Clinical Trials: Overview (Switzerland)

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A Practice Note providing an overview of the regulation of clinical trials of medicinal products in Switzerland.

This Note provides an overview of the regulation of clinical trials of investigational medicinal products (IMPs) in Switzerland, including the legislation and regulatory framework governing the conduct of clinical trials and the relevant regulatory authority. It also outlines the process for applying for clinical trial authorisation in Switzerland, including any pre-trial considerations, and explains the procedural requirements during and after the end of the clinical trial, including requirements for reporting safety information.

This Note also contains a high-level discussion on regulation of decentralised clinical trials in Switzerland and other important considerations.

Legislation and Regulatory Framework

Clinical trials in Switzerland are governed by:

- The *Federal Act on Research Involving Human Beings of 30 September 2011* (Human Research Act) (HRA).
- Articles 53 to 54 of the *Federal Act on Medicinal Products and Medical Devices of 15 December 2000* (Therapeutic Products Act) (TPA).
- The *Ordinance on Clinical Trials with the Exception of Clinical Trials of Medical Devices of 20 September 2013* (Clinical Trials Ordinance) (ClinO).

All clinical trials of therapeutic products must be carried out in accordance with the recognised principles of Good Clinical Practice (GCP) (Article 5(1) of the ClinO provides that the applicable GCP is defined in Annex 1(2) of the ClinO: the term GCP is therefore to be understood generally, as depending on the type of clinical trial, different guidelines will apply). Under the ClinO, trials with medicines must comply with the requirements of the *International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH): Guideline for Good Clinical Practice E6(R2) Guideline for Good Clinical Practice E6(R2)* issued by the *International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use* (ICH) (ICH GCP E6(R2)).

Clinical trials of medical devices are governed by the general framework of the HRA, Articles 53 to 54 of the TPA, and the *Ordinance on Clinical Trials with Medical Devices of 1 July 2020* (ClinO-MD). Under the ClinO-MD, trials with medical devices must comply with the requirements of the applicable European Union (EU) regulations (that is, Regulation (EU) 2017/745 (EU-MDR) and Regulation (EU) 2017/746 (EU-IVDR), as well as *ISO 14155:2020 on Clinical investigation of medical devices for human subject – Good clinical practice* issued by the International Organization for Standardization (ISO). Clinical trials of medical devices are outside of the scope of this Note.

Clinical trials of investigational medicinal products (IMPs) are divided into three categories (categories A, B and C) by Article 19 of the ClinO, depending on the authorisation status of the IMP and the intended use within the clinical trial:

- Clinical trials of authorised medicinal products come under category A (Article 19(1), ClinO) if:
    - they are used in accordance with the prescribing information; or
    - they are used in a different indication or dosage from that specified in the prescribing information while the indication is still within the same disease group, or while the disease in question is self-limiting and the dosage used is lower than that specified in the prescribing information; or
    - if the intended use is recognised as standard in guidelines prepared in accordance with internationally accepted quality criteria.

- Clinical trials of authorised medicines which are not used within the limits already defined for category A come under category B (Article 19(2), ClinO).
- Clinical trials of non-authorised medicinal products come under category C (Article 19(3), ClinO).

The requirements for categories A, B, and C differ mainly concerning:

- The application documents that are required for the clinical trial (Annexes 3 and 4, ClinO).
- The scope of, and the competent authority for, notification and documentation duties related to the progress of the trial, or incidents relating to the trial.
- Certain other information and disclosure requirements that must be made to:
    - *Swissmedic* (the Swiss Agency for Therapeutic Products); or
    - the competent ethics committee; or
    - the *Federal Office of Public Health* (FOPH).

There are several different types of clinical trials for which different requirements apply, as follows:

- Clinical trials involving devitalised human tissue or cells (see *Clinical Trials with Devitalised Human Tissue or Cells*).
- Clinical trials regarding gene therapy or genetically modified or pathogenic organisms. These require additional application documents and are subject to increased scrutiny (Articles 22 and 35, ClinO).
- Clinical trials in emergency situations (see *Informed Consent: Persons in Emergency Situations*).
- Multicentre clinical trials. These require co-ordination by a lead committee and a co-ordinating investigator (Articles 47(2) and 47(3), HRA; Article 27, ClinO).
- Investigations involving radiation sources. These require submission of additional application documents and are subject to increased scrutiny and monitoring (Articles 28 and 44, ClinO).
- Clinical trials involving the transplantation of human organs, tissues, or cells. The categorisation and authorisation procedure for these trials are regulated separately and differ from other clinical trials in certain respects (see *Clinical Trials Involving the Transplantation of Human Organs, Tissue, or Cells*). In addition to authorisation by the competent

ethics committee, an authorisation by the FOPH is required (instead of authorisation by Swissmedic) (Article 52 et seq, ClinO) (see *FOPH Authorisation*).

- Clinical trials that are not trials concerning:
    - medicinal products; or
    - the products listed under Article 2(a)(2) of the TPA; or
    - transplant products; or
    - transplantation.

    These are regulated separately (Article 60 et seq, ClinO). In particular, only an authorisation by the competent ethics committee is required (Article 62 et seq, ClinO).

Regulatory Authority

In general, clinical trials of medicinal products require prior authorisation from Swissmedic, although limited exceptions to this apply (Article 54, TPA). In addition, prior authorisation from the competent ethics committee is also required to conduct a research project (Article 45(1)(a), HRA). Therefore, clinical trials of medicinal products are typically subject to a double authorisation requirement, with prior authorisation being obtained from both:

- The federal authority (Swissmedic).
- The relevant cantonal authority (that is, the competent ethics committee).

The review areas for Swissmedic and the ethics committee to grant these respective authorisations differ in terms of their content, so that in principle the granting of one authorisation has no influence on the granting of the other.

In the case of medicinal products, Swissmedic verifies whether those medicinal products comply with the rules regulating good manufacturing practice (GMP) and medicinal product safety (Article 54(4), TPA).

The ethics committee grants its authorisation if the ethical, legal, and scientific requirements of the HRA are met with respect to the research project (Article 45(2), HRA).

The supervision of clinical trials is not fully integrated between Swissmedic and the relevant ethics committee (though Swissmedic and the ethics committee keep each other informed and can co-ordinate their measures (Article 48(4), HRA; Article 48, ClinO)), and each body has its own supervisory remit:

- Swissmedic can carry out an inspection at any time to determine whether the conduct of a clinical trial meets the requirements specified in the TPA and the HRA (Article 54b, TPA). Inspections can cover clinical trials under categories A, B, or C, and can go beyond the scope of Swissmedic's review area with respect to the authorisation process pursuant to Article 54 of the TPA.
- The competent ethics committee can revoke or suspend its authorisation or make the continuation of the research project subject to additional conditions, if it considers that the health or safety of the project's subjects is at risk. It can request further information or documentation concerning the research project.

FOPH Authorisation

Clinical trials involving the transplantation of human organs, tissues, or cells require prior authorisation from the FOPH (Article 36, of *Federal Act on the Transplantation of Organs, Tissues and Cells of 8 October 2004*) (Transplantation Act). Whilst no authorisation from Swissmedic is required for these types of trials, authorisation from the competent ethics committee is still required, and the FOPH and the competent ethics committee have parallel supervisory competencies over such trials (Article 51 et seq, ClinO). The provisions on the required authorisations are contained in Article 52 (in connection with Articles 24 to 29) of the ClinO (ethics committee) and Articles 52 to 56 of the ClinO (FOPH). The provisions on supervisory competencies are contained in Articles 57 (in connection with Articles 37 to 41, 43, and 44), 58 and 59 of the ClinO.

Regulatory Guidance

Both *Swissmedic* and the *FOPH* have published guidance documents and further information on their practices, forms, and templates, on their websites concerning clinical trials and corresponding applications. Similarly, the *Swiss Association of Research Ethics Committees* (swissethics) has published several guidelines and templates concerning clinical trials.

Register of Clinical Trials

Authorised clinical trials must be recorded in a public registry (Article 56(1), HRA). According to Article 64(1) of the ClinO, the sponsor of the clinical trial must register the data defined in Annex 5 No. 1 of the ClinO in either:

- A primary register recognised by the *World Health Organization* (WHO).
- The registry of the US National Library of Medicine.

To make the data available to the public, the data must additionally be entered into a supplementary federal Swiss database using a Swiss national language under Article 64(2) of the ClinO (the data is published on the *Swiss National Clinical Trials Portal* (SNCTP), which is operated by the *FOPH's portal for human research in Switzerland* (*Koordinationsstelle Forschung am Menschen*) (kofam) (Article 67, ClinO)). The FOPH manages kofam under Article 55(3) of the HRA. The SNCTP is the portal where clinical trials in Switzerland are published. It contains data from two sources:

- From the Business Administration System for Ethics Committees (BASEC), the national platform for submitting applications for research projects to ethics committees.
- From the WHO International Clinical Trials Registry Platform (ICTRP), which covers the 17 primary registries worldwide.

The ICTRP clinical trials shown on the SNCTP are limited to those conducted in Switzerland; there is also an option to display trials conducted in one of Switzerland's neighbouring countries. Regarding the data that must be registered, Annex 5 No. 1 of the ClinO refers to Version 1.2.1 of the WHO Trial Registration Data Set.

The relevant data must be registered before the clinical trial is conducted, except for clinical trials in which the medicinal product under investigation is being administered to adults for the first time (that is, Phase I clinical trials), which must be registered within one year after completion of the trial (Articles 66(1) and 66(2), ClinO).

Clinical trials authorised by the ethics committees are also published on the *Registry of All Projects in Switzerland* (RAPS) of swissethics.

Applying for Clinical Trial Authorisation

When is Clinical Trial Authorisation Needed?

In general, an authorisation from the competent ethics committee is required to conduct a research project that is within the scope of the HRA (Article 45(1)(a), HRA). It therefore follows from the definition of a clinical trial (that is, a research project involving individuals that prospectively assigns them to undergo a health-related intervention to study its effects on health or on the structure and function of the human body (Article 2(a), ClinO)) that every clinical trial requires such authorisation. Whether an additional authorisation from a federal agency (Swissmedic or the FOPH) is also required depends on the nature and design of the clinical trial, as discussed below.

Clinical Trials with Medicinal Products

Clinical trials with medicinal products generally require a prior authorisation from Swissmedic (Article 54(1), TPA). However, clinical trials involving authorised medicinal products used in accordance with the product information are exempt from mandatory authorisation (Article 54(2), TPA). This exemption extends to all category A clinical trials involving medicinal products (Articles 19 and 30, ClinO).

Clinical Trials with Medical Devices

A prior authorisation from Swissmedic is generally also required for clinical trials with medical devices (Article 54(1), TPA). However, category A clinical trials with medical devices are exempt from mandatory authorisation from Swissmedic (Article 7, ClinO-MD). Under the ClinO-MD, a clinical trial is either a clinical investigation or a performance study (Article 2(a), ClinO-MD). Performance studies can be either interventional or non-interventional performance studies.

Clinical investigations fall under category A (and are therefore exempt from Swissmedic authorisation) if all the following conditions apply:

- The device to be investigated carries a conformity marking in accordance with the applicable medical device regulation.
- That device is used in accordance with the instructions for use.
- It is not prohibited to make the device available on the market, put it into service or use it in Switzerland.

(Article 6(1), ClinO-MD.)

Interventional performance studies fall under category A (and are therefore exempt from Swissmedic authorisation) if all the following conditions apply:

- The device to be investigated carries a conformity marking in accordance with the applicable in-vitro diagnostic medical device regulation.
- The device is used in accordance with the instructions for use.
- It is not prohibited to make the device available on the market, put it into service or use it in Switzerland.

(Article 6a, ClinO-MD.)

Non-interventional performance studies fall under category A (and are therefore exempt from Swissmedic authorisation) if they are not yet exempt from the scope of the ClinO-MD under Articles 2a(1) to 2a(3) of the ClinO-MD (for example, because the

conduct of the study is not limited to the further use of already sampled biological material or already collected health-related personal data (Article 6a(1)(b), ClinO-MD).

Clinical Trials with Devitalised Human Tissue or Cells

Medicinal products containing devitalised human tissue or cells (and their derivatives) are subject to the TPA or the Transplantation Act, depending on their nature, composition and intended use (Article 2a, TPA).

Clinical trials with such products fall under category A (and are therefore exempt from Swissmedic authorisation under Article 30 of the ClinO) if:

- the person placing the product on the market has notified Swissmedic of their name and address, and the product to be placed on the market (including their general technology and use) by the time the product is placed on the market.
- The product must be used in accordance with the instructions for use (Article 20(1), ClinO).

Otherwise, authorisation by Swissmedic is mandatory (Article 20(2), ClinO).

There are certain special requirements for clinical trials with devitalised human tissue or cells that are capable of emitting ionising radiation (Articles 36 and 44, ClinO).

Clinical Trials Involving the Transplantation of Human Organs, Tissue, or Cells

Clinical trials involving the transplantation of human organs, tissues, or cells require prior authorisation from the FOPH (Article 36(1), Transplantation Act).

A clinical trial involving the transplantation of human organs, tissues, and cells comes under category A (and is therefore exempt from FOPH authorisation (Article 52, ClinO)) if the transplantation to be investigated is recognised as standard in guidelines prepared in accordance with internationally accepted quality criteria (Article 49(1), ClinO). These internationally accepted quality criteria are defined in the *Appraisal of Guidelines for Research and Evaluation II* (AGREE II), which is used to develop guidelines and to assess methodological stringency and transparency.

Clinical trials of the transplantation of embryonic and foetal tissues and cells come under category C (and therefore require authorisation by the FOPH) (Article 49(3), ClinO).

For clinical trials with transplant products, the rules regarding clinical trials of medicinal products apply by analogy (Article 21, ClinO).

Transplant products are defined as products consisting of or containing human organs, tissues, or cells:

- If these have been substantially processed (that is, a propagation of cells via cell culture, a genetic modification of cells, or a differentiation or activation of cells).
- If they are not intended to perform the same function in the recipient person as in the donor person.
- If the products consist of or contain animal organs, tissues, or cells.

(Articles 2(1)(c) and 2(1)(d), *Ordinance on Transplantation of Organs, Tissues and Cells of Human Origin* (TxV), available in German, French, and Italian).

Application Process

The application process involves the "investigator" and the "sponsor":

- The sponsor means a person or institution headquartered or represented in Switzerland that takes responsibility for organising a clinical trial (in particular, for the initiation, management, and financing of the trial in Switzerland) (Article 2(d), ClinO).
- The investigator means a person responsible in Switzerland for the conduct of a clinical trial and for the protection of the participants at the trial site.

An investigator can also take responsibility for organising a clinical trial in Switzerland, with the result that the investigator is also a sponsor of that trial (Article 2(d), ClinO). Where the investigator and the sponsor are different people, the investigator and the sponsor can simultaneously submit applications to the competent ethics committee and to the relevant federal authority (typically Swissmedic) (Article 23(1), ClinO). Both authorities will then co-ordinate their assessments (Article 23(2), ClinO).

Application Process for Authorisation by the Ethics Committee
See *Ethics Committee, Institutional Review Board, or Equivalent Approval*.

Application Process for Authorisation by Swissmedic
The sponsor must submit the application documents specified in Annex 4 of the ClinO to Swissmedic for review. Swissmedic can request additional information during its review (Article 31, ClinO). Swissmedic acknowledges receipt of the application within seven days of receipt and will notify the sponsor of any formal deficiencies in the application documents. It must then reach a decision within 30 days of acknowledgement of receipt of the formally correct application documents. If a medicinal product or product under Article 2a(2) of the TPA is to be used in persons for the first time or manufactured in a new process, this deadline can be extended by a maximum of 30 days (Swissmedic will inform the sponsor of any such extension). After it has made its decision on whether or not to grant authorisation, Swissmedic informs the competent ethics committee of its decision (Article 33, ClinO).

Application Documents
The application documents required to be submitted to the ethics committee and Swissmedic are specified in Annexes 3 and 4 of the ClinO respectively and differ depending on the type of clinical trial. However, the following documents are typically required.

For authorisation by the ethics committee:

- Basic form, including a summary of the protocol in the national language of the trial site and the reasons for the requested clinical trial categorisation.
- Protocol.
- Case report form (CRF), which is required to enable the collection of all data needed to conduct the clinical trial and analyse its results.
- Information sheet, informed consent form, and recruitment documents (in particular, the wording of announcements or advertisements).

- Any other documents issued to participants.
- Information on the type and amount of any remuneration to be given to participants.
- For clinical trials of medicinal products: specific information in connection with the medicinal product under investigation (for example, the prescribing information, the investigator's brochure (IB), information on conformity, intended use and instructions, proof of compliance with GMP, and so on).
- The investigator's CV, including evidence of their knowledge and experience, and a list of the other persons conducting the clinical trial, indicating their responsibilities and relevant professional knowledge.
- Information on the suitability and availability of infrastructure at the trial site.
- Information on the secure handling of personal data.
- Any agreements between the sponsor, or third parties acting on the sponsor's behalf, and the investigator (in particular, concerning the financing of the clinical trial, the investigator's remuneration, and publication of the trial).
- A certificate of insurance or other proof of coverage for possible damage, including agreements between the sponsor, or a third party acting on the sponsor's behalf, and the investigator.
- Any decisions or opinions of ethics committees located abroad concerning the clinical trial, including any conditions imposed and the reasons given.

(Annex 3, Clin O.)

For authorisation by Swissmedic:

- Basic form.
- Protocol.
- For clinical trials of medicinal products Specific information in connection with the medicinal product under investigation (for example, the prescribing information).
- Documents on the quality of the product, and the CRF.
- The IB, if applicable, including information on risk assessment, or limited to changes in the administration of the medicinal product.
- Proof of compliance with GMP.
- Proof of compliance with correct labelling.
- Any decisions of foreign drug regulatory authorities concerning the clinical trial, including any conditions imposed and the reasons given.
- Information on:
    - any applications currently being reviewed by an ethics committee in Switzerland; and
    - any decisions of ethics committees in Switzerland.

(Annex 4, Clin O.)

Both the ethics committee and Swissmedic can grant their authorisations with ancillary provisions (conditions or limitations). The authorities may also hear the investigator or the sponsor in the context of requests for additional information (RFIs). If necessary, they can also consult external experts as reviewers (Article 1(4), *Ordinance on Organisational Aspects of the Human Research Act*) (OrgO-HRA). The decision to issue any ancillary provisions or further clarifications is solely at the authorities' discretion. Due to the clock-stop rule (Articles 26(3) and 33(4), ClinO), the application process can, in practice, extend beyond the 30 days provided. However, the ethics committee must make its decision within two months of submission of the application at the latest (Article 45(2), HRA).

So far, no shorter, risk-adapted maximum limits for processing periods have been set for clinical trials, although Article 45(2)(a) of the HRA provides for this possibility.

Trial Preconditions That Must Be Met

Trial Sponsor and Legal Representative

Swiss law does not provide for the possibility of several sponsors being involved in a trial. Therefore, Swissmedic only accepts one sponsor for any particular clinical trial. This sponsor assumes the overall responsibility for the clinical trial in Switzerland.

Under Article 2(d) of the ClinO, a sponsor means a person or institution headquartered or represented in Switzerland, so it is not required for the sponsor itself to be established in Switzerland. However, a foreign sponsor must designate a named representative in Switzerland. The responsibility of the representative in Switzerland can be assumed by any individual or legal entity domiciled in Switzerland. Where the representative is a person, it is not necessary for that person to be a Swiss citizen. If the clinical trial application is sent from abroad, further correspondence (including invoicing) will go through the Swiss representative. The Swiss representative will also be the contact person for liability cases.

Insurance

In general, any person who carries out a research project involving persons as subjects will be liable for any damage suffered by them in connection with that project. The general liability and compensation rules of Swiss law apply with regard to any claims for damages (Article 19, HRA).

Liability must be appropriately covered through insurance or in an equivalent manner (Article 20(1), HRA).

For category A clinical trials where any measures for the collection of health-related personal data or the sampling of biological material entail more than only minimal risks and burdens, the insurance policy value must be at least:

- CHF250,000 per person.
- CHF20,000 for damage to property.
- CHF3 million for the entire clinical trial.

For other clinical trials, the policy value must be at least:

- CHF 1 million per person.
- CHF50,000 for damage to property.
- CHF10 million for the entire clinical trial.

(Annex 2, ClinO.)

The liability coverage must cover damage occurring up to ten years after the completion of the clinical trial (Article 13(3), ClinO).

Trial Site or Facilities

The review conducted by the ethics committee also includes a review of the suitability and availability of the infrastructure at the trial site (Article 25(h) and Annex 3, ClinO; *swissethics Guideline to the suitability and availability of infrastructure at the research site*). In this regard, the review covers the following points (among others):

- The experience of members of the investigating group in conducting clinical studies.
- Participating clinics/departments or external institutions (for example, radiology, laboratory, pharmacy).
- Suitability of available resources and facilities on site (room and equipment).
- Suitability of equipment, devices, and room(s) being used for the study.
- Provision of emergency care (including the form in which it is provided).
- The number of patients treated in the indication under research per year, as well as the planned number of patients for the study.
- The number of ongoing studies (in general and in the same indication).
- The handling of overlapping studies (that is, of the same indication or with similar inclusion/exclusion criteria).

Ethics Committee, Institutional Review Board, or Equivalent Approval

Authorisation from the competent ethics committee is required for all clinical trials (Article 45(1)(a), HRA) (see *Application Process for Authorisation by the Ethics Committee*).

The competent ethics committee must review the following review areas:

- The completeness of the application.
- The trial categorisation requested.
- The information intended for registration of the clinical trial.
- The protocol with regard to:
    - the scientific relevance of the topic, the suitability of the chosen scientific methodology and compliance with GCP;
    - the ratio between the likely risks and burdens and the expected benefits;
    - the measures taken to minimise risks and burdens, and to ensure the protection and follow-up of participants (including precautionary measures in the handling of personal data);
    - the need to involve persons (in particular, persons who are particularly vulnerable);

    - the criteria for the selection of participants;
    - the proposed procedure for providing information and obtaining consent (including the appropriateness of the period for reflection);
    - the appropriateness of the remuneration for participants; and
    - compliance with scientific integrity requirements.

- The completeness of the documentation for recruitment, information, and consent, and its clarity (especially with regard to the possible involvement of particularly vulnerable persons).
- The guarantee of the right to compensation in the event of damage.
- The adequacy of the knowledge and experience of the investigator and of the other persons conducting the clinical trial.
- The suitability of the infrastructure at the trial site.
- The financing of the clinical trial and the agreements between the sponsor, third parties and the investigator concerning the allocation of tasks, remuneration, and publication of the trial.
- Any other areas, where this is necessary to assess the protection of participants.

(Article 25, Clin O.)

For information on the application process for authorisation by the ethics committee, see *Application Process for Authorisation by the Ethics Committee*.

At present, it is not possible to submit a single application to both the competent ethics committee and the relevant federal authority.

Informed Consent

The consent of every person involved in a research project must be given in writing. Each person concerned must receive clear oral and written information. Before a decision on consent is made by the persons concerned, they must be allowed an appropriate period for reflection (Article 16, HRA). In any case, appropriate measures must be taken to ensure that the persons concerned have understood the essential elements of the information provided (Articles 7(3) and 7(4), ClinO). The person giving consent must be capable of judgment and give their consent voluntarily.

In exceptional cases, the persons concerned may be given incomplete information regarding specific aspects of a research project before it begins if both:

- This is essential for methodological reasons.
- The research project entails no more than minimal risks and burdens.

However, the participants must subsequently be fully informed as soon as possible (Article 18, HRA).

Persons concerned must be informed on the following aspects:

- The nature, purpose, procedure for, and duration of, the research project.

- The foreseeable risks and burdens.
- The expected benefits of the research project (in particular, for themselves or for other people).
- The measures taken to protect the personal data collected.
- The rights of the participants.

(Article 16(2), HRA.)

In addition to the points in Article 16(2), HRA, the persons concerned must also receive information on:

- Possible alternatives to the intervention under investigation, if the clinical trial is expected to offer a direct benefit.
- The effort involved and the obligations arising from participation.
- The participants' right to withhold or revoke their consent without giving reasons, and without suffering any disadvantages in relation to their medical treatment.
- The consequences of revocation of consent for their subsequent medical treatment, and for further use of the personal data and biological material collected up to that point.
- The participants' right to receive information at any time in response to further questions relating to the clinical trial.
- The participants' right to be informed of results concerning their health, and their right to forgo such information or to designate a person who is to take this decision for them.
- The measures envisaged to cover any damage arising from the clinical trial, including the procedure in the event of a claim.
- Details on the sponsor and the main sources of financing for the clinical trial.
- Any other points relevant to their decision on participation.

(Article 7(1), ClinO.)

Informed Consent: Children and Adolescents

For research projects involving children who are capable of judgement and that can demonstrate an expected direct benefit to the child:

- The informed consent of the child is required.
- The informed consent of that child's legal representative is required.

(Article 22(1), HRA.)

Swiss law does not define a certain age from which the capacity of judgement of a child is presumed. In a medical context, capacity is generally presumed from the age of 16, but this can vary depending on the circumstances of the individual clinical trial and the child.

For research projects involving children who are capable of judgement that cannot demonstrate an expected direct benefit to the child, in addition to the consent requirements above, the research project:

- Cannot entail more than minimal risks and burdens.
- Must be expected to yield substantial findings which could, in the long term, be beneficial to persons with the same disease or disorder, or in the same situation.

(Article 22(2), HRA.)

For research projects involving children who are not capable of judgement, instead of the child's informed consent (the consent of the child's legal representative is still required), it is required that the child does not visibly express opposition to the research intervention either verbally or by their behaviour (Articles 22(3) and 22(4), HRA).

Similar requirements as those expressed above for children who are (or are not) capable of judgement also apply to research projects involving adolescents (that is, minors from 14 years of age and older) (Article 23, HRA). The term "adolescents" is defined in Article 3(k) of the HRA.

Informed Consent: Adults Lacking Capacity

Under Article 24(1) of the HRA, a research project that is expected to provide a direct benefit to the subject of that project can only be carried out on adults who lack the capacity to provide informed consent if:

- Consent was provided by that adult whilst they were in a state of capacity to provide it, and that consent was duly documented.
- Where no duly documented consent is available, informed consent has instead been duly provided in writing by that adult's:
  - legal representative; or
  - designated trusted person; or
  - next of kin.

In any event, the adult concerned must also not visibly express opposition to the research intervention either verbally or by their own behaviour.

For research projects carried out on adults who lack the capacity to provide informed consent, where that project cannot demonstrate an expected direct benefit to the adult concerned, in addition to all the above requirements the project:

- Must not entail more than minimal risks and burdens.
- Must be expected to yield substantial findings which could, in the long term, be beneficial to persons with the same disease or disorder, or in the same situation.

(Article 24(2), HRA.)

Informed Consent: Pregnant Women and Living Embryos and Foetuses

Research projects designed to modify the properties of an embryo or foetus for non-disease-related reasons are prohibited (Article 25, HRA).

Research projects that will have an expected direct benefit for the pregnant woman, or for the embryo or foetus, can only be carried out if the foreseeable risks and burdens (both for the pregnant woman and for the embryo or foetus) are not disproportionate to the expected benefits (Article 26(1), HRA).

Research projects that have no expected direct benefit for the pregnant woman, or for the embryo or foetus, are only permissible if they both:

- Entail no more than minimal risks and burdens for the embryo or foetus.
- Are expected to yield substantial findings which could, in the long term, be beneficial for pregnant women, embryos, or foetuses.

(Article 26(2), HRA.)

A pregnant woman can only be asked to participate in a research project concerning methods of induced abortion after that woman has decided to undergo an abortion, and the woman's consent to participation must also be provided (Article 27, HRA).

Informed Consent: Prisoners

Research projects involving prisoners cannot be conducted if such research would involve the relaxation of the prisoner's conditions of imprisonment (Article 29, HRA).

For a research project involving a prisoner that will have an expected direct benefit for that prisoner, whilst the general requirements for research involving persons apply, the requirements stipulated in Article 11(2) of the HRA do not apply (that is, that a research project involving particularly vulnerable persons can only be carried out if equivalent findings cannot be obtained by other means) (Article 28(1), HRA).

A research project involving prisoners that has no expected direct benefit can only be carried out if it entails no more than minimal risks and burdens (Article 28(2), HRA).

Informed Consent: Persons in Emergency Situations

A research project that will have an expected direct benefit to the person concerned can only be carried out in emergency situations if all the following conditions are met:

- Necessary measures have been taken so that the wishes of the person concerned can be determined as soon as possible.
- The person concerned does not visibly express opposition to the research intervention (either verbally or behaviourally).
- A doctor who is not participating in the research project is called in to safeguard the interests of the person concerned before their involvement in the project. In exceptional cases, where there are good reasons for so doing, the doctor can be called in at a later stage.

(Article 30(1), HRA.)

Where a research project has no expected direct benefit to the person concerned, in addition to the above requirements, it can only be carried out in emergency situations where it both:

- Entails no more than minimal risks and burdens.
- Is expected to yield substantial findings which could, in the long term, be beneficial for persons with the same disease or disorder, or in the same situation.

(Article 30(2), HRA.)

The subject of a research project carried out in an emergency situation must provide their informed consent to that project as soon as is practically possible. Where such consent is refused, the biological material and any data collected cannot be used for the research project (Article 31, HRA; Article 15, ClinO).

Risk Assessment

In general, in every research project, the risks and burdens for the participants must be minimised as far as possible and the likely risks and burdens for the participants must not be disproportionate to the expected benefits of the research project (Article 12, HRA).

In addition to this principle of risk reduction, the risk-based regulation of clinical trials is reflected in various instances. The ethics committee reviews the protocol of a clinical trial with regard to the ratio between the likely risks and burdens and the expected benefits, as well as the measures taken to minimise risks and burdens for participants. For clinical trials of medicinal products, Swissmedic reviews the risk assessment and risk management based on the medicinal product safety data (Article 32(1)(c), ClinO). Further, the categorisation of clinical trials often is directly or indirectly linked to the risks to which participants may be exposed during trials (for example, see Article 61 of the ClinO).

Outcome of Assessment

Appeals against decisions of the competent ethics committee can first be made to the appeal bodies provided for by the respective cantonal law. This ensures a full review of the facts and the accurate application of the law. However, the appropriateness of the decision is expressly excluded from this review (Article 50(2), HRA). The decisions of these appeal bodies can then be further appealed to the Federal Supreme Court (Article 50(1), HRA).

Appeals against decisions of the competent federal authority, in particular of Swissmedic, must first be made to the Federal Administrative Tribunal. The Tribunal's review fully covers the facts, the accurate application of the law, and the appropriateness of the decision. The Tribunal's decision can then also be appealed to the Federal Supreme Court (though the Federal Supreme Court's authority to review is limited to violations of law).

A sponsor can withdraw an application for authorisation of a clinical trial at any time.

Conducting and Managing a Clinical Trial

Ethical Guidelines and GCP

Authorisation will be granted by the ethics committee if, among other things, the ethical requirements of the HRA are met (Article 45(2), HRA). The *Principles and Procedures for Integrity in Scientific Research* issued by the Swiss Academies of Arts and Sciences is applicable in this regard (Annex 1 No. 1,ClinO). Regarding the rules of GCP, the *ICH GCP E6(R2)* applies for clinical trials of medicinal products and transplant products (Annex 1, ClinO). The ICH GCP E6(R2) partly refers to the World Medical Association's (WMA) Declaration of Helsinki (available on the website of the WMA) regarding applicable ethical principles.

Various templates, checklists, and other guidance documents are provided by swissethics and several cantonal ethics committees online. This includes, for example, a comprehensive template for study protocols that cites the relevant provisions of applicable laws and regulations, as well as the ICH GCP E6(R2).

Reporting Safety Information

Reference Safety Information (RSI**)**

The RSI is part of the IB, which must be contained in the clinical trial application dossier for all IMPs:

- Without a marketing authorisation in Switzerland or a country whose GMP control system is recognised as equivalent to the Swiss system (Annex 4 Nos. 2.4, 3.4(a), and 3.5(d), ClinO).
- With a marketing authorisation in Switzerland that are not used in accordance with the approved product information (Annex 4 No. 1.5, ClinO).

According to Swissmedic, the RSI should meet the requirements specified in the Clinical Trial Facilitation Group's (CTFG):

- *Q&A Document - Reference Safety Information* (dated November 2017).
- *RSI Q&A cover note* (dated 8 March 2018).

For IMPs with a marketing authorisation in several GMP-equivalent countries with different product information/summary of product characteristics (SmPC), Swissmedic requires that the sponsor selects the most appropriate product information/SmPC as the RSI. A justification of the choice of RSI must also be provided. If the IB is chosen as the RSI, the IB must be submitted in addition to the product information/SmPC.

If an IMP is identified in the trial protocol only by its active substance, and different products with marketing authorisation containing this substance may be used in the trial, then Swissmedic requires only one product information/SmPC to be selected as the RSI. A justification of that choice, and a list of the products (name and authorisation number) used at Swiss clinical trial sites, must also be provided.

If an IMP with a marketing authorisation in Switzerland or a GMP-equivalent country is not used in accordance with the terms of that authorisation (for example, a new route of administration, a new dosage or frequency, a new indication, and so on), then Swissmedic requires that either an IB specific to that new use is prepared, or a new section to the general IB is inserted. The IB must contain separate RSI sections for each indication. This document must be submitted in addition to the product information/SmPC.

In the context of investigator-initiated trials, if the sponsor does not have access to an IB for the used IMP with a marketing authorisation, then Swissmedic allows the product information or section 4.8 of the SmPC to be used as the RSI, subject to a sufficient justification by the sponsor in the clinical trial application cover letter. Otherwise, the RSI must always be a clearly separated specific section within the IB, as detailed in the CTFG's *Q&A Document – Reference Safety Information* (dated November 2017).

Adverse Events and Serious Adverse Events

For adverse events in clinical trials of medicinal products, the following provisions apply:

- For category C clinical trials, if an adverse event (which is not classified as serious) occurs during the trial, it must be documented by the investigator in a standardised manner.
- For category B clinical trials, if an adverse event occurs during the trial, it must be documented similarly to category C clinical trials, if this is envisaged in the protocol or was requested by the authorities responsible for authorisation.
- For category A clinical trials, there is no obligation to document an adverse event.

(Article 39, ClinO.)

If, during a clinical trial of medicinal products, a serious adverse event occurs, the investigator must document it in a standardised manner and notify the sponsor within 24 hours after the event becomes known. Events which are not to be reported according to the protocol are exempt. In the absence of provisions to the contrary in the protocol, the investigator must notify the competent ethics committee of a fatal serious adverse event occurring at a trial site in Switzerland within seven days (Article 40, ClinO).

Suspected Unexpected Serious Adverse Reactions (SUSARs)

If, during a clinical trial, a SUSAR occurs, the investigator must document this in a standardised manner and notify the sponsor within 24 hours after it becomes known.

The investigator must notify the competent ethics committee of:

- A fatal SUSAR occurring in Switzerland within seven days of its occurrence.
- Any other SUSAR occurring in Switzerland within 15 days of its occurrence.

(Article 41, ClinO.)

For category B and C clinical trials, a similar notification must also be submitted to Swissmedic by the sponsor. For category A clinical trials, however, the sponsor is subject to the notification requirements contained in paragraphs 1 and 2 of Article 59 of the TPA, which requires notification to Swissmedic of any adverse event or reaction of authorised therapeutic products (Article 41, ClinO).

Submitting Safety Update Reports

Once a year, the investigator must present to the competent ethics committee a list of events and deficiencies in the medicinal product under investigation and adverse reactions and, on this basis, must submit a report on their severity and causal relationship to the intervention, and on the safety of participants (this is the annual safety report (ASR)). In the case of clinical trials also conducted abroad according to the same protocol, the events and deficiencies in the medicinal product under investigation and adverse reactions occurring abroad must also be included in the list and the ASR. For category B and C clinical trials, the ASR must also be submitted to Swissmedic by the sponsor (Article 43, ClinO).

Other Reporting Requirements

If immediate safety and protective measures have to be taken during the conduct of a clinical trial, the investigator must notify the ethics committee of these measures, and of the circumstances necessitating them, within seven days of the measures being taken.

In the case of clinical trials with devitalised human tissue or cells, or derivatives of those, this deadline is shortened to two days.

For category B and C clinical trials, these notifications must be submitted to Swissmedic (instead of the ethics committee) by the sponsor (Article 37, ClinO).

Certain notification and reporting duties also apply upon the completion, discontinuation, or interruption of clinical trials (see *Suspension or Termination* and *End of the Clinical Trial*).

Safety and Protective Measures

Anyone who conducts a research project must, before it starts, take all the measures required to protect the participants (Article 15(1), HRA). As a general duty of the investigator, this includes ensuring effective monitoring measures to detect the effects of the clinical trial on each subject's health and any other change in a subject's health status.

If, during the research project, circumstances arise which could jeopardise the safety or health of the participants, or lead to a negative risk-benefit ratio, all the measures required to ensure each subject's protection must be taken without delay (Article 15(2), HRA). Existing protective measures must therefore be reviewed on an ongoing basis and adapted as quickly as possible as new circumstances become known.

Changes to the Clinical Trial

Amendments to the Clinical Trial Documentation

Significant changes to an authorised clinical trial must be authorised by both the competent ethics committee and the competent federal authority (typically, Swissmedic). The investigator must submit to both authorities any affected application documents and provide information on the reasons for the change. Both authorities will reach a decision within 30 days of receipt of the request to change the documentation (Articles 29, 34, and 55, ClinO).

Suspension or Termination

The investigator must notify the ethics committee of the discontinuation or interruption of the clinical trial within 15 days of that discontinuation or interruption. They must state the reasons for the discontinuation/interruption in the notification. Additionally, the investigator must submit a final report to the ethics committee within one year after the completion or discontinuation of the clinical trial, unless a longer period is specified in the protocol. For category B and C clinical trials, the notification and report must be made to Swissmedic (instead of the ethics committee) by the sponsor (Article 38, ClinO).

The competent federal authority can revoke or suspend its authorisation in the following circumstances:

- The health or safety of participants is at risk (for example, as a result of inadequate product safety or manufacturing defects as a result of the manufacturing process of medicinal products).
- The quality of the data collected during the clinical trial is poor.
- The clinical trial is not conducted in accordance with the approved application documents.
- The authorisation and notification requirements have not been complied with.

(Article 47, ClinO.)

The continuation of a clinical trial without authorisation is subject to criminal sanctions (Article 62(1)(a), HRA; Article 86(1)(f), TPA).

End of the Clinical Trial

The investigator must notify the ethics committee of the completion of a clinical trial in Switzerland within 90 days of its completion. Completion of a clinical trial is marked by the last participant's final follow-up visit, in the absence of provisions to the contrary in the protocol. For category B and C clinical trials, this notification must be made to Swissmedic (instead of the ethics committee) by the sponsor within the same timeframe (Article 38, ClinO).

For category B and C clinical trials, the sponsor must submit a final report to Swissmedic within one year after completion of the trial, unless a longer period is specified in the protocol (Article 38, ClinO).

The sponsor is also subject to various retention and registration obligations after completion of the trial.

The sponsor must retain all data relating to the clinical trial until the expiry date of the last batch supplied or manufactured of the medicinal product under investigation, but at least for ten years after the completion or discontinuation of the clinical trial. In the case of devitalised human tissue or cells, or derivatives of those, that can be implanted, the retention period amounts to a minimum of 15 years. The investigator must retain all documents required for the identification and follow-up of participants, and all other original data, for at least ten years after completion or discontinuation of the clinical trial. This retention period amounts to a minimum of 15 years for implantable devitalised human tissue or cells, or derivatives of those (Article 45, ClinO). For clinical trials of transplant products or blood and blood products, the retention period amounts to 30 years (Article 40(1), TPA).

To date, a legal obligation to publish the results of clinical trials is only provided for in the case of clinical trials with medicinal products. The marketing authorisation holder of a medicinal product for human use containing a new active substance must publish the results of clinical trials conducted for its development in the form of a report within three months of the marketing authorisation being granted (Article 71, *Ordinance on Medicinal Products (Verordnung über die Arzneimittel) (VAM)*, available in German, French, and Italian). However, if the regulatory authority of a country with comparable medicinal product control has already made the report on the results publicly available, the marketing authorisation holder can also refer to that publicly available material.

The minimum content of the report is specified in Annex 5 of the VAM. The report can be published in one of the official languages of Switzerland or in English. The report must be anonymised. The marketing authorisation holder can exclude information that constitutes trade or business secrets from publication (Articles 71 to 73, VAM). The relevant legal provisions (Articles 71 to 73 and Annex 5, VAM) do not specify where the trial results must be published, or who must have access to the report.

Decentralised or Hybrid Clinical Trials

The question of whether, and in which specific settings, decentralised clinical trials (DCTs) and hybrid DCTs are permitted under the current Swiss legislation requires a differentiated analysis and examination on a case-by-case basis. Swiss law contains possibilities for integrating new technologies without the need to change the current law. However, it is not possible to identify, in a general manner, which provisions of national (and international) law affect DCTs (and to what extent they are affected), or whether (and how) the required compliance of clinical trials with the legislation can be achieved under different DCT settings. Therefore, researchers are recommended to liaise closely with Swissmedic and the ethics committees beforehand to clarify specific questions relating to the conduct of DCTs.

Subject Recruitment

Given the modalities of recruitment and selection, there is a risk that it will mainly be technically versed individuals who decide to take part in DCTs. However, a representative sample of trial participants must be ensured to avoid any selection bias. If the discussion about participation between the investigator and the subject during the informed consent process is done via electronic platforms, several additional aspects must be considered. Ethical principles and specific requirements such as subject autonomy and time to think about trial participation must be addressed. The requirements of the Federal Act on Data Protection of 19 June 1992 (FADP) (for example, with respect to server location) must be fulfilled (Article 7, FADP). The protection of personal data from unauthorised or accidental disclosure must be safeguarded, in particular by ensuring that during any data transmission of personal data is adequately protected from unauthorised or accidental disclosure to the sponsor or companies involved in this process (*ICH Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2): 2.11*; Article 7(1), FADP).

Use of E-Consent/Electronic Signature

As a principle, Swiss law requires the signature to be handwritten but it also defines a qualified electronic signature as equivalent to a handwritten signature (Article 14(2), Code of Obligations; cf *Federal Act on Electronic Signatures*). However, the use of a qualified electronic signature is not yet a practical solution, because of the effort every single trial participant would have to undertake to be able to deliver such a qualified electronic signature. Therefore, a conventional, handwritten signature is routinely required in Switzerland. It is also necessary that, even when using electronic media, the information and consent process, as well as the respective versions of the patient information and declaration of consent used, are documented in a GCP-compliant manner and are available for monitoring, audits, and inspections. The statutory archiving obligation for these source data must also be observed (Article 45(2), ClinO).

Home Health Visits

If trial-related interventions are performed outside the trial site with the trial subjects' consent (for example, in their homes), these tasks can be performed by commissioned service providers. It is necessary for each person who performs these interventions (at the responsibility of the investigator as part of the study team) to have appropriate training and have proven knowledge and experience (Article 6(4), ClinO; ICH Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2): 4.2.4). It is the responsibility of the investigator in Switzerland to monitor that the trial nurses carry out and document the study-specific interventions on the subject at home in accordance with the protocol. The investigator must ensure adequate medical care if adverse events occur outside the trial site, as well as the standardised documentation and protocol-compliant reporting of adverse events (Articles 39 to 41, ClinO; ICH Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2): 4.3.2).

Direct Deliveries of IMP

An IMP whose stability and safety profile has not yet been adequately characterised due to its early stage of development is unsuitable for dispensing and administration to the trial subjects at home. The same applies for IMPs that require preparation (for example, in a sterile environment) before administration, or those that are associated with a high risk of possible adverse reactions. If the IMP is dispensed outside the trial site, the requirements of GMP (Annex 1, *Ordinance on Licensing in the Medicinal Products Sector* (MPLO); Article 32(1)(d), ClinO), Good Distribution Practice (GDP), and of the applicable cantonal laws, must be fulfilled. If trial subjects are supplied directly, they must be given appropriate information and agree to the necessary transfer of personal data, and they must be instructed in advance about the correct handling, storage, and use of the IMP (to the latter: ICH Guideline for Good Clinical Practice E6 (R2): 4.6.4 and 4.6.5).

Remote Safety Monitoring and Remote Access to Electronic Health Records (EHRs)

Data capture outside the trial site using mobile technologies is addressed in item 2.4. of the *Position Paper on decentralised clinical trials (DCTs) with medicinal products in Switzerland* by Swissmedic and swissethics. Where the intention is to use

mobile technologies to record data outside of the trial site, it must be ensured that the trial subjects have given their prior consent to data being recorded by the device (for example, wearables) or entered by the trial subjects (for example, electronic patient reported outcome (ePRO)). The trial subjects must also be trained in the correct use of the mobile technologies. If source data are recorded directly in the CRF, this must be identified as such in the protocol. If data are recorded automatically, it should be ensured that only trial-specific data are recorded by the mobile technology being used. The data that are considered to be source data must be stated in writing before the clinical trial begins. The mobile technologies must be demonstrably validated and must comply with the relevant standards for accuracy, precision, reproducibility, reliability, and responsiveness (ICH Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2): 5.5.3). The sponsor must define measures to ensure that the recorded data actually originates from the trial subjects or was generated by the trial subjects (and not by a third person). It must be ensured that the sponsor has no access to personal or identifiable information relating to the trial subjects. To ensure the protection of personal data from unauthorised or accidental disclosure, the sponsor must protect this data from any form of intervention from outside, whether accidental or intentional. This protection applies to:

- All personal, identifiable information.
- All personal health-related data.
- Devices and mobile technologies used to collect, store, or transmit data.

If sensitive personal data is stored on a central server, the server must be located in Switzerland, the EU, or a country whose legislation guarantees adequate data protection under Article 6(1) of the FADP.

Requirements for the Use of Computerised Systems

Remote source date verification is addressed in item 2.6 of the Position Paper on decentralised clinical trials (DCTs) with medicinal products in Switzerland by Swissmedic and swissethics. If persons commissioned by the sponsor review uncoded personal data from trial subjects in the course of source data verification, and this review is not performed in person at the trial site but remotely, suitable technical and organisational measures must be taken to ensure compliance with the FADP. If the trial site sets up separate electronic access for the monitors to the trial patients' source data for the purpose of verifying the source data, measures must be taken to ensure that this application is appropriately protected (for example, with two-factor authentication and a VPN). The monitor can only be granted read-only rights. Remote source data verification should be performed from Switzerland. Whenever uncoded personal data, regardless of whether non-genetic or genetic, are reviewed, the trial subjects must be informed comprehensively and must give their explicit consent.

Other Important Considerations in Clinical Trials

Data Privacy

Various federal and cantonal regulations govern data protection in the context of clinical trials. Principally, the HRA contains rules for the processing of personal data by researchers. Articles 58 to 60 of the HRA also contain rules for the enforcement authorities (Swissmedic, the ethics committees, FOPH, and so on). Depending on the type of the clinical trial, the data protection provisions of the relevant sector law (for example, the TPA and the Transplantation Act) will also apply. In addition, the FADP must be observed, which regulates the processing of personal data by private persons or organisations, and federal authorities. If individual provisions of the FADP are stricter than those of the HRA, the former take precedence. Finally, the cantonal data protection laws apply to data processing by cantonal authorities.

To date, as far as can be seen, no specific guidance is available from the authorities on the implementation of data protection legislation in the context of clinical trials. Additional guidance on data protection is made available on the website of the *Federal*

Data Protection and Information Commissioner (FDPIC) and upon request by the competent authorities (Swissmedic, FOPH, and the ethics committees).

Confidentiality

Persons who initiate and carry out research projects (sponsors, investigators, and so on) are subject to a duty of professional confidentiality when conducting research involving human beings. That duty is subject to criminal law (Article 321 bis, *Swiss Criminal Code* (SCC)).

Similarly, the HRA provides for a duty of confidentiality for persons responsible for the enforcement of the HRA (Article 57, HRA). The following are also subject to criminal sanctions:

- A breach of official secrecy by any person in their capacity as a member of an authority, or as a public official.
- A breach of professional confidentiality by the following persons from the health sector in their professional capacity:
    - doctors;
    - dentists;
    - chiropractors;
    - pharmacists;
    - midwives;
    - psychologists;
    - nurses;
    - physiotherapists;
    - occupational therapists;
    - dieticians;
    - optometrists;
    - osteopaths;
    - assistants to any of the foregoing persons; and
    - students who have come to their knowledge in the course of their studies.

(Articles 320 and 321, SCC.)

Requirements Related to IMPs

Labelling Requirements

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 (see *Application Documents*). The compulsory elements of the labels

for IMPs are laid down in the *European Commission: Public Health: Eudralex – Volume 4 – Good Manufacturing Practice (GMP) guidelines* (EU GMP Guidelines) (at *Annex 13: Manufacture of Investigational Medicinal Products*). If a commercially available medicinal product is used as test product or comparator product, a considerable amount of information (such as the batch number, expiry date, and storage conditions) is already included on the normal commercial label. In these cases, it is possible to only use an additional label with the following elements:

- Trial number or trial ID.
- Trial subject number or patient ID.
- Name of the sponsor, investigator, or contract research organisation.
- Contact details of the main contact for information.

(*Swissmedic's FAQ on clinical trials with medicinal products*, p11.)

It is acceptable to indicate the global sponsor's name and phone number, as appropriate. 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. 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.

Manufacturing and Importing/Exporting IMP

As part of the authorisation procedure for clinical trials, Swissmedic must verify, in the case of medicinal products, whether they comply with the EU GMP Guidelines (Article 54(4), TPA; Annex 4, ClinO). *Commission Directive 2003/94/EC* (EU GMP) laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use applies for IMPs for human use under the EU GMP Guidelines (Annex 1, MPLO). IMPs used in clinical trials in Switzerland must therefore have been manufactured in accordance with these rules.

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. No further import licences are required where new trial centres are added to the original authorised trial. This licence is restricted to the IMPs used in the clinical trial, and its validity is restricted to the duration of the clinical trial. However, this licence is not required if the importing person or institution already holds a general import licence for medicinal products (Article 19, MPLO).

Payments and Incentives

No person can receive payment or any other non-cash advantage for their participation in a research project which has an expected direct benefit. Participation in a research project which has no expected direct benefit can be appropriately compensated (Article 14(1), HRA). In addition, it is permissible to reimburse a trial subject for their expenses and lost income as a result of participating in a trial. However, no person can demand or accept payment or any other non-cash advantage from another in return for the latter's participation in a research project (Article 14(2), HRA).

Any person who wilfully or negligently makes a payment or provides any other non-cash advantage to a person to participate in a research project with an expected direct benefit, or demands or accepts payment or any other non-cash advantage from a person for participation in a research project, will be liable to a fine (Article 63(1), HRA).

GxP

Regarding the applicable GMP rules, Annex 1, No. 1 of the MPLO refers to the following provisions:

- EU GMP, laying down the principles and guidelines of Good Manufacturing Practice in respect of medicinal products for human use and investigational medicinal products for human use.
- Commission Directive 91/412/EEC, laying down the principles and guidelines of Good Manufacturing Practice for veterinary medicinal products.
- Guide to Good Manufacturing Practice for medicinal products for human use and medicinal products for veterinary use of the European Commission (EudraLex, Volume 4).
- Principles and Guidelines for Good Manufacturing Practice in accordance with the Convention for the mutual recognition of inspections in respect of the manufacture of pharmaceutical products of 8 October 1970. There are no references to good laboratory practice rules in connection with clinical trials.

END OF DOCUMENT