swissmedic

Guidance document

Authorisation human medicinal product under Art. 13 TPA

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1 Definitions, terms and abbreviations

1.1 Definitions and terms

1.1.1 Countries with comparable control systems for medicinal products

The current list of countries recognised by Swissmedic as countries with comparable human medicinal product control in accordance with Art. 16 para. 4 TPO is published on the Swissmedic website under the Directory *List of all countries with comparable control of human medicinal products*.

The regulatory authorities for medicinal products in these countries are referred to in this guidance document as *foreign authorities*.

1.1.2 Reference authority

The term *reference authority* refers to the foreign authority which has already authorised the medicinal product in question, and whose evaluation is used by the applicant as the basis for the authorisation of the product in Switzerland.

1.2 Abbreviations

AI	Additional indication
ASMF	Active Substance Master File
Auth.	Authorisation (standard procedure)
CHM	Complementary and herbal medicines
CHMP	EMA Committee for Medicinal Products for Human Use
COMP	EMA Committee for Orphan Medicinal Products
CP	EU Centralised Procedure
CxMP	EMA Committee for Medicinal Products
DCP	EU Decentralised Procedure
DMF	Drug Master File
eCTD	Electronic submission as Common Technical Document
EFTA	European Free Trade Association
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
EU	European Union
EU-SmPC	Summary of Product Characteristics (EU)
FDA	Food and Drug Administration (USA)
FeeO-Swissmedic	Ordinance on the Fees charged by the Swiss Agency for Therapeutic Products of 14 September 2018 (SR 812.214.5)
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GxP	Good x Practices
HMPC	Committee on Herbal Medicinal Products
ICH E2E	International Council on Harmonisation Guideline Pharmacovigilance Planning
IHP	Information for healthcare professionals
KAS	Medicinal products with known active substances
LoQ	List of Questions
LoOI	List of Outstanding Issues
MRP	EU Mutual Recognition Procedure
NAS	Medicinal products with new active substances
NOC	Notice of Compliance
NtA	Notice to Applicant
Ph. Eur.	European Pharmacopoeia
Ph. Helv.	Pharmacopoeia Helvetica
PI	Patient information
PMDA	Pharmaceuticals Medical Devices Agency (Japan)
RiskMAP	Risk Minimization Action Plan
RMP	Risk Management Plan
RMS	EU Reference Member State
RUP	Repeat Use Procedure
SBA	Summary Basis of Approval

temp.auth.	Temporary new authorisation
tempAI	Temporarily authorised additional indication
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPLO	Ordinance of the Swiss Agency for Therapeutic Products of 22 June 2006 on the Simplified Licensing of Therapeutic Products and the Licensing of Therapeutic Products by the Notification Procedure (SR 812.212.23)
TPLRO	Ordinance of the Swiss Agency for Therapeutic Products of 9 November 2001 on the Licensing Requirements for Therapeutic Products (SR 812.212.22)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
WL	Wegleitung = guidance document

2 Introduction and objective

If an applicant requests the authorisation, extension or a variation of an authorisation for a medicinal product or procedure[1] for which authorisation has already been granted in a country with a comparable control system for medicinal products, Swissmedic will take into consideration the results of the assessments carried out by the foreign regulatory agency provided that certain requirements are fulfilled. Consideration of the results of foreign authorisation procedures is intended to assist in processing authorisations of medicinal products in Switzerland in such a way that medicinal products already authorised in foreign countries are made available to patients in Switzerland as rapidly as possible, and also to ensure the targeted, risk-assessed use of Swissmedic's resources (Art. 1 para. 2 letter c and Art. 1 para. 3 letter a TPA).

This guidance document is primarily intended for administrative bodies and does not directly specify the rights and obligations of private individuals. Swissmedic uses it first and foremost as a resource for applying the legal provisions in a uniform and equitable manner. For applicants, its publication is intended to elucidate the specific preconditions and requirements that must be fulfilled so that applications for the authorisation of human medicinal products and procedures according to Art. 13 TPA can be processed as quickly and efficiently as possible.

3 Scope

This guidance document is valid in the following cases:

1st For the following authorisation and variation applications for human medicinal products and for procedures based on Art. 16–19 TPO and related to an authorisation already granted in a country with a comparable control system for medicinal products:

a. New authorisation applications for medicinal products with known active substances
b. New authorisation applications for biosimilars that have already been authorised by the European Commission or the US FDA
c. New authorisation applications for medicinal products with new active substances and their additional indications, provided that the criteria specified in section 7 are fulfilled

[1] according to Art. 9 para. 3 TPA in conjunction with Art. 31 - 34 TPO

d. New authorisation applications for medicinal products that are not eligible for simplified authorisation based on Art. 12 para 5 TPLO, provided that the criteria specified in section 6.3 are fulfilled
e. New authorisation applications for medicinal products with new active substances or with known active substances (KAS: when an application is submitted for a previously unauthorised indication) and their additional indications, for which temporary authorisation is to be granted under Article 9*a* TPA, provided that the criteria specified in section 7 or 8 are fulfilled
f. Applications for minor variations (types IA / IA_{IN} / IB), as long as they meet the criteria in section 5.1
g. Applications for major variations (type II); (extended indication for medicinal products with new active substance, provided they meet the criteria set out in section 7)
h. Applications for extensions

2nd For parallel processing of applications in Switzerland and abroad in accordance with Art. 20 TPO

By analogy, for the authorisation of procedures in accordance with Art. 9, para. 3, TPA

3rd For the authorisation of human medicinal products whose extensions and variations, provided that the applicant requests the application of the procedure according to Art. 13 TPA and all the following requirements are fulfilled:

a. The submitted documents from the foreign procedure, including all variations, are no older than five years[2] and correspond to the authorisation status in the other country.
b. The assessment decisions submitted in connection with the foreign authorisation procedures, including the associated complete and final Assessment Reports, are available.
c. The documents contain all the information required for Switzerland according to section 11, particularly the medicinal product information and labelling texts.
d. The documents are available in an official language, in English or in a translation into one of these languages. If a translation is submitted, the applicant must confirm that it is correct.

4th For extensions and variations for human medicinal products that were initially authorised by Swissmedic without reference to Art. 13 TPA, and for which the applicant confirms according to section 5.1 that the status of the submitted dossier is identical to that submitted to the foreign authority.

The guidance document is not valid for:

- Authorisation applications for medicinal products in the notification procedure in accordance with Art. 15 TPA in conjunction with Art. 32 para. 1 TPLO

4 Legal basis

The procedure for taking into account the results of assessments carried out during the course of foreign authorisation procedures is derived in particular from the following legal bases (legal provisions and ordinances):

Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (TPA[3]):

- Art. 13 Medicinal products and procedures authorised in foreign countries

Ordinance of 21 September 2018 concerning Medicinal Products (TPO[4]):

- Section 2: Medicinal products and procedures authorised in foreign countries (Art. 13 TPA): Art. 16 - 20

[2] Date of the official decision on the new authorisation or the approval of the extension / variation
[3] SR **812.21**
[4] SR **812.212.21**

5 Requirements relating to documentation (Art. 16 TPO)

If a medicinal product has already been authorised in a country with a comparable control system for medicinal products according to section 1.1.1, Swissmedic will take into account the results of the assessment by the reference authority during the authorisation procedure, provided that the applicant explicitly requests Swissmedic to do so in the form *New authorisation of human medicinal products* or *Variations and extensions*. In this case Swissmedic will also check that all the documents required for this procedure have been submitted in full.

5.1 Documentation submitted to the reference authority

- *Comparability of foreign and Swiss documentation*

The documentation submitted to Swissmedic (Modules 2.4, 2.5, 2.6, 2.7, 4 and 5) must be identical to that on which the reference authority has based its authorisation of the medicinal product or a variation thereof.[5] Deviations regarding Modules 2.3 and 3 are outlined in full in section 5.7. If the product has been authorised in more than one country with comparable medicinal product control, the authorisation documentation must be completely identical to that submitted to the reference authority. For subsequent applications for variations, the originally selected reference authority must remain the same.
The full documentation must be submitted to Swissmedic in CTD format[6] together with the country-specific Module 1 assessed by the reference authority and the Swiss Module 1. If the documentation was authorised in NtA format (Parts I - IV) by the reference authority, it may also be submitted in the same format to Swissmedic. The Guidance document *Guidance Industry eCTD* must be considered for eCTD submissions.

- *Variations and / or additions after the decision by the foreign authority*

In parallel with the application for new authorisation, the variations and additions approved since the reference authority granted the authorisation must also be submitted to Swissmedic. This additional or replacement documentation can either be integrated within the application documentation or the module in question, or be submitted separately. The variations must be referred to in the cover letter, and a comparison showing the changes (old / new) must be appended to the corresponding final assessment report.

Until such time as a procedure has been completed, subsequently submitted variations that have been approved by the reference authority count as part of the ongoing procedure. Depending on the extra workload incurred, it may be necessary to extend the duration of the procedure and levy an additional fee.

- *Documentation for variation applications and authorisation extensions*

In order for Art. 13 TPA to be applied to applications for variations for medicinal products, an Assessment Report by the reference authority must be submitted. Minor variations (types IA / IA_{IN} and IB) are only possible if they are addressed in an Assessment Report by the foreign reference authority

[5] For exceptions, see section 5.7

[6] Common Technical Document according to the ICH guidelines M2 (eCTD) and M4 (CTD) (International Conference on Harmonization). Consists of the following modules: 1 (Country specific), 2 (Summary), 3 (Quality), 4 (Preclinical), 5 (Clinical).

and do not contradict the legal requirements in Switzerland. All variations submitted in a multiple application must appear in the same Assessment Report.

For applications for medicinal products that were authorised by Swissmedic without reference to Art. 13 TPA, a confirmation signed by a person entitled to act as a signatory must be submitted, stating that the documentation for the reference authority (prior to the approval of the variation) and that for Switzerland are identical. For applications for extensions without prior reference to Art. 13 TPA in accordance with section 6, the documentation and the corresponding documents for the first authorisation must also be submitted if they are the main source of reference.

Variation applications and applications for authorisation extensions in eCTD format must 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.

- *Information regarding safety signals*

In connection with ongoing nationally and internationally recorded safety signals, all relevant information and relevant correspondence with the reference authority, such as communications regarding the initiation of a procedure, LoQ letters, experts' reports, interim results (milestones) and final reports, should be submitted. If applicable, relevant updates taking place during the authorisation process must be sent subsequently. For safety signals which occur after the authorisation abroad and the submission to Swissmedic and which have been concluded, only the final report and any modified product information texts need be submitted.

- *GLP / GMP / GCP*

The GLP / GMP / GCP compliance of the medicinal product to be authorised must be confirmed. Pending investigations (e.g. correction of deficiencies, required follow-up inspections) must be stated in the cover letter.

- *Risk Management Plan in accordance with ICH E2E*

The Risk Management Plan must be submitted for NAS and their additional indications in accordance with the Guidance document *RMP ICH E2E Information for submission HMP*.

- *Drug Master File (DMF / ASMF)*

If a DMF / ASMF has been submitted to the reference authority for the application in question, the DMF / ASMF holder must submit an identical copy of the complete DMF (Applicant's and Restricted Parts) to Swissmedic. Modules 2.3 and 3 must be submitted in consolidated form together with a Module 1 according to Swiss requirements that includes Form Part B, the Letter of Access, the Assessment Report from the Restricted Part, the LoQ and the Response of the DMF holder to the Restricted Part. If the DMF / ASMF has been subsequently modified (i.e. after first authorisation abroad and before submission in Switzerland), the approved variations, with the corresponding Assessment Report, must be submitted separately in parallel and noted in the cover letter together with a comparison showing the changes (old / new).

5.2 Date of the authorisation or the last revision of the documentation

The first authorisation or the last updated version of the entire documentation approved by the reference authority must not be older than 5 years[7], taken from the date on which the application was submitted to Swissmedic. Deviations from currently valid guidelines that were not yet in force at the

[7] Date of the official decision on the new authorisation or the approval of the extension / variation

time of the authorisation in a foreign country are possible. These should be critically assessed and mentioned in the cover letter.

- *Repeat Use Procedure RUP*

If a Repeat Use Procedure RUP or DCP is implemented in the EU, a complete, updated dossier must be submitted for the new group of Member States. This dossier is assessed by the national authority of the Reference Member State that conducted the initial MRP or DCP. This updated dossier must also include all variations approved since the first authorisation. Only the updated dossier, including the associated assessment reports and decisions, must be submitted, irrespective of when it was authorised in the MRP or DCP.

5.3 Results of the assessment and decisions on the part of the reference authority

Results of the assessment that are provided to Swissmedic must facilitate an understanding of the reference authority's decision process. The documents required are listed in section 11 (Annex).

Basically, the complete, final, scientifically substantiated Assessment Report of the reference authority must be submitted to Swissmedic. If the foreign reference authority provides the applicant in Switzerland only with an Assessment Report that is not wholly legible, Swissmedic will accept the submission of this incomplete Assessment Report. However, in these situations Swissmedic reserves the right to conduct its own scientific assessment for the inaccessible parts of the Assessment Report, while referring to the underlying documentation. The corresponding extra work involved will usually lead to a time-based surcharge[8] and correspondingly higher fees[9].

If a medicinal product has been authorised in several countries with a comparable control system for medicinal products (according to section 1.1.1), the authorisation decisions (official decisions) of all authorities and the Assessment Report (results of the assessment according to section 11) from the reference authority specified by the applicant should be submitted to Swissmedic.
If the applicant requests the authorisation or extension of an authorisation for a medicinal product for which conflicting decisions have been issued by foreign authorities, the assessment results (Assessment Reports) for the deviating decisions by the corresponding foreign authorities or the correspondence connected with the withdrawal of an application should be submitted to Swissmedic. If another foreign authority issues a deviating decision while a procedure under Art. 13 TPA is still in progress, Swissmedic must be notified of the decision, and the associated Assessment Report must be submitted to the Agency. Conflicting decisions by foreign authorities constitute concerns. The diverging assessment result will feed into Swissmedic's ongoing review process.

Any negative decisions concerning authorisation, a withdrawal by the applicant, an ongoing examination procedure or a suspension of the product for which the application is made, must be listed for all foreign authorities, in accordance with Section 1.1.1, on the form *Status of authorisation applications abroad*. The cover letter must present, in a transparent manner, such differing authorisation decisions of other authorities (rejection, communications leading to the withdrawal of the application, divergences regarding indications, dosage, storage instructions, shelf life, other restrictions etc.).

[7] See WL *Time limits for authorisation applications*
[9] See FeeO-Swissmedic

For the application of Art. 13 TPA for applications for the authorisation of medicinal products authorised in the EU by a hybrid procedure, the assessment of the reference authority must be plausible for Swissmedic. This assumes that the medicinal product on which the EU hybrid authorisation is based is or was also authorised in Switzerland, otherwise a medicinal product would be authorised without Swissmedic possessing the complete documentation (particularly also concerning certain aspects of safety and efficacy in the requested indications (incl. clinical trials) to which it could refer if necessary.

5.4 Remarks that are specific to Swiss module 1

In addition to the documentation submitted to the reference authority, Swissmedic requires the administrative data of Swiss Module 1 in accordance with the guidance document *Formal requirements* and the associated Directory *Overview of documents to be submitted*.
The applicant must ask for the assessments of foreign authorities to be taken into account, in accordance with Art. 13 TPA and Art. 16–20 TPO, using the forms *New authorisation of human medicinal products* and *Variations and extensions*.
All required annexes and forms for Module 1 (or, for CHM: Parts 1A and 1B NtA) are listed in the *Table of documents to be submitted*. Additional documents that are not stated in the table must be referred to in the cover letter.
Proof that the current requirements of the Ph. Eur. / Ph. Helv. are met can be integrated within Module 3 CTD (for NtA: Part II) or attached separately and must be confirmed in the form *Information for application Art. 13 TPA*. If, instead of the corresponding methods of Ph. Eur. / Ph. Helv., other methods are used, their equivalence with the methods of Ph. Eur. / Ph. Helv. should be demonstrated.

The ERA (Module 1) only needs to be submitted for medicinal products that have been authorised in a country with a comparable control system for medicinal product that is not a member of the EU.

5.5 Product information

If an authorisation has been granted in a centralised EU procedure (European Commission Scientific Decision) or in a member state of the EU or EFTA, Swissmedic can also approve the relevant applicable form of the medicinal product information so that the medicinal product can be placed on the market in Switzerland (Art. 16 para. 3 TPO). However, Swissmedic must check those aspects that are specific to Switzerland, such as compliance with the requirements for the medicinal product information (e.g. storage instructions) or the agreement with the wording of the product information for medicinal products with a comparable data situation. This usually means that a word-for-word adoption of the medicinal product information approved by the reference authority without checking by Swissmedic is not possible. If there are differences in content from the Swiss requirements, Swissmedic must check those aspects that are specific to Switzerland. In all cases, the language requirements and mandatory declarations regarding genetically-modified organisms or substances from genetically-modified organisms must be respected.

The medicinal product information for a KAS without innovation must be identical to that for the reference medicinal product in Switzerland. An adoption of the form and wording of the medicinal product information of the foreign reference authority for placing the medicinal product on the market in Switzerland is not possible for this type of application. If the reference medicinal product is no

longer authorised in Switzerland and no reference can therefore be made to current information for healthcare professionals, the applicant must create updated information for healthcare professionals and patients in which reference is made to the new aspects.

All appropriate text passages of the product information for a biosimilar must be identical to those for the reference medicinal product at the time the application for authorisation for the biosimilar was submitted. The Information for healthcare professionals must clearly indicate that a biosimilar is involved.

The Swiss requirements relating to the information and texts on containers and packaging should be respected (Art. 12 and annexes, TPLRO).

5.6 Requirements regarding languages and translation of the documentation

The documentation (Modules 2 to 5 and the country-specific Module 1 or Parts I - IV) and the documentation required as stated in section 11 (Annex) must be submitted to Swissmedic in one of Switzerland's official languages or in English. Translations into one of these languages are also accepted, provided that the applicant confirms in writing that the translations are correct. The Switzerland-specific Module 1 (or, for CHM, Parts 1A and 1B), as well as the medicinal product information and the packaging texts, must be submitted in one of Switzerland's official languages.

5.7 Differences compared to the product authorised by the reference authority

As a rule, the product authorised in the foreign country must be identical to the product that is the subject of the application in Switzerland. Differences relating to the following are possible:

- batch release
- quality control(s)
- secondary packaging or the secondary packer
- the pack size, if this does not conflict with the use of the product
- the name of the medicinal product authorised in the foreign country

Since differences relating to the manufacturing site of the finished product, the primary packaging and the primary packager must be subjected to a scientific assessment, they are not permitted in connection with an application according to Art.13 TPA.

On the other hand, it is possible that fewer

- manufacturers of the active substance
- manufacturers of the finished product
- primary packers
- primary packagings

were requested for Switzerland than were authorised in the reference country.
The forms in the Swiss Module 1 (e.g. form *Manufacturer information*) must be completed accordingly for Switzerland. If the documentation is submitted using eCTD, the deviations that are not applied for must not be removed from the consolidation sequence.

If minor differences exist between the authorisation in the foreign country and the application to Swissmedic, the documentation presented to the reference authority for authorisation should be submitted. The differences should be presented in the cover letter and confirmed on the form

Information for application Art. 13 TPA. These are assessed by Swissmedic in the same way as a variation, but do not involve lengthy processing times.

5.8 Compliance with Swiss-specific requirements

The requirements specific to the various types of application mentioned in the following Swissmedic guidance documents must be respected, and the associated documentation should be submitted to Swissmedic together with the application for authorisation:

- Guidance document *Authorisation of human medicinal product with known active substance*
- Guidance document *Authorisation of human medicinal product with new active substance*
- Guidance document *Authorisation biosimilar*
- Guidance document *Authorisation of allergen product*
- Guidance document *Authorisation of herbal medicinal products*
- Guidance document *Authorisation of antidote*
- Guidance document *Authorisation of medicinal gas*
- Guidance document *Authorisation of radiopharmaceutical*
- Guidance document *Temporary authorisation for human medicinal products*
- Guidance document *Variations and extensions*

5.9 Other documentation specific to certain authorities

The documents to be submitted to the reference authority are listed in section 11 (Annex). In its assessment, Swissmedic refers exclusively to documents submitted to it by the applicant. A direct transfer of the assessment documents from a foreign country by the relevant authority to Swissmedic is not possible. By way of exception, Swissmedic accepts the direct submission of the assessment report for Drug Master Files (DMF) by consortium partner authorities. However, in these situations Swissmedic reserves the right to conduct its own scientific assessment for the directly submitted assessment report for the DMF, while referring to the underlying documentation. The corresponding extra work involved will usually lead to a time-based surcharge and correspondingly higher fees.

5.10 Information and documentation after authorisation by Swissmedic

Once the official decision is taken by Swissmedic to approve or (partially) reject the authorisation, the authorisation procedure according to Art. 16 - 19 TPO is concluded.
Conditions imposed by the reference authority that have not yet been fulfilled by the time of the authorisation decision by Swissmedic are usually also imposed by Swissmedic.
Decisions concerning the fulfilment of conditions taken by the reference authority should be submitted to Swissmedic without delay. So that Swissmedic can base its own decisions on those of the foreign authorities, the documentation submitted to the reference authority and/or the corresponding Assessment Report must be submitted.
The requirements for submission of applications to fulfil conditions are based on the Guidance document *Formal requirements*.

5.11 RMP-related conditions

Study reports on studies that were performed for an RMP must be submitted to Swissmedic only if submission of these study reports is expressly stipulated as a condition by Swissmedic. A routine submission of RMP study reports is not envisaged.

Detailed information on submission of RMP updates is given in the Guidance document *RMP ICH E2E Information for submission HMP*.

6 Assessment principles for medicinal products with known active substances (Art. 17 TPO)

The following statements apply to the assessment of applications for the authorisation of medicinal products with known active substances, biosimilars and other non-innovative medicinal products in the categories listed in Art. 12, para 5 TPLO. The consideration of results of assessments by foreign authorities within the framework of an application for an extension and for a variation for a medicinal product with a known active substance is also subject to these provisions, provided the document requirements set out in section 5 are met.

6.1 Medicinal products with known active substances

As regards applications for the authorisation of a KAS for which authorisation has already been granted in a country with comparable medicinal product control (section 1.1.1), and which satisfies the requirements for the application of Art. 13 TPA according to section 3, Swissmedic dispenses with its own scientific assessment provided that the requirements relating to the documentation according to Art. 16 TPO are respected. These applications are evaluated according to the following criteria:

Swissmedic checks the following based on the history and context

- whether safety signals requiring special consideration exist
- whether material differences exist between the authorisation decisions of two authorities (e.g. authorisation by one and rejection or partial rejection by the other, differing indication wording and / or therapeutic regimen)
- whether major concerns exist in respect of quality, safety and/or efficacy based on an earlier assessment of a medicinal product with the same active substance or the same substance class
- whether new findings from the published specialist literature or information arising from cooperation with other regulatory authorities exist.

If the decisions made in two or more foreign countries differ, or if major concerns about the authorisation decision of the foreign regulatory authority arise in light of the points mentioned above, the application is evaluated on the basis of the Assessment Report of the reference authority. If the points giving cause for concern cannot be rectified in the review of the Assessment Report, a targeted inspection of the underlying documentation, restricted to the mentioned points, is carried out (Flowchart I).

If the Swiss regulations applicable to the assessment of the medicinal product differ significantly from those of the reference authority (e.g. complementary and herbal medicines, specification of the dispensing category), Swissmedic reserves the right to carry out its own assessment. The results of the foreign authority are also taken into account as far as possible.

6.2 Biosimilar

As regards applications for the authorisation of a biosimilar that has already been authorised by the European Commission or US FDA and that satisfies the requirements for the application of Art. 13 TPA according to section 3, Swissmedic dispenses with its own scientific assessment provided that

the requirements relating to the documentation according to Art. 16 TPO are respected. These applications are evaluated similarly according to the criteria described in section 6.1.

If differing decisions are made by the European Commission and the US FDA, or if major concerns about the authorisation decisions of these two authorities arise in light of the points mentioned above, the application is evaluated on the basis of the Assessment Report of the reference authority. If the points giving cause for concern cannot be rectified in the review of the Assessment Report, a targeted inspection of the underlying documentation, restricted to the relevant points, is carried out.

If, for the authorisation of a biosimilar, the applicant refers to the authorisation granted by another foreign authority with comparable medicinal product control according to section 1.1.1 - apart from the European Commission or the US FDA - Swissmedic will carry out its own assessment (Flowchart II), taking account, insofar as possible, of the complete assessment results of the relevant reference authority submitted to it by the applicant.

6.3 Other non-innovative medicinal products in the categories listed in Art. 12 para. 5 TPLO

Since the active substances covered by the medicinal product categories listed in Art. 12 para. 5 TPLO differ from classic medicinal products (which are defined by their molecular structure) in that they cannot normally be completely identical to the active substance of an existing authorised medicinal product, they generally require a more extensive authorisation procedure than classic medicinal products with known active substances (biosimilars are subject to the requirements in 6.2 above). In terms of authorisation requirements, this fundamental difference aligns the medicinal product categories in question more closely with the category of medicinal products with new active substances. For this reason, the medicinal products in Art. 12 para. 5 TPLO were excluded from the scope of the simplified authorisation procedure for medicinal products with known active substances, and for many years it was Swissmedic's regulatory practice to treat them like innovative medicinal products when considering foreign authorities' authorisation decisions. Nevertheless, it is possible to foresee scenarios under which these medicinal product categories could quite closely approximate the category of medicinal products with known active substances. On request, or on an ex officio basis, Swissmedic can thus partially scale back its assessment if a medicinal product that has been authorised by the EU Commission or US FDA is sufficiently similar to a medicinal product already authorised in Switzerland. However, this is only possible if the following criteria are all fulfilled:

- **Active substances**
  The medicinal product must contain an active substance that is contained in a medicinal product that is or was authorised by Swissmedic. If the medicinal product consists of more than one known active substance (i.e. is a fixed medicinal product combination), both/all active substances must be contained in at least one medicinal product that is or was authorised by Swissmedic (see also guidance document: *Authorisation of human medicinal product with new active substance* or guidance document *Authorisation of human medicinal product with known active substance*).
- **Active substance manufacturer**
  The active substance manufacturer's production sites must be known to Swissmedic.
- **Manufacturing process**
  The manufacturing process must be known to Swissmedic.

- **Indication**
  The requested indication wording for the medicinal product submitted for authorisation must be identical to the indication wording authorised by the foreign reference authority.
- **Administration route**
  The requested administration route for the medicinal product submitted for authorisation must be identical to the administration route authorised by the foreign reference authority.

If applicable:

- **Extension by the addition of similar components**
  The new components must have been produced using the same/known manufacturing process.

If the above-mentioned criteria, the requirements for the application of Art. 13 TPA set out in chapter 3, and the documentation requirements set out in chapter 5 are all fulfilled, Swissmedic will not normally conduct its own scientific assessment. These applications will be evaluated correspondingly in accordance with the criteria described in chapters 6.1 and 6.2 (Flowchart III).

6.4 Transparency regarding major concerns

The reasons for concerns leading to Swissmedic carrying out an independent assessment will be provided to the applicant with the List of Questions or – if no List of Questions is compiled – the preliminary decision.

7 Assessment of medicinal products with new active substances and their additional indications (Art. 18 TPO)

Applications for the authorisation of a medicinal product with a new active substance or an additional indication for this product are subjected to a comprehensive independent scientific assessment by Swissmedic based on all the submitted documentation. In justified cases, however, Swissmedic may reduce the scale of such assessments, either on request or *ex officio*, based on the result of the corresponding assessment by the foreign authority (see Flowchart IV).

7.1 Reduced assessment on request for orphan drugs

A reduced assessment of an application under Art. 13 TPA for a medicinal product with an NAS or for its additional indications is possible (provided that the indication wording applied for is identical to that authorised in the reference country) only for medicinal products that are classified and authorised as Orphan Drugs by the EMA Committee for Orphan Medicinal Products (COMP) or the FDA Orphan Drug Act.

For an application requesting the consideration of the assessment results of a foreign authority for an orphan drug, the corresponding recognition of orphan status and authorisation by the EMA or the FDA must be submitted. Moreover, Swissmedic must have approved the Orphan Drug Status before submission of the application for authorisation. If the above criteria (orphan drug) are not fulfilled, an interim decision (rejection of the application of Art. 13 TPA) is issued and the application is then

subject to the normal authorisation process according to the guidance document *Authorisation of human medicinal product with new active substance*.

The reduced assessment is usually restricted to an examination of the submitted authorisation decisions of the foreign authorities with comparable medicinal product control (section 1.1.1) and the assessment result of the foreign reference authority, provided that the documentation requirements according to Art. 16 TPO were respected (see section 5).

The quality, efficacy and safety of the medicinal product are evaluated and assessed regarding whether the reference authority's examination results can be used by Swissmedic to reach a decision regarding authorisation, based on the reference authority's assessment reports. Reasonable evidence for a potential unfavourable risk-benefit ratio may arise from this approach, which will be further assessed on the basis of a targeted, in-depth review of the underlying documentation. Swissmedic also reviews the background and the context of such applications to ascertain whether reasons exist for carrying out its own scientific evaluation. Such reasons may include an earlier rejection or withdrawal of an application for this medicinal product or for one from the same class of substances in Switzerland or in another country with a comparable control system for medicinal products as stated in section 1.1.1, or if new scientific findings have emerged since the authorisation abroad was granted.

7.2 Streamlining of the review procedure on request for special medicinal product categories

In application of Art. 13 TPA in conjunction with Art. 18 para. 2 TPO, Swissmedic may, on request, reduce its assessment of an application for the authorisation of a medicinal product that has already been authorised by the EU Commission or US FDA if the product in question fulfils all the following conditions. Concise reasons in support of the request must be provided in the covering letter.

a) *The medicinal product is intended to prevent a transmissible infectious disease that may cause severe harm or serious suffering with potentially fatal consequences.*

b) *The requested indication wording is identical to the indication wording approved by the reference authority.*

If the medicinal product fulfils the above criteria, Swissmedic will review its efficacy, safety and quality using the reference authority’s assessment report, and determine whether the outcome of the foreign authority’s assessment can be adopted for Swissmedic’s authorisation decision. Swissmedic will authorise the medicinal product if its anticipated benefits outweigh its risks. If the above criteria are not fulfilled, an interim decision (rejection of the application of Art. 13 TPA) will be issued and the application will then be subject to the normal authorisation procedure according to the guidance document *Authorisation of human medicinal product with new active substance*. A reduced assessment in accordance with Art. 13 TPA will be performed accordingly using the criteria listed in chapter 7.1.

7.3 Application of Art. 13 TPA in special cases

If required in the interests of public health (e.g. authorisation of a vaccine in the event of a pandemic), Swissmedic can, ex officio, accelerate an authorisation procedure by restricting its own assessment,

even if the application was not submitted according to Art. 13 TPA in conjunction with Art. 16 – 19 TPO.

8 Application for medicinal products with limited and/or temporary authorisation (Art. 9a TPA, Art. 19 TPO, Art. 18ff. TPLO)

For authorisation applications for a medicinal product with a new active substance or with a known active substance (KAS: when an application is submitted for a previously unauthorised indication), whose authorisation – granted by a country with comparable medicinal product control according to section 1.1.1 – has been limited and made subject to special conditions due to the lack of data on quality, safety and efficacy, the assessment results of the foreign authority for granting a temporary authorisation (temp.auth.) according to Article 9a TPA will be taken into account. This also applies to applications for temporarily authorised additional indications (tempAI) in another country for NAS or KAS. Provided that the documentation requirements for NAS and the criteria specified in section 7 for temp.auth. and tempAI are also fulfilled and provided Swissmedic has approved the preceding application for the granting of a temporary authorisation, the application can be assessed according to Article 13 TPA.
The assessment is usually restricted to the review of the risk-benefit ratio based on the Assessment Report of the foreign reference authority. If a medicinal product has been granted temp.auth. or tempAI in another country, Swissmedic will likewise only grant a temporary authorisation according to Art. 9a TPA in conjunction with Art. 18ff TPLO. All submitted data and all assessment results of the foreign authority relating to the fulfilment of the specific conditions applicable to this authorisation should be submitted to Swissmedic without delay (see WL *Temporary authorisation for human medicinal products* and *Flowchart IV*).

9 Application for parallel processing of applications in Switzerland and abroad (Art. 20 TPO)

When submitting an application for authorisation using the standard procedure, the applicant should state on the form *Status of authorisation applications abroad HMV4* whether an authorisation application for the same medicinal product has already been submitted in a country with a comparable control system for medicinal products.
If, during the current authorisation procedure in Switzerland, the EMA issues a recommendation to the EU Commission, or a positive authorisation decision is issued in a country with comparable medicinal product control*, Swissmedic may, on receipt of a corresponding request by the applicant, apply* Articles 16 - 19 TPO by analogy*, provided that there are no major concerns based on Swissmedic's own assessment and it appears likely that this procedure (procedure in accordance with Art. 13 TPA) will lead to an earlier decision. If major concerns about the assessment results of the foreign reference authority arise during the assessment conducted by Swissmedic, the Agency will proceed to carry out its own independent scientific assessment (Flowchart V).*

10 Process at Swissmedic

10.1 Processing of the application

During the formal control, Swissmedic checks whether the requirements for the application of Art. 13 TPA according to section 3 are fulfilled and that the required complete documentation exists (see section 11 (Annex)). It also checks whether the documentation requirements according to Art. 16 TPO were respected. The applicant is informed about the rejection of the application of Art. 13 TPA or about any formal complaints. The applicant must present its statement on the negative preliminary decision on the application of Art. 13 TPA to Swissmedic – or, as the case may be, submit the missing documentation – within 30 days.

The process for minor variations (types IA / IA_{IN} and IB) is based on the requirements in the guidance document *Variations and extensions*.

Applications for NAS or their additional indications and products under Art. 12 para. 5 a, b, c and e TPLO, as well as applications for temp.auth. or tempAI (after a previously approved application) or for extensions or variations of a NAS will be checked to ensure that the criteria as stated in section 7 are fulfilled and that the application is therefore eligible for processing in accordance with Art. 16 - 20 TPO.

At the request of the applicant, the assessment according to Art. 13 TPA will be applied to all authorisation applications for medicinal products with known active substances and biosimilars, and also to its applications for extensions or variations according to section 6, provided that these satisfy the conditions stated in Art. 16 - 20 TPO, as well as to applications for a temp.auth. of a KAS or its tempAI (after a previously approved application).

If no questions are identified that require the issuing of an LoQ, the applicant will be sent the preliminary decision directly.

10.2 Costs of the procedure

If the authorisation holder submits an application for the assessments of foreign authorities to be taken into account in accordance with Art. 13 TPA in conjunction with Art. 16 - 20 TPO, and the requirements described in this guidance document are met, and if Swissmedic's decision can be based on the results of the reference authority's assessment, the overall fees applicable to individual cases are reduced by 60% in accordance with Art. 10 FeeO-Swissmedic.

11 Annex

The following documents (decisions and additional documentation) must be submitted as additional information:

11.1 Documents to be submitted for applications to all reference authorities

- Modules 1 to 5, or Parts I to IV (NtA) as submitted to the foreign authority (for applications for extension, additional indication and the authorisation of a new dosage recommendation without prior reference to Art. 13 TPA according to section 5, the documents for the first authorisation should also be submitted if they are the main source of reference).
- For minor variations of types IA / IAIN / IB and type II major variations: the complete final Assessment Report of the reference authority.
- If applicable: for DMF / ASMF an identical copy of the complete DMF (Applicant's und Restricted Parts) should be submitted (see under section 5.1).
- Swiss Module 1 (according to the guidance document Formal requirements and corresponding Directory Overview of documents to be submitted)
- Cover letter (according to the guidance document Formal requirements and corresponding Directory Overview of documents to be submitted). If applicable, confirmations, explanations, critical assessments or additional documentation must be submitted in the following situations:
  - In the case of differing authorisation decisions, e.g. concerning indications, dosage, storage instructions, shelf life, or other restrictions and similar issues, and in the case of withdrawal, rejection, suspension or ongoing investigation procedures
  - For differences or additions with regard to the documentation and / or the DMF / ASMF (Applicant's Part and Restricted Part) that have taken place since the authorisation decision: a comparison (old / new), incl. a critical evaluation and assessment report
  - If, instead of the corresponding methods of Ph. Eur. / Ph. Helv., other methods are used, their equivalence with the methods of Ph. Eur. / Ph. Helv. should be stated and substantiated accordingly in the form Information for application Art. 13 TPA.
  - For extensions and variations without prior reference to Art. 13 TPA, confirmation signed by a person entitled to act as a signatory stating that the documentation for Switzerland and that for the reference authority (before approval of the variation) are identical
  - In the event of ongoing GxP investigations (e.g. correction of deficiencies, required follow-up inspections)
  - In the event of deviations from currently valid guidelines that were not yet in force at the time of the authorisation in a foreign country
  - For translations: confirmation that the translations are correct
  - If information regarding safety signals is required
- Authorisation decisions of the foreign authorities, Assessment Report of the reference authority and additional documentation according to sections 11.2 – 11.10. (If differing decisions are made by the foreign authorities, see section 5.3)

11.2 Authorisation based on the EU Centralised Procedure (CP)

Basis for foreign decision:	CxMP / HMPC Opinion The EU Commission decision should be submitted as soon as it is available.
Additional documentation:	Day 80 Assessment Report Day 120 LoQ Day 180 LoOI Answers to Day 120 LoQ Answers to Day 180 LoOI Day 210 Assessment Report Risk Management Plan RMP (for NAS and their additional indications) Paediatric Investigation Plan and amendments (if available)

11.3 Authorisation based on the EU Mutual Recognition Procedure (MRP) and Decentralised Procedure (DCP)

Basis for foreign decision:	Marketing Authorisation in RMS (Letter of approval or Letter end of procedure)
Additional documentation:	LoQ Answers to LoQ Day 90 RMS Assessment Report (for MRP) Day 70 Preliminary Assessment Report (for DCP) Final Assessment Report (MRP = Day 90 DCP ≥ Day 105) In the event of arbitration to CHMP (EMA), *if applicable,* the EMA opinion should be submitted Risk Management Plan RMP (for NAS and their additional indications)

11.4 Authorisation based on EU/EFTA States and the UK: National authorisations

Basis for foreign decision:	Marketing Authorisation (Letter of approval or Letter end of procedure)
Additional documentation:	LoQ Answers to LoQ Assessment Report Risk Management Plan RMP (for NAS and their additional indications)

11.5 Authorisation based on authorisation in USA / FDA

Basis for foreign decision:	Approval Letter
Additional documentation:	LoQ Answers to LoQ Assessment Report: Standard or Priority Review

If available: Summary Basis of Approval (SBA)
ERA
If requested: Risk Minimization Action Plan (RiskMAP)
(for NAS and their additional indications)

11.6 Authorisation based on authorisation in Japan / PMDA

Basis for foreign decision:	Marketing Authorisation
Additional documentation:	LoQ (translated into German, French or English) Answers to LoQ (translated into German, French or English) Review Reports of New Drug Applications PMDA (translated into German, French or English) Review Summaries and Overall Summary Basis of Decision (translated into German, French or English) ERA Risk Management Plan RMP (for NAS and their additional indications)

11.7 Authorisation based on authorisation in Canada / Health Canada

Basis for foreign decision:	Notice of Compliance (NOC)
Additional documentation:	LoQ Answers to LoQ Assessment Report *If available:* Summary Basis of Decision ERA Risk Management Plan RMP (for NAS and their additional indications)

11.8 Authorisation based on authorisation in Australia / TGA

Basis for foreign decision:	Marketing Authorisation
Additional documentation:	LoQ Answers to LoQ Assessment Report ERA Risk Management Plan RMP (for NAS and their additional indications)

11.9 Authorisation based on authorisation in Singapore / HSA

Basis for foreign decision:	Marketing Authorisation
Additional documentation:	LoQ (translated into German, French or English) Answers to LoQ (translated into German, French or English) Assessment Report (translated into German, French or English)

ERA
Risk Management Plan RMP (for NAS and their additional indications)

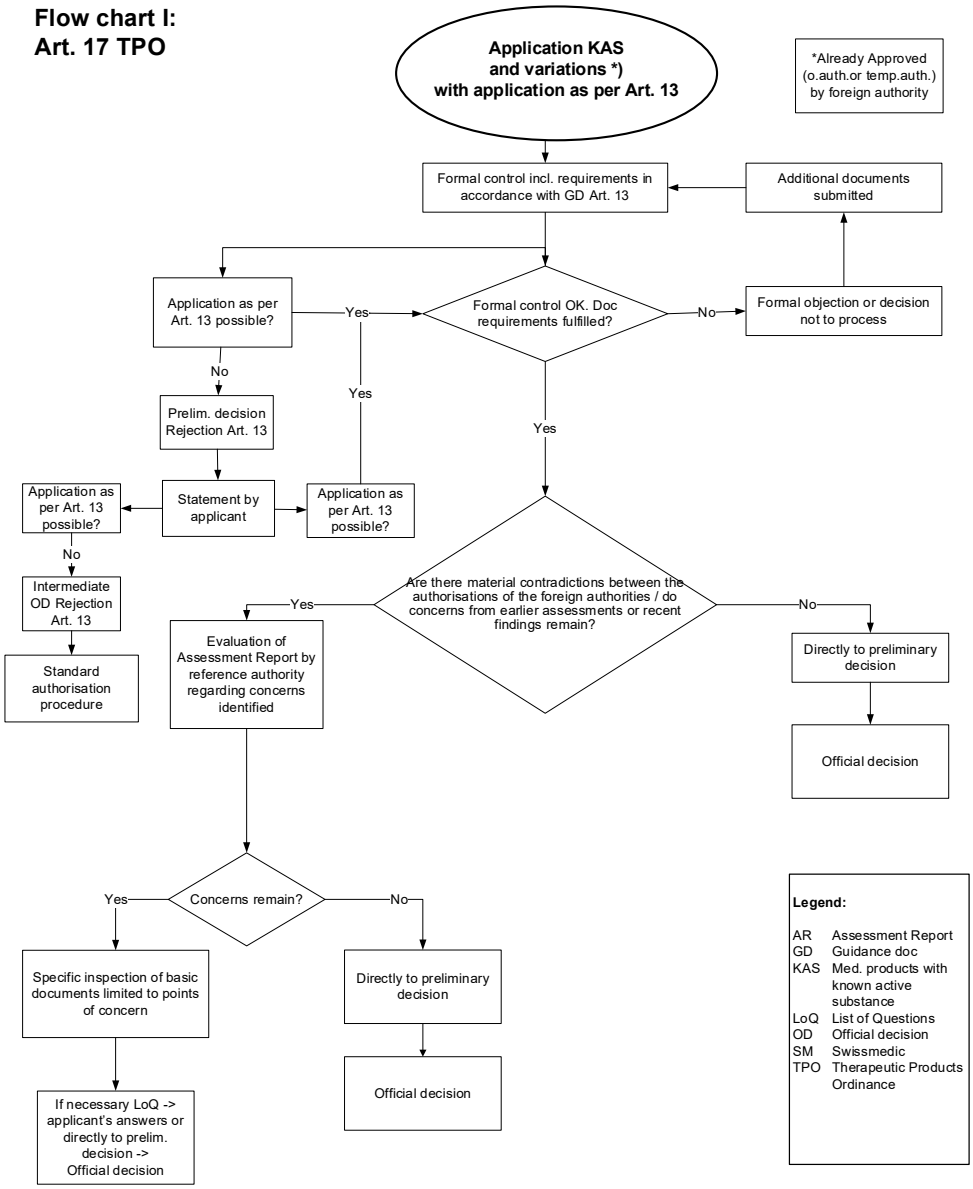
11.10 Authorisation based on authorisation in New Zealand / Medsafe

Basis for foreign decision:	Marketing Authorisation
Additional documentation:	LoQ Answers to LoQ Assessment Report ERA Risk Management Plan RMP (for NAS and their additional indications)

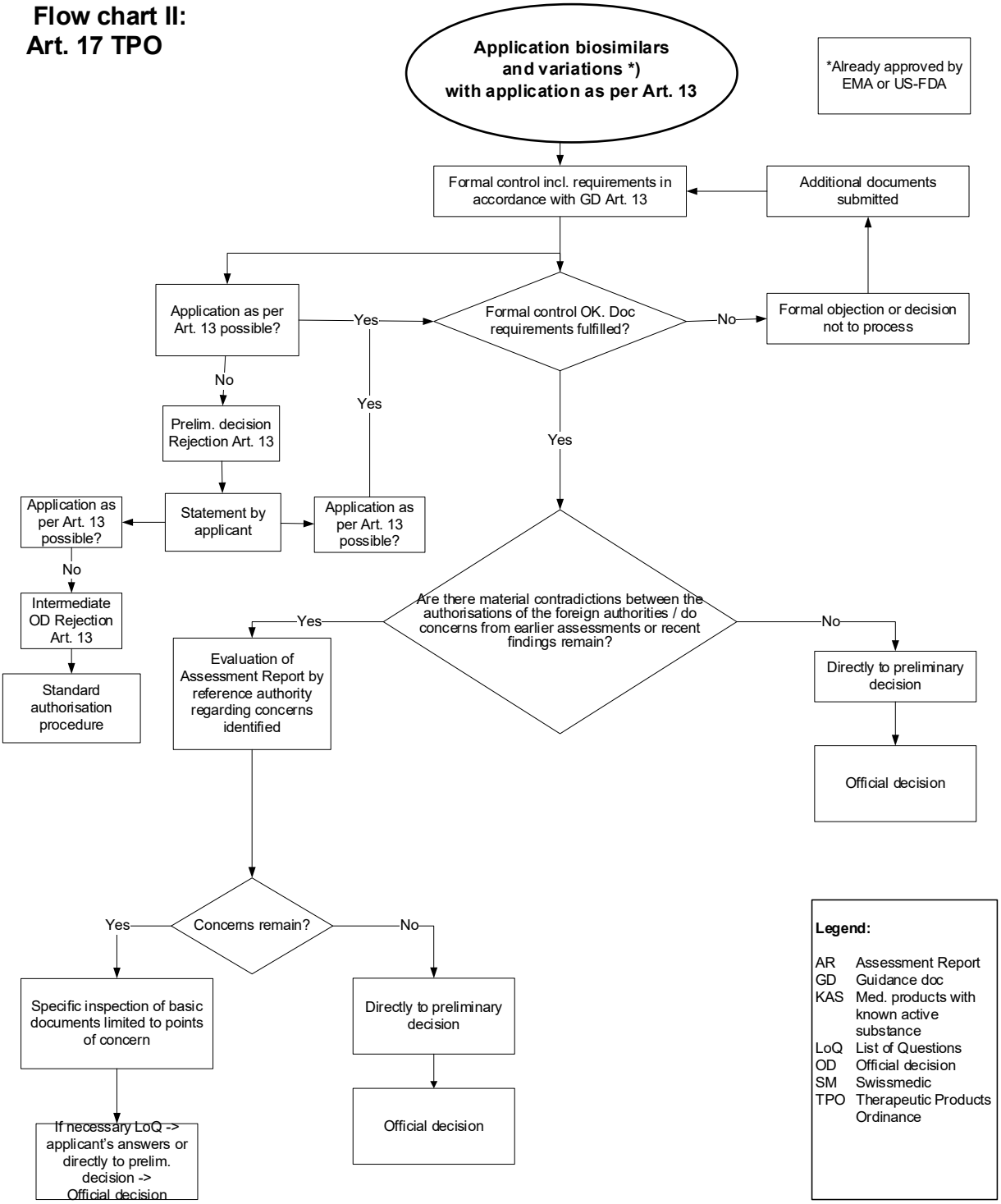
11.11 Flowcharts relating to application procedures

Flowchart I: Authorisation application for KAS (auth. or temp.auth.) and variations with application under Art. 13 TPA (Art. 17 TPO)
Flowchart II: Authorisation application for biosimilar and variations with application for Art. 13 TPA (Art. 17 TPO)
Flowchart III: Authorisation application for a non-innovative medicinal product in the categories listed in Art. 12 para. 5 TPLO (Art. 17 TPO)
Flowchart IV: Authorisation application for NAS (auth. or temp.auth.) and its additional indications with application under Art. 13 TPA (Art. 18 TPO)
Flowchart V: Parallel procedures in Switzerland and abroad (Art. 20 TPO)

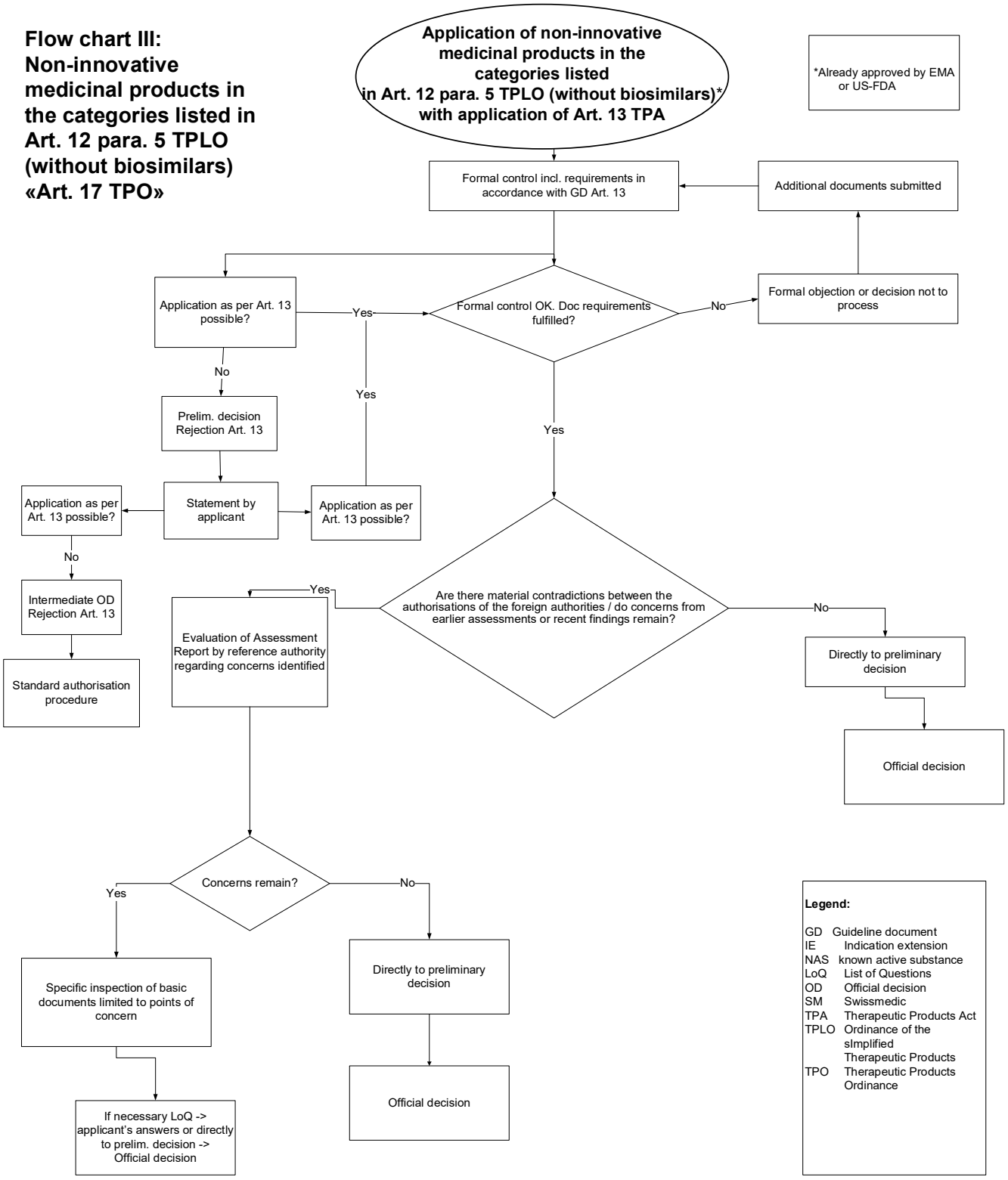
Flow chart I:
Art. 17 TPO



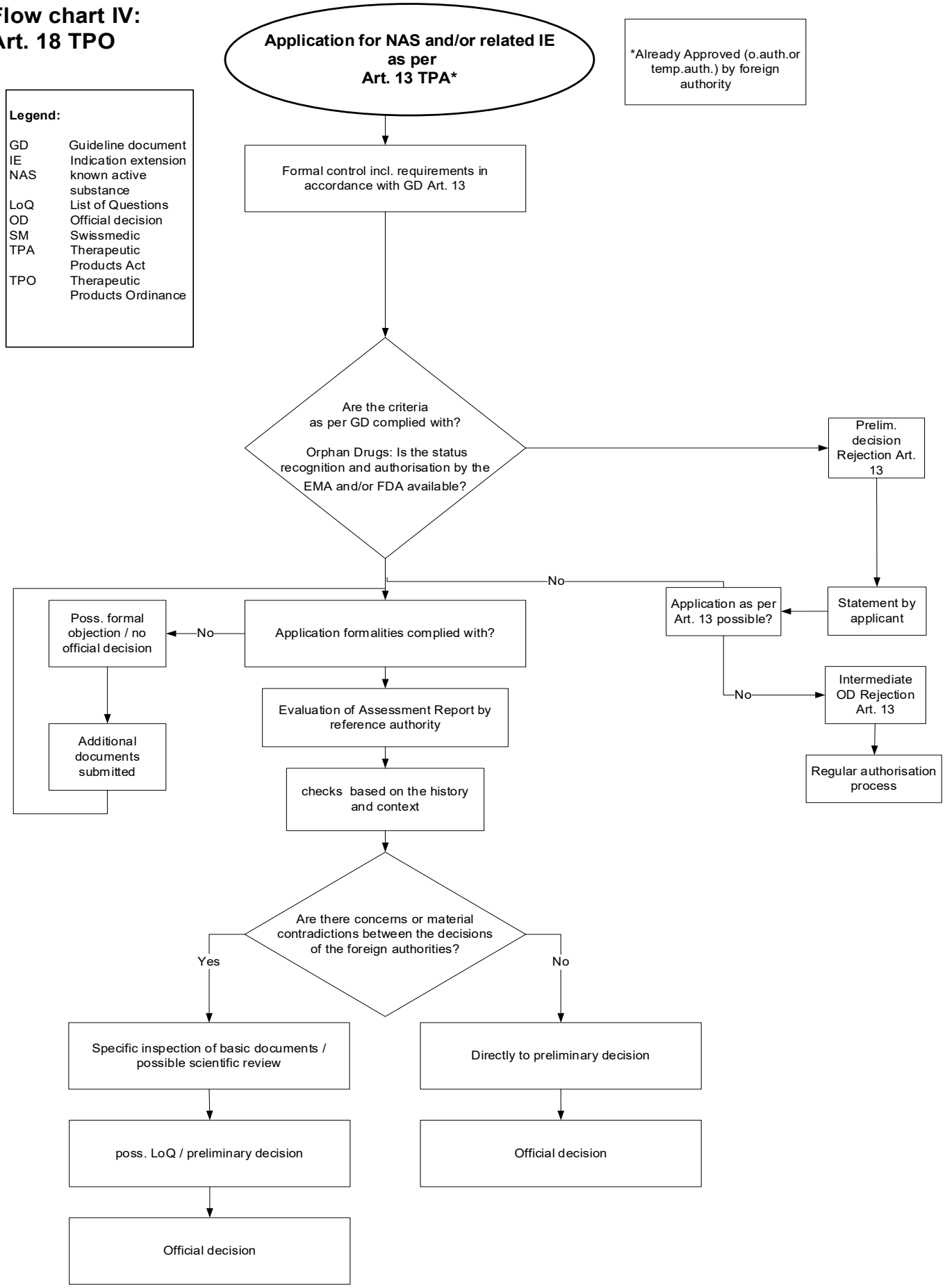
Flow chart II: Art. 17 TPO



Flow chart III: Non-innovative medicinal products in the categories listed in Art. 12 para. 5 TPLO (without biosimilars) «Art. 17 TPO»



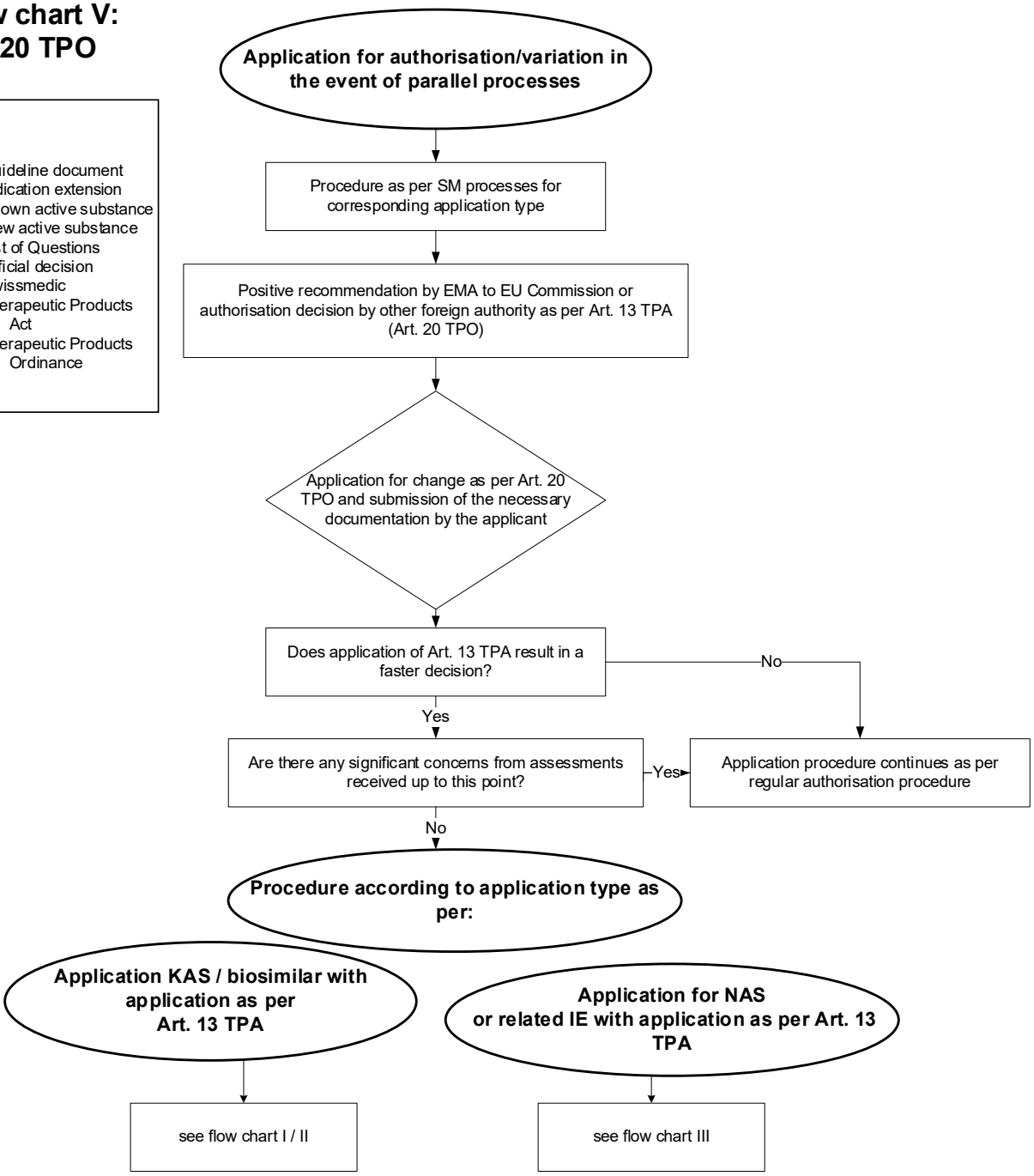
Flow chart IV: Art. 18 TPO



Flow chart V: Art. 20 TPO

Legend:

GD	Guideline document
IE	Indication extension
KAS	Known active substance
NAS	New active substance
LoQ	List of Questions
OD	Official decision
SM	Swissmedic
TPA	Therapeutic Products Act
TPO	Therapeutic Products Ordinance



Change history

Version	Change	sig
5.0	Clarifications regarding eCTD applications in section 5.1 Clarifications regarding consistency of foreign and Swiss documentation in sections 5.1, 5.7 and 11.1 Clarification in section 5.2 regarding RUP procedure Clarification regarding medicinal product information for reference products that are no longer authorised in section 5.5 Clarification regarding submission of documentation in section 5.10 Clarification of the wording “indication” and “indication wording” in sections 6.1 and 7.1 Clarification regarding RMP HMV4 suffix deleted, further editorial changes	fg/cho/hv
4.0	Changes in sections 3, 8 and 10.1 and in KAS and NAS flowcharts in section 11: Temporary authorisation also for KAS and temporary additional indication for NAS and/or KAS, additions to section 1.2 concerning temporary authorisation / additional indication Clarification in section 5.1 concerning additions since the foreign decision / DMF submission and section 11 concerning DMF submission Clarification in section 5.2 concerning the Repeat Use Procedure Clarification in section 5.3: Decisions of the reference authority / EU hybrid authorisation Clarification in section 5.7 concerning other possible deviations from the reference product	fg/hv/cho
3.1	Formal adjustments to the header and footer No content adjustments to the previous version.	dei
3.0	Clarifications in sections 3 and 5: Art. 13 TPA can be applied for minor variations of types IA / IA_{IN} / IB as long as these are addressed in an Assessment Report	fg
2.0	Clarification in chapter 6.3: medicinal products listed in Art. 12 para. 5 TPLO Clarification in chapter 7.2: reduced assessment for special medicinal product categories	fg
1.3	Explanation in chapter 10 Process	nma/fg
1.2	Correcting a single typo: Correcting ATP to TPA.	dts
1.1	Explanation in chapter 5.9 re submission of the assessment report for the DMF by consortium partner authorities Explanation in chapter 7.1 re orphan drug status	fg
1.0	Implementation of TPO4	fg