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1. GENERAL QUESTIONS

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

- Therapeutic Product Act (TPA / HMG / LPT_h) (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

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

The Clinical Trials Division evaluates all aspects related to the safety and quality of the 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).

What is a clinical trial?

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

- I. *Clinical trial* means a research project in which persons 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.

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).

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.

What is an Auxiliary Medicinal Product (AxMP)?

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

Definition of an AxMP:

“A medicinal product 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 (5)].

AxMPs are medicinal products that do not fall within the definition of an IMP given above.

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

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.

(This document was previously called Guidance on Investigational Medicinal Products [IMPs] and Non-Investigational Medicinal Products [NIMPs]).

See also information on this topic in Chapter 4 below.

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 products with an MA in a country whose GMP control systems is recognised as equivalent to the Swiss system*. For products 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 www.swissmedic.ch > Clinical trials on medicinal products > Clinical Trial Application > Guidelines for CTA dossiers submitted”.

2. APPLICATIONS

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

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

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

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 www.swissmedic.ch/clinicaltrials > **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.

Is the trial protocol (or protocol amendment) to be signed, and by whom?

For submission to Swissmedic, only the sponsor's signature is necessary on the trial protocol and the amendment(s).

It goes without saying that the trial protocol must be signed by the sponsor and the investigator prior to the 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.

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

The applicant can be any authorised person (sponsor, sponsor representative, CRO, etc.).

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

What is the "previous assessment status" mentioned in sections 7 and 8 of the *Guideline Clinical Trial Application Dossier*?

The "previous assessment status" refers to the marketing authorisation status of the IMP used in the clinical trial. The assessment status also takes into consideration the fact that a drug substance is contained in a product with marketing authorisation. Depending on this status, a different kind of mandatory information has to be submitted, as described in sections 7 and 8 of the *Guideline Clinical Trial Application Dossier*.

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.

Which document should contain the Reference Safety Information?

For an IMP with no marketing authorisation in Switzerland (or in a country with a recognised GMP control system), the RSI should always be a clearly separated specific section within the IB.

If it is proposed to use an IMP outside the (Swiss) terms of marketing authorisation (or from a country with a recognised GMP control system) within the trial and/or if the sponsor does not have access to an IB for the marketed IMP, section 4.8 of the SmPC for the IMP(s) could be used as the RSI, if justified by the sponsor in the clinical trial application cover letter. Otherwise the RSI should always be a clearly separated specific section within the IB as detailed in point 1 above.

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 grounds 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). In most cases, the clinical trial cannot start until Swissmedic has confirmed that the conditions have been fulfilled.

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.

3. SPECIAL CATEGORIES OF CLINICAL TRIALS

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

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

Cat. B: Trials with products authorised in Switzerland, not used according to the Swiss SmPC

Cat. C: Trials with products not authorised in Switzerland.

If a trial with products authorised in Switzerland, used according to the SmPC, is blinded (e.g. with a placebo, a comparator, etc.) it can no longer be categorised as a category A trial. The reason for this is that the blinding processes are manufacturing steps (labelling, packaging, or possibly production of a placebo and the blinding process itself), and since these manufacturing steps may impact on the quality of the IMP, they must be reviewed by Swissmedic.

Based on these considerations, a trial with products authorised in Switzerland used according to the SmPC, blinded with a placebo or an authorised comparator, would theoretically fall into category C. However, it was decided in agreement with the Federal Office of Public Health (FOPH) to classify such trials as category B according to ClinO art 19 para 4. Documents on the quality referring to the changes as compared to the authorised product and proof of compliance with Good Manufacturing Practice must be submitted according to ClinO Annex 4 points 1.4 and 1.6.

The classification of a clinical trial is the responsibility of the sponsor. The REC (not Swissmedic) is responsible for checking if the category is correct. Nevertheless, Swissmedic may see the need for changing the category when reviewing the PQD. In such a case, Swissmedic will ask the sponsor to re-discuss the category with the REC.

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. For multicentre trials, the sponsor must send the request of change of category to the Lead REC that approved the clinical trial. The other (local) RECs must be informed by the sponsor about the decision of the Lead REC.

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

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 capable of 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 need 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: www.swissmedic.ch/clinicaltrials > 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).

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

Being of a commercial or non-commercial nature does not affect the characterisation of the trial as a clinical trial. If IITs fall within the scope of the definition of a clinical trial (Art. 2 ClinO), they are not different from commercially operated clinical trials from a legal point of view (Art. 53, TPA).

When planning and carrying out IITs, all requirements as laid down in the TPA, the ClinO and the ICH GCP Guideline must therefore be respected.

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 and override the nature of the trials (commercial or non-commercial).

When should trial subjects be considered as voluntary trial subjects 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 the 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 volunteer trial subjects and not patients.

These are the only two cases for which trial subjects may be paid by the sponsor of the clinical trial to compensate for their time. In principle, no financial incitement for participants to take part in a clinical trial is permitted.

What is the submission procedure for clinical trials in which both Investigational Medicinal Products (IMPs) and Medical Devices (MDs) are investigated?

In combined trials, both medical devices and medicinal products (including e.g. transplant products) are the subject of investigation. The requirements for trials with medicinal products and those for trials of medical devices must both be met.

The following cases can be distinguished for submissions to Swissmedic:

Conforming medical device*	Conforming medicinal or transplant product**	How to submit to Swissmedic
No	No	Submit a full documentation for clinical trials of medical devices according to the submission procedure for medical devices. In addition, insert the form for clinical trials with medicinal or transplant products and all the additional documents required for medicinal or transplant products.
No	Yes	Make a submission with the form and according to requirements for clinical trials of medical devices. In the trial protocol, describe pharmacovigilance reporting duties for the medicinal or transplant product.
Yes	No	Make a submission with the form and according to requirements for clinical trials of medicinal products. In the trial protocol, describe materiovigilance reporting duties for the medical device.
Yes	Yes	No submission of the clinical trial to Swissmedic. Materiovigilance and pharmacovigilance reporting duties apply.

* is CE-marked, is used in the clinical trial according to its CE-marked instructions for use, and has not been forbidden in Switzerland

** is authorised by Swissmedic and is used in the clinical trial according to its authorised label

Detailed information on clinical trial applications, reporting and submission of modifications in ongoing clinical trials for IMPs and MDs combination trials can be found on the information sheet on clinical trials with medical devices and on the Swissmedic website www.swissmedic.ch > Medical devices > Clinical trials of medical devices.

4. IMP: PHARMACEUTICAL QUALITY DOCUMENTATION; GMP; LABELLING: IMPORT

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
www.swissmedic.ch/clinicaltrials > Clinical trials on medicinal products > Clinical Trial Application.

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

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 Chapter 1 above, and to "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". In particular, reference is made to Appendix 1 and the examples for AxMPs such as "rescue medication", "challenge agents", "background treatment", etc.

Making a distinction between IMPs and AxMPs is relevant since it has a bearing on costs borne by sponsors or health insurance companies.

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 subject (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. It may, however, be assessed during a GCP inspection.

**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

Must labels be provided in several national languages?

Depending on the Canton and the geographical location of the trial centre in Switzerland, the labels must be provided in one or several of the official national languages.

Exception: For clinical trials in which the IMP is exclusively administered directly at the clinic or hospital by the investigator, and is not dispensed to the trial subjects, Swissmedic also accepts texts on the labels in English.

What information must be provided on the label?

In order to be used within the framework of a clinical trial, all IMPs must have a trial-specific label. Samples of the labels of all IMPs must be submitted as part of the application dossier.

The compulsory elements of the labels for IMPs are laid down in Annex 13, "Manufacturing of investigational medicinal products" to Volume IV of the EU guideline to Good Manufacturing Practice.

If a commercially available medicinal product is used as test product or comparator product, a considerable amount of information such as batch number, expiry date and storage conditions is already included on the normal commercial label.

In these cases, it is possible to use only an additional label with the following elements:

- Trial number or Trial ID;
 - Trial subject number / Patient ID;
 - Name of the sponsor, investigator or CRO, and contact details of the main contact for information. It is acceptable to indicate the global sponsor's name and phone number, as appropriate.
-

5. LEGAL QUESTIONS

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

No. Such official decisions are sent to the applicant by post only.

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.

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 [www.swissmedic.ch/clinical trials](http://www.swissmedic.ch/clinical%20trials).

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.

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?

Please refer to the "Guideline on amendments in clinical trials" available on our website www.swissmedic.ch/clinicaltrials > Clinical trials on medicinal products > Submission of changes.

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

Please refer to the "Guideline on amendments in clinical trials" available on our website www.swissmedic.ch/clinicaltrials > Clinical trials on medicinal products > Submission of changes.

What are the requirements for sending data or biological samples abroad?

When sending data or biological samples abroad, the sponsor must guarantee the same level of data protection as in Switzerland. They may only be sent abroad if the receiving country has an appropriate level of data protection legislation (corresponding to the standards of Switzerland or the EU), or if specific precautions (written information for the trial subjects and their consent, or contractual provisions) are taken [Art. 6 of the Data Protection Act, DPA].

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.

How are follow-up studies to be classified?

Based on the definition of “clinical trial” given in the HRA article 3 letter I, all studies that do not involve the prospective assignment to a health-related intervention cannot be classified as clinical trials:

*“Clinical trial means a research project in which persons 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”.*

Most follow-up studies are safety or efficacy follow-up studies that do **not** involve the administration of medicinal products. Therefore, all these studies should be seen under the Human Research Ordinance (HRO) on “research other than clinical trials”. The evaluation is therefore only done by the REC.

These studies do not require Swissmedic evaluation since patients are not at risk because of no administration of the medicinal product. There might be other risks associated with the procedures (biopsies, CT scans, blood extraction) in the study, which are not evaluated by Swissmedic but by the EC.

If the extended follow-up on long-term safety and efficacy of a medicinal product is an integrated part of the original clinical trial protocol or is submitted as an amendment to the clinical trial protocol, the follow-up will remain under the Clinical Trials Ordinance ClinO and be categorised as the original protocol.

6. MANDATORY INFORMATION AND REPORTS BY SPONSORS

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.

SUSARs must fulfil 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, e.g. in the Investigator's Brochure).

Only SUSARs observed at Swiss trial centres must be announced immediately to Swissmedic, also when it concerns international trials.

Other adverse drug reactions must be announced to Swissmedic in the Annual Safety Report (ASR).

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

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

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

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

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

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 of end of trial.

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).

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

If a Swiss trial site taking part in a multicentre trial is closed prematurely, Swissmedic must be informed of the premature closure only if it is linked with immediate safety and protective measures (art. 37 ClinO).

When is the clinical trial considered to be 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 by the final trial subject ("last patient last visit", LPLV), or the last data point recorded for a patient in accordance with the trial protocol.

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

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.

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.

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**What are the requirements for on-site reconstitution (Zubereitung) of cytostatic compounds?**

If the cytostatic compound is already on the market in Switzerland and if the reconstitution intended for open-label or double-blind administration is done according to the professional information (PI), only the PI must be submitted with the CTA.

The personnel in charge of the reconstitution (e.g. pharmacist, nurses) must be properly trained for this task. It is the responsibility of the sponsor to ensure that the personnel is adequately trained. Swissmedic verify it during a GCP inspection.

It is the responsibility of the sponsor to ensure adequate and correct accountability of the therapeutic product, and correct labelling of the end container (usually infusion bag).

Must preclinical investigations on whose basis the safety of an IMP for use in humans is assessed be drawn up in accordance with GLP?

Yes. Broadly speaking, 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. 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	Valid and binding as of:	Description, comments (by author)	Author's initials
24	01.09.2021	Information on IMP and MD combination trials updated	plp
23.1	05.03.2020	Minor corrections in the Table of content	jaf
23	01.02.2020	Clarifications and minor corrections	jaf
22	15.03.2019	Clarifications of RSI and minor corrections	jaf
21	11.07.2018	Clarifications and minor corrections	jaf
20	10.10.2017	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	02.06.2017	clarifications for submission requirements	jaf
18	15.12.2016	Addition of information concerning reporting requirements and use of NIMPs, clarifications	hch, jaf
17	12.02.2016	Minor text changes and precisions.	jaf
16	30.04.2015	Transfer of some information to the “Guideline amendments in clinical trials” / Deletion of some information not specific for Swissmedic	jaf
15	24.02.2015	Chapter 5: „A sentence was deleted for clarification. The remaining content of the document is unchanged.“	sel
14	27.01.2015	full revision	coa
13	31.07.2014	New change history inserted in the document, dropdown field inserted in the header	wis