Guidance document

Temporary authorisation for human medicinal products

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1 Definitions, terms, abbreviations

1.1 Definitions

1.1.1 Temporary authorisation

Temporary authorisation (temporary new authorisation: temp.auth and temporary additional indication: temp.AI) is based on Art. 9*a* TPA in conjunction with Art. 18–22 TPLO, includes as yet incomplete documentation at the time of authorisation and is granted for a maximum of two years with special conditions (Art. 21 TPLO). Temporary authorisation either results from a temporary authorisation procedure, which was previously approved after company request, or is granted “ex officio” by Swissmedic.

1.1.2 Authorisation

The authorisation of a medicinal product is based on full documentation and results either from an ordinary procedure according to Art. 11 TPA (also called *standard procedure* in this guidance document) or after conversion of a temporary authorisation to an authorisation without special conditions (Art. 21 a para. 2 TPLO). The initial authorisation period is 5 years (Art. 16 para. 2 TPA). *Authorised* is used synonymously with *unlimited authorisation* and *authorised without special conditions*.

1.2 Abbreviations

AAA	Accelerated Application Hearing
AE	Adverse Event
AI	Additional indication
Auth.	Authorisation
COMP	Committee for Orphan Medicinal Products
DP	Document protection

EMA	European Medicines Agency
FC	Formal check
FDA	Food and Drug Administration
FDHA	Federal Department of Home Affairs
FeeO-Swissmedic	Ordinance on the Fees charged by the Swiss Agency for Therapeutic Products of 14 September 2018 (SR 812.214.5)
FTP	Fast-Track authorisation Procedure
IRB	Institutional Review Board
KAS	Known active substance
LoQ	List of Questions
MPI	Medicinal product information
NAS	New Active Substance
PD	Preliminary decision
SAE	Serious Adverse Event
ST	Standard Treatment
TEAE	Treatment-Emergent Adverse Event
temp.AI	Temporary additional indication
temp.auth	Temporary authorisation
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (Therapeutic Products Act, SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (Therapeutic Products Ordinance, TPO) (SR 812.212.21)
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)

2 Introduction and objective

It is possible for temporary authorisation to be granted under certain conditions defined by law in order to make medicinal products for the treatment of life-threatening diseases available to patients as quickly as possible. The submitted clinical documentation in particular does not have to be complete for a temporary authorisation (temp.auth) and the temporary authorisation procedure has an accelerated deadline. In contrast to the standard procedure, temporary authorisation must first be requested and this process may only be used if the request has been approved. An application for temp.auth/temp.AI cannot be submitted until the request has been approved. If authorisation is requested for a medicinal product or an additional indication using the standard procedure, but Swissmedic considers the data submitted to be insufficient, Swissmedic may propose an “ex officio” temporary authorisation to the applicant provided the criteria per Art. 9*a* TPA in conjunction with Art. 18 TPLO are fulfilled.

Section 5, *Request for temporary authorisation,* of this guidance document outlines the conditions that must be met before a **request** for temp.auth or temp.AI can be approved, and presents the detailed procedure for the meeting with applicants (AAA) during which this request is processed and evaluated (see annexes 1, 2 A and 2 B for the detailed AAA procedure). The formal and content

requirements for an **application** for the temp.auth or temp.AI, as well as the evaluation procedure itself, are described in **section 6** *Application for temporary authorisation*.

Swissmedic uses this guidance document first and foremost as a resource for applying the legal provisions in a uniform and equitable manner. For applicants, the document is intended to make clear the specific requirements that must be fulfilled so that corresponding applications can be processed by Swissmedic as quickly and efficiently as possible.

3 Scope

Temporary authorisation is possible in the following circumstances provided the criteria per Art. 9*a* TPA in conjunction with Art. 18 TPLO are fulfilled:

- New authorisation of human medicinal products with new active substance (NAS)
- New authorisation of human medicinal products with known active substance (KAS) if an indication not previously authorised is requested (KAS with innovation).
- Additional indication for human medicinal products

4 Legal framework

Temporary authorisation is regulated in Article 9*a* TPA.

Articles 18 - 22 TPLO set out in detail the conditions for the granting of temp.auth or temp.AI.

5 Request for temporary authorisation

5.1 Principle

The temp.auth or temp.AI should be granted if the conditions outlined in section 5.2 are met cumulatively. The documentation that was incomplete when the application for temp.auth or temp.AI was assessed should be supplemented only after the official decision has been issued. This information, required in connection with the conditions imposed, will subsequently be reviewed by Swissmedic; if the documentation is approved the temporary authorisation, if duly requested, can be converted into an authorisation without special conditions.

5.2 Material preconditions for temporary authorisation

The fulfilment of criteria stipulated in Art. 18 let. a to e TPLO is first checked by Swissmedic in the request for temporary authorisation. The criteria must continue to be met cumulatively up to, and including, the date on which the authorisation decision is issued.

Criteria

a. *The product is used "to identify, prevent or treat a disease that can lead to serious invalidity, severe suffering possibly resulting in death or to the death of a patient in the short term".*
   - The target population should comprise patients with an established clinical presentation. Reference may also be made to a subgroup that is at a certain stage of the underlying disease or that exhibits a recognised molecular pathogenic entity with specific characteristics in terms of course, prognosis or therapy. Please refer to Annex 2 D *Annex on tissue-independent or tumour-agnostic indications* for information on these indications, which are relevant owing to the growing significance of molecular diagnostics, particularly in oncology.

- The risk of serious invalidity or a possible fatal outcome is intended to apply to all the patients in the target population.
- The target population should be reflected explicitly in the indication.

b. *No alternative and equivalent medicinal product is authorised or available in Switzerland.*
   - Applies in particular to diseases for which no prophylactic or treatment options with authorised medicinal products exist.
   - Authorised or available medicinal products are authorised medicinal products with full or completed documentation; i.e. either authorised in the standard procedure (ordinary procedure according to Art. 11 TPA) or that have been converted from a temporary authorisation (authorisation without special conditions according to Art. 21*a* para. 2 TPLO) (see also section 1.1.2 *Authorisation*).
   - The existing treatment options with authorised medicinal products do not adequately reduce the risk of serious invalidity or a possible fatal outcome.
   - Criteria for checking the equivalence of medicinal products include:
     Indication, target population, mechanism of action, ease of use (administration route, pharmaceutical form, dosage recommendation, availability, etc.) and/or the benefit/risk profile.

c. *Major therapeutic benefit is expected from use of the product for which authorisation is being requested.*
   - Major therapeutic benefit should be demonstrated in clinical studies in the target population in a clinically and scientifically convincing manner. The following three aspects must be fulfilled in this respect:
     1. The selected trial end point(s) must be clinically relevant, i.e. survival rates, or Surrogate Markers for survival or the prevention of serious invalidity that are validated and recognised in the target population should be available.
     2. The events attributed to the trial endpoints(s) must occur with sufficient frequency in order to permit an assessment of the effect size; and
     3. Causality between treatment and clinical effect must be evident. Prevention or therapy of the disease achieves a relevant reduction in the risk of invalidity or threat to life.
   - Based on the clinical documentation submitted with the request for a temporary authorisation, it should be possible, even without an evaluation of the detailed data, to assess whether the therapeutic benefit is superior to that of the current authorised treatment/standard therapy to a clinically relevant extent (comparative basis).
     The evaluation of the clinical data considers not just the control arm of the clinical trial as a basis for comparison, but also all treatments for the proposed indication(s) with authorised medicinal products (used as monotherapy or in combination) that are available in Switzerland at the time of submission of the request for a temporary authorisation.
   - To generate a basis for comparison, the company must compare the study results on efficacy (endpoints accepted from the regulatory standpoint) and safety (in addition to TEAEs, a table of grade 3-5 TEAEs; SAEs and TEAEs that resulted in death) with the existing treatments with authorised medicinal products that are available in Switzerland in a tabular overview. This applies particularly if the submitted clinical trial was not randomised and therefore lacks a control arm. A standard treatment (ST) is considered to be the treatment with the non-temporarily authorised medicinal products that are available in Switzerland for the corresponding indication.

   For the **request** for temporary authorisation, the following applies:
   The date on which the request for an AAA for a planned application for temp.auth or temp.AI is submitted is considered to be the key date for the evaluation of the high therapeutic benefit. If the ST (control arm during the study) has changed in the interim, the applicant must demonstrate that a medicinal product proposed for temp.auth. also offers a greater therapeutic benefit compared to the **current** ST (when submitting the request).
   - The assessment of the clinical relevance depends on the individual clinical presentation and the corresponding clinical and scientific practice.

d. *The applicant is expected to be able to supply the necessary data per section 2 of the TPLO before the temporary authorisation expires.*
   - One or more studies decisive for authorisation will be completed before the temp.auth. or temp.AI expires, and corresponding reports will be submitted to Swissmedic (in accordance with ICH E3).
   - The final study protocol (i.e. the version approved by the Ethics Committee/IRB) for the pivotal study must be submitted with the application for temp.auth or temp.AI, together with confirmation of the above-mentioned undertaking to submit documentation *post hoc*. The expected date of the *data cut-off point* and the date on which the report will be submitted should be stated with binding effect.

e. *It takes so long to compile all the required data and to process and evaluate the data under letter d in a regular authorisation procedure as per Art. 11 TPA that irreversible damage in patients would result or worsen or this would be associated with severe suffering.*
   - The above-mentioned target population must be in immediate danger of invalidity or imminent death. Diseases that are associated with an increased risk, but classified as 'chronic' are not within the scope of temp.auth or temp.AI.

In any case, a positive evaluation of the request for an AAA for a planned temp.auth or temp.AI is possible only if the applicant can demonstrate, separately for each proposed indication, that the criteria a to e are all fulfilled. Criteria a to e per Art. 18 TPLO must be fulfilled throughout the entire process for temporary authorisation. Swissmedic can withdraw the authorisation at any time if any of the conditions are no longer fulfilled or the authorisation holder does not fulfil the special conditions specified in Art. 21 para. 1 TPLO.

5.3 Formal preconditions

When submitting the request for a temp.auth. or temp.AI, the applicant should demonstrate that the preconditions stipulated in Art. 18 TPLO are fulfilled. Section 5.6 regulates the processes for the request for, and implementation of, an AAA. The request should be submitted between 3 and 12 months before the authorisation application so that planning and procedural certainty can be guaranteed.

5.4 Scientific Advice

The applicant has the option of attending a pre-submission meeting in the form of a Scientific Advice Meeting to discuss the available data (see the guidance document *Meeting for applicants held with the Authorisation sector).* This option is explicitly encouraged by Swissmedic.

5.5 Documentation to be supplied

The request for temp.auth or temp.AI must be submitted to Swissmedic in writing by the applicant. The request must be substantiated scientifically and be backed up by the required documentation. The following documents should be submitted:

a) Covering letter stating the indication(s) requested for Switzerland. The wording of the scheduled indication should be based on the patient populations that have been or are being investigated and documented by the results of studies. If applicable, the covering letter must also refer to authorisation applications pending in other countries and the existence of questions or decisions from other authorities where these exist.
b) Justification of why the applicant believes the conditions for temp.auth or temp.AI are fulfilled (5 to a maximum of 15 pages). Specific position statements on all criteria stated in Art. 18 let. a to e TPLO should be provided (see section 5.2 *Material preconditions for temporary authorisation*).

The argumentation must be documented (e.g. summary of the data from the pivotal studies that are available or will be submitted *post hoc*).

c) If several indications are proposed for the medicinal product, the applicant must demonstrate that the criteria stated in Art. 18 let. a to e TPLO are all fulfilled for each individual indication.
d) Supportive information in the form of available relevant top-line[1] results of ongoing studies (see also criterion c in section 5.2 *Material preconditions for temporary authorisation*).
e) Overview of the data package intended for the application for temp.auth or temp.AI at the time of submission, with a tabular listing and brief overview of the ongoing studies, number of patients for efficacy and safety results. The CTD module 5.2 “Table of All Clinical Studies” can be used as a template for this listing.
f) Confirmation that the complete data for pharmaceutical quality (module 3) are available and will be submitted with the application for temp.auth and temp.AI if applicable (if, for example, a new pharmaceutical form or dosage strength is required). This refers to the medicinal products for which temporary authorisation is being requested.
g) Draft of the risk management plan (RMP) for the medicinal product scheduled for temp.auth or temp.AI with the risk aspects of the medicinal product, the planned pharmacovigilance activities and risk-mitigation measures. The principles of the RMP that must be submitted in the context of temp.auth or temp.AI are described in the documents “ICH E2E Guideline - Pharmacovigilance Planning”, the European Medicines Agency (EMA) Guideline “Good pharmacovigilance practices (GVP): Module V – Risk management systems” and the Swissmedic guidance document “RMP/ICH E2E information submission HMP”.
h) If available: Draft version of the Information for healthcare professionals or the EU or FDA *Summary of Product Characteristics* or the *FDA Prescribing Information*.
i) *Decision minutes from Accelerated Application Hearing* form in PDF and Word format, incl. details of the planned date of submission of the authorisation application (+/- 2 calendar weeks).

5.6 Request for a temp.auth or temp.AI

After the request for a temp.auth. or temp.AI has been received, the documentation is formally checked within 5 calendar days. Swissmedic will decide, no later than 30 days after completion of the formal checks, whether the criteria for a temp.auth. or temp.AI per Art. 18 let. a - e TPLO are met.

Depending on the result of the assessment of the Briefing Document and the submitted documentation, one of the following three processes, a), b) or c), will be applied:

a) Criteria stipulated in Art. 18 let. a to e TPLO are fulfilled

If, after receiving the applicant's request, Swissmedic unconditionally agrees to review its authorisation application in the context of a temp.auth. or temp.AI, and if the evaluation of the submitted documentation does not reveal any aspects requiring clarification, Swissmedic can dispense with the implementation of an AAA. In this case, Swissmedic will directly issue an official decision to approve the request for a temp.auth. or temp.AI. The approval will be recorded in the decision minutes. These will be included as an integral part of the official decision.

b) Criteria stipulated in Art. 18 let. a to e TPLO cannot be conclusively evaluated following the assessment of the Briefing Document

If the criteria for a temp.auth. or temp.AI cannot be conclusively evaluated by Swissmedic following the assessment of the Briefing Document, Swissmedic will inform the applicant accordingly no later than 30 days after the completion of the formal control and advise the applicant of the date of an AAA.

[1] Available results evaluated statistically as per study protocol, but no complete studies or interim reports as per ICH-E3 available

The applicant will be informed of the specific criterion that cannot yet be conclusively evaluated. The applicant will also be informed of the specific unresolved questions that will need to be clarified in connection with the AAA, or the specific aspects that must be fulfilled before the request for a temp.auth. or temp.AI can be conclusively evaluated. The applicant will be informed of the final decision on the request for a temp.auth. or temp.AI in connection with the AAA.

c) Criteria stipulated in Art. 18 let. a to e TPLO are not fulfilled

If the evaluation of the submitted documentation reveals that the criteria stipulated in Art. 18 let. a to e TPLO are not fulfilled, Swissmedic will issue the applicant with a preliminary decision to reject the request. The applicant will be granted a time limit period of 10 days in which to submit a written statement or inform Swissmedic whether it would like to participate in an AAA. If the applicant decides not to take part in an AAA, after assessing the statement Swissmedic will inform the applicant of its final decision on the request for a temp.auth. or temp.AI in the form of an official decision subject to appeal.

5.7 Procedure for an AAA (see annex for detailed procedure)

During the AAA, Swissmedic discusses with the applicant whether, on the basis of the submitted documents, the preconditions of Art. 18 let. a to e TPLO are satisfied and whether a temp.auth or temp.AI is possible. The applicant can issue a position statement on Swissmedic's line of reasoning and, if applicable, present counterarguments that justify the implementation of a procedure for a temp.auth or temp.AI.

Based on the provisional result of the review of the documents submitted with the request for a temp.auth or temp.AI and the supplementary reasons presented to the applicant during the AAA, Swissmedic will reach a binding decision during the AAA on whether an application for temp.auth or temp.AI can be approved or not. The decision taken by Swissmedic is recorded in writing in the minutes with the rationale.

The relevant discussion items are documented concisely by the applicant in the decision minutes. The applicant confirms that it has been informed of all the reasons for Swissmedic's decision during the AAA, that the applicant has been granted a fair hearing in accordance with the law, and that the applicant has orally presented its position statement on the intended decision.

The applicant is given the opportunity to finalise the minutes after the AAA. The finalised minutes are submitted by the applicant to Swissmedic via the eGov portal at the latest three working days after the AAA. Swissmedic reviews the minutes and makes any necessary corrections and additions.

Following the AAA, the applicant will receive the decision in writing in the form of an official order. The final minutes (i.e. the rationale for the decision) will be enclosed as an appendix and as an integral part of the official order concerning the request for temp.auth or temp.AI.

The procedure for the AAA is described in detail in Annex 1.

5.8 Presubmission Meeting

If the request for temp.auth or temp.AI has been approved, a Presubmission Meeting can be held if required between one and two months before the application for temp.auth or temp.AI is submitted. The aim of the meeting is to establish whether all the documentation required to process the

application is available. In particular, the following formal aspects of the authorisation application to be submitted will be considered:

- Index of scientific and administrative documentation
- Any unresolved questions concerning incomplete clinical documentation and the times at which it will be submitted

The definitive submission date is established at the Presubmission Meeting.

The following information / documentation must be sent to Swissmedic, with an appropriate covering letter, at the latest 2 weeks before the Presubmission Meeting:

- List of questions: Presentation of the issues to be clarified during the Presubmission Meeting, usually in the form of a Briefing Book (see Section 3.2 List of questions/documentation in the guidance document *Meeting for applicants held with the Authorisation sector*)
- Draft agenda with the points to be discussed
- Proposal for the type of meeting: in person, teleconference or videoconference
- List of participants and their functions

The guidance document *Meeting for applicants held with the Authorisation sector* also applies.

5.9 Planning the submission of the authorisation application following the approval of the request

If the request for a temp.auth. or temp.AI is approved, the authorisation application can be submitted on the planned date stated on the decision minutes. Applicants must inform Swissmedic in writing of the exact date on which they intend to submit the authorisation application as soon as possible but at least one month before submission of the authorisation application.

6 Application for temporary authorisation

6.1 Formal aspects and the documentation to be submitted

The applicant must submit the application for temp.auth. or temp.AI together with all documentation required according to the application type to Swissmedic by the agreed date. Up to, and including, the date of completion of the application for temporary authorisation, the criteria stipulated in Art. 18 let. a to e TPLO must continue to be met cumulatively (see section 5.2 *Material preconditions for temporary authorisation*).

6.1.1 Labelling in the Information for healthcare professionals

The specific requirements to be fulfilled by the Information for healthcare professionals for medicinal products with temporary authorisation are derived from the guidance document *Product information for human medicinal products*.

6.2 Review phases

The process of assessing an application for temp.auth or temp.AI is described in in Annex 2 A *Procedure for request and application for temporary authorisation*. The assessment is performed using process New authorisation or Variations and extensions for human medicinal products (see

guidance document *Authorisation of human medicinal product with new active substance* and the guidance document *Variations and extensions HMP*).
On the dates of the preliminary decision and official decision on the application for temporary authorisation, the criteria stipulated in Art. 18 let. a to e TPLO must be met cumulatively (see section 5.2 *Material preconditions for temporary authorisation*).

6.3 Review time limits

The time limits given in the guidance document *Time limits for authorisation applications* apply. Answers to the LoQ must be submitted within the time windows published on the Swissmedic website. To ensure that applications are processed promptly, the applicant must also notify Swissmedic in advance of the date on which the responses to the List of Questions (LOQ) and to the preliminary decision (PD) will be submitted within 14 calendar days of receipt of the LOQ or PD.

6.4 Grant of the temporary authorisation

The temp.auth or temp.AI is granted for a maximum of two years. **No document protection** is granted when an application for temp.auth. or temp.AI is approved, and the following is stated on the authorisation certificate: “Temporary authorisation as per Art. 9*a* TPA” or “New indication with temporary authorisation per Art. 9*a* (SR 812.21) (Product information: information last revised Month Year)”.

6.5 Phase after temporary authorisation

The phase after temporary authorisation is characterised by the following:

6.5.1 Risk management plan and post-marketing activities

The risk management plan (RMP) describes the risk aspects of the medicinal product, the planned pharmacovigilance activities and the risk-mitigation measures. The pharmacovigilance activities and the risk-mitigation measures cannot be planned or assessed definitively yet since knowledge of the risk aspects is still incomplete at the time the authorisation application is assessed. Specific conditions regarding safety specifications, the further collection of pharmacovigilance data and implementation of risk-mitigation measures may therefore be imposed.

6.5.2 Fulfilment of conditions and conversion

The conversion to an authorisation is contingent on the fulfilment of the conditions imposed on such a conversion.

- **Fulfilment of conditions**
  All documentation on the fulfilment of conditions must be submitted to Swissmedic for review **at least 90 calendar days before expiry of the temporary authorisation**.
- **Conversion:**
  At the same time as the documentation on the fulfilment of the latest condition(s), the authorisation holder must also submit the application for conversion. If this application for authorisation is approved, an authorisation with a validity of five years is issued and corresponding document protection granted. The authorisation number and packaging code are unchanged. The regulations governing document protection in the context of conversion

can be found in the guidance document *Document protection.*
The relevant texts must be submitted with the documentation on conversion for modifications of the MPI (information for healthcare professionals) associated with the conversion.

- **Extension of the "ex officio" temporary authorisation:**
  If Swissmedic receives the documentation on the fulfilment of conditions within the specified period, the temp.auth or temp.AI is extended until the new documentation has been reviewed.
- **Updating the product information:**
  If the fulfilment of conditions requires modification of the product information (PI), the relevant texts must be submitted with the documentation on the fulfilment of conditions. An additional application for modification of the product information is not required.

If, after reviewing the documentation on the fulfilment of conditions, Swissmedic concludes that the conditions are not or cannot be met, the temp.auth is revoked or lapses.

6.5.3 Extension or discontinuation of the temporary authorisation by the authorisation holder

If the documentation on the fulfilment of conditions for a temp.auth or temp.AI cannot be submitted within the specified period, it may be possible to extend the temp.auth or temp.AI in scientifically justified exceptional cases, subject to an application being submitted, in accordance with Art. 21 para. 3 TPLO. This application for the extension of the temp.auth or temp.AI must be submitted to Swissmedic **at least 90 calendar days before the end of the temporary authorisation** period for assessment. For the application for extension, an interim report is prepared on the conditions specified in the official decision, focusing particularly on the required analyses and study results. In addition, the marketing authorisation holder should propose new submission deadlines for the documentation on the fulfilment of conditions in its application to extend temp.auth or temp.AI.

For the authorisation to be extended, the criteria stipulated in Art. 18 let. a to e TPLO must continue to be met cumulatively (see section 5.2 *Material preconditions for temporary authorisation*). If an equivalent medicinal product was authorised in the interim, the initial authorisation period (usually 2 years) cannot be extended at the request of the applicant.

If the marketing authorisation holder wishes to discontinue the temp.auth or temp.AI it must send an application to Swissmedic for discontinuation of the authorisation or deletion of a therapeutic indication (OT Discontinue preparation or an application for a type IB variation: VA IB C.I.6.b)) **at least 90 calendar days before the end of the temporary authorisation period**. In addition to justification for waiver of a plan, this application includes details of how already treated patients will continue to be treated or switched to other therapies.

7 "Ex officio" temporary authorisation

If, during its review of an authorisation application, Swissmedic determines that the clinical documentation does not adequately support the requested indication(s), Swissmedic will always consider the possibility of an "ex officio" temp.auth or temp.AI (see Annex 2 B *"Ex officio" temporary authorisation*). If the criteria under Art. 18 TPLO are fulfilled, Swissmedic issues a preliminary notification of approval with partial rejection. The company has the following options depending on whether it accepts the "ex officio" temp.auth / temp.AI or not:

1. **"Ex officio" temp.auth or temp.AI: YES:**
   The applicant accepts the temp.auth or a temp.AI and submits a corresponding confirmation and any outstanding documentation as necessary in response to the preliminary notification. The original time limit schedule continues with the change to an “ex officio” temp.auth. or temp.AI. No reduced time limits are applied.
2. **"Ex officio" temp.auth or temp.AI: NO:**
   a. The applicant does **not** accept a temporary authorisation or a temporary AI and withdraws the application or agrees with the official decision of rejection in its response to the preliminary decision.
   b. The applicant does **not** accept a temp.auth or temp.AI and submits a statement in response to the preliminary notification justifying why the preconditions for an authorisation without special conditions or AI are met using new arguments/evidence. The application continues in the procedure initially requested.

Swissmedic is entitled to switch to a temporary authorisation procedure and this decision is submitted to the applicant with the preliminary notification, as described above. If the company wishes on its own initiative to switch from the current procedure to a temporary authorisation procedure, it must withdraw the ongoing application. The applicant can subsequently initiate a procedure for the granting of temp.auth or temp.AI by means of a prior request for temp.auth or temp.AI (in with the context of an AAA, see section 5 *Request for temporary authorisation*) along with a subsequent application for temp.auth or temp.AI (see section 6 *Application for temporary authorisation*).

8 Variations and extensions for temporarily authorised medicinal products

After a temp.auth has been approved for the medicinal product, the authorisation holder is required to submit any variations to Swissmedic in accordance with Art. 21 to 24 TPO.

AI are possible both with a complete data record and with incomplete documentation. It may be possible to conclude the procedure for authorisation of a fully documented AI with an approval before the end of the temp.auth period for the medicinal product. This means that the medicinal product’s authorisation is converted when the AI is approved and that document protection is granted. The regulations on this can be found in the guidance document *Document protection.*

Indications with temporary and non-temporary authorisation are identified as such in the product information (see requirements in the guidance document *Product information for human medicinal products*) and included in the lists published on the Swissmedic website from this time onwards.

9 Application of Art. 13 TPA

The regulations for applying Art. 13 TPA in the context of temporary authorisations can be found in the guidance document *Authorisation human medicinal product under Art. 13 TPA.*

10 Time limits

The time limits are based on the guidance document *Time limits for authorisation applications*.

11 Fees

The fees specified in FeeO-Swissmedic apply.

For requesting a temp.auth. or temp.AI, Swissmedic invoices the applicant for its administrative and scientific costs. The costs are calculated on the basis of Art. 4 FeeO-Swissmedic.

The fees for reviewing the documentation on the fulfilment of conditions (including modification of the PI) will be calculated according to the work involved.

Annex 1

Accelerated Application Hearing (AAA) procedure

Before the AAA

- The AAA takes place 6-8 weeks following receipt of the request for temp.auth or temp.AI. The AAA lasts up to 1.5 hours, including two time-outs. The aspects to be clarified for the conclusive evaluation of a request for temp.auth. or temp.AI and the confirmation of the date on which the AAA will be held is sent to the applicant in writing no later than 30 days after completion of the formal control.

- The applicant's line of reasoning to substantiate fulfilment of the criteria set out in Art. 18 let. a to e TPLO must be presented on slides. If the indication wording is amended as a result of questions posed by Swissmedic, this should be documented on the presentation slides. No further change to the indication wording is accepted during the AAA. The final presentation slides are submitted to Swissmedic as a PDF via the eGov portal by the applicant at least 10 calendar days before the AAA.

- Approx. one hour before the AAA begins, Swissmedic makes the draft decision minutes available in Word format via the eGov portal so that the applicant can work on them.

During the AAA

- During the AAA, the applicant presents the prepared presentation regarding the request for temp.auth or temp.AI. No changes may be made to the content of the presentation slides sent to Swissmedic before the AAA.

- If Swissmedic has asked for any clarification regarding the data submitted, the applicant must provide this information on a differentiated basis during the AAA. However, no additional or new data that are not included on the presentation slides submitted in advance are accepted during the AAA.

- During the AAA, the applicant can ask questions, issue a position statement on Swissmedic's line of reasoning and, if applicable, present counterarguments that justify the implementation of the requested temp.auth or temp.AI procedure.

- The applicant concisely documents its opinion and relevant points for discussion in the decision minutes.

- Before the AAA ends, Swissmedic reaches a binding decision on the basis of the provisional result of the documentation review and the supplementary line of reasoning presented by the applicant at the AAA. Swissmedic can allow itself a 15-minute time-out for decision-making after discussing the data with the applicant.

- After the time-out, Swissmedic will present its decision to the applicant by word of mouth. The decision will be recorded in the decision minutes by the applicant. If the request for temp.auth or temp.AI is rejected, Swissmedic can recommend the applicant to submit an application for temp.auth or temp.AI via an alternative procedure.

- Once Swissmedic has communicated its decision, the applicant is granted a 15-minute time-out, if it wishes to have one. The applicant then has the chance to discuss the decision and, where required, to discuss the proposal for the submission of another authorisation procedure without Swissmedic being present.

After the AAA

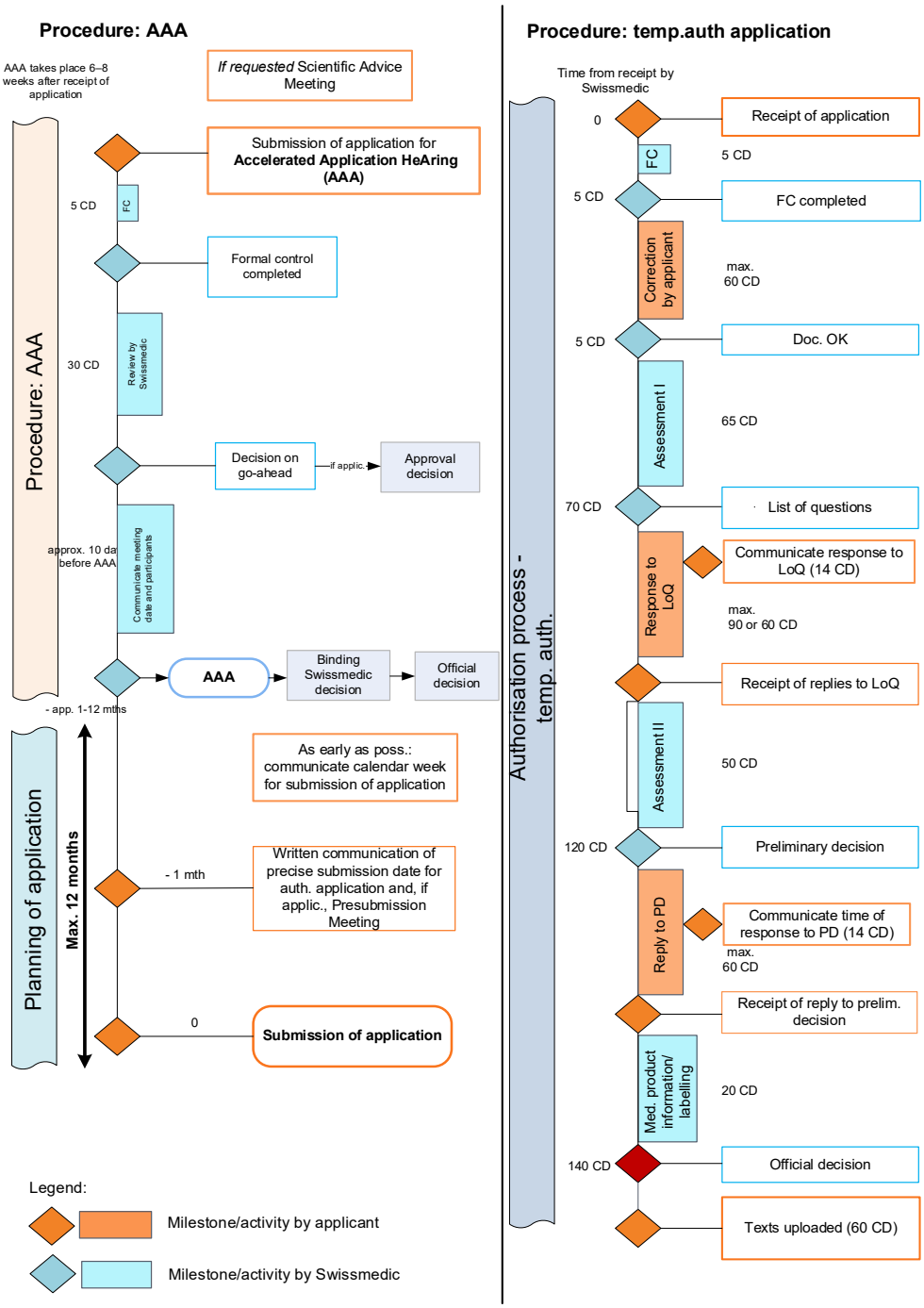
- The finalised minutes are submitted to Swissmedic by the applicant via the eGov portal at the latest three working days after the AAA. Swissmedic reviews the minutes and makes any necessary corrections and additions.

- After the AAA, Swissmedic informs the applicant of the decision taken at the AAA in the form of a written official order. The final minutes are enclosed as an appendix and as an integral part of the official order concerning the application for temp.auth. or temp.AI.

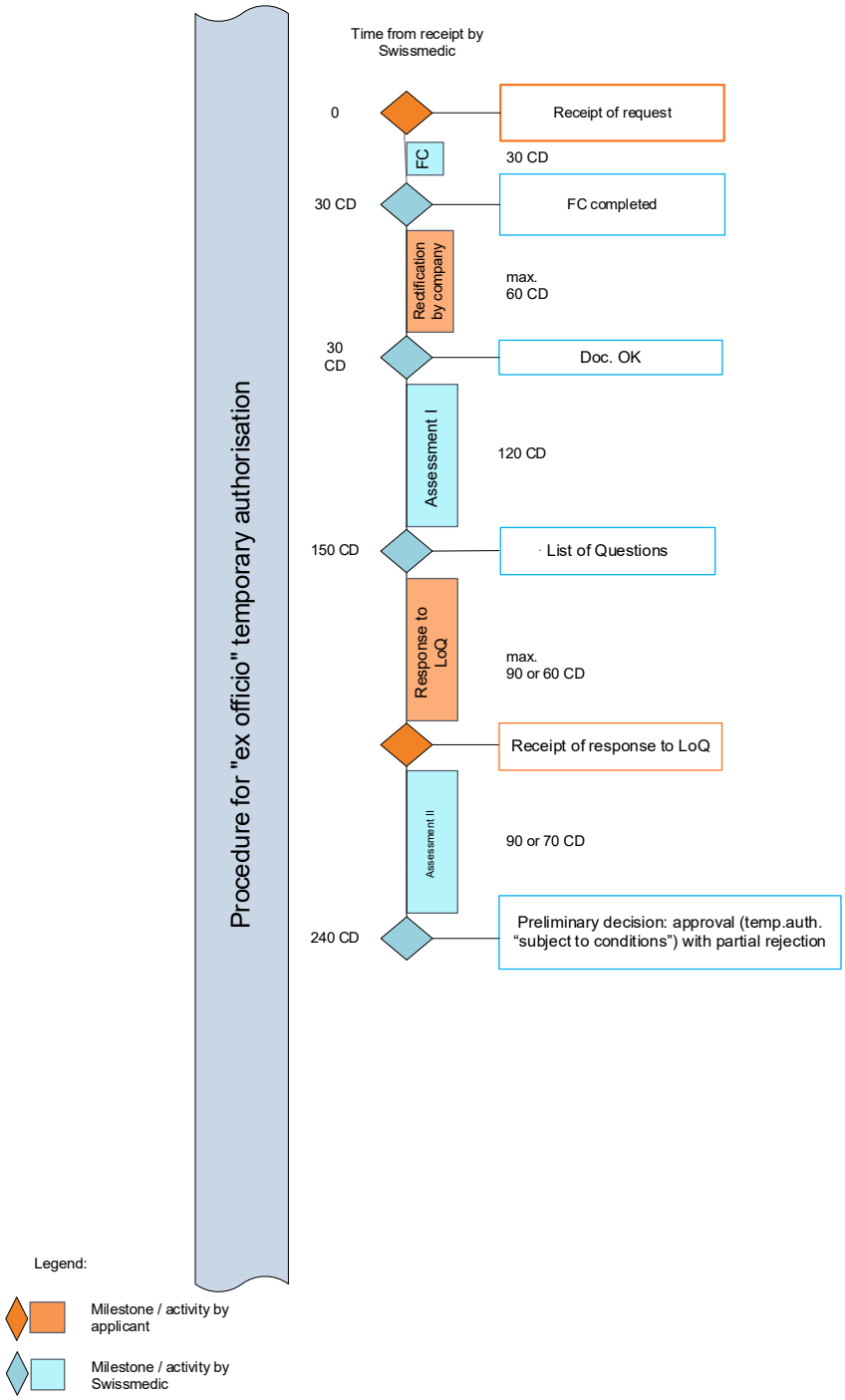
Annex 2

In the following illustrations, temp.auth refers both to temporary new authorisations and temporary authorisation of additional indications.

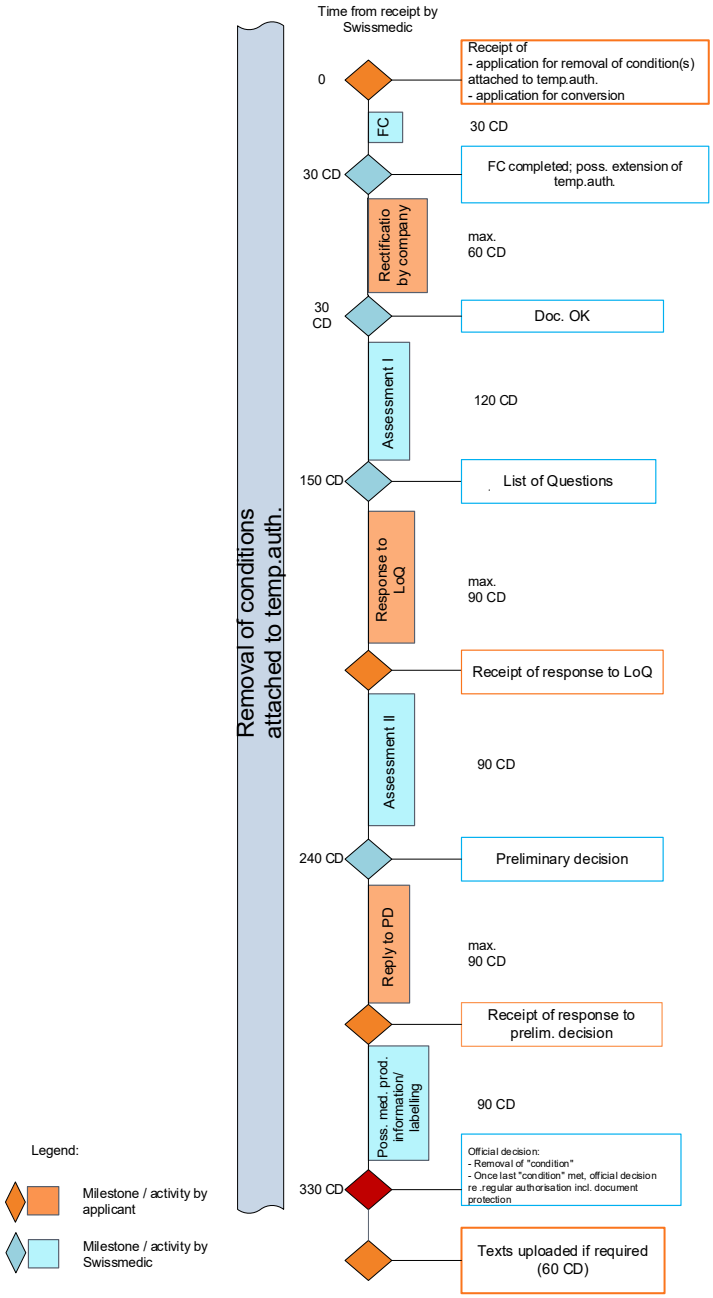
A. Procedure for request and application for temp.auth



B. “Ex officio” temp.auth



C. Application for removal of condition(s) attached to a temp.auth



D. Annex on tissue-independent or tumour-agnostic indications

Definition

A tissue-independent or tumour-agnostic indication is characterised by the fact that its wording describes a patient population with a particular molecular abnormality that is not restricted to a localised, tissue-specific tumour entity, but that extends to all tumour entities regardless of their location (e.g.: “medicinal product A is indicated for all patients whose tumours display genetic abnormality xyz”).

Application

In principle, an application for a procedure for temp.auth or temp.AI can be submitted for oncologicals with tissue-independent or tumour-agnostic indication wording in connection with an AAA.

Guidance on the fulfilment of criteria of Art. 18 let. a to e. TPLO

A disease or a subgroup of a disease may be deemed “recognised” or “established” in the context of a “tissue-independent” indication if it can be unequivocally distinguished from other subgroups within an entity by virtue of its prognosis, treatment and course, and by the fact that the medicinal product demonstrates general efficacy. It is incumbent on the applicant to demonstrate plausibly that in terms of prognosis and/or as a result of the treatment, the molecular tumour marker behaves differently in all tissue types, regardless of nature, when compared with histological subgroups without this marker. The relevant specialist guidelines should be consulted for this purpose.

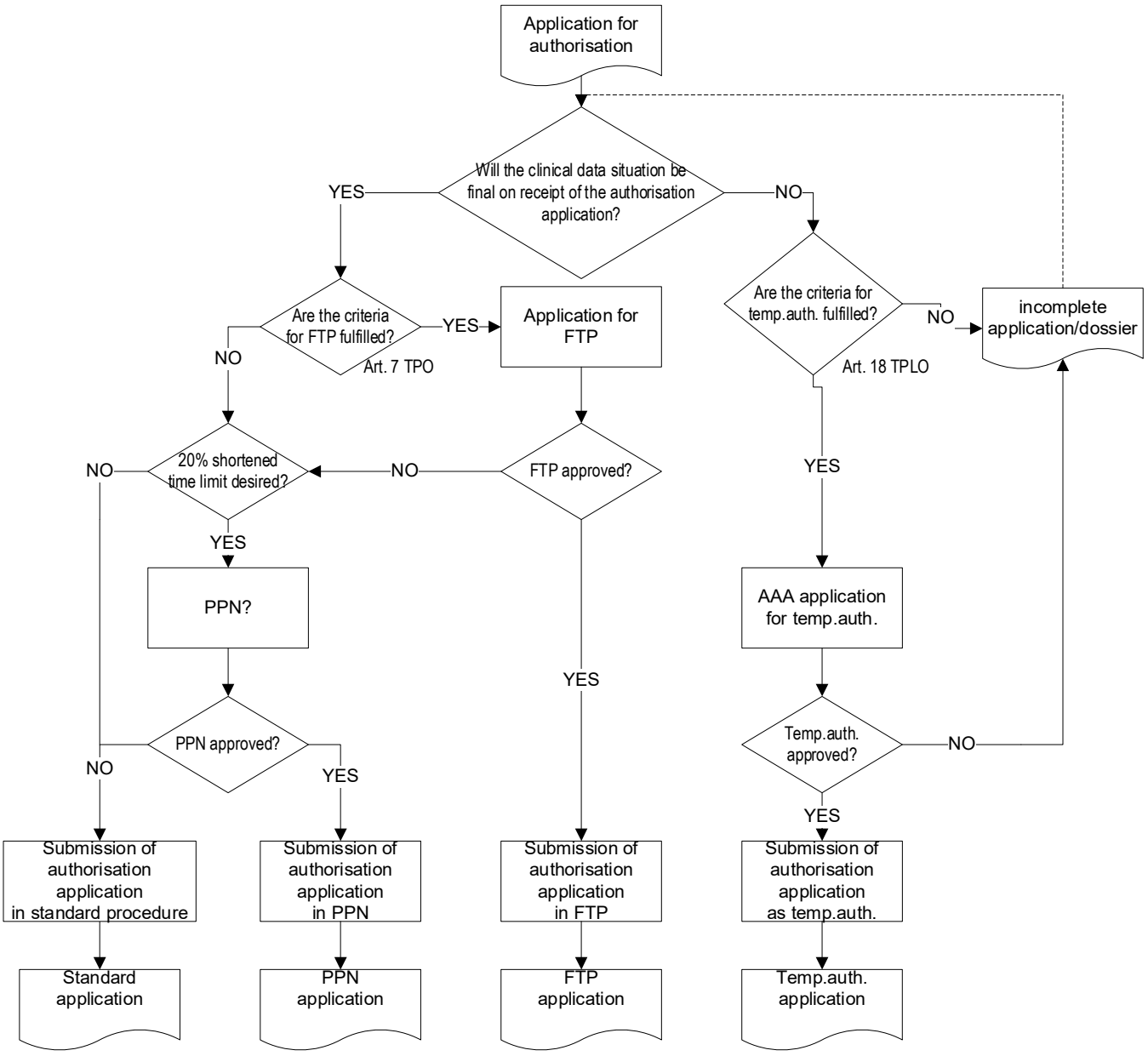
Tumour-agnostic indications will be assessed for compliance with criteria a to e on a case-by-case basis using the evidence base submitted. For this purpose, convincing proof of efficacy obtained from an adequate number of patients for each case must be presented for tumours in peripheral and central nervous system locations and from different tissues of origin (sarcomas, carcinomas, or haematologic tumours if appropriate).

The temp.auth or temp.AI process will pay particular attention to the extent to which the applicant is able to subsequently supply such data as the Agency may require to ensure adequate case numbers in the above-mentioned different tumour locations and tissues of origin. The decision will also take account of this (criterion d). This approach is intended in particular to acknowledge the fact that – in contrast to applications for fast-track authorisation (see Guidance document *Fast-track authorisation procedure HMV4* in Annex 2 B) – any review of an application for temporary authorisation is a provisional evaluation rather than one based on a final evidence base.

If an application for an authorisation procedure for temp.auth or temp.AI is approved, a decision will be taken during the process of conversion, and on the basis of the final submitted evidence base, as to whether the authorisation of the indication wording will be retained or has to be modified or, if applicable, whether the temp.auth or temp.AI must be withdrawn (without conversion) in accordance with Article 21a paragraph 1, TPLO.

E. Decision tree

The key criterion for distinguishing between a temp.auth and FTP is the **degree of finalisation of the clinical data package** on receipt of the authorisation application. If the pivotal clinical trials have been completed and evaluated (incl. CSR) at the time of application submission, then an FTP is possible. However, if clinical trials are still ongoing at the time of application receipt, a temp.auth is required.



F. Interpretation in respect of the criterion of Art. 18 let. c TPLO when applying for temp.auth in connection with an AAA

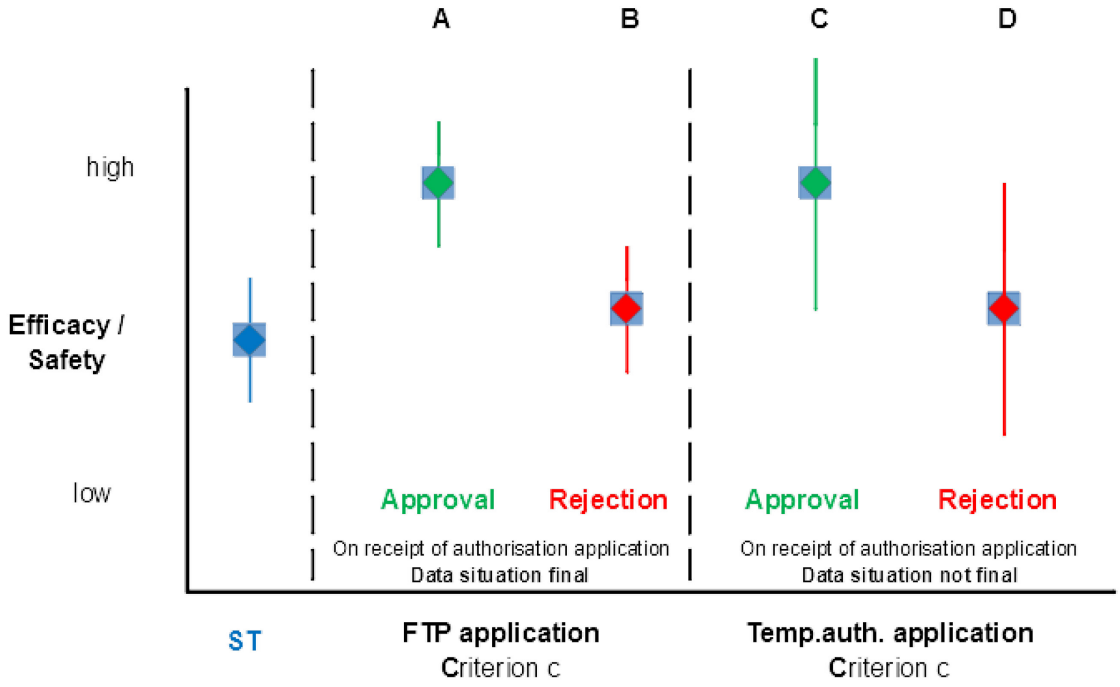
Due to the differing degree of finalisation of the clinical data package on receipt of an application for temp.auth or temp.AI compared to an FTP application (see Annex 2 D), the requirement pertaining to the **point estimate** in respect of efficacy and safety and its **dispersion** (usually the 95% confidence interval) also differs.

A. An **approval of the application for an FTP** is probable if the point estimate is appreciably higher than that for the ST and the confidence intervals **do not overlap**.
B. A **rejection of the application for an FTP** is probable if the point estimate is higher but the confidence intervals **overlap**.
C. An **approval of the temp.auth or temp.AI application** is probable if the point estimate for safety and efficacy is appreciably higher than that for the ST. However, the confidence intervals (ST – temp.auth.) may overlap in this case.
D. A **rejection of the temp.auth / temp.AI application** is probable if the point estimate is only slightly higher and the confidence intervals overlap appreciably with those for the ST.

The efficacy and safety of the latest ST always form the basis for comparison in demonstrating the high therapeutic benefit (criterion c). Although the effect size for the temp.auth / temp.AI candidate must be higher – to a clinically relevant extent – than that for the ST, the fact that the data situation is not yet final is taken into account and a larger confidence interval (possibly with overlapping with the ST) is acceptable (greater *uncertainty*).

The required difference in effect sizes (ST vs. proposed medicinal product for temp.auth / temp.AI) in terms of safety and efficacy depend on the clinical situation, the currently marketed medicinal products for the respective indication and the prevalence and incidence of the illness.

Statistically verified effects are basically expected at the time of the final data situation (FTP), whereas a conclusive statistical assessment – particularly from studies that are still in progress – might still be outstanding at the time of the prefinal data situation (temp.auth / temp.AI).



Change history

Version	Change	sig
14.0	Section 5.2 – Criterion b (Art. 18 TPLO): Clarification of the criteria for checking the equivalence of medicinal products Section 6: Clarification regarding the times when the criteria for the temporary authorisation must be fulfilled according to Art. 9*a* TPA and Art. 18 TPLO (specifically: on receipt and completion of the application and when an extension is requested by the applicant). Process optimisations for the request for temp.auth. or temp.AI	stb, fg, ru, hv, nma, lm, tsc, fco
13.0	Section 5.2 - criterion B (Art. 18 TPLO): authorised and available medicinal products refers to authorised medicinal products (with unlimited authorisation) with complete or incomplete documentation. Section 6.5 – Harmonisation of deadlines for applications before expiry of temporary authorisation period (in all cases at least 90 calendar days before expiry of temporary authorisation period) Changes to terminology (incl. *authorisation without special conditions* instead of *ordinary authorisation*).	ru, nma, hv, lm, fg, stb, tsc, fco
12.0	Section 5.7: Clarification of the AAA procedure; new deadline for finalising the decision protocol. Further editorial changes	fg, zsa, rc, pfc, ru
11.1	New layout, no content adjustments to the previous version.	dei
11.0	Sections 6.1.7 and 8.1: New deadline for finalising the decision minutes, exchange of documentation now via the eGov portal.	fg, rc
10.0	Extension of scope (section 4): - Temporary new authorisations including for KAS with innovation (new indication) and - Temporary additional indications if criteria per Art. 9*a* TPA in conjunction with Art. 18 TPLO are fulfilled. Additional information on, among other things, aspects relating to AAA, labelling in the Information for healthcare professionals (reference to the guidance document *Product information for human medicinal products HMV4*), document protection (reference to the guidance document *Document protection HMV4*) and application of Art. 13 TPA in conjunction with the extended scope (reference to the guidance document *Authorisation human medicinal product under Art. 13 TPA HMV4*). Term “ordinary” changed to “regular”	lm, hv, nma, ru, stb, fg
9.1	Change in wording in prelim. decision from: “rejection with partial approval” to: “approval with partial rejection” (sections 6.3 and 8.2)	stb
9.0	Sections 6.2.5.2 *Fulfilment of conditions and conversion to an ordinary authorisation* and 6.2.5.3 *Extension of the temporary authorisation or discontinuation by the authorisation holder*: various clarifications. The content of section 6.2.5.4 has been incorporated into section 6.2.5.2. Section 6.2.5.4 has therefore been deleted. Section 6.3: *“Ex officio” temporary authorisation*: clarification of time limits. Section 6.7 *Fees*: clarification of fees.	lm, hv, vy, stb
8.0	Clarification re. lead times before request and between official decision on request and submission of application for temp.auth. (sections 6.1.3 and 6.1.8). Amendment of guidance document due to simplification of process for “ex officio” temp.auth. (section 6.3 and annex 2). Clarification of terminology re. request for temp.auth. (processing and assessment thereof at AAA) and application for temp.auth. (various sections). Addition of definitions of “ordinary authorisation” and “temporary authorisation” (section 1).	stb, zsa, dts, fg
7.0	Clarification of process / procedure AAA	fg, gf, ru, zsa
6.0	Accelerated Application Meeting replaces application for temporary authorisation. Clarification in section 6.4 regarding retention of the “temporary” status when the indication extension with the complete data record is approved.	fg, gf, ru, zsa, stb

5.0	Inclusion of a decision tree and criteria for demarcating between temporary authorisation and FTP in Annexes 8.1 and 8.2	stb
4.0	Complete revision with explanations in sections 4, 6.2.1.1, 6.2.5, 6.3 (previously 6.7) and 6.5 (previously 6.8), and new sections 6.4 (Variations and extensions for temporarily authorised medicinal products) and 6.6 (Time limits). In addition, new flowchart 8.2.1. in Annex: - All documents for the fulfilment of conditions must be submitted to Swissmedic together with the submission of an application for ordinary authorisation (conversion) within a maximum of two years following the official approval decision for temporary authorisation (Section 6.2.5.2). - Variations and extensions for temporarily authorised medicinal products are possible (particularly applications for additional indications). However, all clinical trial data must be available, i.e. the data situation must be definitive (Section 6.4). Updates regarding the "ex officio" temporary authorisation (Section 6.3) and the temporary authorisation in accordance with Art. 13 TPA (Section 6.5).	fg, stb
3.0	Clarification inserted in Section 6.3 Ex officio temporary authorisation Sections 6.1.1 and 6.4: SMC position on tissue agnostic indications	fg, ru
2.0	Section 6.2.3, Time limits for assessment: Addition regarding time windows for submitting answers to the List of Questions	sjo
1.1	Section 6.4, Procedure / application for temporary authorisation: Response to prelim. decision max. 60 CD.	sjo
1.0	Implementation of HMV4	sjo