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 ch. 4 (art. 32-35) and HRO ch. 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.

Apart from the further use of genetic personal data and biological material in uncoded form, general consents from patients are also possible. Various institutions have meanwhile drawn up general consents for patients.

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 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

✂ **... 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 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.:

HRA	Human Resarch 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.

4. Origin of the data/biological material
Where does the data/biological material come from? Is the data source public, private, or from a commercial company? Is the data source credible and of good quality?

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. Information and consent of participants
It must be ensured that adequate and comprehensible information has been given.
How was/is the information provided? Reference to the information leaflet with the consent document 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 must be notified of any change of project leader in advance. The completion or discontinuation of the research project must be reported to the ethics committee within 90 days.

10. 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 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 the project management (Prof. Petra Muster). 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.

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. Hans Muster."

11. 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 still used, a system must be put in place to improve data privacy and data reliability, such as using a protected cloud system with controlled access and user rights.
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 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).

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."

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).

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?).

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

Information on incidental findings: Indicate whether there could be incidental findings. 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.

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