Template from swissethics
for the submission of a project "Further use with consent" according to HRA/HRO.

Legal basis for Further use with consent projects

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

The requirements for correct information and consent for the further use can be found in the HRA art. 28-32. For the further use of coded, health-related personal data (HRA art. 32), the right of objection is sufficient. For all projects where the patient must give explicit consent, swissethics has provided templates that can be found on the homepage under "Study information and consent / Collection of data/biological materials". These templates must be adapted both to the institution (e.g. letterhead, name and address of the project management) and to the respective research question.

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).

The sponsor and the project management must ensure that the groups of people from which the data/biological material is used in the research project, and which is relevant for answering the scientific question, are adequately represented (Art. 2 let. c HRO in conjunction with Art. 4a ClinO). 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), 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** (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 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 must be uploaded in an OCR PDF format (Optical Character Recognition, i.e. a searchable PDF format).

The content of the protocol must be identical to the content of the BASEC research project application form. In the research project application form in BASEC you can refer to the protocol to avoid redundancies, but not vice versa.

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
		X	Added note to chapter 11 on the use of Excel.	PG
		X	Added note to chapter 3 on the SPHN risk assessment tool for health-related data de-identification.	PG
		X	Instructions on sex and gender-equitable research have been added on page 1	PG
4.1	16.09.2024		New version adapted to the amended HRO, status as of November 1, 2024.	PG

✂ **... 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 pursuant to Articles 32 and 33 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.:

EC	Ethics Committee
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: 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 SPH webpage (Link).
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? Is the data source from a registry, collected data for xx purpose or xx (public, private, or from a commercial company)? Is the data source credible and of good quality?

The sponsor and the project management must ensure that the groups of people from which the data/biological material is used in the research project, and which is relevant to answering the scientific question, are adequately represented. This must particularly take into account the distribution of age groups and sex ratio is balanced. If this is irrelevant provide a justification.

If applicable for the further use: how was the original data collected for the present analysis? E.g. from the relevant medical history, online via questionnaire, via app or similar.

Which population is to be studied using the data/biological material? Does this population belong to a vulnerable population (e.g. minorities, minors, persons unable to consent)?

E.g. "We want to examine biological material from all adult patients with depression who have been treated for infectious diseases at our centre in the last 10 years for as yet unknown biological markers for depressive diseases. "
Or e.g. "Health-related data and all imaging data (CT, MRI, etc.) of knee joint operations from January 1st, 2011- December 31st, 2015, ..." The data comes from xy.

Or: "We are analysing the genome from PBMCs with regard to the following gene sequences xy using Next Generation Sequencing."

5. Inclusion criteria
What criteria must the data/biological material meet in order to be used for this evaluation?
e.g. "Adult male patients with a confirmed diagnosis of depression." "Signed informed consent."

6. Exclusion criteria
What criteria exclude the data/biological material from being used in this evaluation?
e.g. "Presence of documented refusal (if applicable for coded data)." Which data sets would distort the evaluation if they were included?
e.g. "Data sets with an ambiguous diagnosis, etc.".

7. Informed consent and information of participants
It must be ensured that adequate and comprehensible information has been given.
How was/is the information provided? Reference to the patient information and consent form or, if applicable, to the general consent form and the confirmation that consent was obtained.
e.g. "All data originate from our daily clinic routine and were captured between 2014 and 2015. All patients have signed the general consent of the university hospital … (copy enclosed)."

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

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.
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?

9. Reporting obligations
The ethics committee is notified of any change of project leader in advance.
The project leader notifies the ethics committee of the completion or early termination of the research project within 90 days.

10. Data protection
Note: 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.

Coding: Biological material and health-related personal data are correctly coded if, without access to the key or to the source data, it is only possible with disproportionate effort to link the biological material or the health-related data to a specific person (Art. 26 HRO).

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, personal data is only identified by a unique participant number. Coding is done using a method based on the current state of the art (Art. 26 HRO). The key is stored separately from the personal data by a person or organisational unit that is designated in the application to the ethics committee, and which is not involved in the research project.

Describe if uncoded or coded (genetic or non-genetic) data is used. Indicate the person or organizational unit that holds the key (Art. 26 para. 2 HRO), 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. See example given below.

If applicable: **Biological material** in this project is not identified by participant name but by a unique participant number. Coding is done using a method based on the current state of the art (Art. 26 HRO). The key is stored separately from the biological material by a person or organisational unit that is designated in the application to the ethics committee, and which is not involved in the research project.

Describe if uncoded or coded biological material is used. Indicate the person or organizational unit that holds the key (Art. 26 para. 2 HRO). 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 research project are to be shipped outside the research site, indicate the receiving 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. See example given below.

E.g. "As part of a Master's degree, medical student Felix 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. Mr. 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 an independent person (Prof. Petra Muster, if available give the full address) for storage. Dr. Keller and Mr. 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."

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 person or organizational unit that holds the key (Art. 26 para. 2 HRO).

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 an independent person (Prof. Petra Muster, if available give the full address)."

11. Information on the storage of data and samples / completion of the research project

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 organisational measures (Art. 5 HRO).

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=Itz8v_z7ha4).
Note: 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 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. 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.

Describe what happens to the biological materials and health-related data at project end: e.g. all biological materials are destroyed and health-related data are anonymised upon termination of data analysis.

Note on the **anonymisation** of biological material and health-related personal data: Biological material and health-related personal data is considered anonymised when its association with a specific person is rendered impossible or eliminated in such a way as to allow this association to be re-established only with disproportionate effort. Anonymisation must be effected using a method based on the current state of the art . Items of data which, individually or in combination, allow the association with a specific person to be re-established, such as the first name, surname, address, date of birth or unique identification numbers, must be deleted or modified (Art. 25, paa 2, HRO).

If applicable, the method used for anonymisation must be documented, including a description of the residual risk of reidentification (Art. 25 para 3, HRO).

12. 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." Refer to the note on the anonymisation in chapter 11, if appliable.

13. Ethical and regulatory requirements

Risk-benefit assessment:
Preliminary remark: Please carefully consider the benefits and risks. Some statements are particularly relevant for Big Data projects, for example.

What benefits are expected from this project? Is there a societal and/or personal benefit? Who will benefit from the results? Is the benefit only for the project's sponsors? Do the data donors also benefit, if any? Do the benefits outweigh the risks? For example, will low-quality or potentially discriminatory data be processed?

What data risks are associated with the project and how are they prevented or mitigated? How will data linkage be governed? How can you prevent data from being disclosed to any unintended recipients? Could this result in personal disadvantages for participants and/or inaccurate assumptions or predictions resulting from the research project? If applicable, are particularly vulnerable groups concerned?

What harm could result from these risks (e.g. physical, emotional, financial, etc.)? What would be the extent of the harm? Do the risks and harms affect all stakeholders equally? Will some risks or damages be permanent?

Who assumes liability, e.g. for data related damages? It is the responsibility of the project leader to take appropriate precautions (note: separate project insurance is not usually required).

If applicable and incidental findings are possible: consider the right to know and not to know for results and possible incidental findings. Describe the process how the ethical challenges regarding incidental findings are addressed. Consult the “Guideline for handling incidental findings in medical research” published on swissethics.ch / topics / position papers / incidental findings. Note: The communication of incidental findings only makes sense if they have a high medical relevance for the persons concerned and if the findings are appropriately validated (you can refer to chapter 7 “Informed consent and information of participants” above, if applicable).

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.

14. 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?).

Are the persons concerned informed about the results of the project?

15. 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.

16. References