

# Clinical Protocol Template for ClinO, Chapter 4 «Other Clinical Trials»

## General information and instructions

### Legal basis for other clinical trials

The laws applicable in this template are the Federal Act on Research involving Human Beings (HRA) and its applicable ordinance (ClinO e/KlinV d/OClin f/OSRUm i) and the ICH-GCP E6, section 6.

The template is intended for studies:

- which are interventional clinical trials according to the definition given in HRA, Art. 3 lit. I and fall into the scope of ClinO Chapter 4 other clinical trials\*,
- performed in Switzerland, respectively where the Investigator is located in Switzerland, (possibly there are additional international sites)
- where the study question does not relate to the use of drug(s), medical device(s), transplant products, gene therapy, genetically modified or pathogenic organisms and transplantation effect(s), but to other kinds of medical, psychological, physiological interventions or other procedures,

\* Intervention means any action performed on the trial participant whose effect on that person shall be investigated.

For multicenter studies, the language used in the protocol should be English.

For monocentric studies the protocol may also be written in a national language, i.e. German, French or Italian, even though the template is in English.

Ensure that the criteria for selecting the persons intended to participate and the trial design allow an appropriate representation of the groups of persons who are relevant for answering the scientific question; in particular, they must take into account the distribution of genders and age groups. All applications submitted to the Ethics Committee should also address the issue of **sex and gender** (unless totally irrelevant). Based on the recommendations “sex and gender in research involving humans according to the HRA” ([swissethics.ch / topics / sex and gender equitable research](http://swissethics.ch/topics/sex-and-gender-equitable-research)), a set of instructions has been elaborated by a group of experts to guide researchers in the writing of their research documentation, including a grid inspired by the SAGER guidelines. Researchers need to know that the check-up grid provided in the instructions are used by ethics committees' members to review all protocols and related documents.

- Please use the text passages that are written in black.
- Please delete all instructions and explanations that are written in blue, including this page and the table 'Change History'.
- Write the protocol in a gender-neutral language.
- Header and footer should contain the following information on all pages: [Study ID], [version x, DD/MM/YYYY], [Page x of xx].
- In places where the information is redundant, it is acceptable to refer to another section or to state its redundancy but the section must not be deleted.
- The protocol must be submitted via BASEC in an Optical Character Recognition (OCR) PDF format, i.e. in a searchable PDF format.

- The protocol has to be signed by the principal investigator, the sponsor (if applicable) and in case of a multicentric project by the different local principal investigators as well. Electronic signatures are accepted under the following conditions: The service provider used for the electronic signature process must have a system that verifies that the electronic signature is correct and genuine and properly embedded in the document. Copy-paste of scanned signatures are not accepted. If the protocol is signed by hand, the scans of the wet-ink signed signature pages are uploaded to BASEC separately.
- Refer questions regarding use of this template to swissethics, [info@swissethics.ch](mailto:info@swissethics.ch), phone: +41 31 306 93 95, [www.swissethics.ch](http://www.swissethics.ch).

**Be aware that the content of the protocol has to be identical to the content of the BASEC research study application form. You can refer to the trial protocol in the research study application form in BASEC to avoid redundancies but not vice versa.**

### Change history

Version Nr	Version date	Modified without version change	Description, comments	Control
1.0	30.08.2018		Initial version	PG
		X	Corrected Typo chapters' numbers in table of contents	PG
1.1	02.12.2020		Added sub-chapter "notification of safety and protective measures" in chapter 6.2.	PG
		X	Add note for gender research to chapter 4.1, 11.4, and 10. Updated 'General information and instructions' with a note on the use of the electronic signature.	PG
1.2	30.12.2021		Updated chapter 6.7 "Notification and reporting upon completion, discontinuation or interruption of the study" with the reporting obligation according to ClinO Art. 38.	PG
		X	Replaced 'ASR/DSUR' by 'ASR' throughout the template. Corrected some typos	PG
1.3	20.07.2022		Chapter 6.8 Insurance: substantial revision.	PG
1.4	22.11.2022		Deleted reference to ClinO, Art. 44 and corresponding paragraph from chapter 6.4 Radiation	PG
		X	Instructions on sex and gender-equitable research have been added on page 1	PG
2.0	16.09.2024		New version adapted to the amended ClinO, status as of November 1, 2024.	PG
		X	Removed duplicate "statistical consideration" in the synopsis. Added reference to 'Clinicaltrials.gov' in chapter 9	PG
2.1	13.11.2024		Updated chapter 8.3 Confidentiality, according to art. 6 ClinO	PG
2.2	08.01.2025		Updated Chapter 4.2 Recruitment, according to art 62 lit. c ClinO, resp. art 38 ClinO	PG



**Please remove the 'General information and instructions'**

**and the table 'Change history'**



## Protocol Title

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Study Type:	Other Clinical Trial according to ClinO, Chapter 4
Risk Categorisation:	Risk category A or B according to ClinO, Art. 61
Study Registration:	1. Name of primary study registry and registration number (if not yet registered, name the intended registry) 2. Registration number from the FOPH portal SNCTP (Swiss National Clinical Trial Portal) and, if applicable, other registries and numbers
Sponsor:	Name and contact details of Sponsor or Sponsor-Investigator
Principal Investigator	Name and contact details of Principal Investigator
Investigated Intervention:	Description of investigated intervention
Protocol ID	If applicable, e.g. Protocol number
Version and Date:	Version x (dated DD/MM/YYYY)

### CONFIDENTIALITY STATEMENT

If applicable, add an institutional confidentiality statement here respecting that it is not in conflict with the applicable transparency rules.

e.g. "The information contained in this document is confidential and the property of xx (or "the sponsor"). The information may not - in full or in part - be transmitted, reproduced, published, or disclosed to others than the applicable Competent Ethics Committee(s) and Regulatory Authority(ies) without prior written authorisation from the sponsor except to the extent necessary to obtain informed consent from those who will participate in the study.

## PROTOCOL SIGNATURE FORM

Study Title        Full study title as written out on title page

Study ID            If applicable

The Sponsor or the Sponsor-Investigator has approved the protocol version x (dated DD/MM/YYYY) and confirm hereby to conduct the study according to the protocol, current version of the World Medical Association Declaration of Helsinki, and ICH-GCP guidelines as well as the local legally applicable requirements.

A clinical trial covered by ClinO Chapter 4 may be conducted in accordance with other rules than ICH-GCP guidelines, provided that such rules are recognised in the specialty in question and the protection of participants and data quality and security are guaranteed (ClinO Art. 5, Abs 2). If the clinical trial is not conducted according to ICH-GCP guidelines, the paragraph above must be adapted accordingly.

If Sponsor and Principal Investigator are the same person (Sponsor-Investigator), please delete the additional signature line for the Principal Investigator of the study.

### **Sponsor:**

Name: *Name in print*

Date: \_\_\_\_\_

Signature: \_\_\_\_\_

### **Principal Investigator:**

Name: *Name in print*

Date: \_\_\_\_\_

Signature: \_\_\_\_\_

(only for multicentric studies, delete this page for monocentric studies)

**Local Principal Investigator at study site:**

In multicenter studies, this page must individually be signed by all participating Local Principal Investigators.

Site: *Name and address of site*

Principal Investigator: *Name in print*

Date: \_\_\_\_\_

Signature: \_\_\_\_\_

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## GLOSSARY OF ABBREVIATIONS

<i>AE</i>	<i>Adverse Event</i>
<i>BASEC</i>	<i>Business Administration System for Ethical Committees</i>
<i>CRF</i>	<i>Case Report Form</i>
<i>CTCAE</i>	<i>Common Terminology Criteria for Adverse Events</i>
<i>FADP</i>	<i>Federal Act on Data Protection (in German: DSG, in French: LPD, in Italian: LPD)</i>
<i>eCRF</i>	<i>electronic Case Report Form</i>
<i>FOPH</i>	<i>Federal Office of Public Health</i>
<i>GCP</i>	<i>Good Clinical Practice</i>
<i>HRA</i>	<i>Human Research Act (in German: HFG, in French: LRH, in Italian: LRUm)</i>
<i>ICH</i>	<i>International Conference on Harmonisation</i>
<i>ClinO</i>	<i>Ordinance on Clinical Trials in Human Research (in German: KlinV, in French: OClin, in Italian: OSRUm)</i>
<i>SAE</i>	<i>Serious Adverse Event</i>

Please expand the list of abbreviations as needed.

# 1 STUDY SYNOPSIS

<b>Sponsor / Sponsor-Investigator</b>	Name(s) and contact details of Sponsor / Sponsor-Investigator
<b>Study Title</b>	Full protocol title
<b>Short Title / Study ID</b>	Abbreviated protocol title or, if applicable, study ID, e.g. study number
<b>Protocol Version and Date</b>	Version x (dated DD/MM/YYYY)
<b>Study Registration</b>	Name of study registry, registration number (if not yet registered, name the intended registry).
<b>Study Category and Rationale</b>	Risk category and rationale. State the risk category of the study according to ClinO, Art. 61 Refer to ClinO Art 2 for what was intended for minimal risks and burdens and for a list of examples.
<b>Background and Rationale</b>	Provide a short background and the rationale for the study, this includes the health condition studied. Are "sex and gender" dimensions relevant to the topic of the study (specifying genetic/biological or social mechanisms at play)? To address this question, refer to the recommendations "sex and gender in research involving humans according to the HRA" (swissethics.ch / topics / sex and gender equitable research). If it is considered that "sex and gender" dimensions are not relevant, provide a justification.
<b>Risk / Benefit Assessment</b>	Risk / benefit assessment.
<b>Objective(s)</b>	Primary objective(s) and, if applicable, secondary including safety objective(s).
<b>Endpoint(s)</b>	Primary endpoint(s) and, if applicable, secondary including safety endpoint(s).
<b>Study Design</b>	Design attributes (e.g. confirmatory, non-randomised / randomised, open / single-blinded / one-arm / two-arm, cross-over/controlled).
<b>Inclusion- / Exclusion Criteria</b>	Brief description of the anticipated study population, the key inclusion and exclusion criteria and if applicable, the reasons for inclusion of vulnerable participants. Are "sex and gender" dimensions relevant to the topic of the study? To address this question, refer to the recommendations "sex and gender in research involving humans according to the HRA" (swissethics.ch / topics / sex and gender equitable research).
<b>Number of Participants with Rationale</b>	Number of participants in the entire study, provide the total number as well as the number for each treatment group. Briefly explain the rationale for the number of participants.
<b>Study Intervention</b>	Description of the study intervention.
<b>Control Intervention</b>	If applicable, description of the control group.
<b>Study procedures</b>	Description of the overall study procedures.
<b>Study Duration and Schedule</b>	Estimated duration for the main investigational plan, i.e. from start of screening of first participant to last participant last visit and finishing the study.  Planned MM/YYYY of First-Participant-In Planned MM/YYYY of Last-Participant-Out
<b>Investigator(s)</b>	Name(s) and contact details of Investigator(s).
<b>Study Center(s)</b>	Name(s) and address of Study Center(s). If multicenter study, number of centers to be involved. If multinational study, countries to be involved.
<b>Statistical Considerations:</b>	A very brief description of the main elements of the statistical methodology to be used in the study. Explanation to sample size. Are "sex and gender" dimensions relevant to the topic of the study? To address this question, refer to the recommendations "sex and gender in research involving humans according to the HRA" (swissethics.ch / topics / sex and gender equitable research).
<b>Data privacy</b>	Explain how the privacy of data is guaranteed. Mention coding and confidentiality while handling data and if applicable biological material.



<b>Ethical consideration</b>	Explain the scientific value of the study, justify the methodology give a statement to the risks and the benefit. Explain if you include vulnerable populations.
<b>GCP Statement</b>	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP, the HRA as well as other locally relevant legal and regulatory requirements. A clinical trial covered by ClinO Chapter 4 may be conducted in accordance with other rules than ICH-GCP guidelines, provided that such rules are recognised in the specialty in question and the protection of participants and data quality and security are guaranteed (ClinO Art. 5, Abs 2). If the clinical trial is not conducted according to ICH-GCP guidelines, the paragraph above must be adapted accordingly.

## 2 BACKGROUND AND RATIONALE

The study must address a relevant scientific question and potentially provide valuable generalizable knowledge. Scientific value is essential for the ethical conduct of every study (HRA, Art. 5). The legal requirements must be fulfilled and the ethical standards must be guaranteed. Note that research on humans is only allowed as long as an equivalent new knowledge cannot be gained otherwise (HRA, Art. 11).

Provide information about the following points:

- given the scientific background of the study (e.g. (disease) background, epidemiology, current standard of care, etc.);
- give a scientific rationale for the study;
- cite relevant literature including relevant systematic reviews;
- describe the research question and explain why you chose the research question that will be answered through this study;
- provide information about the intended intervention (e.g. surgery, physiotherapy, psychology, examination method or whatever applies);
- explain why the study generates new scientific generalizable knowledge.
- state the risk category of the study according to ClinO, Art. 61 and explain the rationale behind the risk categorisation. Refer to ClinO Art 2 for what is intended for minimal risks and burdens and for a list of examples.

Are “sex and gender” dimensions relevant to the topic of the study (specifying genetic/biological or social mechanisms at play)? To address this question, refer to the recommendations “sex and gender in research involving humans according to the HRA” ([swissethics.ch / topics / sex and gender equitable research](http://swissethics.ch/topics/sex-and-gender-equitable-research)). If it is considered that “sex and gender” dimensions are not relevant, provide a justification.

## 3 STUDY OBJECTIVES AND DESIGN

### 3.1 Hypothesis and primary objective

Describe a clear hypothesis that will be answered through the study and the primary objective. In rare cases a hypothesis might not be required (e.g. exploratory studies).

If applicable, describe secondary objectives.

### 3.2 Primary and secondary endpoints

The primary endpoint is the main result that is measured during or at the end of an intervention to verify whether the intervention (i.e. the administrated treatment, the surgical procedure, the physiotherapy etc.) was successful or not. Describe the variable of primary interest, the rationale for its selection, the method and as applicable the time point of assessment. In general, a single variable and a single time point are used for the primary endpoint. Under certain circumstances, a combined primary endpoint is possible, but should be carefully determined together with trial statistician.

If applicable, provide a description of all secondary endpoint variables to be assessed. The secondary endpoint(s) are used to answer the secondary objectives.

If applicable, provide a description of the safety endpoint variables referring to e.g. specific adverse events (AEs), the rate of adverse events in general, laboratory parameters/vital signs, etc.

Describe baseline factors that may have an influence on the endpoints (e.g. age, gender, history, morbidity etc.).

### **3.3 Study design**

Both the study design and the selected methods should be appropriate to answer the research question and address the hypothesis.

Describe the general study design (e.g. confirmatory, non-randomised / randomised, one-arm / two-arms, open / single-blinded / cross-over) and the study setup (monocentric / multicenter, national / international). Discuss known or potential problems associated with the trial design.

Describe the methods of minimising bias (e.g. randomisation or other methods of minimising bias, such as the use of validated questionnaires).

### **3.4. Study intervention**

Describe the planned intervention (e.g. surgical procedure, physiotherapy or other) in detail. What exactly is done?

## **4 STUDY POPULATION AND STUDY PROCEDURES**

### **4.1 Inclusion and exclusion criteria, justification of study population**

Describe the study population and specify the total number of participants, including the control groups. Justify the choice of study population.

Ensure that the criteria for the study participant selection criteria and the trial design allow an appropriate representation of the groups of persons who are relevant for answering the scientific question; in particular, they must consider the distribution of genders and age groups. The exclusion or intended underrepresentation of relevant groups of persons must be stated and justified. See Art. 4a ClinO.

Describe how recruitment of the participants is conducted to ensure “sex and gender” balance is achieved, or give an explanation why this would not be possible and how this imbalance would impact the scientific validity of the investigation result. Refer to the recommendations “sex and gender in research involving humans according to the HRA” ([swissethics.ch / topics / sex and gender equitable research](http://swissethics.ch/topics/sex-and-gender-equitable-research)) to address “sex and gender” issues in this chapter.

List the study inclusion criteria, e.g.

- Group of people undergoing the intervention,
- Target disease / diagnosis,
- Able to give informed consent as documented by signature,
- Age,
- Clinical history,
- Ethnic or sociodemographic background,
- Lifestyle factors, etc.

List the study exclusion criteria, e.g.

- Pregnant or lactating women,
- Inability or contraindications to undergo the investigated intervention,
- Clinically significant concomitant diseases,
- Inability to follow the procedures of the study, e.g. due to language problems, psychological disorders, dementia, etc.,

- Previous enrolment in a clinical trial, etc.

For vulnerable participants (e.g. minors, participants incapable of judgment or participants under tutelage), the following questions need to be addressed (HRA, Art. 21 – 24):

- Rationale for the inclusion of vulnerable participants, i.e. reasons why comparable findings cannot be obtained from adults or those capable of judgment,
- Describe how the legal representative is informed regarding the procedures of the study and how his or her consent is obtained,
- In the event of a participant capable of judgment, describe how their assent is collected in addition to the consent of their legal representative,
- In the event of a participant incapable of judgment, mention that symptoms showing that the participant is unwilling to participate in the study will result in the participant being excluded from participation

For emergency situations with regard to vulnerable patients refer to HRA, Art. 30 f.

#### **4.2 Recruitment, screening and informed consent procedure**

Describe the location of recruitment (e.g. hospital, general practice, city, etc.) and procedures for participant recruitment (e.g. consecutive ongoing recruitment through the study coordinator in daily clinical practice, or recruitment through referring physician). When using advertisements or flyers as a recruitment tool, the documents must be submitted to the Ethics Committee for approval through BASEC and have to be in line with the guidelines published on [www.swissethics.ch](http://www.swissethics.ch).

swissethics strongly recommends to exclusively use the swissethics templates for writing the patient information documents and informed consent forms (ICF). They meet the legal requirements of Switzerland. The templates can be downloaded in German, French and Italian from [swissethics.ch / templates](http://swissethics.ch/templates) and checklists / patient information and declaration of consent.

In addition, a Guidance document on “How to write comprehensible patient information and consent forms for research” and a “Glossary for medical terms and abbreviations” are available on [swissethics.ch/templates/patient information and declaration of consent](http://swissethics.ch/templates/patient%20information%20and%20declaration%20of%20consent). swissethics strongly recommends to read the guidance document before writing the ICF. Check that the layout of the information respects the epicene language, or it is written in an inclusive format. Make sure that the information covers the study’s aspect related to “sex and gender” appropriately. If applicable, ensure that the issue of contraception and pregnancy are fully, clearly and appropriately presented (also eliminate or adapt the information to the considered participant population and study aspects)..

If the sponsor or investigator plan to develop an electronic ICF for the study, swissethics strongly recommends referring to the Guidance document on the development and use of an Electronic Informed Consent (eIC), published on [swissethics.ch/topics/position papers](http://swissethics.ch/topics/position%20papers), to meet international and national requirements.

Describe the informed consent process (HRA, Art. 7, 16 - 18, 42; ClinO, Art. 7 - 9) including ample time for consideration given to the participants as well as the opportunity to ask questions.

The investigators will explain to each participant the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail. Each participant will be informed that the participation in the study is voluntary and that he or she may withdraw from the study at any time and that withdrawal of consent will not affect his or her subsequent medical assistance and treatment.

The participant will be informed that his or her medical records may be examined by authorised individuals other than their treating physician.

All participants for the study will be provided a participant information sheet and a consent form describing the study and providing sufficient information for participant to make an informed decision about their participation in the study. **Enough time needs to be given to the participant to**

decide whether to participate or not. Please specify the time frame given.

The formal consent of a participant, using the approved consent form, will be obtained before the participant is submitted to any study procedure.

The consent form will be signed and dated by the investigator or his designee at the same time as the participant sign. A copy of the signed informed consent will be given to the study participant. The consent form will be retained as part of the study records. The informed consent process must be documented in the patient file and any discrepancy to the process described in the protocol must be explained.

If applicable: In case prenatal and presymptomatic genetic tests are provided for in the protocol, the ICF must comply with the provisions of Art. 7e ClinO. That is, the study participants must be informed that incidental findings are to be expected as a result of the genetic tests. The following aspects should be addressed and described:

- Describe how genetic counselling is provided to study participants, when prenatal or presymptomatic genetic testing is performed as part of the study. Describe how study participants will be informed of any incidental genetic findings that directly affect their health.

If applicable, if non-genetic incidental findings are expected in the study (e.g., radiological findings) that directly affect health care provided to the study participants, describe how they will be informed.

In case of vulnerable population the following aspects should be addressed and described:

- Describe how the legal representative is informed regarding the procedures of the study and how his or her consent is obtained;
- In the event that a minor and / or participant under tutelage is capable of judgment, describe how their consent (or assent) is collected in addition to the consent of their legal representative;
- In the event of a participant lacking capacity of judgment, mention that signs and symptoms showing that the participant is unwilling to participate in the study will result in the participant being excluded from participation.

Additionally, for emergency situations, the following aspects should be addressed and described (a guidance document and templates for writing ICF for investigations in emergency situations are available on [swissethics.ch/topics/research](http://swissethics.ch/topics/research) in an emergency situation):

- How the will of the participant can be elucidated without unjustified delay (e.g. patient's provision);
- Mention that signs and symptoms showing that the participant is unwilling to participate in the study will result in the participant being excluded from participation;
- The guarantee that a physician not participating in the investigation, safeguards participant interest and ensures proper medical care;
- How the informed consent for the use of the data is obtained from the participants after they have regained capacity, and in case of death of the participants before they regain capacity;
- How to obtain the informed consent from the legal representative of participants that are permanently lacking capacity, minors or participants under tutelage.

If necessary, describe screening process and screening procedures to meet inclusion and exclusion criteria. Any screening procedure that is not routine or daily practice can only be performed once informed consent has been obtained.

If applicable, describe any compensation or payments given to the participants. For guidelines concerning the remuneration of participants refer to HRA, Art. 14.

An ethical guideline concerning the remuneration of participants is also available on [www.swissethics.ch](http://www.swissethics.ch).

The first study participant must be included in the trial within two years following the issuance of the authorization by the Ethics Committee. An application for an extension is a substantial amendment; in the event of non-compliance, the study is deemed interrupted.

The investigator or the sponsor notifies the Ethics Committee of the first study participant, in accordance with art 62 lit. c ClinO, resp. art 38 ClinO. If the first participating person is not included in the trial within two years following the issuance of the authorization, the trial is considered interrupted (art. 23a ClinO). The clinical trial may not be commenced until an application for an extension of the time limit has been approved. The application for the extension is submitted to the CEC as a substantial amendment.

#### **4.3 Study procedures**

State the planned overall study duration, including the recruitment period and study duration for each patient. Provide a detailed description of the planned intervention (e.g. surgery, physiotherapy etc.) as well as all the additional planned procedures, such as examinations etc.

If applicable: Describe the material sampled and stored as well as methods and tests used for sample collection and analysis.

Compile a summary table listing all study visits, relevant procedures, and samplings as well as all timelines, i.e. a schedule of assessment. For the table, please refer to appendix 1. A table or a flowchart is always helpful.

Describe any expected biases to the study and measures taken to reduce them.

#### **4.4 Withdrawal and discontinuation**

Describe criteria for which a participant is withdrawn from the study (e.g. withdrawal of informed consent, disease progression, etc.).

Describe procedures to follow upon premature participant withdrawal or upon withdrawal of informed consent (e.g. final examinations, etc.). Describe how the data and material is anonymised in case of withdrawal. If this is not possible, provide a justification.

## **5 STATISTICS AND METHODOLOGY**

### **5.1. Statistical analysis plan and sample size calculation**

If a statistician is involved, please mention his or her name and responsibilities. State the hypotheses (null, alternative hypotheses) in terms of the primary endpoint. Describe the statistical rationale for sample size in terms of the power to test the primary endpoint. If this is not possible, the sample size should nonetheless be justified. Give a description of the planned statistical methods for the primary endpoint. State the level of significance used (e.g. significance level will be two-sided,  $\alpha = 0.05$ ). Give definitions for the different sets of analysis populations. In the event of multiple endpoints, statistical adjustments for multiple testing need to be considered. If applicable, explain the reason of any planned interim or safety analyses.

If “sex and gender” dimension is of primary interest, does the sample size estimation integrate this aspect? Are the statistical analyses appropriate? Include a statement that analyses of gender differences are planned. If such an analysis is not possible, please state the reasons.

Name the statistical software package(s) to be used.

If different statistical methods for each hypothesis testing are used, please describe them in detail. Mention procedures for reporting any deviations from the original statistical plan (e.g. any

deviation from the original statistical plan will be described and justified in the final trial report).  
Describe the stopping rules

## 5.2. Handling of missing data and drop-outs

Describe how missing data (e.g. multiple imputation, last observation carried forward, complete case analysis, etc.) will be handled.

Describe how drop-outs will be handled in order to ensure an adequate number of participants in the study (e.g. drop-outs are replaced by recruitment of new participants, etc.).

## 6 REGULATORY ASPECTS AND SAFETY

### 6.1 Local regulations / Declaration of Helsinki

This study is conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP [If the clinical trial is not conducted according to ICH-GCP guidelines, the paragraph above must be adapted accordingly \(ClinO Art. 5, Abs 2\)](#), the HRA as well as other locally relevant legal and regulatory requirements.

### 6.2 (Serious) Adverse Events and notification of safety and protective measures

An Adverse Event (AE) is any untoward medical occurrence in a patient or a clinical investigation participant which does not necessarily have a causal relationship with the trial procedure. An AE can therefore be any unfavourable or unintended finding, symptom, or disease temporally associated with a trial procedure, whether or not related to it.

A Serious Adverse Event (SAE) (ClinO, Art. 63) is any untoward medical occurrence that

- Results in death or is life-threatening,
- Requires in-patient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability or incapacity, or
- Causes a congenital anomaly or birth defect

Both Investigator and Sponsor make a causality assessment of the event to the trial intervention, (see table below based on the terms given in ICH E2A guidelines). Any event assessed as possibly, probably or definitely related is classified as related to the trial intervention.

Relationship	Description
Definitely	Temporal relationship Improvement after dechallenge* Recurrence after rechallenge (or other proof of drug cause)
Probably	Temporal relationship Improvement after dechallenge No other cause evident
Possibly	Temporal relationship Other cause possible
Unlikely	Any assessable reaction that does not fulfil the above conditions
Not related	Causal relationship can be ruled out
*Improvement after dechallenge only taken into consideration, if applicable to reaction	



Both Investigator and Sponsor make a severity assessment of the event as mild, moderate or severe. Mild means the complication is tolerable, moderate means it interferes with daily activities and severe means it renders daily activities impossible. [Other grades of severity, such as the terminology from the CTCAE, may be used, if appropriately referenced.](#)

#### **Reporting of SAEs** (see ClinO, Art. 63)

All SAEs are documented and reported immediately (within a maximum of 24 hours) to the Sponsor of the study.

If it cannot be excluded that the SAE occurring in Switzerland is attributable to the intervention under investigation, the Investigator reports it to the Ethics Committee via BASEC within 15 days.

[In multicenter studies the following should be added:](#)

If the SAE occurs at one of the study sites, the coordinating Investigator reports the events to the Ethics Committee concerned, within 15 days.

[Exemptions from expedited reporting may be possible if the SAE is either a clear result of the underlying disease or well-known. Please define those SAEs that are exempted from expedited reporting.](#)

[A template of the SAE is available at www.swissethics.ch.](http://www.swissethics.ch)

#### **Follow up of (Serious) Adverse Events**

[Describe the follow up procedures of participants terminating the study with reported ongoing \(S\)AEs until resolution or stabilisation.](#)

#### **Notification of safety and protective measures** (see ClinO, Art 62, b)

If immediate safety and protective measures have to be taken during the conduct of the study, the investigator notifies the Ethics committee of these measures, and of the circumstances necessitating them, within 7 days.

#### **6.3 Periodic reporting of safety and general progress of the clinical trial.**

Once a year, the investigator submits to the Ethics Committee a list of the safety events including the severity of the events, their causality to the intervention and the safety of the study participants. The investigator also informs the Ethics Committee about the general progress of the clinical trial (ClinO, Art. 43).

[The safety report and the general study progress report can be merged in one single report.](#)

[In international multicenter studies the following should be added:](#)

In international multicentric studies the safety report and the general study progress report contain information from all sites including information from sites outside of Switzerland. The Sponsor-Investigator distributes the reports to all the participating Investigators.

#### **6.4 Radiation**

[If applicable, refer to the swissethics template of clinical trials for IMPs and Medical Devices.](#)

[Note: FOPH Radiological Protection examines all accompanying investigations involving ionizing radiation when a radiopharmaceutical is employed that is not used in accordance with the authorisation or is not authorised in Switzerland; or when a medical device is employed which is capable of emitting ionising radiation that is not used in accordance with the instructions or that does not bear a conformity marking in accordance with Article 13 MedDO. Or when some other](#)



radioactive source is used. (Art. 36a ClinO).

## 6.5 Pregnancy (if applicable)

Depending on the study, reporting of pregnancies may not be necessary. If reporting is necessary, state how pregnancies will be reported (usually within a maximum of 24 hours to the Sponsor), and how occurrence of pregnancy will be handled in the study (usually patient is withdrawn, outcome of the pregnancy is followed up, etc.).

## 6.6 Amendments

Substantial changes to the study setup and study organization, the protocol and relevant study documents are submitted to the Ethics Committee for approval before implementation. Under emergency circumstances, deviations from the protocol to protect the rights, safety and well-being of participants may proceed without prior approval of the Ethics Committee. Such deviations shall be documented and reported to the Ethics Committee as soon as possible.

Substantial amendments are changes that affect the safety, health, rights and obligations of participants, changes in the protocol that affect study objective(s) or central research topic, changes of study site(s) or of investigator and sponsor (ClinO, Art. 29).

A list of substantial changes is also available on [www.swissethics.ch](http://www.swissethics.ch).

A list of all non-substantial amendments will be submitted once a year to the competent EC together with the safety report / general study progress report.

## 6.7 Notification and reporting upon completion, discontinuation or interruption of the study

Upon regular study completion, the Ethics Committee is notified via BASEC within 30 days (ClinO, Art. 38). The investigator reports the global completion of an international trial to the Ethics Committee within 90 days (remove if not applicable).

Unless otherwise specified in this protocol, the last follow-up visit of the last study participant is defined as the end of the trial.

Provide a statement that the Sponsor and any other competent authority may terminate the study prematurely according to certain circumstances, e.g:

The Sponsor may terminate the study prematurely according to certain circumstances, e.g.

- Ethical concerns,
- Insufficient participant recruitment,
- When the safety of the participants is doubtful or at risk (e.g. when the benefit-risk assessment is no longer positive),
- Alterations in accepted clinical practice that make the continuation of the study unwise, or
- Early evidence of harm or benefit of the experimental intervention

Upon premature study termination or study interruption, the Ethics Committee is notified via BASEC within 15 days (Article 38 ClinO).

Please refer to [www.swissethics.ch](http://www.swissethics.ch) for a template concerning the notification of completion, discontinuation or interruption of the clinical trial.

Describe what happens to the biological materials and health-related data at the end of the study (e.g. all biological materials and health-related data are anonymised upon end of data analysis).

*Add if applicable:* If any use is made of ionising radiation, the investigator documents all information relevant to radiation protection in the final study report and includes a retrospective participant dose estimation. There is no reporting obligation for radiopharmaceuticals used in

conformity with the authorization and for medical devices with a conformity mark in accordance with Art. 13 Medical Devices Ordinance (MedDO) and used in accordance with the instructions. The FOPH may also provide for exemptions from the reporting obligation or on request (Art. 44, ClinO).

**Add if applicable:** Within a year of the completion or discontinuation of the clinical trial which included accompanying investigations involving radioactive sources, the investigator submits to the FOPH the final study report including all information of relevance for radiological protection. The final study report is submitted to the FOPH if the FOPH has issued an opinion in accordance with ClinO Art. 36a.

A final report is submitted to the Ethics Committee via BASEC within a year after completion or discontinuation of the study, unless a longer period is specified in the protocol (ClinO, Art. 38).

## **6.8 Insurance**

The insurance (guarantee) must cover damage occurring up to 20 years after the end of the clinical trial. Refer to ClinO Art. 10 for exemptions from liability and to ClinO Art. 12 for exemptions from liability coverage requirements.

**For category A studies:** In the event of study-related damage or injuries, the liability of the institution *xy* provides compensation, except for claims that arise from misconduct or gross negligence.

**For category B studies:** A separate study insurance is necessary, the sponsor needs to document the guarantee of liability (insurance certificate or equivalent guarantee). The policy value shall be set in accordance with ClinO Annex 2.

## **7 FURTHER ASPECTS**

### **7.1 Overall ethical considerations**

Provide overall ethical considerations of the study, such as generalizability of results, i.e. overall social and scientific value of the study, justification of the study design, the study population and of the study procedures. Provide information about other study-specific ethical aspects (e.g. handling of incidental findings, right of information, special risks in studies using genetic data, methodological critical points, voluntary study participation, vulnerable population, etc.). Ensure that there is an overall fair balance for the study participant.

### **7.2 Risk-benefit assessment**

Assess the potential risk or anticipated adverse effects for participants against a potential benefit for society, science and the participant. Describe how risks to participants are mitigated or minimised. The risk of a study includes the risks of the trial intervention itself (e.g. MRI, psychiatric questionnaires with potential of traumatization, etc.) as well as the risk of unauthorised data access through third parties or unwanted identification of participants.

For studies without immediate benefit to the study participant, a rationale should be provided stating how the results of the study could benefit future patients (e.g. due to a better understanding of the disease, surgical procedures, etc.).

## **8 QUALITY CONTROL AND DATA PROTECTION**

### **8.1 Quality measures**

Describe measures taken for quality assurance and quality control (e.g. double data entry, study personnel trained on all important study related aspects, planned quality visits or independent data review through an independent Data- or Safety Monitoring Committee or a trial monitor, etc.).

For quality assurance the sponsor, the Ethics Committee or an independent trial monitor may visit the research sites. Direct access to the source data and all study related files is granted on such occasions. All involved parties keep the participant data strictly confidential.

## **8.2 Data recording and source data**

Describe how study data is recorded (e.g. electronic Case Report Form (eCRF) such as secuTrial® or Redcap®). An audit trail is obligatory. For each participant a CRF is maintained. CRFs must not identify participants by their name or birth date, but must provide appropriate coded identification.

Please refer to [www.swissethics.ch](http://www.swissethics.ch) for an acceptable coding of trial participants.

List the source data used in the study. Source data is all information in original records, certified copies of original records of clinical findings, questionnaires, observations, or other recorded activities in a clinical investigation. Clearly differentiate between source data collected on study specific documents (e.g. study CRF, study specific forms or questionnaires, etc.), and routinely collected data during the daily practice. Only routinely collected data is part of participant file but it may be transferred to the participant's CRF under the condition that, in this case, the CRF will no longer be considered as source data.

## **8.3 Confidentiality and coding**

The investigator affirms and upholds the principle of the participant's right to privacy and that they shall comply with applicable privacy laws. Especially, anonymity of the participants shall be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals.

The investigator has appropriate knowledge and skills in the areas of data security and data protection or is able to ensure compliance by calling in appropriate expertise (Art. 6, ClinO).

Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited.

Trial and participant data will be handled with the utmost discretion and is only accessible to authorised personnel who require the data to fulfil their duties within the scope of the study. On the CRFs and other study specific documents, participants are only identified by a unique participant number.

Describe who stores the participant identification list, how the data is protected from unauthorised or accidental disclosure, alteration, deletion, copying and theft. Describe the processes in place to ensure traceability (audit trail; ClinO, Art. 18). Mention password access and safety back-ups on storage media to prevent misuse.

In multicenter studies, the process can be described in an annex to cover all sites' specificities.

Describe if uncoded or coded genetic or only non-genetic data are used.

If applicable:

Biological material in this study is not identified by participant name but by a unique participant number. Biological material is appropriately stored in a restricted area only accessible to the authorised personnel.

Describe the measures taken to prevent unauthorised or accidental disclosure, alteration, destruction and theft of biological material.

Describe the processes in place, which are essential to ensure traceability.

Describe appropriate storage and technical requirements to be met (e.g. the maintenance of a cooling system).

If biological material or data collected during the study are to be shipped outside the study site, include the receiver address, the responsible person to whom the materials or data are sent, the purpose of shipment, if applicable, temperature control and how participant confidentiality is guaranteed. Biological material or genetic data can only be sent abroad in the scope of the research study, if the participant involved has given his or her consent to do so upon having been sufficiently informed. Non-genetic health-related personal data can be sent abroad for research if the requirements of Swiss data protection law are met (FADP, Art. 6).

#### **8.4 Retention and destruction of study data and biological material**

The investigator retains all documents necessary for the identification and follow-up of the trial participants and all other original data for at least twenty years after completion or discontinuation of the clinical trial.

Specify time-period and location of archiving of the study data and the biological material.

If applicable, describe how biological materials will be destroyed after termination of the research study and how this will be documented.

If it is planned to further use the study data or the biological materials (e.g. for a Biobank), describe the planned use and the duration (HRA, Chapter 4).

### **9 MONITORING AND REGISTRATION**

Mention the institution that is fulfilling the monitoring duties. Describe the regular monitoring visits at the investigator's site prior to the start and during the course of the study. Give a description of what data and documents will be monitored. Alternatively, the extent and nature of monitoring activities based on the objective and design of the study can be defined in a study specific monitoring plan.

Provide a statement that the source data/documents are accessible to monitors and questions are answered during monitoring.

The study must be registered in the Swiss National Clinical trial Portal (SNCTP) via BASEC in the national language of Switzerland in which recruitment is intended.

In addition, the study must be registered in a primary registry recognized by the WHO (International Clinical Trials Registry Platform: <https://www.who.int/clinical-trials-registry-platform>), or in the registry of the U.S. National Library of Medicine (<https://clinicaltrials.gov>), if it satisfies the definition given therein.

### **10. FUNDING / PUBLICATION / DECLARATION OF INTEREST**

Describe funding sources, publication policy of the study (e.g. authors, raw data access, timelines, etc.), data sharing policy and possible conflict of interests (e.g. independence, intellectual, financial, proprietary, etc.). If applicable, make reference to other contracts or documents where this information is captured.

In multicenter studies, if there is no contract or any written agreement between the institutions, the specifics of the collaboration can be given here.

Publication: Confirm that if "sex and gender" effects are observed, they will be published in the final study report. If an analysis is performed but no "sex and gender" effects are observed, this should also be published in the final study report.

The sponsor enters and publishes a summary of the trial results in a public register in accordance with ClinO Art. 65a within one year of completion or discontinuation of the trial. An interruption lasting more than two years is considered a discontinuation of the trial.

For the purpose of publication in the public register the sponsor also ensures that a lay summary of the trial results is entered in BASEC within one year of completion or discontinuation of the trial. The entry is made at least in the national languages of Switzerland in which the study participants were recruited.

The investigator will provide each study participant with the lay summary of the trial results at the end of the study, directly. The investigator should ensure that study participants are adequately informed about this in the patient information document and that they are informed where the lay summary of the study results will be published online.

## 11. REFERENCES

1. Common Terminology Criteria for Adverse Events (CTCAE):  
<https://evs.nci.nih.gov/ftp1/CTCAE/>
2. Declaration of Helsinki: <https://www.wma.net>
3. Federal Act on Data Protection (FADP):  
<https://www.fedlex.admin.ch/eli/cc/2022/491/en>
4. Human Research Act (HRA)  
<https://www.fedlex.admin.ch/eli/cc/2013/617/en>
5. International Conference on Harmonization (ICH) E6(R2) Guideline for Good Clinical Practice: <https://www.ich.org>
6. International Conference on Harmonization (ICH) E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting: <https://www.ich.org>
7. Medical Device Ordinance (MeDO): <https://www.fedlex.admin.ch/eli/cc/2020/552/en>
8. Ordinance on Clinical Trials in Human Research (ClinO):  
<https://www.fedlex.admin.ch/eli/cc/2013/643/en>

Add all relevant study specific references that justify the study background, objectives, study population and sample size considerations.

## Appendix 1: Schedule of assessments (if applicable)

Time (hour, day, week)	>-1 day	0	+1	+3
Visit	Information	Screening	1 <sup>st</sup> visit	2 <sup>nd</sup> visit
Oral and written patient information	+			
Written consent		+		
Inclusion-/ exclusion criteria		+		
Medical history		+		
Physical examination		+		
Participant characteristics		+		
Procedures			+	+
Intervention		+	+	+
Questionnaire		+	+	+
Sampling			+	+
Safety		+	+	+

Please amend and expand the above schedule according to the specific study.