swissmedic

Guidance document
Fast-track authorisation procedure

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List of contents

1 Abbreviations

AAA	Accelerated Application HeAring
AE	Adverse event
temp.auth.	Temporary authorisation
FTP	Fast-track authorisation procedure
FeeO-Swissmedic	Ordinance on the Fees charged by the Swiss Agency for Therapeutic Products of 14 September 2018 (SR 812.214.5)
HMEC	Human Medicines Expert CommitteeLoQ List of Questions
NAS	New Active Substance
OD	Official decision
ODS	Orphan Drug Status
PD	Preliminary decision
PPN	Procedure with prior notification
SAE	Serious Adverse Event
ST	Standard Treatment
TEAE	Treatment-Emergent Adverse Event
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)

2 Introduction and Purpose

A fast-track procedure (FTP) is possible for the authorisation of a medicinal product, provided that the criteria stated in Art. 7 TPO are cumulatively fulfilled. Therefore, in contrast with the standard procedure, in all cases the FTP requires a previously approved request for the implementation of this procedure. An application for an FTP cannot be submitted until the request has been approved.

An FTP application must include the same scientific documentation as an application in a standard procedure and is reviewed according to the same criteria. However, this faster review procedure is possible thanks to the targeted advance planning of resources.

Section 5 of this guidance document describes the conditions and criteria that must be met before an application for implementation of an FTP can be approved, and specifies the detailed procedure for the meeting with the applicant (Accelerated Application HeAring, AAA) scheduled in connection with this application (see Annex 1 for the detailed procedure for the AAA). **Section 6** describes the formal and content requirements for an **application** for authorisation of a medicinal product through an FTP, as well as the review procedure itself.

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

This guidance document applies to applications regarding authorisation of human medicinal products within the Swissmedic sectors Medicinal Product Authorisation and Vigilance and Medicinal Product Licences and Surveillance.

4 Legal basis

The fast-track authorisation procedure is regulated in Art. 7 TPO.

5 Application for a fast-track authorisation procedure

5.1 Material preconditions for an FTP

The following criteria **must all be met** in accordance with Art. 7 of the TPO for a human medicinal product, or any variations thereto, to be evaluated by means of a fast-track authorisation procedure:

a. *It is promising prevention against, or treatment for, a severe, disabling or life-threatening disease.*
This criterion is fulfilled if it can be assumed that the respective prevention or treatment of the disease will reduce the risk of disability or loss of life. This must be demonstrated in clinical trials with one or more primary endpoints (see criterion c).

b. *Treatment using currently authorised medicinal products is either unavailable or unsatisfactory.*
   - Lack of treatment options:
     Applies only to diseases for which no treatment options with authorised medicinal products exist.
   - Unsatisfactory treatment options:
     The available treatment options with authorised medicinal products may be unsatisfactory in several ways, such as insufficient effect, unsatisfactory safety or no established standard treatment (ST) with authorised medicinal products with complete documentation. The proposed new treatment should significantly improve the treatment options based on new evidence (see also point c).

c. *A high therapeutic benefit is expected from using this new medicinal product.*
   A high 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 application for an FTP, it should be possible, even without an in-depth evaluation of the detailed data, to assess whether the therapeutic benefit is superior to that of the current authorised treatment/standard therapy (as a basis for comparison) to a clinically relevant extent. 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 requested indication(s) with authorised medicinal products (used as monotherapy or in combination) that are available in Switzerland at the time of submission of the application for an FTP for the proposed indication(s).

- To generate the comparative basis, in a tabular overview, 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 TEAE AEs that resulted in death) with the existing treatments with authorised medicinal products that are available in Switzerland. This applies particularly if the submitted clinical trial was not randomised and therefore did not have a control arm. A standard treatment (ST) is considered to be the treatment with the permanently authorised medicinal products that are available in Switzerland for the corresponding indication.
- In an application for an FTP, the following applies:
  The **submission date** of the application for the implementation of an FTP 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 the medicinal product proposed for the FTP still offers a higher therapeutic benefit than the current ST (when submitting the application). The assessment of the clinical relevance depends on the individual clinical presentation and the associated clinical and scientific practice.

In any case, an application for the implementation of an FTP will only receive a positive evaluation if the applicant can demonstrate, separately for each proposed indication, that the criteria a and b (Description/evaluation of the medical environment) and c (Description/evaluation of the FTP candidate compared to authorised treatments/ST) are all fulfilled.

5.2 Formal preconditions

When submitting the application for an FTP, the applicant should demonstrate that the preconditions stipulated in Art. 7 TPO are fulfilled. Section 5.3 regulates the processes for the application and the implementation of an AAA. The application should be submitted between 3 and 12 months before the authorisation application so that planning and procedural certainty can be guaranteed. The application for an FTP must be submitted to Swissmedic in writing by the applicant. The application must be substantiated scientifically and backed up by the required documentation. The following documents should be submitted:

a) Cover letter describing the indication(s) scheduled for Switzerland as precisely as possible. The wording of the scheduled indication(s) should be based on the investigated study population and substantiated by study results. If applicable, the covering letter must also refer to authorisation applications or the existence of questions or decisions from other authorities.
b) Rationale stating the extent to which the medicinal product to be notified for authorisation satisfies all the criteria for an FTP. Specific position statements on all criteria specified in Art. 7 let. A to c

TPO should be provided (see point 5.1). The rationale should be substantiated by existing data and by references (e.g. summary of the pivotal study) and should not usually exceed 15 pages.

c) If several indications are proposed for the medicinal product, the applicant must demonstrate that the criteria specified in Art. 7 let. A to c TPO are all fulfilled for each individual indication.
d) Relevant top-line results (still no complete study or interim reports according to ICH-E3) of ongoing studies, if available, should also be submitted (see also criterion c under section 5.1).
e) An overview of the data scheduled for the future authorisation application: tabular listing with a brief description of the pivotal studies, number of patients for efficacy and safety results, and stating whether interim or final study reports are involved. The table from CTD module 5.1 "Table of All Clinical Studies" can be used as a template for this listing. In this case, the pivotal studies should be presented in the ICH E3 format when the authorisation application is submitted.
f) Draft version of the Information for healthcare professionals or the Summary of Product Characteristics or the US Prescribing Information.
g) Form *Company meeting*
h) *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).

5.3 Application for an FTP

After the request for an FTP has been received, the documentation is formally checked within 5 calendar days. Swissmedic will decide within 30 days of completion of the formal checks of the application whether the criteria for an FTP under Art. 7 TPO are met.

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

a) Criteria stipulated in Art. 7 TPO are fulfilled

If, after receiving the applicant's application, Swissmedic unconditionally agrees to review its authorisation application in the context of an FTP, 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 application for an FTP. In this case, the applicant can submit the authorisation application for the FTP on the date stated in the decision minutes. If the applicant would like to submit the FTP application on an earlier date, the applicant can contact Swissmedic in order to check whether earlier submission is possible. The application for the FTP can be submitted, at the earliest, one month after the application for the implementation of an FTP is approved. At least one month before they intend to submit the authorisation application, applicants must confirm to Swissmedic the exact date on which they intend to submit the authorisation application (see section 5.7).

b) Criteria stipulated in Art. 7 TPO cannot be conclusively evaluated following the assessment of the submitted documents

If the criteria for an FTP cannot be conclusively evaluated by Swissmedic following the assessment of the submitted documents, Swissmedic will inform the applicant accordingly no later than 30 days after the completion of the formal check and advise the applicant of the date of an AAA. The applicant will be informed of the specific criteria 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 application for an FTP can be conclusively evaluated.

Applicants can present their line of reasoning to substantiate fulfilment of the criteria set out in Art. 7 TPO for the planned FTP on slides to be submitted for the AAA and concisely comment on the aspects and questions expressed by Swissmedic.

Applicants will usually be informed of the final decision on the application for an FTP during the AAA. Swissmedic can dispense with the implementation of an AAA if the additional documents submitted by the applicant for the scheduled AAA show that all of the criteria for the implementation of an FTP procedure are fulfilled. In this case, Swissmedic will issue an official decision to approve the application for the implementation of an FTP.

c) Criteria stipulated in Art. 7 TPO are not fulfilled

If the evaluation of the submitted documentation reveals that the criteria stipulated in Art. 7 TPO are not fulfilled, Swissmedic will issue the applicant with a preliminary decision to reject the application. 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 application for an FTP in the form of an official decision subject to appeal.

5.4 Procedure for the AAA (see annex 1 for detailed procedure)

During the AAA, Swissmedic discusses with the applicant whether on the basis of the submitted documents the preconditions of Art. 7 let. a to c TPO are satisfied and an FTP 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 an FTP.

Based on the provisional result of the review of the documents submitted with the application for an FTP and the supplementary reasons presented by the applicant at the AAA, Swissmedic will reach a binding decision during the AAA on whether implementation of an FTP is accepted or not. The decision taken by Swissmedic is recorded in writing in the minutes.

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 decision 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.

Following the AAA, the applicant will receive the decision in writing in the form of an official order. The final decision minutes will be enclosed as an appendix and as an integral part of the official order concerning the application for an FTP.

5.5 Combination of application for an FTP with request for PPN

A request for a PPN procedure can be submitted at the same time as the application for an FTP under the terms of Art. 7 TPO. To this end, all the required information and documentation for the

application for an FTP and the request for a PPN must be submitted concurrently and the intended timing of the submission of the FTP and PPN specified.

By combining the FTP application with a request for PPN, in the event of a negative evaluation of the application for the implementation of an FTP the application can be submitted at the earliest possible date. A request for PPN can be submitted as a separate application at any time, even after a decision to reject the FTP application. However, the latter option will lead to a delay in application submission due to the sequentially arranged processes. The information in the guidance document *Request for a procedure with prior notification* also applies.

5.6 Fee for an application for an FTP

Swissmedic invoices the applicant for its costs associated with the application for an FTP. The fees stated in FeeO-Swissmedic apply.

5.7 Submission of the authorisation application following the approval of the application for an FTP

If the implementation of an FTP is approved, the authorisation application can be submitted on the planned date stated on the decision minutes. Applicants must confirm to Swissmedic in writing the exact date (exact day) on which they intend to submit the authorisation application, but at least one month before submitting the authorisation application. At the same time, applicants must indicate whether documentation on quality and preclinical aspects (ERA and/or modules 2.4/2.6/4) and an RMP are being submitted so that Swissmedic can schedule the recruitment of all the specialist assessors needed for assessing the application. The applicant may, if required, apply for a preliminary discussion of the dossier with Swissmedic at a pre-submission meeting. The aim of this Presubmission Meeting is to ensure that the authorisation application is complete upon submission and will not lead to any formal objections (see guidance document *Meetings for applicants held with the Authorisation sector*).

6 Application in the fast-track procedure

6.1 Formal aspects and the documentation to be submitted

In the FTP, the applicant must submit the authorisation application together with all documentation required according to the application type to Swissmedic by the agreed date (see WL *Formal requirements* and VZ *Table of documents to be submitted).*

6.2 Review phases

The application is reviewed according to the processes described in the guidance document *Authorisation of human medicinal product with new active substance* or the guidance document *Variations and extensions*.

6.3 Review time limits

The time limits are those stipulated in the guidance document *Time limits for authorisation applications*. Answers to the LoQ must be submitted within the time windows published on the Swissmedic website in connection with HMEC meeting dates. To ensure that applications are processed promptly, the applicant must also notify Swissmedic in advance of the date on which the responses to the LoQ and to the preliminary decision will be submitted within 14 calendar days of receipt of the LOQ or PD.

7 Time limits

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

8 Fees

The fees specified FeeO-Swissmedic apply.

In the case of new authorisations of medicinal products with Orphan Drug Status (ODS) in the FTP, the supplement for the FTP is payable, but no flat fee is charged.

9 Annex 1

Accelerated Application HeAring (AAA) procedure

Before the AAA

- The AAA takes place 6-8 weeks following receipt of the application for a planned FTP. The AAA lasts up to 1.5 hours, including two possible time-outs. The aspects to be clarified for the conclusive evaluation of an application for an FTP 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 check.

- The applicant's line of reasoning to substantiate fulfilment of the criteria set out in Art. 7 let. a to c TPO for the planned FTP authorisation procedure must be presented on slides. If the indication wording is amended as a result of Swissmedic's questions, 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 to the applicant in Word format via the eGov portal so that the applicant can work on them.

During the AAA

- During the AAA, the person authorised by the applicant to manage the application presents the prepared presentation of the application for an FTP. 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 requested implementation of an FTP.

- The applicant 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 Hearing. 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 verbally. The decision will be recorded in the decision minutes by the applicant. If the application for an FTP is rejected, Swissmedic can recommend the applicant to submit an application for authorisation via an alternative procedure (e.g. temporary authorisation (temp.auth)).

- 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.

- If suggested by Swissmedic, the applicant may decide to switch to a temp.auth. procedure during the AAA. If the applicant does not wish to take the decision to switch to a temp.auth. during the AAA, an application for a temp.auth. procedure may be submitted at a later date. Equally, if the FTP application is rejected at the AAA, the applicant may switch to a PPN provided that this is indicated in the decision minutes when requesting the FTP. The applicant also has the option, after the AAA, of submitting a request for a PPN as a separate application (see section 5.5).

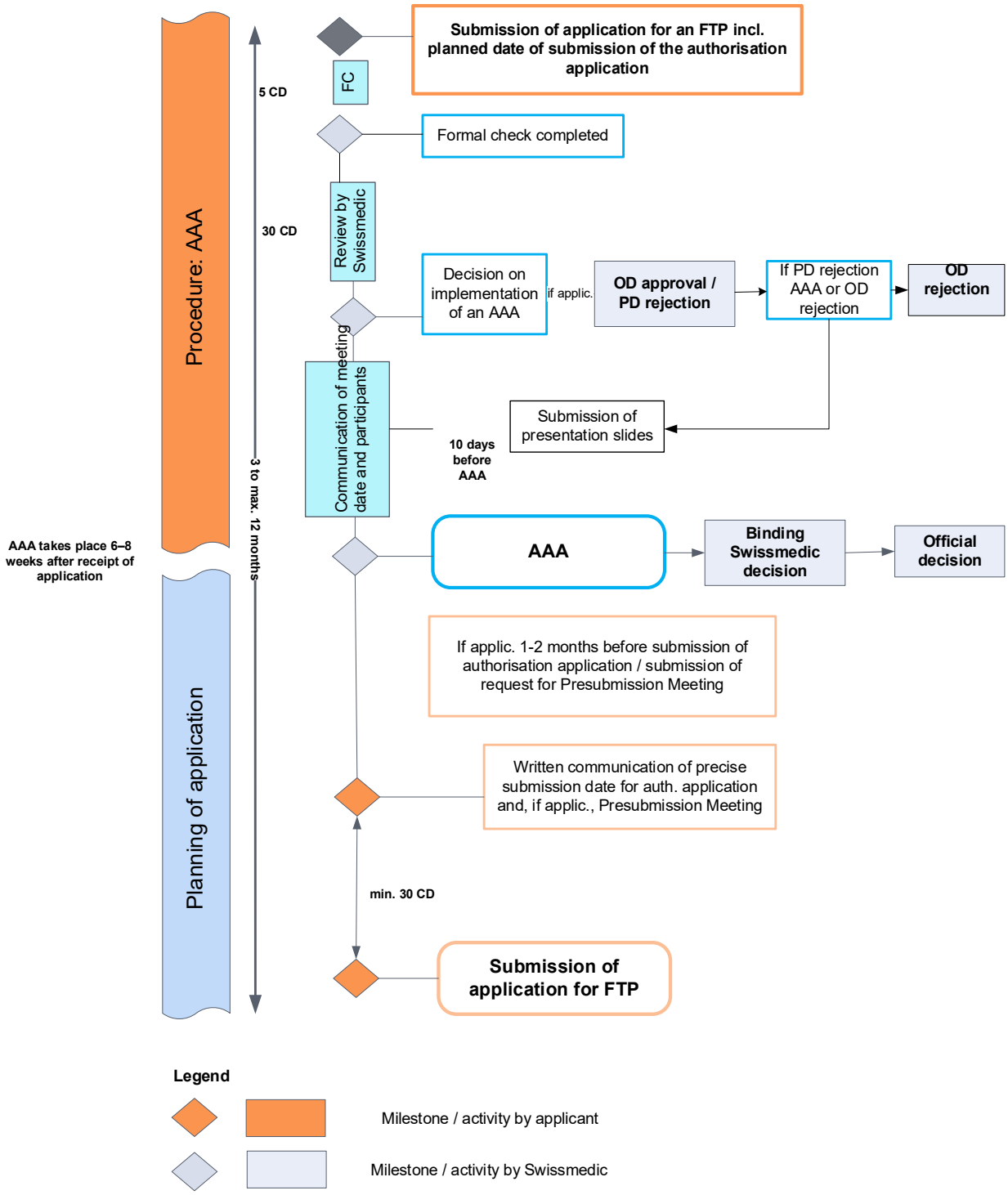
After the AAA

- 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.

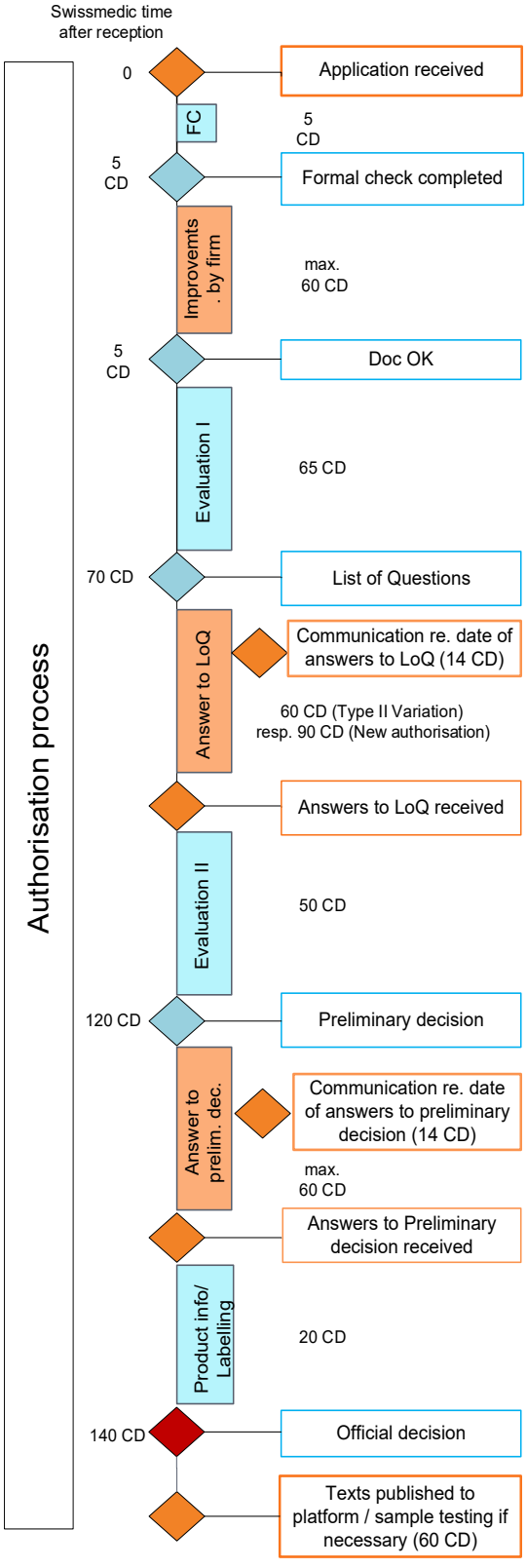
- After the AAA, Swissmedic informs the applicant of the decision taken at the AAA in the form of a written official order. The final decision minutes are enclosed as an appendix and as an integral part of the official order concerning the application for an FTP.

10 Annex 2

A. Procedure for an FTP application / FTP request



After receipt of application



B. Annex on tissue-independent or tissue-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

Although an FTP involving a tumour-agnostic indication is not excluded in principle, it is subject to a thorough case-by-case review for compliance with criteria of Art. 7 let. a to c TPO (see Guidance below).

Guidance on the fulfilment of the criteria of Art. 7 let. a to c TPO

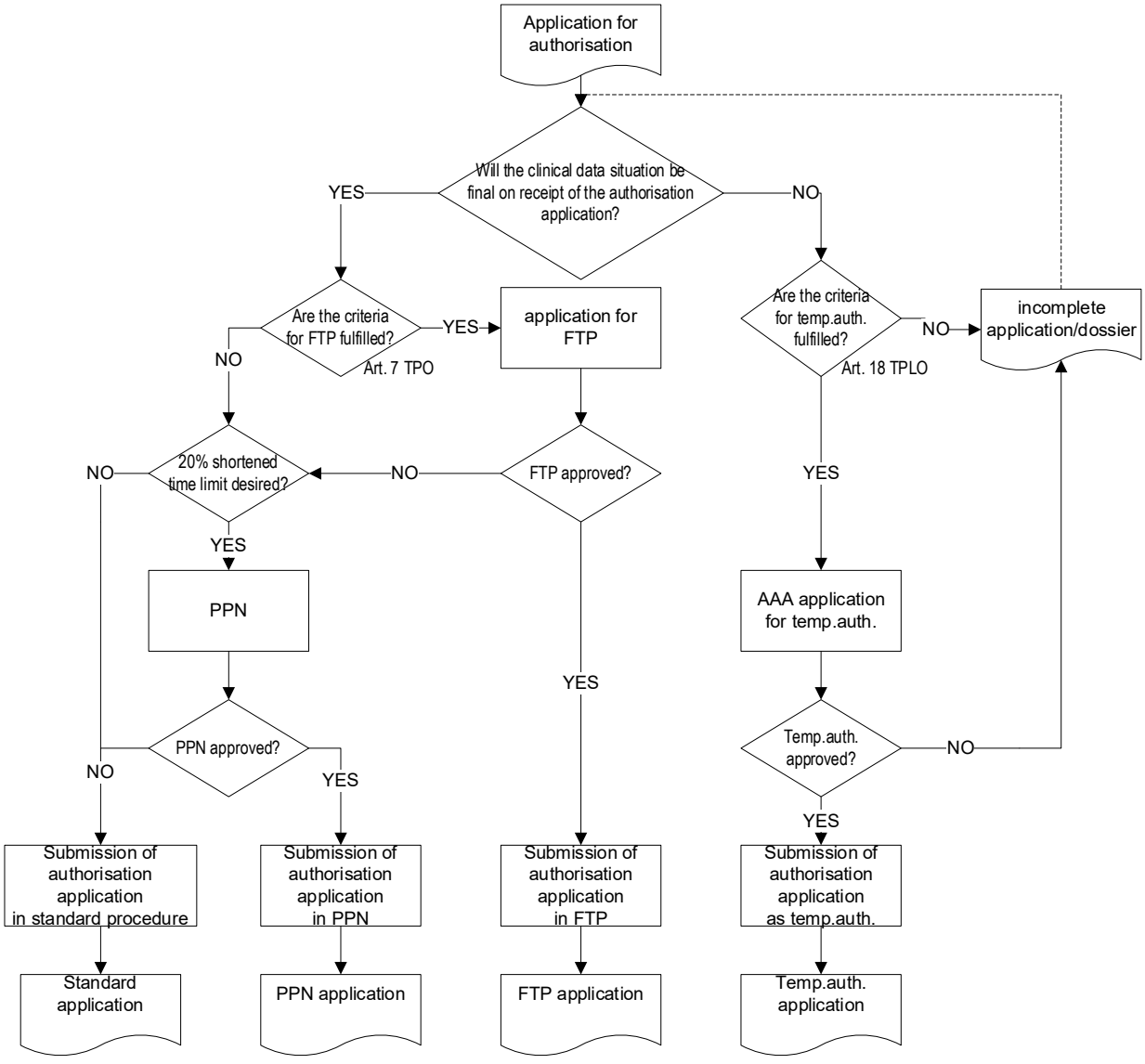
A disease or a subgroup of a disease may be deemed “recognised” or “established” in the context of a “tissue-agnostic” indication if it can be unequivocally distinguished from other subgroups by virtue of its prognosis, treatment and course, and by the fact that the medicinal product demonstrates general efficacy. It is incumbent on the applicant to present appropriate evidence. The relevant specialist guidelines should be consulted for this purpose.

The validity of a tissue-independent or tumour-agnostic indication wording in terms of compliance with criteria a to c is reviewed on a case-by-case basis using the evidence base submitted. Evidence demonstrating unequivocal efficacy in the form of a clinical response resulting predominantly from the medicinal product’s mechanism of action on the molecular aberration, regardless of tumour type, must have been obtained from an adequate number of patients with tumours in peripheral and central nervous system locations and from different tissues of origin (sarcomas, carcinomas, or haematologic tumours if appropriate).

Since the aim of the FTP – in contrast to temporary authorisation (temp.auth., see WL *Temporary authorisation for human medicinal products*, Annex 2.D) – is the granting of an authorisation without special conditions, the data submitted to demonstrate efficacy will be reviewed in detail to ensure that they are complete, i.e. that they represent an adequate number of patients with tumours in the appropriate location and in different tissues of origin.

C. Decision tree

The key criterion for demarcating between FTP and temp.auth. 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.



D. Interpretation in respect of the criterion of Art. 7 let. c TPO when applying for fast-track authorisation in connection with an AAA

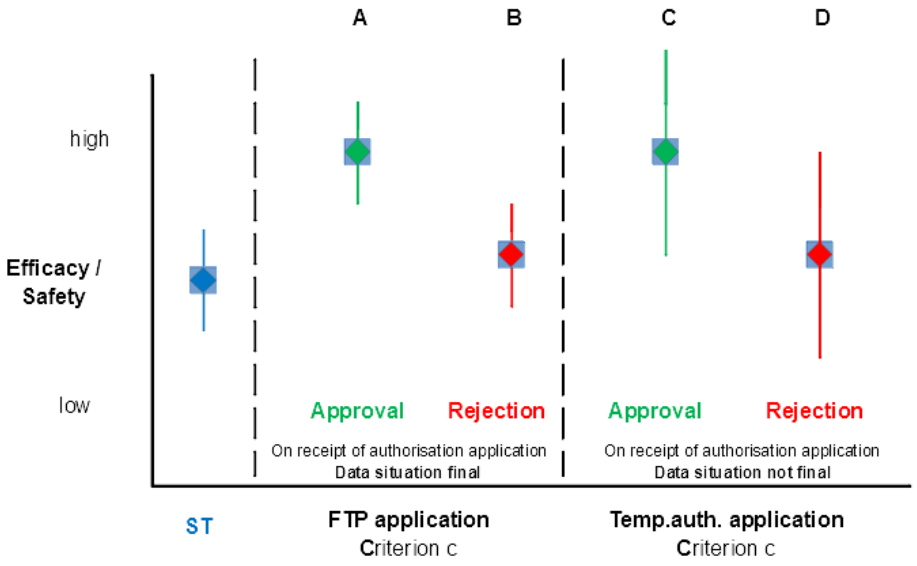
Due to the differing degree of finalisation of the clinical data package on receipt of an FTP application compared to a temp.auth application (see Annex 2 F), the requirement pertaining to the **point estimate** in respect of efficacy and safety and its **variation** (usually the 95% confidence interval)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

A. An **approval of the application for an FTP** is likely 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 likely if the point estimate is higher but the confidence intervals **overlap**.
C. An **approval of the application for a temp.auth.** is likely 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 application for a temp.auth.** is likely 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). The effect size for the FTP candidate must be higher, to a clinically relevant extent, than that for the ST for an application in connection with an AAA to be approved. The confidence intervals (ST – FTP) must not overlap.

The required difference in effect sizes (ST vs. proposed medicinal product in the FTP) 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. For an FTP application in connection with an AAA and the final study situation on receipt of the application, the high therapeutic benefit must be clearly assessable at the time of high-level data submission.

Basically, statistically verified effects are 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.).



Change history

Version	Change	sig
11.0	Clarification in section 5.3 - AAA procedure Other editorial changes	fg, pfc, ru, zsa, rc
10.0	Optimisation of the FTP application procedure	fg, pfc, rc, ru, zsa,
9.1	New layout, no content adjustments to the previous version.	dei
9.0	Section 5.4: Clarification of AAA procedure; new deadline for finalising the decision minutes. Other editorial changes.	fg/zsa/rc/pfc/ru
8.0	Sections 5.4 and 9.1: New deadline for finalising the decision minutes, exchange of documentation now via the eGov portal. Editorial changes.	fg/rc
7.0	Clarification of process/procedure AAA	fg/gf/ru/zsa
6.0	Accelerated Application Hearing replaces FTP application	fg/gf/ru/zsa
5.0	Inclusion of a decision tree and criteria for distinguishing between FTP and temporary authorisation in Annexes 9.3 and 9.4	stb
4.0	SMC position on tissue-agnostic indications	ru
3.0	Section 5.7: For FTP applications for medicinal products with ODS, no flat fee will be charged in light of the status; however, the FTP supplement will be invoiced.	fg
2.0	Section 4.2: Explanation regarding formal requirements Section 5.3: Addition regarding time windows for submitting answers to the List of Questions Sections 5.5/5.6: Explanation regarding sample testing	fr/rc
1.2	Modification of the Time limits for the authorisation applications submitted subsequently (Flowchart)	fg/rc
1.1	Explanation re planning the submission after approval of the application Explanation re fast-track authorisation criteria	fba/fg/rc
1.0	Implementation of HMV4	fg