

Template from swissethics

for the submission of a project "Further use **without consent**" according to HRA art. 34/HRO.

Legal basis for Further use without consent projects

The legal requirements for research projects involving re-use can be found in HRA ch. 4 (art. 32-35) and HRO ch. 3 (art. 24-40).

If the requirements for consent and information according to articles 32 and 33 HRA are not met, biological material or health-related personal data **may only be used for research purposes by way of exception and only if the requirements of art 34 lit. a-c HRA are met.**

The following template is to be used as a basis for the protocol. The use of this template is mandatory.

In addition to this template, further documents must be submitted to the responsible ethics committee. These documents are listed in detail on the BASEC web portal (Business Administration System for Ethics Committees).

- Please use the text passages that are written in black.
- Please **delete all instructions and explanations** (written in blue), including this page.
- The information required in the protocol depends on the type of reuse project: A retrospective evaluation of a medical history without consent requires different information in the protocol than a project from the field of big data. If certain information is not applicable to the project at hand, it should be omitted.
- Please use gender-neutral language.
- Submission via the BASEC web portal (<https://submissions.swissethics.ch/en/>) to all Swiss ethics committees is mandatory.
- 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. 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. If the protocol is signed by hand, the scans of the wet-ink signed signature pages are uploaded to BASEC separately.
- The protocol has to be uploaded in an OCR PDF format (Optical Character Recognition, i.e. a searchable PDF format).

Change history of the template

Version Nr	Version date	Modified without version change	Description, comments	Control
4.0	26.08.2021		First version in English. Translated from the corresponding version in German	PG
		X	Minor changes to some of the examples given (text in blue), added 'samples size' to title chapter 8. Scientific method.	PG
4.1	27.04.2022		Updated text of chapter 15 to match the provisions of art. 14 and art 40 HRO and the versions of the template in DE, FR, and IT.	PG
		X	Added note to chapter 17 on the use of Excel. Corrected error in table chapter 8.	PG
		X	Added note to chapter 3 on the SPHN risk assessment tool for health-related data de-identification.	PG



... Please delete the instruction text and the table "Change history"...



Research plan/Protocol for HRO:

Further use of biological material and health-related personal data for research **without consent pursuant to Article 34 HRA**

Title of the research project

Identical to the title on the "Research Project Application Form".

Name and address of the project leader

The project leader is the person responsible for the practical implementation of the further use project in Switzerland. In a clinical study, this would be the "principal investigator". In the case of Master's theses and medical doctoral theses, the supervisor is the project leader.

Salutation, first name, surname, position e.g. senior physician, institution

Address, telephone number, e-mail

If applicable: Name and address of the sponsor

The sponsor is the person responsible for the overall research project, namely for its initiation, management and financing. If the project management also initiates the research project, it is also the sponsor. Only to be filled in if the project leader and sponsor are not the same person.

Salutation first name, surname, position e.g. senior physician, institution

Address, telephone number, e-mail

Confirmation of the project leader and (if applicable) the sponsor

With my signature, I attest that all information in this protocol is correct and that I will comply with the information I have given and with national legislation, namely data protection law.

Project leader:

Place, date

Signature

If applicable and not identical with the project leader: Sponsor:

Place, date

Signature

This page is only needed for multicentre projects in Switzerland; please remove this page for monocentric research projects.

Local project leader at the local centre/site:

This page must be signed individually by all local project leaders. Add as many sections as there are local centres/sites.

Local Project leader:

Salutation first name, surname, position e.g. senior physician, institution

Place, date

Signature

Abbreviations

List the abbreviations used in the document, e.g.:

HRA	Human Research Act
HRO	Human Research Ordinance
PCR	Polymerase Chain Reaction

1. Background

Describe here the scientific background to your research question and justify the scientific relevance of the project in context. Will this project create new generalisable knowledge and investigate a relevant research question?

2. Objectives

Describe the primary and, if applicable, secondary objectives of the project. What is the aim of the analysis of the data or the biological material? The primary objective must be clearly and precisely defined.

Describe the endpoint for the primary objective and, if applicable, describe the endpoints for the secondary objectives. Endpoints are those parameters that are measured to achieve the objective.

If you do not define endpoints, describe the relationship between the parameters that you are evaluating and what conclusions this should allow.

3. Design

How is the study actually executed? Which evaluation methods/techniques are used?

e.g. "From the available blood samples, the laboratory blood values are further used. Data already collected from the medical history will also be evaluated."

What is to be investigated? e.g. "Biomarkers in liver carcinomas".

Indicate here the "period of collection" for this research project.

Note: For Article 34, it is important to use as few data/ biological material as possible, just enough to statistically answer the project question. In no case should a particularly large sample size of data/biological material be aimed for.

Note: SPHN has elaborated a methodology and created a tool to assess the risk for health-related data de-identification. The methodology consists in evaluating in a project-specific case-by-case manner the risk of re-identification and applying data de-identification rules and potentially other safeguards (contractual and/or technical) in order to reduce such a risk under an acceptable threshold. The tool consists in the guidance document «De-identification of health-related data – Recommended phased approach» and in the Excel file «Template use case evaluation and risk assessment». The guidance document and the Excel file can be downloaded from the [SPHN webpage](#).

Although the use of the tool is not mandatory, swissethics recommends it. If used, the Excel file can be uploaded to screen 6. Lead EC, section 39. Varia/Miscellaneous of the project form in BASEC.

4. Origin of the data/biological material

Where does the data/biological material come from? Which population is to be studied using the data/biological material?

E.g. "We want to investigate the survival data of thyroid cancer patients treated with experimental antibody x in the years y to z. Many patients have already died (see below for further justification). For the subgroup of still living persons, we will obtain the informed consent (e.g. by means of a general consent or a study-specific consent).

5. Inclusion criteria

What criteria must the data/biological material meet in order to be used for this evaluation?

e.g. "From patients with papillary thyroid cancer and therapy with antibody x for at least y months."

6. Exclusion criteria

What criteria exclude the data/biological material from being used in this evaluation? "Which data sets would distort the evaluation if they were included?"

e.g. "Data sets with an ambiguous diagnosis, etc. Data of persons with"

Presence of a documented refusal.

7. Scientific methods and sample size

Describe the intended statistical methods for assessing the primary endpoint and, if applicable, the secondary endpoints. If possible, formulate a hypothesis. The statistical evaluation should confirm or reject the hypothesis. Please use established statistical methods whenever possible. It must be stated what is to be analysed or measured using which method.

State the sample size and justify the amount of data sets and biological samples to be analysed with respect to the primary endpoint and, if applicable, secondary endpoints. For all projects, the sample size of data and material to be analysed must be justified. If different statistical methods (e.g. descriptive statistics or artificial intelligence/algorithms) are used instead of statistical tests to confirm or reject a hypothesis, these should be described and justified.

In the case of multiple endpoints, statistical adjustments for multiple testing should be considered.

If applicable: Indicate which statistical software package(s) will be used.

Note: For purely exploratory projects, the formulation of a hypothesis is not required.

If applicable, please critically question the methodology to be used and list potential limitations of the methodology (risk of bias):

Will the analysis be reproducible, transparent and justifiable?

Does the selection process lead to bias? (e.g. by over- or under-sampling a gender, ethnicity, socio-economic or religious group)? How is this bias mitigated?

8. For which health-related personal data/biological material should the authorization be granted?

Preliminary remark: The consent for the participation, respectively the consent for further use of samples and data, resp. the collection of the general consent has the highest priority and is an expression of the autonomy of the individual. Therefore, all efforts to obtain the consent of the persons - wherever possible, must be described.

Most projects will be categorized as "mixed projects", i.e. the consent is available for some persons, for other persons the consent is not available and an approval from the ethics committee for the exemption is applied for. This exemption can only be granted for a special subgroup if, for example, the persons are already deceased or cannot be contacted for reasons that need to be specified. In general, the consent for further use is always required from all those persons who have either already been asked or can still be asked for the general consent. An existing documented refusal must be taken into account.

For consideration for approval by the EC, it is necessary to provide detailed information on the sample size at the site (or at all participating sites in the case of multicentre projects). In addition, it must be stated for which subgroup a consent (e.g. a signed general consent) is already available or for which subgroup the exemption is requested.

Which data/biological material should be further used to answer the scientific question?

Note: All data/biological material that is to be used for the research project must be specified here.

e.g. "Personal and medical data and all images (CT, MRI, etc.) of the operated knee joint of approx. 1000 patients from the years 2000-05 at..."

It is important that the time periods when the data were originally collected are indicated and that it is mentioned when the general consent was introduced at the respective sites/hospitals. This is the only way to ensure that all efforts to obtain consent are evident.

Note: Often it is not possible to provide completely correct information on the number. Please then provide an estimate.

	total number of data/ samples	number of data/ samples with consent	number without consent – person deceased	number without consent – person not contactable	total number of data/ samples without consent
Site ZH					
Site BE					
Site VD					
total	xy	xy	xy	xy	xy

9. Application for an exemption according to Art. 34 HRA.

Ad art.34 lit.a: Justification why it is impossible or disproportionately difficult to obtain consent of the participants or justification why this would impose an undue burden on the person concerned, or to their relatives if the persons concerned have died:

E.g., "We want to examine 200 records of thyroid cancer individuals from the last 10 years. For the past two years, we have requested patients with general consent for continued use of data/samples at our hospital. Consent was given as part of the hospital stay. A copy of the general consent used is attached to the application.

However, the bulk of the data is from previous years. We have to assume that about three quarters of the patients have died in the meantime. It is therefore difficult and involves a disproportionate amount of effort to locate the patients, or the relatives if they have died."

Ad Art. 34 lit.c: Reason why the interests of research outweigh the interests of the person concerned in deciding on the further use of his or her biological material and data:

If the expected increase in knowledge will benefit future patients or if important findings in a field of research can be expected that can only be obtained in this way, then there is a good reason why the interests of research outweigh the interest of the persons concerned.

10. Confirmation that there is no documented refusal:

Ad Art.34 lit.b: The project leader confirms that no health-related personal data and no biological material will be used if there is a written or documented verbal refusal from the person concerned.

11. Which group of persons is authorized to release the biological material and the health-related personal data?

Individual persons must be listed here by name (e.g. "Prof. Jane Doe and Dr. Felix Muster at the dept. vascular surgery at hospital x) and/or groups of persons (e.g. "the attending physicians at the dept. vascular surgery at hospital y) who, by virtue of their treatment assignment, have a right to view/access/all uncoded data/uncoded biological material of the persons concerned.

12. Who takes responsibility for the reception of this data/biological material?

As a rule, this is one person, usually the project leader. This person can decide who all should have direct access to the uncoded data/uncoded biological material in the context of this research project. The person named here is responsible for ensuring that no data/biological material is further used other than under this authorization.

13. Which group of persons should be authorized to access the health-related personal data within the scope of this research project?

All persons who are to have access to uncoded data and/or biological material within the scope of this work must be listed here.

These persons should preferably be identified by name. However, it is also permissible to leave this open (e.g. "A future master's student and a future doctoral student are to copy the data from the patient register. The assistant physician, Dr. John Smith, who supervises the trainees, should also be authorized to view the uncoded data.") Handling of the data/biological material is to be restricted to those persons who need it to perform their study-related tasks.

14. Who is responsible for the protection of the data that have been released?

A person must be indicated here by name; generally, this is also the project leader.

15. Reporting obligations

The ethics committee must be notified of any change of project leader in advance and of any changes to the information given in the authorisation.

The completion or discontinuation of the research project must be reported to the ethics committee within 90 days.

16. Data protection

Uncoded data, coding and storage of the key

For uncoded data/biological material:

The source data in most projects in a clinical setting are almost always uncoded (inspection of medical records). For the analysis, the data must be correctly coded. Please mention where the key is kept.

E.g. "As part of a Master's degree, medical student Petra Müller will transcribe all data from the hospital's patient charts into a table, coding them with a neutral number. At the same time, she will keep a key document with which the data can be assigned to the patients. Ms Müller will also take a paraffin block of the surgical material of each of the thyroid cancer subjects from the Institute of Pathology and code it with the same neutral study number. The key will then be sent to the project management (Prof. Jane Doe). Dr. Keller and Ms Müller will evaluate the sections together, enter the results in the data sheet and correlate them with the survival times of the patient chart. All coded data and biological materials will be evaluated according to the information in this protocol, in compliance with data protection.

For coded data/biological material:

If the data or biological material is already coded for analysis, e.g. in a research registry or research biobank, this must be mentioned, as well as the location where the key is securely stored.

E.g. "The data described above are available in coded form in the European Cancer Registry. The study team only sees the registry number (e.g. CH-ZH-0025). The first two letters stand for the donor's country of origin, the second pair of letters for the canton. The number comes from a consecutive numbering system. The key is kept by Prof. Jane Doe."

17. Information on the storage of data and samples

What is done to ensure the privacy of participants is protected?

When storing health-related personal data and/or biological material for research, their protection must be ensured by appropriate operational and organizational measures (HRO art. 5). Unauthorized or accidental disclosure, alteration, deletion or copying of health-related personal data must be prevented.

A paper data collection sheet or suitable software e.g. SecuTrial® or REDCap allows changes to be traced.

E.g.: "We will extract the data from the electronic medical record and enter it into SecuTrial®. This way, all subsequent changes can be tracked. Access is password protected."

Note: Microsoft Office programs such as Excel spreadsheets do not guarantee data privacy and reliability, as changes can be made in an uncontrolled manner. Use of such programs is discouraged.

If Microsoft Excel is used, a system must be put in place to improve data privacy and data reliability. That is with a protected cloud system that combines controlled access and user rights with tracking of changes at file / document level, and using the feature "Track changes" (see instruction for use of this functionality [here](#). Training videos on how to use this feature are available on the YouTube channel, e.g.: https://www.youtube.com/watch?v=ltz8v_z7ha4). Ethics committees will review the use of Microsoft Office programs based on a risk-adapted approach.

All identifying data (names, addresses, date of birth and hospital patient number, etc.) must be kept separate from the actual study data. All digital documents must be password protected. Paper data must be securely locked away.

If applicable: Please mention server locations, cloud services if applicable and other security standards ("security framework" incl. quality control). Servers should be located in Switzerland or Europe. This always requires study-specific contractual agreements.

Server locations in the USA should be avoided. If this is not possible, it must be explicitly justified including all efforts/contractual agreements made to ensure data security.

Biological material must also be appropriately coded or anonymised. The technical requirements for proper storage must be guaranteed and the necessary resources for storage must be available. Unauthorised persons are denied access to the material. The necessary measures to protect the biological material must be described in this section.

If possible and provided for in the project: If anonymization takes place, the anonymization process must be described (e.g. destruction of the key).

18. Retention period

Specify the place and period of retention.

e.g. "The biological material will be destroyed after the evaluation and the data will be stored for x years". Or: "The biological material will be anonymised after evaluation, i.e. the key code will be destroyed and the data will be stored for x years." Or: "The remains of the unused biological materials are sent back to the hospital biobank xy and stored there."

19. Ethical and regulatory requirements

Risk-benefit assessment:

Preliminary remark: Please carefully consider the benefits and risks.

What benefits are expected from this project? Is there a societal benefit? Who will benefit from the results? Do the benefits outweigh the risks?

What data risks are associated with the project and how are they prevented or mitigated?

This project complies with the regulatory requirements of the HRA and the HRO. The prerequisite for carrying out the research project is the approval of the competent ethics committee.

20. Results / transparency / publication

Are the results scientifically valid and justifiable (e.g. is there a correlation or even a causality)?

Can the results be generalised?

If applicable: Are the results being shared? Which other stakeholders are involved? Is an administrative fee paid for this?

Where and how are the results disseminated? (e.g. as coded or anonymised data?).

Note: Information about results and on incidental findings for the cohort without consent is not applicable. If the sub-cohort with consent is large, it must be considered whether and in which form results and/or incidental findings are communicated. Note: The communication of incidental findings only makes sense if they have a high medical relevance for the persons concerned and only if these results are appropriately validated.

21. Funding / Data sharing / Declaration of interest

Describe the funding sources, the publication policy of the project, the data sharing practices and possible conflicts of interest. If applicable, refer to contracts or documents in which this information is recorded. For multicentre projects, if there is no contract or written agreement between the institutions, the details of the collaboration can be provided here.

If applicable: Note on data exchange: The templates for writing the 'Consortium Agreement' (CA), the 'Data Transfer and Use Agreement' (DTUA) and the 'Data Transfer and Processing Agreement' (DTPA) can be found on the Swiss Personalized Health Network (SPHN) website ([link](#)). Please use the information provided on the SPHN website to find out about the various legal agreements required for the establishment of research consortia, as well as for data transfer and data use in collaborative research projects. Please contact the Personalised Health Informatics (PHI) Group directly for advice and support at dcc@sib.swiss.

22. References