Guideline

Temporary Authorisation to Usean Unauthorised Medicinal Product

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1 Introduction

Based on art. 9b para 1 of the Therapeutic Products Act (TPA; SR 812.21) and art. 52 of the Medicinal Products Licensing Ordinance (MPLO; SR 812.212.1), a temporary authorisation for use of an unauthorised medicinal product under restricted conditions can be granted to the sponsor of a clinical trial approved in Switzerland, to use the Medicinal Product (MP) without marketing authorisation tested in the clinical trial in patients outside of this trial.

With this temporary authorisation for use of an unauthorised medicinal product, hereinafter referred to as temporary authorization, the sponsor has the possibility to make the Medicinal Product (MP) available to patients who could not be included in this clinical trial but would benefit from the therapy.

A prerequisite is that the Medicinal Product (MP) is identical to the Investigational Medicinal Product (IMP) used in the clinical trial approved by Swissmedic and the competent Ethics Committee (EC).

The present guideline clarifies the requirements for submission of new applications for **temporary authorisations for use of an unauthorised medicinal product**, as well as the requirements for submission of changes and reporting during the conduct of a temporary authorisation.

Before submitting the dossier for authorisation to Swissmedic, the sponsor must obtain a positive decision from the Ethics Committee which approved the reference clinical trial (the lead-Ethics Committee in case of multi-centre trials).

You will find more information regarding the documents that need to be submitted to the Ethics Committee on the Swissethics website.

2 Timelines and application fees

The MPLO does not foresee special timelines. However, Swissmedic shall evaluate each case as soon as possible depending on the specificities of each project.

For administrative actions in the context of its supervisory duties, Swissmedic levies charges that are calculated either on the basis of the flat fees set out in Annexes 1 and 2 of the Ordinance on the fees charged by the Swiss Agency for Therapeutic Products (Fee Ordinance-Swissmedic; SR 812.214.5) or according to the actual work incurred (Art. 4 para. 1 FeeO-Swissmedic). Any additional work incurred shall be invoiced in addition as per Art. 5 FeeO-Swissmedic. The fees are payable by the entity that requested the administrative action (Art. 3 para. 1 FeeO-Swissmedic).

For temporary authorisations fees are levied according to the actual work incurred (Art. 4 para. 1 FeeO-Swissmedic).

3 New application for a temporary authorisation project

The dossier for a temporary authorisation project must cover the information as listed in Annex 6 of the MPLO (SR 812.212.1). Swissmedic may request further information if needed.
For the submission requirements and corresponding instructions, please refer to the Guidelines:

Guidance on the new submission process and Quick instruction for use of new submission form.

Incomplete submission dossiers will not be processed. We therefore ask you to ensure that all necessary documentation is provided, in order to avoid queries and delays.

The Sponsor should complete the application form and submit to Swissmedic the following documents:

- **Ethics Committee Decision:** Decision on the temporary authorisation application from the competent Ethics Committee which approved the referenced clinical trial(s) or the lead Ethics Committee – in case of multicentre clinical trial(s).
- **Decision of Other Countries:** Any available decision on the same project of "Compassionate Use" (approval, approval with condition including reasons, refusal including reasons) **from a European Competent Authority or a Competent Authority from a country whose GMP-control system is considered equivalent to the Swiss one** [1] (art. 13 TPA) for this medicinal product.
- **Description of the project:** It should cover all aspects listed under Art. 52 Letters b-g MPLO (as submitted to the competent Ethics Committee).
- **Information notice for participating patients**: It should emphasise the special status of the medicinal product and its use under a temporary authorisation for the use of unlicensed medicinal products (as submitted to the competent Ethics Committee).
- **Agreement between sponsor and treating physician on their respective responsibilities** (as submitted to the competent Ethics Committee).
- **Reference Investigator's Brochure (IB):** Current version of the reference Investigator's Brochure. The version/date of the Investigator's Brochure (IB) last approved for the reference clinical trial(s) must be indicated. If Swissmedic approved an earlier version of the IB for the referenced clinical trial(s), any changes made since the last approved IB version must be summarised in a summary of changes or shown as track-changes. The clean version of the IB must always be submitted.
- **Sponsor's confirmation Identical IMP:**

[1] For information about which countries are considered GMP equivalent, please refer to "List of countries with recognised GMP control systems" on the Swissmedic homepage www.swissmedic.ch/licensing > Clinical trials on medicinal products > Clinical Trial Application > Guidelines for CTA dossiers submitted.

Confirmation of the sponsor that the MP used is identical to the IMP that was approved by Swissmedic and the competent Ethics Committee or lead Ethics Committee for the reference clinical trial(s).
The version/date of the Pharmaceutical Quality Dossier (PQD) -or Investigational Medicinal Product Dossier / (IMPD) last approved for the reference clinical trial(s) must be indicated.

- **Reference Pharmaceutical quality documentation (PQD):**
  If Swissmedic approved an earlier version of the PQD / IMPD for the reference clinical trial(s), the new version must be submitted in the following format: the changes to the PQD / IMPD must be documented in a tabular summary of changes and the updated PQD / IMPD version must be submitted in track change mode.
  The clean version of the PQD / IMPD must only be submitted if there are no changes to the previously approved version.

  IMPORTANT: Please note that the primary condition for a temporary authorisation is that the MP is identical to the IMP already authorised by Swissmedic in the reference clinical trial.
  Therefore, changes between the PQD/IMPD of the reference clinical trial and the PQD/IMPD for the temporary authorisation are restricted to minor updates.

  Examples of permitted changes (non-exhaustive list):

  Purely administrative changes: inclusion of the International Non-proprietary Name (INN) of the Drug Substance (DS) once granted by World Health Organization (WHO), change of name of a manufacturer (when physical location remains the same).

  Changes to Drug Substance (DS):

  Tightening of acceptable ranges of in process parameters of the manufacturing process, tightened limits in the specification, (re)-validation of already approved analytical methods, addition of a new testing site provided that the specifications (limit and analytical method) for the test are the currently approved ones and no changes are introduced, submission of updated stability data, extension of the re-test period (Chemical DS) / shelf-life (Bio DS), as foreseen in the already approved stability protocol.

  Changes to Drug Product (DP):

  Tightening of acceptable ranges of in process parameters of the manufacturing process, minor differences in drug product (printing), tightened limits in the specification, (re)-validation of already approved analytical methods, addition of a new testing site provided that the specifications (limit and analytical method) for the test are the currently approved ones and no changes are introduced, secondary packaging, submission of updated stability data, extension of the shelf-life, as foreseen in the already approved stability protocol.

  Examples of non-permitted changes (non-exhaustive list):

  Non-permitted changes are those that cannot be considered to render an IDENTICAL MP compared to the already approved IMP for the reference clinical trial:

  New manufacturers of starting materials for the DS, new manufacturing sites for DS (including manufacturers of intermediates), new manufacturing sites for DP (including manufacturers of intermediates), changes in the manufacturing process of the DS and DP, widening of specifications limits for the control of DS, DP or intermediates.

- **Other relevant documents**: as applicable

4 Submission of changes to an approved temporary authorisation project

The Sponsor must notify all **significant (major) changes** to the MP or its application to Swissmedic, following the definition/provisions of Art. 34 para. 3 ClinO (SR 810.305)[2].

The Sponsor should provide a rationale for the proposed change(s).

Please note that changes to a temporary authorisation are only permitted if the MP used in the project remains identical to the IMP used in the reference clinical trial, and if the essence of the project remains the same.

Changes modifying the project or the IMP in such a way that we are faced with a different project must be submitted as new projects necessitating a new temporary authorization.

The Sponsor should complete the application form and submit to Swissmedic the relevant documents.

For the submission requirements and corresponding instructions, please refer to the Guideline: **Guidance on the new submission process and Quick instruction for use of new submission form.**

Incomplete submission dossiers will not be processed. We therefore ask you to ensure that all necessary documentation is provided, in order to avoid queries and delays.

If significant changes related to safety or quality documentation are submitted for the reference clinical trial, the sponsor must also submit these changes for the temporary authorisation project. When submitting these changes for the temporary authorisation project, a cross-reference to the approved changes in the reference clinical trial should be indicated.

Please note that only major changes need to be submitted to Swissmedic in accordance with Art. 54, paragraph 1 of the Medicinal Products Licensing Ordinance (MPLO; SR 812.212.1). Changes that do not qualify as major changes according to the legal provisions indicated above, should not be submitted to Swissmedic.

Significant changes that must be submitted to Swissmedic for notification are:

Changes to Description of the project:

All significant changes related to the use and/or safety of the medicinal product or any other significant modification according to Art. 34 para. 3 ClinO must be submitted to Swissmedic prior to implementation.

Modifications to the description of the project must be documented in a summary of changes and the updated document version submitted in a **track change** mode.

Changes to Investigator's Brochure and risk-benefit evaluation:

Significant changes to the IB must be submitted until the end of the temporary authorisation. The changes to the IB must be documented in a summary of changes and the updated version shall be submitted in **track change** mode.

[2] Clinical Trial Ordinance, SR 810.305, 20. September 2013

Moreover, it must be indicated if, and to what extent, the changes impact the **risk-benefit evaluation** of the medicinal product and the temporary authorisation. Should any measures have been taken on the basis of the new analysis, these should also be described.

Changes to Pharmaceutical Quality Documentation (PQD) of the medicinal product:

All significant changes to the PQD or IMPD related to the temporary authorisation must be submitted to Swissmedic.

Please see the guideline “Amendments Clinical Trials” section 5 for more information on what changes are considered significant (or substantial).

The primary condition for a temporary authorisation is that the MP is identical to the IMP already authorised by Swissmedic in a clinical trial.

Therefore, changes between the PQD/IMPD of the reference clinical trial and the PQD/IMPD for the temporary authorisation are restricted to minor updates.

In this respect, the same approach is followed as for the initial authorisation of a temporary authorisation project.

See non-exhaustive list of examples of permitted and non-permitted changes under that section.

The changes to the PQD / IMPD must be documented in a tabular summary of changes and the updated PQD / IMPD version shall be submitted in **track change** mode.

5 Reporting during the conduct of a temporary authorisation project

The sponsor must comply with the reporting obligations described in Art. 54 para. 2 and 3 MPLO and Art. 55 para. 3 MPLO regarding the safety of the participants and the end of the temporary authorization.

The Sponsor should complete the application form and submit to Swissmedic the relevant documents.

For the submission requirements and corresponding instructions, please refer to the Guideline:

Guidance on the new submission process and Quick instruction for use of new submission form.

Incomplete submission dossiers will not be processed. We therefore ask you to ensure that all necessary documentation is provided, in order to avoid queries and delays.

Reporting obligations

1st The Sponsor must notify **all adverse events or reactions** and other incidents to Swissmedic, following Art. 59 TPA[3] (Art. 54 para. 2 MPLO). For further information please visit the following site: www.swissmedic.ch > Human medicines > Market Surveillance.

2nd The sponsor must submit an annual safety report (ASR) to Swissmedic (Division Clinical Trials). The annual safety report is a summary of the current status of knowledge and describes the identified and potential risks of medicinal products.

[3] Therapeutic Products Act, SR 812.21, 15. December 2000

The report must comply with the requirements of ICH E2F, the following formats are accepted: DSUR, PSUR, PBRER, ASR. The report must be submitted once a year throughout the duration of the temporary authorisation.

The following details must be included in the ASR: Report No. (consecutive numbering), product name, Swissmedic reference number(s) of the temporary authorisation, time period covered by the report, date of the report, name and address of the sponsor.

3rd The sponsor must notify Swissmedic of the effective availability of the MP on the Swiss market after the marketing authorisation has been granted, in order to initiate the **revoke of the Temporary Authorization by Swissmedic.**

Swissmedic may revoke the temporary authorisation at any time due to safety reasons or if the marketing authorisation was rejected by the Agency.

6 Relevant documents

Guidelines: Guidance on the new submission process and Quick instruction for use of new submission form.

Change history

Version	Change	sig
4.3	New layout, minor editorial changes, no content adjustments to the previous version	tsj/lkr
4.2	Correction of typographical errors	lam
4.1	Renewed in 2022. No modifications	lam
4.0	New submission instructions	lam
3.0	Introduction of a non-exhaustive list of examples of permitted and non-permitted changes in the IMPD	lam
2.1	Correction of the reference to the application form and to the form for submission of changes and reporting	jaf
2.0	Added paragraph on Ethics Committee procedure to introduction Added the fees to section “timelines” Added information on submission of Quality amendments to the reference clinical trial	lel
1.0	New Document	lel / hch