

Project plan template: Research involving human subjects with the exception of clinical trials

General information and instructions

Legal basis for human research projects with the exception of clinical trials

The laws applicable in this template are the Federal Act on Research involving Human Beings (HRA, RS 810.30) and the Ordinance on Human research **with the exception of clinical trials** (HRO, RS 810.301, Art. 6-23).

Reporting guidelines and checklist for the main study types are listed by the Equator network (<http://www.equator-network.org/reporting-guidelines/>) and should accordingly be addressed in the project protocol (STROBE statement).

The template is intended for research projects with persons in which health-related personal data and/or biological material are to be collected (not yet available) in order to answer a scientific question. For further use projects, please use the appropriate protocol template (either with or without consent) on the homepage swissethics.ch.

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

- Please use the text passages that are written in black.
- Please **delete all instructions and explanations** (written in blue), including this page.
- The protocol has to be signed by the project leader, sponsor (if applicable) and in case of a multicentric project by the different local project leaders as well. The protocol should be uploaded in an OCR PDF format (Optical Character Recognition, i.e. a searchable PDF format). The scan of the wet-ink signed signature page should be uploaded separately.
- The protocol as well as the signature page and other necessary documents must be submitted through the web-portal BASEC (<https://submissions.swissethics.ch/en/>).
- In places where the information is redundant, it is acceptable to refer to another section, to document or to state its redundancy but the section must not be deleted.

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

Change history

Version Nr	Version date	Modified without version change	Description, comments	Control
1.0	2013		Initial version	AGEK
2.0	19.07.17		Total revision of all paragraphs (which have been either simplified, condensed or deleted).	PG
		X	Removed 'logo of the institution' on project title page	PG
2.1	07.10.17		Added 'project title' on signature page	PG

Project Title

Research legislation: Ordinance on human research with the exception of Clinical trials (HRO) [1].

Type of Research Project: Research project involving human subjects

Risk Categorisation: Provide Risk category A or B acc. to ordinance HRO Art.7

Project Leader: Title, Name, Position, Address, Phone, e-mail.

The project leader is a qualified individual by education and training (HRO Art.4), who is responsible for the whole project. In case of a multicenter project, list the centers names and the names of the local responsible project leaders. Please ensure compatibility with BASEC research application form.

PROTOCOL SIGNATURE FORM

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

Study Title *Full study title as written out on title page*

The project leader has approved the protocol version [**x (dated DD.MM.YYYY)**] (version and date must coincide with the footer), and confirms hereby to conduct the project according to the protocol, the Swiss legal requirements [1, 2], current version of the World Medical Association Declaration of Helsinki [3] and the principles of Good Clinical Practice.

Project leader:

Site *[name and address of site]*

Name:

Date: _____ Signature: _____

If applicable and not identical with project leader:

Sponsor:

Name:

Date: _____ Signature: _____

PROTOCOL SIGNATURE FORM

(only for multicentre projects, delete this for monocentric projects)

Study Title *Full study title as written out on title page*

The project leader (main center) and the investigator (at the local center/site) have approved the protocol version **[x (dated DD.MM.YYYY)]** (version and date must coincide with the footer), and confirm hereby to conduct the project according to the protocol, the Swiss legal requirements [1,2], the current version of the World Medical Association Declaration of Helsinki [3] and the principles of Good Clinical Practice.

Project leader (lead center/site)

Site *[name and address of site]*

Name:

Date: _____ Signature: _____

If applicable and not identical with project leader:

Sponsor:

Name:

Date: _____ Signature: _____

Local Project Leader at local center/site:

This page must individually be signed by all participating local Project Leaders.

Site *[name and address of site]*

Name of Local Project Leader: _____

Date: _____ Signature: _____

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GLOSSARY OF ABBREVIATIONS

<i>BASEC</i>	<i>Business Administration System for Ethical Committees</i>
<i>CRF</i>	<i>Case report form</i>
<i>FOPH</i>	<i>Federal Office of Public Health</i>
<i>HRA</i>	<i>Human Research Act</i>
<i>HRO</i>	<i>Ordinance on Human</i>

1 BACKGROUND AND PROJECT RATIONALE

The project must address a relevant scientific question and potentially provide valuable generalizable knowledge. The legal requirements must be fulfilled and the ethical standards must be guaranteed. Please provide information about the actual scientific background, cite relevant literature including relevant systematic reviews, and explain why you chose the question that will be answered through this project. Provide information about the disease background, epidemiology, current standard of care, pre-clinical and clinical data, scientific rationale and significance according to HRA Art.5 and 10. Explain why the question of the project provides new scientific input for the community, what is the potential project benefit and expected new information to be gained. Note that scientific value is essential for ethical conduct of every project. State the risk category for research projects according to art. 7 (HRO): A or B and explain rationale behind the risk categorization. Evaluate overall risk of project in relation to formal categorization.

2 PROJECT OBJECTIVES AND DESIGN

2.1 Hypothesis and primary objective (and if applicable also secondary objectives)

Describe a clear hypothesis that will be answered through the conduct of the project and the primary objective. In very rare cases a hypothesis might not be required for all project types (e.g. exploratory projects). If applicable: secondary objectives.

2.2 Primary and secondary endpoints

Describe the variable of primary interest and the rationale for its selection. In general, a single variable and a single time point are used regarding the primary endpoint. Describe baseline factors that may have an influence on the primary endpoint, e.g. age, gender, etc. In rare cases, for example for qualitative project designs the listing of endpoints may not be possible or needed. If applicable: provide a list of all secondary endpoint parameters to be assessed. The secondary endpoint(s) are used to answer the secondary objectives. Describe also the baseline factors that may have an influence, e.g. smoking, blood pressure, etc.

Any endpoint should be measurable and should give information towards the project objective. If you do not choose endpoints to measure, please provide information about the association between exposure and outcome and how you plan to quantitate this.

2.3 Project design

Both the study design and selected methods should be appropriate to answer the research question and address the hypothesis. Specify regarding observational study, project design and rationale (e.g. exploratory, confirmatory qualitative research, fundamental research; project set-up e.g. multicenter / single center; national / international).

3 PROJECT POPULATION AND STUDY PROCEDURES

3.1 Project population, inclusion and exclusion criteria

Describe project population, total number of participants, including the control groups. Justify with respect to choice of project population. List all project **inclusion criteria**, such as for example: target disease, diagnosis, therapeutic method, surgical procedure(s), clinical history, etc.; age; ethnic, sociodemographic background; life style factors e.g. exercise, smoking history etc. List all project exclusion criteria such as for example: pregnant or lactating women; specific medication or treatment, other clinically significant concomitant diseases (e.g. hepatic dysfunction,

cardiovascular disease, etc.); life style factors, inability to follow procedures or insufficient knowledge of project language, inability to give consent.

3.2 Recruitment, screening and informed consent procedure

Describe location (hospital, community, city etc.) of recruitment. Describe procedures for participant recruitment, e.g., “consecutive ongoing recruitment through project leader in daily clinical practice”, or “participant recruitment through referring physician”. When using advertisement/flyer as a recruitment tool, the document should be uploaded in BASEC and have to be in line with the guidelines published on www.swissethics.ch.

If applicable, describe screening process and list any screening procedures, such as laboratory or diagnostic tests necessary to meet inclusion and exclusion criteria. Any screening procedure that is not routine/daily practice can only be performed once informed consent has been obtained. Describe the informed consent process including ample time for consideration given to the participants and opportunity to ask questions.

If applicable, describe any compensation or payments given to the project participants. A guide on the monetary contributions to patients participating in research projects is available on www.swissethics.ch. The templates for the informed consent in German, French and Italian are available on www.swissethics.ch

3.3 Study procedures

Describe overall project duration, incl. recruitment period and project duration for each patient. Provide a description and sequence of all planned procedures, such as the use of questionnaires, project visits, and permitted timeframe for each visit. Describe material sampled and stored, as well as methods and tests used for sample collection and analysis. Compile a summary table listing all project visits including relevant procedures, sampling and timelines (i.e. a schedule of assessment): attach the table here or refer to appendix 1.

Describe any expected biases to your project and measures taken to reduce them.

3.4 Withdrawal and discontinuation

Describe reasons for which a participant is “withdrawn from the project”, e.g. withdrawal of informed consent, disease progression, etc.

Describe procedures to follow upon premature participant withdrawal (i.e. final examinations, etc.) or upon withdrawal of informed consent. Describe how the data is anonymized and the material destroyed in case of withdrawal. If this is not possible, provide a justification. In longitudinal studies, refer how to handle drop-outs.

4 STATISTICS AND METHODOLOGY

4.1. Statistical analysis plan

The consultation of a statistician is recommended to state the hypotheses (null, alternative hypotheses). Describe the statistical rationale for sample size in terms of the power to test the primary endpoint. If this is not possible, the planned sample size should still be justified. Give a description of the planned statistical methods for the primary endpoint. Level of significance used, e.g. significance level will be two-sided $\alpha = 0.05$. In the event of multiple endpoints, statistical adjustments for multiple testing need to be considered. If applicable: include the statistical software package(s) to be used. Include any planned interim analyses (if applicable).

If different statistical methods rather than hypothesis testing are used, please describe them in detail.

4.2. Handling of missing data

Describe how missing data will be handled in the analysis. Ensure an adequate number of participants will be evaluated, e.g. by compensating for expected drop-outs or by replacement.

5 REGULATORY ASPECTS AND SAFETY

5.1 Local regulations / Declaration of Helsinki

This research project will be conducted in accordance with the protocol, the Declaration of Helsinki [3], the principles of Good Clinical Practice, the Human Research Act (HRA) and the Human Research Ordinance (HRO) [1] as well as other locally relevant regulations. The Project Leader acknowledges his responsibilities as both the Project Leader and the Sponsor (if there is no separate Sponsor).

5.2 Notification of safety and protective measures (HRO Art. 20)

The project leader (and if applicable the sponsor) is promptly notified (within 24 hours) if immediate safety and protective measures have to be taken during the conduct of the research project. The Ethics Committee will be notified via BASEC of these measures and of the circumstances necessitating them within 7 days.

5.3 Serious events (HRO Art. 21)

If a serious event occurs, the research project will be interrupted and the Ethics Committee notified on the circumstances via BASEC within 7 days according to HRO Art. 21¹.

Note: a template to report safety events to the Ethics Committee is available on www.swissethics.ch. If a serious event occurs in connection with an investigation involving a radiation source on which the Radiation Protection Division of the Federal office of Public Health (FOPH) has delivered an opinion in accordance with Art.19 (HRO) this must be additionally reported to the FOPH within 7 days.

5.4 Radiation

If radioactive sources are used in the research project, e.g. tracers, and the expected individual radiation dose is higher than 5 mSv per year **and**:

- a. a radiopharmaceutical is used which is not authorised in Switzerland;
- b. a radiopharmaceutical is used which is authorised in Switzerland, and the intervention in question is not a routine nuclear medicine examination; or
- c. some other unsealed or sealed radioactive source is used the FOPH must also authorize the research project. Please consider the requirements according to HRO Art. 19 and Art.23.

5.5 Amendments

Substantial changes to the project set-up, the protocol and relevant project documents will be submitted to the Ethics Committee for approval according to HRO Art. 18 before implementation. Exceptions are measures that have to be taken immediately in order to protect the participants. Substantial amendments are changes that affect the safety, health, rights and obligations of project participants, changes in the protocol that affect project objective(s) or central research

¹ A serious event is defined as any adverse event where it cannot be excluded, that the event is attributable to the sampling of biological material or the collection of health-related personal data, and which:

- a. requires inpatient treatment not envisaged in the protocol or extends a current hospital stay;
- b. results in permanent or significant incapacity or disability; or
- c. is life-threatening or results in death.

topic (category B only), changes of project site(s) or of project leader and sponsor. Note: List of substantial changes is available on www.swissethics.ch.

5.6 End of project

Upon project termination, the Ethics Committee is notified within 90 days. Describe what happens to the biological materials and health-related data at project end: e.g. all biological materials and health-related data are anonymized upon termination of data analysis.

If the project also requires a FOPH approval: Within a year of completing or discontinuing a research project which included investigations involving unsealed or sealed radioactive sources, the project leader shall submit to the FOPH a final report including all information of relevance for radiological protection, and in particular a retrospective dose estimation. Routine nuclear medicine examinations involving authorized radiopharmaceuticals are exempt from these reporting requirements.

5.7 Insurance

In the event of project-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 research projects, an additional insurance package is needed. See Annex 1 of HRO for policy values for liability coverage.

6 FURTHER ASPECTS

6.1 Overall ethical considerations

Overall ethical considerations of the project: generalizability of results, i.e. overall social and/or scientific value of the whole project; justification of the study design and of procedures (burden and time effort) for participants (refer to chapter 1). Provide information about other project-specific ethical aspects, like handling of incidental findings, right of information, special risks in studies using genetic data, voluntary study participation, etc. Is there an overall fair balance for the study participant?

6.2 Risk-Benefit Assessment

Assess the risk for project participants against a potential benefit and include a description how risks to project participants are minimized and can be managed. Each (potential) risk must be justifiable. The risk of a project includes the risks of the procedure itself (e.g. MRI, psychiatric questionnaires with potential of traumatization) and the risk of unauthorized data access and/or unwanted identification of project participants.

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

6.3 *If applicable*: Rationale for the inclusion of vulnerable participants

Describe all vulnerable participants that shall be included in the research project. State why equivalent findings cannot be obtained by other means (subsidiarity). Describe the procedures taken, including how the informed consent is obtained:

Guidelines to conduct research in emergency situations are available in German, French and Italian (see HRA Art. 30, 31) and Guidelines to conduct research with children, adolescents and adults with incapacities (see HRA Art. 21, 22, 23, 24) are available on www.swissethics.ch.

7 QUALITY CONTROL AND DATA PROTECTION

7.1 Quality measures

Describe measures taken for quality assurance and quality control: e.g. double data entry, project personnel trained on all important project related aspects, planned quality visits or independent data review, etc. For quality assurance the Ethics Committee may visit the research sites. Direct access to the source data and all project related files and documents must be granted on such occasions.

7.2 Data recording and source data

Describe how project data is recorded, e.g. with paper Case Report Forms (CRF) or an electronic Case Report Form (eCRF) such as secuTrial® or Redcap®. Efforts should be made not to use any software, like Microsoft Office software's (e.g. Excel), that do not have an audit trail. If paper CRFs are used, describe how data is transferred to an electronic database for later analysis. An electronic database is recommended.

List the source data used in the project. 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 project specific documents (e.g. project CRF, project specific forms or questionnaires, not part of participant file), and routinely collected data during the daily practice. The routinely collected data is part of participant file but can also be transferred to the participant CRF.

7.3 Confidentiality and coding

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

Describe if uncoded or coded (genetic or non-genetic) data is used. Describe who stores the participant identification list, how the data is protected from unauthorized or accidental disclosure, from alteration, deletion, copying and theft. Describe the processes in place, which are essential to ensure traceability (audit trail). Mention password access and safety back-ups on storage media to prevent misuse. If applicable for multicentric trials: the process can be described in an annex to cover all sites' specificities.

If applicable: **Biological material** in this project is not identified by participant name but by a unique participant number. Biological material is appropriately stored in a restricted area only accessible to authorized personnel. Describe the measures taken to prevent unauthorized or accidental disclosure and to prevent the biological material to be altered, destroyed or stolen. Describe the processes in place, which are essential to ensure traceability of the biological material.

Describe appropriate storage and technical requirements to be met, i.e. maintenance of the cooling system. If biological material or data collected during the study are to be shipped outside the study site, include: receiver address, responsible person to whom materials or data are sent, purpose of shipment, temperature control if applicable and how participant confidentiality is guaranteed. Biological material or genetic data can only be sent abroad in the scope of the research project, if the participant involved has given his/her consent to do so upon having been sufficiently informed (HRO, Section 2).]

7.4 Retention and destruction of study data and biological material

Specify time-period and location of archiving of the study data and the biological material; e.g. health related data are stored for x (for example 10) years after publication of the research project

(in clinical trials the data is archived for at least 10 years after study end). If applicable, describe how biological materials will be destroyed after termination of the research project and how this will be documented.

If it is planned to further use the data and/or the biological materials, such as for biobanking, describe the planned use and the duration.

8 FUNDING / PUBLICATION / DECLARATION OF INTEREST

Describe funding sources, publication policy of the project, data sharing policy and possible conflict of interests. If applicable, reference to other places or contracts/documents where this information is captured. If applicable in multicentric projects, if there is no contract or any written agreement between the institutions, the specifics of the collaboration can be given here.

9 REFERENCES

1. Ordinance on Human Research with the Exception of Clinical trials (HRO)
<http://www.admin.ch/opc/en/classified-compilation/20121177/201401010000/810.301.pdf>
2. Human Research Act (HRA)
<http://www.admin.ch/opc/en/classified-compilation/20121176/201401010000/810.305.pdf>
3. Declaration of Helsinki (<http://www.wma.net/en/30publications/10policies/b3/index.html>)
4. STROBE statement ([http://www.jclinepi.com/article/S0895-4356\(07\)00436-2/pdf](http://www.jclinepi.com/article/S0895-4356(07)00436-2/pdf))

If applicable: **Appendix 1: Schedule of assessments**

Note: Amend and expand the below example according to the specific project

<i>Time (weeks)</i>	<i>>-1 day</i>	<i>0</i>	<i>+1</i>	<i>+3</i>
<i>Visit</i>	<i>Information</i>	<i>Screening</i>	<i>1st visit</i>	<i>2nd visit</i>
<i>oral and written Information</i>	+			
<i>Written consent</i>		+		
<i>check inclusion-/exclusion criteria</i>		+		
<i>Medical history</i>		+		
<i>Participant Characteristics</i>		+		
<i>Procedures</i>			+	+
<i>Questionnaire</i>		+	+	+
<i>Sampling</i>			+	+