concerning referenced legal documents	OSS Division
1.5	Update, minor corrections	OSS Division
1.4	Final version, published on Swissmedic website	OSS Division
1.3	Final version	Submissions Division
1.2	Final version, published on Swissmedic website	Submissions Team
1.1	Final version, published on Swissmedic website	Submissions Team
1.0	Final version, published on Swissmedic website	SIMES Step 3 Working Group