swissmedic

Information sheet

Questions and answers on clinical trials with medicinal products

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1 GENERAL QUESTIONS

1.1 Relevant laws and guidelines for clinical trials with medicinal products in Switzerland

- Therapeutic Product Act (TPA / HMG / LPTh) (SR 812.21)
- Human Research Act (HRA / HFG / LRH) (SR 810.30)
- Clinical Trials Ordinance (ClinO / KlinV / OClin) (SR 810.305)
- Therapeutic Products Fees Ordinance (HGebV / OEPT) (SR 812.214.5)
- Data Protection Act (DPA / DSG / LPD) (SR 235.1)
- Medicinal Products Licencing Ordinance (MPLO / AMBV / OAMéd) (SR 812.212.1)
- ICH Good Clinical Practice Guideline (ICH E6(R2); 2016)
- Declaration of Helsinki
- Any other relevant national law or international guideline

1.2 What are the responsibilities and competencies of Swissmedic's Clinical Trials Division?

The Clinical Trials Division evaluates all aspects related to safety and quality of Investigational Medicinal Products (IMPs) as well as the risk-analysis and risk management plan (Art. 32 ClinO) of clinical trials on **medicinal products** of **category B and C**, as defined in the HRA and the related ClinO. Within this frame, the Clinical Trials Division approves new clinical trials on medicinal products and modifications in ongoing clinical trials.

The Clinical Trials Division is also responsible for conducting the following types of inspections:
- Good Clinical Practice (GCP) inspections in clinical research (i.e. clinical trials on medicinal products of category A, B and C)
- Inspections of pharmacovigilance systems (Good Vigilance Practice, GVP).

Clinical trials on medical devices and clinical trials on transplant products, gene therapy and GMO are handled by other Swissmedic divisions (see Swissmedic website).

Combined studies, wich include both, clinical trials with a medicinal product and interventional performance studies with in vitro diagnostics or clinical investigations with medical devices are jointly evaluated by the Clinical Trials Division and the Division Medical Devices Clinical Investigation. For more information on combined studies, please see swissmedic.ch > Medical devices > Clinical trials > Combined studies.

1.3 What is a clinical trial?

Definition of a “clinical trial” given in Art. 3 HRA:

l. *Clinical trial* means a research project, in which individuals (patients or healty volunteers) are prospectively assigned to a health-related intervention in order to investigate its effects on health or on the structure and function of the human body.

The term “health-related intervention” is defined in Art. 2 ClinO:

a. *health-related intervention* means a preventive, diagnostic, therapeutic, palliative or rehabilitative measure investigated in a clinical trial.

Research projects involving medicinal products and not complying with the above definition of a clinical trial do not need the approval of Swissmedic.

1.4 What is a medicinal product?

Medicinal products are products of chemical or biological origin, which are intended to have, or are presented as having, a medicinal effect on the human or animal organism, in particular in the diagnosis, prevention or treatment of diseases, injuries and handicaps; blood and blood products shall also be considered as medicinal products (Art. 4 letter a, TPA).

1.5 What is an Investigational Medicinal Product (IMP)?

Definition of an IMP:

“A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use” (ICH E6, Chapter 1.33).

“*A medicinal product which is being tested or used as a reference, including as a placebo, in a clinical trial”* [Regulation (EU) No 536/2014 Article 2 (5)].

It follows that medicinal products with a marketing authorisation are also considered IMPs when they are to be used as the test product, reference product or comparator in a clinical trial.

In order to classify a "medicinal product" as an "investigational medicinal product" a sponsor must consider both its intended use and the objectives of the clinical trial.

1.6 What is an Auxiliary Medicinal Product (AxMP)?

[Auxiliary Medicinal Products (AxMPs) were previously called “Non Investigational Medicinal Products (NIMPs)]”.

Definition of an AxMP:

“AxMPs are medicinal products used for the needs of a clinical trial as described in the protocol, but not as an investigational medicinal product” [Regulation (EU) No 536/2014 Article 2 (8)]. AxMPs are medicinal products that do not fall within the definition of an IMP given above.

They could be used as rescue medication, challenge agents, to assess end-points in the clinical trial, or background treatment. Further, the medicinal product should be related to and relevant for the design of the clinical trial, which excludes ‘concomitant medications’.

Further detailed information on AxMPs can be found in the following document:

Auxiliary Medicinal Products in Clinical Trials: Recommendations on the use of Auxiliary Medicinal Products in Clinical Trials written and endorsed by the Clinical Trials Coordination and Advisory Group (CTAG), March 2024

Of note, this document should also be read in combination with the Clinical Trials Regulation (EU) No 536/2014 and Eudralex 10 - 1 March 2024.

These documents supersede: “The rules governing medicinal products in the European Union, Volume 10 – Chapter III – *Auxiliary Medicinal Products in Clinical Trials* – Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use - 28 June 2017.”

See also information on this topic in Chapter 4 below.

1.7 Which rules apply to the use of Auxiliary Medicinal Product (AxMP)?

AxMPs without a marketing authorisation (MA) in Switzerland may be used, if no alternative to the foreseen AxMP is available in Switzerland or if a justification for the use of an AxMP non-authorised in Switzerland is provided.

If AxMPs without an MA in Switzerland are foreseen to be used in a clinical trial, preference should be given to AxMPs with an MA in a country whose GMP control systems is recognised as equivalent to the Swiss system*. For AxMPs without such an MA, a quality dossier must be submitted (for more information please refer to our Guideline Clinical Trial Application Dossier).

*For information about which countries are considered GMP equivalent, please refer to “List of countries with recognised GMP control systems” on the Swissmedic homepage swissmedic.ch > Clinical trials on medicinal products > Clinical Trial Application > Guidelines for CTA dossiers submitted”.

2 APPLICATIONS

2.1 What is the format and the content of a clinical trial application (CTA) or of the submission of modifications in regards to an approved clinical trial to Swissmedic?

Detailed information on clinical trial applications, reporting and submission of modifications in ongoing clinical trials can be found on Swissmedic website **swissmedic.ch > Clinical trials on medicinal products.**

These requirements are based on ClinO Annex 4 in relation to Art. 31, 34–36, 54, 55.

2.2 Within which timeframe can Swissmedic's answer to a CTA or to the submission of modifications and reports be expected?

Detailed information on timeframes for CTA review can be found in the "Guideline Clinical Trial Application Dossier" available on Swissmedic website **swissmedic.ch > Clinical trials on medicinal products.**

The same timeframes apply to the submission of modifications to ongoing clinical trials and reports.

The deadlines are based on ClinO art. 33, 34, 36.

2.3 Does the trial protocol or protocol amendment need to be signed, and if so by whom?

Yes, those documents need to be signed for the submission to Swissmedic. However, only the Sponsor's signature is necessary on the trial protocol and the amendment(s). The protocol could also be signed electronically. In general, please ensure, that on the signature page the reference to the study and version of the protocol is visible.

It goes without saying that the trial protocol must be signed by the Sponsor and the Investigator prior to start of the clinical trial. With their signatures, both parties confirm their agreement to the protocol or protocol amendment(s) (ICH E6 8.2.2).

See also further information on sign-off of trial documentation in Section 5 of this FAQ document.

2.4 Who is allowed to sign the submission forms (i.e. CTA form and the forms for submission of changes and for reporting)?

The applicant as well as any other authorised person (Sponsor, Sponsor`s representative, CRO, e.t.c) is allowed to sign the submission form. In case of KLV portal submissions, no signature page is required.

Swissmedic does not need to receive the delegation log for signatures.

2.5 Do I have to submit the documentation of new trial sites to Swissmedic for approval?

Information on additional trial sites does not have to be submitted to Swissmedic. The Research Ethics Committee (REC) will approve the new site(s) in line with Art. 27 ClinO.

2.6 Which document should contain the Reference Safety Information (RSI)?

The reference safety information could be part of the Investigator's Brochure, of the Professional information / SmPC or of the clinical trial protocol as well as another document containing the RSI.

In addtion, the Reference safety information must comply with the "Q&A document – Reference Safety Information" dated November 2017 and also comply with the covernote dated March 2018 of the Clinical Trial Facilitation Group CTFG (published on the Heads of Medicines Agency HMA – CTFG website (http://www.hma.eu)/

2.7 What does it mean to receive a "Preliminary decision letter of approval with conditions"?

If you receive a "Preliminary decision ["Vorbescheid" (D) / "Préavis" (F) / "Decisione preliminare" (I)] letter of approval with condition(s)" as an answer to your application, it means that the clinical trial will be approved with condition(s).

In such a case, the deadline given in the "Vorbescheid" letter is not meant as the deadline to fulfil the condition(s), but it is the deadline given to the sponsor to comment if they do not agree with the condition(s). After the deadline, if the sponsor has not raised sufficient arguments against the condition(s), Swissmedic will issue the letter of approval with condition(s).

After this approval, the sponsor has time to fulfil the condition(s). If Swissmedic imposes conditions to be fulfilled prior to the First Patient First Visit, the clinical trial cannot start until Swissmedic has confirmed that the conditions have been / are fulfilled.

2.8 What does it mean to receive a “Preliminary decision letter of refusal”?

If you receive a “Preliminary decision” ["Vorbescheid" (D) / “Préavis” (F) / “Decisione preliminare” (I)] letter of refusal” as an answer to your application, it means that the clinical trial will be rejected, if you do not answer the points listed in the letter within the given timeline.

If the answer from the Sponsor is not sufficient, the clinical trial will be rejected. If the answer from the Sponsor is sufficient, the clinical trial will be approved or approved with conditions.

Please note, that this is different from the Preliminary decision letter of approval with conditions (see above), where the conditions do not have to be fulfilled before the final approval is issued.

2.9 What needs to be submitted additionally for a complex clinical trial at submission and for any modification?

Please submit a study overview chart, where the respective arms and their status (recruiting, interrupted or closed) are indicated, in addition to the documents listed in the Guidelines for the Clinical Trial Application Dossier for conventional clinical trials. Please remember to include the updated study overview chart (track change and clean versions) within the specific modification to the study documentation, in case of changes to the status of the arms.

3 SPECIAL CATEGORIES OF CLINICAL TRIALS

3.1 How are the trial categories defined in Art. 19 ClinO to be understood?

Cat. A: Trials with drug products authorised in Switzerland, used according to the Swiss SmPC in the respective indication, dose, population, etc.

Be aware that trials with investigational medicinal products **authorised in a country with comparable control of human medicinal products** (according to Art 13 TPA) could never been catergorized as A.

Cat. B:

1) Trials with investigational medicinal products **authorised in Switzerland**,

- but not used according to the Swiss SmPC in the respective indication, dose, population e.t.c.

  and/or

- have undergone only a low-risk modification as described in Annex 2bis ClinO

2) Trials with investigational medicinal products **authorised in a country with comparable control of human medicinal products** (according to Art 13 TPA)

  and/or

- have undergone not more than a low-risk modification as described in Annex 2bis ClinO

3) Trials with an investigational medicinal product that is a **placebo specifically manufactured** for the clinical trial. This is also the case if the placebo is being compared to IMPs that are authorized in Switzerland and used according to the Swiss SmPC.

Cat. C:

1) Trials with drug products **not authorised in any country** worldwide. In most cases, these are the trials investigating new compounds.

2) Trials with products **authorised in Switzerland or in a country with comparable control of human medicinal products** (according to Art 13 TPA), which have undergone **more than** a low-risk modification as described in Annex 2bis ClinO.

The classification of a clinical trial is the responsibility of the Sponsor. The Research Ethics Committee (REC) is responsible for checking the correctness of the category.

Request for changing the category of a previously approved trial must be submitted to the institutions (REC and Swissmedic) which already gave the approval for the trial as a substantial amendment.

Trials approved by the REC and/or Swissmedic before 01.01.2014 are categorised in category C.

3.2 What are the special requirements for clinical trials with therapeutic products capable of emitting ionising radiation?

Special requirements apply to clinical trials investigating therapeutic products emitting ionising radiation, with regard to radiological protection of trial subjects.

Cat A: The Sponsor must submit one copy of all required documents to the REC, in line with ClinO Annex 3 number 5.

Cat B: The Sponsor must submit one copy of all required documents to Swissmedic (Clinical Trials Division), in line with ClinO Art. 36 and Annex 4 number 5.

Cat C: The Sponsor must submit one copy of all required documents to Swissmedic (Clinical Trials Division), in line with ClinO Art. 36 and Annex 4 number 5, as well as a copy to the Radiological Protection Division of the Federal Office of Public Health (FOPH). Changes during the course of a clinical trial need to be submitted to Swissmedic only.

For the above-mentioned clinical trial applications, the following forms needs to be submitted in addition to the above-mentioned documents:

- For category C studies: Form for clinical trials of radiopharmaceuticals or radiolabelled compounds (form on FOPH website: www.bag.admin.ch)
- For category B studies: Form for clinical trials category B with medicinal products capable of emitting ionising radiation (form on Swissmedic website: swissmedic.ch > Clinical trials > Clinical trials with medicinal products).

The processing time for trial applications with products capable of emitting ionising radiation is **60 calendar days** for **category C** trials and **30 calendar days** for **category B** trials, after the confirmation that the documentation is formally complete has been issued (Art. 36 para. 4 ClinO).

3.3 Is a simplified procedure possible for investigator-initiated trials (IITs)?

Commercial or non-commercial studies enroll individuals and the ethical requirements must be the same for both kind of sponsorships.

When planning and carrying out IITs, all requirements as laid down in the Therapeutic Products Act (TPA), the ClinO, the ICH GCP E6-Guideline and the WMA Declaration of Helsinki-Ethical Principes for Medical Research must therefore be respected and followed by every Sponsor based on the most actual versions.

The above-mentioned laws, regulations and guidelines do not foresee simplifications for IITs, since their main goals of protecting rights, safety, and well-being of trial subjects and credibility of trial data are imperative for all trials independent whether they are commercial or non-commercial.

However, for academic clinical trials without commercial third-party funding, a fee reduction in accordance with Art. 12 FeeO-Swissmedic may be requested.

3.4 When should trial subjects be considered as volunteers and not as patients?

A trial on voluntary subjects (a so-called volunteer trial) can include the following groups:

- Healthy volunteers (most frequent);
- Persons with pre-existing conditions that have no connection to the subject of research (e.g., women with slight anaemia, in whom the influence of two medicinal products on the rigidity of the erythrocytes is compared using several analytical methods). The pre-existing condition, in this case, is only a prerequisite for enrolment in the experimental trial, but is not central to the research (and no therapeutic effect on the condition will be assessed during the trial). The women concerned are thus considered to be volunteers and not patients.

These are the only two situations for which trialindividuals may be compensated fortheir time invested. In principle, no financial incitement is permitted for trial participants.

3.5 How is the submission procedure for clinical trials, where both Investigational Medicinal Products (IMPs) and Medical Devices (MDs) or in vitro Diagnostics are being investigated ?

Combined studies, wich include both clinical trials with a medicinal product and interventional performance studies with in vitro diagnostics or clinical investigations with medical devices are jointly evaluated by the Clinical Trials Division and the Division Medical Devices Clinical Investigation.

For more information and for guidance on the submission requriements for combined studies, please refer to swissmedic.ch > Medical devices > Clinical trials > Combined studies.

4 MP: PHARMACEUTICAL QUALITY DOCUMENTATION; GMP; LABELLING; IMPORT

4.1 What documentation is required with regard to the pharmaceutical quality documentation of IMPs?

Please refer to our Guideline Clinical Trial Application Dossier available on our website swissmedic.ch > Clinical trials on medicinal products > Clinical Trial Application.

4.2 How are the requirements of EU GMP regulated under Swiss law?

Annex 1 of the MPLO refers to the EU GMP directives and guidelines. The documents listed therein are thus legally binding in Switzerland. The various links can be found on the Swissmedic website under the “General legal basis” section.

Further applicable guidelines concerning quality of IMPs are presented in Eudralex Vol. 10 Chapter III. Link: https://ec.europa.eu/health/documents/eudralex/vol-10_en

4.3 Which medicinal products should be listed as IMPs in the trial application?

In most cases, a clear distinction should be made regarding which of the medicinal products used in the test group and comparator group should be regarded as IMPs and which should be regarded as AxMP. In certain cases, however, such a distinction can be difficult (e.g., within the framework of trials in which combinations of medicinal products are used, such as in oncology).

In order to decide whether a product is an IMP or an AxMP, please refer to the chapter “What is an Auxiliary Medicinal Product (AxMP)” and to “*Recommendations on the use of Auxiliary Medicinal Products in Clinical Trials written and endorsed by the Clinical Trials Coordination and Advisory Group (CTAG), March 2024”.*
In particular, reference is made to Appendix 1 and the examples for AxMPs such as "rescue medication", “challenge agents", "background treatment" e.t.c.

Be aware, that making a distinction between IMPs and AxMPs is relevant, since it may have an influence on labelling and costs and safety reporting.

4.4 What is drug accountability and to which medicinal products does it apply?

Drug accountability means maintaining documentation that accounts for the whereabouts of IMPs used in a clinical trial up to the level of the individual trial participant (volunteer, patient) and medication units.

This involves the following steps:

- Receipt and storage by the trial centre
- Dispensing to the patient or administration at the trial centre
- Return of unused units and empty containers
- Return to the sponsor or destruction of remaining product on site

Note: Drug accountability is a GCP aspect but is not part of the CTA review by Swissmedic. Therefore, no documentation with regards to drug accountability needs to be submitted to Swissmedic. It may, however, be assessed during a GCP-inspection.

4.5 What must be taken into consideration when importing IMPs from abroad? Is it necessary to obtain a special import licence?

For direct deliveries of the IMP to trial centres from abroad, Swissmedic grants a trial-related import licence within the framework of the authorisation to perform the trial.

This means that no further import licences need be applied for in case new centres are added to the authorised trial. This licence is restricted to the IMPs used in the clinical trial only, and its validity is restricted to the duration of the clinical trial.

It is the responsibility of the clinical investigator to ensure that the IMPs are only accessible on site to a person with the necessary knowledge (Chapter 4.6, ICH GCP).

If a third party is included in the distribution activities of the IMP (e.g. Swiss affiliate, distributor, local pharmacist or CRO), the concerned entity must possess the appropriate licence(s) provided by Swissmedic that includes the import and distribution of medicinal products.

For further information on import, please refer to our Guideline Clinical Trial Application Dossier available on our website www.swissmedic.ch/clinicaltrials > Clinical trials on medicinal products > Clinical Trial Application

4.6 Which labels should be submitted in case a study category changes from C to B as a result of the Art. 19 of the Clinical Ordinance Revision (01.11.2024)?

If the IMP is marketed in one of the countries with equivalent medicinal product control (according to Art. 13, TPA) and a recategorization from category C to category B has been requested at the latest by 31st October 2025, please submit together with this application also the full labels for the IMP(s) (Annex VI of the Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use).

5 LEGAL QUESTIONS

5.1 Is it possible to receive Swissmedic's approval for the trial or the amendment by e-mail or fax?

No. Official decisions are being sent to the applicant by post only.

5.2 Does Swissmedic accept electronic signatures or scanned signatures in documents related to clinical trials?

Swissmedic accepts electronic or scanned signatures on documents such as trial protocols, Investigator's Brochures, etc. only if the submission of such documents is accompanied by a letter (in case of a CTA), a CTA form, or a form for submission of changes or for reporting with the original ("wet-ink") signature of an authorised person.

The person signing the accompanying letter or the form thus takes the responsibility for the submitted documents.

In general, please ensure, that on the signature page the reference to the study and version of the respective document is visible.

5.3 What should be taken into account if the sponsor has registered offices abroad?

According to Art. 2 ClinO, "Sponsor" means a person or institution headquartered or represented in Switzerland. Therefore, a foreign Sponsor must designate a representative in Switzerland.

The responsibility of Swiss representative can be assumed by any individual or a legal entity domiciled in Switzerland or with registered offices in Switzerland. It is not necessary for the person to be a Swiss citizen.

If the Clinical trial Application is sent from abroad (by the Sponsor or by a CRO), further correspondence (incl. invoicing) will be held with the Swiss representative. The Swiss representative will also be the contact person for liability cases.

For further information regarding Sponsor representation in Switzerland, please refer to the Interpretation Guide *"Obligations of representatives of foreign sponsors"*, available on our website Human medicines > Clinical trials on medicinal products > Clinical Trial Application.

5.4 What is Swissmedic's position regarding the co-sponsorship of clinical trials?

Swiss law does not foresee several sponsors for a given trial. Therefore, Swissmedic accepts only one Sponsor for a clinical trial. This Sponsor assumes the overall responsibility for the clinical trial in Switzerland.

5.5 What happens if a new Sponsor takes over a clinical trial that has been authorised for another Sponsor or if the name or the address of the Sponsor changes during the course of a clinical trial?

The study needs to be amended. For more details, please refer to the “Guideline on amendments in clinical trials” available on our website swissmedic.ch > Clinical trials on medicinal products > Submission of changes.

5.6 What happens in case of change of Sponsor representative in Switzerland or if the name or address of the Sponsor representative changes?

Please ensure to have a representative in Switzerland and inform Swissmedic about any changes as soon as possible. For more details, please refer to the “Guideline on amendments in clinical trials” available on our website swissmedic.ch > Clinical trials on medicinal products > Submission of changes.

5.7 How is the function of the qualified person reflected in Swiss law?

The Swiss equivalent to a “Qualified Person” (QP) is the “Responsible Person” (RP).

The RP must be able to execute his/her responsibility, understand the Swiss GMP/GDP requirements and meet regulatory compliance.

RP Responsible Person:

German: ”Fachtechnisch verantwortliche Person”
French: “Responsable technique”
Italian: “Responsabile tecnico”

The holder or applicant of an establishment license is responsible to have a suitable RP available. The responsibilities of a RP are described in art. 5, art. 10, art. 14 and art. 15 of the MPLO.

5.8 What happens if the deadline of two years for authorisation by the second authority (Art. 23 para. 1bis or Art. 50 para. 1bis) is exceeded?

The authorisation of the first authority expires, if there are more than two years between the date of authorisation by the first authority and the date of authorisation by the second authority. Swissmedic will not inform the Sponsor of the expiry of the authorisation. It is the responsibility of the Sponsor

- to monitor this period
and

- not to undertake any study activities without a valid authorisation.

5.9 How could I extend the deadline of two years for the authorisation of the second authority?

Before the deadline expires, the extension of the deadline must be requested by the Sponsor from both authorities - Swissmedic and the Ethics Committee - as a substantial modification (Art. 23 para. 1ter and Art. 50 para. 1ter) (receipt by the authority) and approved by both authorities.

5.10 What happens, if the deadline for enrolment of the first participant (Art. 23a) is exceeded?

If there are more than two years between the date of authorisation by the second authority and the date of the first inclusion of the first participant, the trial is considered to be interrupted. Swissmedic will not inform you about the interruption.

It is the responsibility of the Sponsor to monitor this period and not to carry out any participant visits in case of the trial interruption.

5.11 What should I do, if I want to extend the deadline for enrolment of the first participant (Art. 23a)?

Before the deadline expires, the extension of the deadline must be requested from both authorities - Swissmedic and the Ethics Committee - as a substantial modification (Art. 23a para. 3) (receipt by the authority) and approved by both authorities.

5.12 When will the new law be implemented?

All authorisations as of 01.11.2024 of a new clinical trial (CTA) and for applications for amendments to ongoing clinical trials will be issued according to the new law.

For flawless (= complete and error-free documentation, no formal and/or content-related deficiencies or ambiguities), that are submitted after 20 September 2024 (60-day assessment period) or after 6 October 2024 (30-day assessment period) and that do not correctly reflect the law applicable from 1 November 2024, Swissmedic will grant authorisation on condition that the points identified that do not comply with the new law are fulfilled before the first visit of the first patient.

In case of deficient applications under the old legislation (= formal and/or content-related deficiencies or ambiguities) that can only be issued after 1 November 2024, Swissmedic will request applicants to address the points that do not comply with the new legislation in addition to the formal and content-related deficiencies by means of a ‘Further Information Request’.

6 MANDATORY INFORMATION AND REPORTS BY SPONSORS

6.1 Must all adverse drug reactions be reported immediately to Swissmedic?

No, only SUSARs (suspected unexpected serious adverse reactions) in clinical trials of categories B and C must be immediately reported to Swissmedic, in line with Art. 41 ClinO.

Of note, only SUSARs observed at Swiss trial centres must be announced immediately to Swissmedic, also when being observed as part of international trials.

SUSARs must fulfill all three of the three following criteria:

- serious (based on the usual definitions);
- suspected (a connection with the IMP cannot be excluded);
- unexpected (in terms of type of AE or degree of severity, the event has not been described previously for the IMP as part of the Reference Safety Information, e.g., in the Investigator's Brochure or SmPC 4.8.).

All other adverse events and adverse drug reactions must be announced by the Sponsor to Swissmedic within the Annual Safety Report (ASR).

Further information can be found on the Swissmedic website swissmedic.ch > Clinical trials on medicinal products > Safety measures in clinical trials.

6.2 When must SUSARs be reported, using which channels, and to whom?

Fatal and life-threatening SUSARs:

- Initial notification of Swissmedic within 7 days,
- follow-up report within 8 days after initial notification (even if no influence on causality assessment).

Other SUSAR events requiring notification:

- Initial notification of Swissmedic within 15 days.

Detailed information can be found on the Swissmedic website swissmedic.ch > Clinical trials on medicinal products > Safety measures in clinical trials.

6.3 What formats does Swissmedic accept for the Annual Safety Report (ASR)?

Detailed information can be found on the Swissmedic website swissmedic.ch > Clinical trials on medicinal products > Safety measures in clinical trials.

6.4 Is it necessary to announce the end of recruitment or end of treatment?

The (scheduled) end of recruitment or treatment is usually not the same as the end of trial, and Swissmedic only has to be notified about the end of trial on local and global level.

In case of life-long follow-up, the sponsor can inform Swissmedic about the “last patient last treatment” date. This, however, does not discharge the Sponsor of announcing the end of the trial.

The end of recruitment has to be announced to Swissmedic only, if it is linked with immediate safety and protective measures (art. 37 ClinO).

6.5 Is it necessary to inform Swissmedic about safety measures taken in international clinical trials, even when no individual has been recruited yet at Swiss sites?

Yes, please inform Swissmedic immediately in detail about the safety measures taken such as e.g. “Dear investigator letter”. This is also the case, when the safety risk has been observed in a different indication, but for the same compound.

Detailed information can be found on the Swissmedic website swissmedic.ch > Clinical trials on medicinal products > Safety measures in clinical trials.

6.6 Must Swissmedic be informed if a trial site (i.e., in a multicentre trial) is closed prematurely in Switzerland?

Swissmedic must be informed of the premature closure only, if it is linked with immediate safety and protective measures (art. 37 ClinO).

6.7 When is the clinical trial considered to have ended?

In accordance with international standards, as well as Art. 38 ClinO, the trial is considered to have ended on the date of the final visit for the final trial subject ("last patient last visit”, LPLV), or the last data point recorded for a patient in accordance with the trial protocol. There are two LPVL, one on global study level, if it is an international trial and one on local Swiss level. Both need to be reported to Swissmedic (Art. 38, para. 1 ClinO).

In order to avoid lack of clarity or misunderstandings, the definition for the potential end of the trial should be explicitly mentioned in the trial protocol. Any change of the potential end of this trial must be submitted to Swissmedic as a substantial amendment, together with a justification.

6.8 When and within what time limits must the Sponsor inform Swissmedic that the trial has ended?

Swissmedic must be informed of the end of a trial in Switzerland within a time limit of **90 days** (i.e., LPLV at the last Swiss centre) (Art. 38, para. 1 ClinO).

If a trial is stopped prematurely for safety-relevant reasons globally or in Switzerland, Swissmedic (and the competent REC) must be informed within **7 days** of sponsor's decision (Art. 37 and 38 ClinO).

If the trial as a whole is stopped prematurely for other reasons (premature termination) or put on hold globally or in Switzerland, Swissmedic (and the competent REC) must be informed within **15 days** of sponsor's decision (Art. 38, para. 2 ClinO).

In addition, a written explanation for the premature end must be submitted.

6.9 For which trials and within which time limits must the Sponsor submit a final report to Swissmedic?

Independently of whether the trial is a commercial or non-commercial one, and whether it ends normally or is prematurely discontinued, a final report must **always** be submitted to Swissmedic. The time limit laid down in ClinO is **one year** after last patient last visit following the end of the trial (Art. 38, para. 3 and 5 ClinO).

Swissmedic does not, however, stipulate any binding format for the report. The final report should nevertheless be in line with ICH GCP requirements (although it is not mandatory for it to be in ICH E3 format) and in accordance with current medical and scientific standards.

6.10 Must Serious Breaches be announced to Swissmedic?

In Switzerland it is not required by law to notify serious breaches in clinical trials to the competent authority.

However, if the serious breach is systematic and it results in safety concerns for the subjects enrolled in the clinical trial, then the sponsor should implement Urgent Safety Measures to minimise this risk immediately. Urgent Safety Measures must be reported to Swissmedic according to article 47 ClinO.

7 CLINICAL AND NON-CLINICAL QUESTIONS

7.1 Do preclinical investigations for IMPs have to be carried out according to Good Laboratory Praxis (GLP)?

Yes. Swissmedic expects that all preclinical investigations (*in vitro* and *in vivo*) regarding toxicology and safety pharmacology of a new medicinal product be carried out in accordance with international standards (ICH). Deviations from this rule must be subject to a well-founded justification.

The GLP provisions define a framework for planning, monitoring, documenting, reporting and archiving of such trials. Only the data collected in the framework of GLP-compliant trials provide authorities such as Swissmedic with sufficient guarantees that the data submitted is a true reflection of the results observed during the trial and can serve as the basis for the assessment of the risk-benefit ratio of the trial applied for.

Change history

Version	Change	sig
25.0	Updates associated with the revision of ordinances relating to the Human Research Act, additional questions, clarifications and revisions of the text	kro
24.2	New layout, no content adjustments to the previous version	tsj
24.1	Information on IMP and MD combination trials updated	plp
24.0	Information on IMP and MD combination trials updated	plp
23.1	Minor corrections in the Table of content	jaf
23.0	Clarifications and minor corrections	jaf
22.0	Clarifications of RSI and minor corrections	jaf
21.0	Clarifications and minor corrections	jaf
20.0	Information on regulatory requirements for follow-up studies / Changes due to new EMA recommendations in Eudralex Vol. 10 „Auxiliary Medicinal Products in Clinical Trials, rev 2, June 2017 (Chapter III)“ / Clarifications & corrections	jaf
19.0	clarifications for submission requirements	jaf
18.0	Addition of information concerning reporting requirements and use of NIMPs, clarifications	hch, jaf
17.0	Minor text changes and precisions.	jaf
16.0	Transfer of some information to the “Guideline amendments in clinical trials” / Deletion of some information not specific for Swissmedic	jaf
15.0	Chapter 5: „A sentence was deleted for clarification. The remaining content of the document is unchanged.”	sel
14.0	full revision	coa
13.0	New change history inserted in the document, dropdown field inserted in the header	wis