UNIVERSITÄT
BERN

Medizinische Fakultät
Institut für Sozial- und Präventivmedizin

Collaboration agreement on the Swiss Rare Disease Registry

BETWEEN:

The Executive Office of the Swiss Rare Disease Registry (SRDR) based at the **Institute of Social and Preventive Medicine** (ISPM)**,** University of Bern, Mittelstrasse 43, 3012 Bern, Switzerland, represented by the actual **SRDR Director**, **named in Appendix II**

AND

The Steering Board of the SRDR, represented by the **President** and the **Vice-President, named in Appendix II**.

Date: 08.04.22
Version: 1.0
Authors: Swiss Rare Disease Registry (SRDR)

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Foreword

This document regulates the organization of the SRDR. It describes the authority of the different structures within the SRDR: the Executive Office, the kosek, the Steering Board, the Council of the Steering Board, the Data Provider Board, and the Patient Organization Board. The regulations for sharing data, collaboration with research projects, and publication and dissemination of SRDR information and data are set in the document “SRDR: Regulations for research, collaborations, data sharing, and publications”. If requested, the collaboration between the ISPM and data providers such as University Hospitals and Centres for Rare Diseases is set in a “Data Transfer and Use Agreement” (DTUA).

1 Definitions and abbreviations

Rare Disease (RD)
In Europe, a disease is rare when fewer than one in 2'000 people are affected. Today, more than 7'000 rare diseases are known. Rare diseases are described in Orphanet, an online portal for rare diseases and orphan drugs. In Switzerland, the estimated combined prevalence for all rare diseases is 7.2%, corresponding to 580'000 people. Each year 6'000 people are newly diagnosed with a rare disease in Switzerland.

Swiss Rare Disease Registry (SRDR)
The SRDR is a population-based registry with long-term follow-up. The SRDR aims to collect data from all people living with a rare disease in Switzerland. Inclusion criteria are people of any age with a diagnosed rare disease (defined in the Orphanet's list of rare diseases) or a high suspicion of a rare disease treated or living in Switzerland. Participation is voluntary.

kosek
The kosek has the patronage of the SRDR. The kosek supports the SRDR in political issues and its cooperation with the Centres for Rare Diseases.

SRDR Director
The SRDR Director leads the Executive office and is named in Appendix II.

Executive Office and SRDR Team
The Executive Office is based at the ISPM, University of Bern. It includes the SRDR Team at the ISPM (SRDR Director, project manager, scientists, students, data manager, and IT experts from SwissRDL) and their tasks.

Steering Board
The Steering Board includes representatives from University Hospitals, Non-University Hospitals, Private Practices, including pediatrics, adult medicine, and representatives of the patient organizations, kosek, Orphanet Suisse, ISPM, and SwissRDL. The Steering Board is the SRDR Director's superordinate organ and is a supervisory authority. Members of the Steering Board are named in Appendix II.

Council of the Steering Board
The Council of the Steering Board consists of the President, the Vice President of the Steering Board, representatives from ISPM, SwissRDL, and 1-2 members who do not hold any of the functions mentioned above. The Council of the Steering Board is designed to facilitate decision-making between Steering Board meetings. It prioritizes issues for the Steering Board to address.

Data Provider
A Data Provider might be Centres for Rare Diseases, Reference Centres for specific rare diseases, University Hospitals, Non-University Hospitals, private practices, patients, and disease-specific registries that provide the Core Data Set or the Minimal Data Set.

Data Provider Board
The Data Provider Board consists of representatives of data providers. The Data Provider Board supports the SRDR in different matters.

The Patient Board
The Patient Board consists of patient organizations of rare diseases and patients suffering from a rare disease and their representatives. The Patient Board supports the SRDR in different matters.

Stakeholders
Stakeholders compromise stakeholders from different areas, including federal bodies, research platforms, quality assurances, and medical societies. The Stakeholder Group supports the SRDR in various matters.

Centres for Rare Diseases
Centres for Rare Diseases are cross-disease care structures or units. They serve as interdisciplinary contact points for the clarification and coordination of treatments. They have information and provide training tasks, and coordinate experts.

Reference Centres
Reference centres and their network partners are specialized in the care and support of people affected by a specific disease or group of diseases. The specialists of the reference centres coordinate the various tasks in care, develop guidelines for treatment or coordinate further training.

Working Groups
Working Groups for specific questions can be formed.

Abbreviations

CSB	Council of Steering Board
CRF	Case Report Form
DTUA	Data Transfer and Use Agreement
EO	Executive Office
FOPH	Federal Office of Public Health
HRA	Human Research Act
HRO	Human Research Ordinance
IC	Informed Consent
IT	Information Technology
ISPM	Institute of Social and Preventive Medicine
KEK-BE	Kantonale Ethikkommission Bern
PI	Principal Investigator
RD	Rare Disease
SB	Steering Board
SRDR	Swiss Rare Disease Registry

2 Name, history, and current situation

2.1 Name

swiss rare disease registry (srdr)
schweizer register für seltene krankheiten (srsk)
registre suisse des maladies rares (rsmr)
registro svizzero delle malattie rare (rsmr)

2.2 History

Prof. Dr. med. Claudia Kuehni, University of Bern (head of research group on Child and Adolescent Health) and Prof. Dr. med. Matthias Baumgartner, University Children's Hospital Zurich (Director of the Children's Research Center at the University Children's Hospital Zurich), launched 2013 the Swiss Rare Disease Registry (SRDR).
In 2014 the Federal Council passed the National Rare Disease Policy and its implementation plan. Subsequently, an interdisciplinary working group of epidemiologists, clinicians, and data scientists developed a detailed concept for the SRDR. In 2017, this concept was reviewed by a broad range of stakeholders, adapted, revised, and submitted to the ethics committee of Bern, which approved it in 2018.

2.3 Current situation

The SRDR is a population-based registry with long-term follow-up. It fulfills one of the 19 measures proposed in the "National concept for rare diseases" implementation plan, published by the FOPH in 2014. The SRDR is hosted at the ISPM at the University of Bern in the research group on Child and Adolescent Health. Its long-term goal is to collect a Core Data Set from all patients with RD in Switzerland, enabling monitoring and benchmarking of clinical and epidemiological studies on RD, improving the diagnosis, treatment, and quality of life of people with rare diseases in Switzerland, and facilitating patients' participation in national and international studies.

3 Ethical and legal aspects

3.1 Ethics Approval

Ethics Committee: Kantonale Ethikkommission Bern (KEK-BE)
Approval: 11. December 2018, Project-ID: Nr. 2017-02313 and related amendments
Duration of validity of approval: No end of the study is planned. The KEK-BE did not define a duration of validity of approval.
Categorization: "Risk Category A" (HRO Art.7, Abs. 3, lit.a.)

- Details are described in the research plan of the ethics application.
- The ethics application does cover
    - Studies using the Core Data Set (Appendix V) or the Minimal Data Set (Appendix VI).
    - Data linkage with, e.g., data from the FSO, whereby the ethics committee must be informed in advance.
    - Ancillary studies that use the patient information and informed consent of SRDR (see Appendix I).
- Studies that require an amendment to the ethics application are
    - Questionnaires for patients and physicians.
- Studies that require a separate ethics application are:
    - observational studies that collect new data not available in medical records
    - clinical investigation studies that collect new data involving patient examination
    - studies investigating research questions outside of the scope of SRDR.

3.2 Legal authority of the SRDR

The SRDR is based at the ISPM of the University of Bern. The ISPM, University of Bern, is the legal authority of the SRDR. The Steering Board is the superordinated organ.

3.3 Provision of FOPH

The FOPH approved financial subsidies under Article 24 of the national law on cancer registration for five years (2020-2024) under the following conditions:
The SRDR report to the FOPH annually on

- the management of the registry
- monitoring and benchmarking
- national and international publications
- other forms of use of the registry data (e.g., reporting for treating clinicians).

The report shall also include, as a minimum requirement, the following information:

- evidence of the correct use of the grant awarded
- a qualitative report on the use of the grant awarded
- the data structure
- the number of registered patients by calendar year
- the list of data providers and an estimate of the completeness of registrations
- special activities, special occurrences, and relevant developments

3.4 Legislation

The SRDR will be carried out in accordance with the HRA and the HRO and the Swiss Data Protection Act as applicable.

3.5 Data Transfer and Use Agreements

DTUA governs the transfer and use of data made available by a data provider (e.g., Centres for Rare Diseases, disease-specific registries) to the ISPM, represented by the actual SRDR Director, Prof. Dr. med. Claudia Kuehni. The DTUA defines data providers' rights, responsibilities, and obligations and the ISPM regarding permitted use, ownership, publications, intellectual property, and liability when data is being transferred or accessed in the frame of this project.

4 Objective of the SRDR

The SRDR will provide representative data on RD in Switzerland as a basis for monitoring RDs by FOPH; it will facilitate research on RDs and enable the participation of Swiss patients in national and international studies. The SRDR will thus help to improve patient care and health care planning on a national and cantonal level.
The primary objectives of the SRDR are to:

- Collect representative, population-based epidemiological data on RDs in children and adults in Switzerland (incidence, prevalence, risk factors).
- Monitor outcomes (survival, morbidity) and assess predictors of long-term outcomes.
- Collect relevant data for health service research (treating institutions, diagnostics, management, quality indicators).
- Constitute a platform for clinical, epidemiological, basic, and translational research.
- Facilitate and document patient participation in national and international (clinical) studies.
- Integrate or connect to data from existing disease registries to harmonize data on RDs in Switzerland.
- Enabling networking between patients.
- Be part of the international RDs registry network.

5 Organization of the SRDR

Figure 1 visualizes the interaction of the organs and indicates the documents that regulate these interactions.

Governing bodies of the SRDR are:

- Patronage kosek
- Steering Board
- Council of the Steering Board
- Executive Office

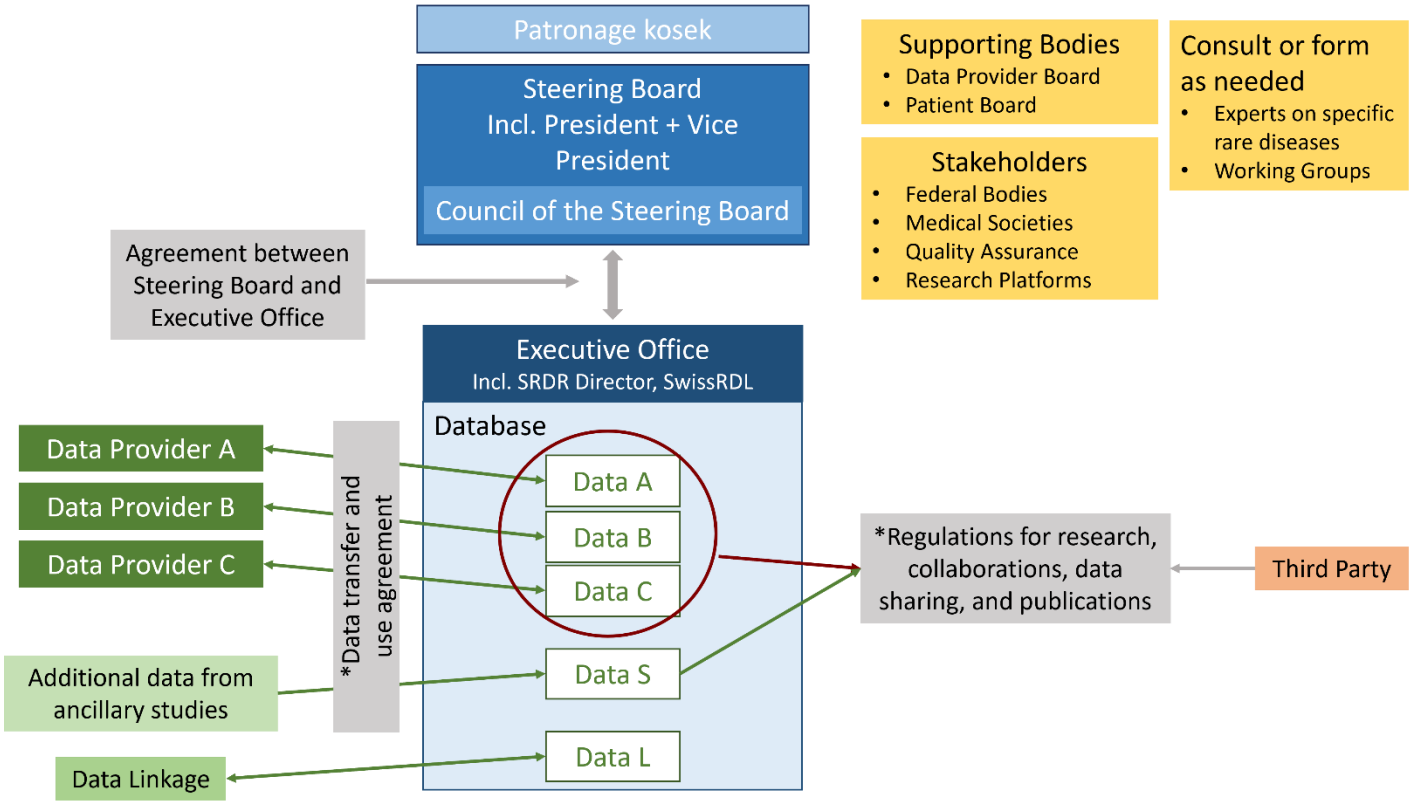
Supporting bodies of the SRDR are

- Data Provider Board
- Patient Board

Further structures

- Stakeholders
- Experts on specific rare diseases
- Working Groups

Figure 1 SRDR Organisation



5.1 kosek

The kosek has the patronage of the SRDR. The kosek supports the SRDR in its collaboration with the Centres for Rare Diseases and the Reference Centres.

5.2 Steering Board

5.2.1 Members of the Steering Board

Formation of the Steering Board:

a) The Steering Board consists of 9-13 members, including the President and the Vice President.
b) The Steering Board should include at least 4 representatives from health care providers (University Hospitals, Non-University Hospitals, Private Practices, including pediatrics, and adult medicine), 1 representative from a patient organization, 1 representative from kosek, 1 representative from Orphanet Suisse, 1 representative from ISPM, ideally the SRDR Director, and 1 representative from SwissRDL.
c) The Steering Board should comprise members from all regions of Switzerland and not include more than 1 member from the same University Hospital, Non-University Hospital, or Private Practice.
d) Each member of the Steering Board may designate a Substitute.
e) The Steering Board Members and their substitutes are named in Appendix II.

5.2.2 Admission, resignation, and expulsion

a) The Steering Board appoints all members of the Steering Board based on an absolute majority of votes cast.
b) The Steering Board agrees collegially on the appointment of the President and the Vice President.
c) Applications for new members have to be proposed and supported by a member of the Steering Board. The Steering Board assesses applications for Steering Board members and decides based on an absolute majority of votes cast (ideally consensus).
d) A vacancy does not need to be replaced as long as the Steering Board comprises at least 9 members.
e) A membership expires as a result of resignation or expulsion. Notification of the intention to resign must be given in writing, allowing a notice period of three months.
f) The expulsion of a member of the Steering Board by the Steering Board shall be subject to a two-thirds majority of votes cast. The reason for excluding a member of the Steering Board must be profound, e.g., a violation of Swiss law.
g) The Steering Board seeks to have a healthy renewal of the leadership position to ensure knowledge transfer to younger members.

5.2.3 Authorities and tasks of the Steering Board

The Steering Board is the SRDR Director's superordinated organ and has a steering function. The authorities and tasks of the Steering Board are summarized as follows:

a) Represents the objectives and interests of the SRDR
b) Revises and approves agreements
c) Revises and approves modalities of the database and data transfer
d) Supports the SRDR in financial aspects
e) Defines procedures of research within SRDR and third parties

A list of the authorities and tasks is provided in Appendix VII, tables 1 and 3.

5.2.4 President and Vice President

The President and the Vice President should belong to different organizations.

Authorities and tasks of the President

a) Presides the Steering Board and the Council of the Steering Board
b) Is the primary contact person for the Executive Office
c) Is the contact person in urgent situations

d) Mediates in case of conflicts
e) Has deciding vote in case of a tie (50:50)

Authorities and tasks of the Vice President

a) Is the contact person in urgent situations
b) Mediates in case of conflicts
c) Substitutes the President

5.2.5 Convocation of the Steering Board

The face two face or virtual meetings of the Steering Board are held at least twice per year. Any member may request an extraordinary appointment by contacting the Executive Office.

5.2.6 Right to vote and resolutions

a) Each Steering Board member shall have one vote.
b) The Steering Board shall constitute a quorum if at least two-thirds of those eligible to vote are present.
c) Votes may be cast by a show of hands unless at least three voting members request a secret ballot.
d) The members shall act in good faith to cooperate and seek agreement concerning issues to be decided. The members shall first try to reach a consensus. However, if consensus cannot be reached, decisions of the Steering Board will require a two-thirds majority.
e) A resolution may be adopted by written consent (including votes via email) provided that at least two-thirds of all Steering Board members are voting and none of the persons with voting rights requests that the matter is discussed in person and the resolution is adopted at a meeting. The voting or the request for discussion and decision at a meeting must occur within two weeks.

5.3 Council of the Steering Board

5.3.1 Members of the Council of the Steering Board

a) The Council of the Steering Board consists of 5-6 members.
b) The Council of the Steering Board includes the President and the Vice President of the Steering Board, 1 representative from ISPM, ideally the SRDR Director, 1 representative from SwissRDL, and 1-2 members who do not hold any of the functions mentioned above.
c) The Council of the Steering Board Members are named in Appendix III.

5.3.2 Admission, resignation, and expulsion

a) The members of the Council of the Steering Board must
    i. Be a member of the Steering Board
    ii. Invest a significant part of his/her working time in supporting the objectives of the SRDR
b) The members of the Council of the Steering Board must meet one or more of the following requirements
    i. Strong scientific track record (publishing in peer-reviewed scientific journals)
    ii. Successful grant applications as PI at large peer-reviewed funding organizations (SNSF or EU level)
    iii. High-level experience in health policy
    iv. Broad experience in performing registry-based clinical studies
    v. Strong experience in rare diseases with a national or international network
c) The Steering Board members vote about the admission, resignation, and exclusion of the members of the Steering Board Council.

5.3.3 Authorities and tasks of the Council of the Steering Board

The Council of the Steering Board has the power to act on behalf of the Steering Board. It is designed to facilitate decision-making between Steering Board meetings or in urgent situations. It prioritizes issues for the Steering Board to address. The decisions and documents resulting from the meetings of

the Council of the Steering Board are passed on to the Steering Board for processing and final approval, or the Council of the Steering Board consults the Steering Board as needed. The authorities and tasks of the Council of the Steering Board are described in Appendix VII, Tables 1 and 3.

5.3.4 Convocation of the Council of the Steering Board

The meetings or phone/video conferences of the Council of the Steering Board shall take place at least every second month.

5.3.5 Right to vote and resolutions

a) Each Council of the Steering Board member has one vote.
b) The Council of the Steering Board shall constitute a quorum if at least three-quarters of those eligible to vote are present.
c) Votes may be cast by a show of hands unless at least one voting member requests a secret ballot.
d) The members shall first try to reach a consensus. However, if consensus cannot be reached, decisions of the Council of the Steering Board will require a two-thirds majority.
e) A resolution may be adopted by written consent (including votes via email) provided that at least three-quarters of all Council of the Steering Board members are voting and none of the persons with voting rights requests that the matter is discussed in person and the resolution is adopted at a meeting. The voting or the request for discussion and decision at a meeting must occur within two weeks.

5.4 Executive office

The executive Office hosts the database (all variables, archived documents, and related documents). The SRDR Director leads the Executive office. The team around the SRDR Director executes the activities under the guidance of the SRDR Director and the President of the Steering Board.

5.4.1 Authorities and tasks of the Executive Office

The Executive Office holds the operational lead of the SRDR.
The authorities and tasks of the Executive Office are summarized as follows:
Prepares meetings

a) Develops, prepares, and revises documents such as agreements, ethics applications, annual reports
b) Main contact point for the data providers to discuss modalities of data transfer
c) Together with the Steering Board and the Council of the Steering Board, defines procedures of research within SRDR and third parties

The authorities and tasks of the Executive Office are described in Appendix VII **Fehler! Verweisquelle k onnte nicht gefunden werden.**.

5.5 Data Provider Board

5.5.1 Members of the Data Provider Board

a) Members of the Data Provider Board are all entities who provide the Core Data Set and the Minimal Data Set (Appendix V and Appendix VI).
b) Each entity that provides data designates a representative to be a member of the Data Provider Board
c) The formation of the Data Provider Board will be redefined as soon as the data provider board contains more than 15 members.

5.5.2 Authorities and tasks of the Data Provider Board

The Data Provider Board supports the SRDR in different matters. The authorities and tasks of the Data Provider Board are described in Appendix VII Table 2.

5.5.3 Convocation of the Data Provider Board

The Executive Office organizes a meeting with the Data Provider Board annually. Members of the Data Provider Board may request additional appointments from the Executive Office.

5.6 The Patient Board

5.6.1 Members of the Patient Board

a) The Patient Board consists of 15 members.
b) Invited are patients as well as patient organizations.
c) Orphanet Suisse provides a list of patient organizations upon request.
d) Each patient organization that is a member designates a representative.
e) The representatives of the patient organizations may elect a substitute if they so wish.
f) The members of the Patient Board select an organization which:
    - chairs the patient organization board
    - is the main contact person for the Executive Office
    - regulates the membership

5.6.2 Authorities and tasks of Patient Board

The Patient Board supports the SRDR in different matters. The authorities and tasks of the Patient Board are described in Appendix VII Table 2.

5.6.3 Convocation of the Patient Board

The Executive Office organizes an information event for Patient Board on an annual basis. Members of the Patient Board may request additional meetings from the Executive Office.

The Chair of the Patient Board is in regular contact with the Executive Office.

5.7 Stakeholders

5.7.1 Members

Stakeholders are from different areas, including federal bodies, research platforms, quality assurances, and medical societies (Appendix VIII)

5.7.2 Information Event for Stakeholders

The Executive Office organizes an information event for the stakeholders on an annual basis. Stakeholders may request additional meetings from the Executive Office as needed.

5.8 Experts on specific rare diseases

The Steering Board or the Council of the Steering Board will consult experts on specific rare diseases as required. National and international experts will be identified via Orphanet, the European Reference Networks, and data providers and contacted for different projects and questions.

5.9 Working Groups

a) To discuss specific questions, Working Groups can be formed. The SRDR forms the Working Groups as needed. The members of the Steering Board, the Data Provider Board, the Patient Board, or the Stakeholder can request to form a Working Group by contacting the Executive Office, who will inform the Council of the Steering Board.
b) The Council of the Steering Board forms and defines Working Groups. The Steering Board approves the proposed Working Groups.
c) Within each Working Group, one member shall be appointed collegially to lead the Working Group. The Working Group Leader shall be in close contact with the Executive Office. If needed, the Executive Office shall attend the Working Groups' meetings.
d) The Executive Office informs the Steering Board about the activities of the Working Groups during the meetings of the Steering Board or as needed.
e) The Working Groups are named in Appendix IX.

f) The Working Group shall be dissolved by the Steering Board upon completion of its work.

5.10 Data providers

A data provider can be, for example, Centres for Rare Disease, Reference Centres for specific rare diseases, University Hospitals, Non-University Hospitals, clinics, private practices, patients, and disease-specific registries (Appendix IV) that provide the Core Data Set (Appendix V) or the Minimal Data Set (Appendix VI). If desired, the collaboration with the data providers is regulated by DTUA.

a) For each data provider, the specific procedure for data collection is elaborated with the Executive Office. Local conditions are taken into account.
b) Data providers inform patients with RD about the SRDR, ask for consent, and regularly provide data to the SRDR.
c) The Executive Office gives regular feedback to the data providers.
d) For each data provider, it is specified who is the contact person for modalities of data transfer, consents, Orpha coding, and legal issues.

6 Confidentiality and Data Protection

Confidentiality and data protection are described in detail in the ethics application research plan in Section 7. Shortly, some critical points:

a) Health-related personal data captured during this project are strictly confidential.
b) Access to personal identifying data is only given to persons who need this information to perform their duties (e.g., data entry, mailing of questionnaires, data linkage).
c) Each member of the SRDR Team working with sensitive patient data is informed in detail by the project manager about the legal situation, the duty of care, the privacy laws, and security.
d) Each user has a personal password for the medical documentation software MEMDoc. A role concept (site investigator, statistician, monitor, administrator, etc.) regulates the access rights to specific variables and patients in the database.
e) Physicians and selected staff in the participating medical sites only have access to personal information from the patients attending their medical site.
f) In cases where the transfer of medical information from the medical site to the MEMDoc database cannot be done online, such as private practices, digitalized medical information is collected on-site and either transferred via a secure email connection (HIN) or transported in an encrypted HardDisk or TrueCrypt container (typically Advanced Encryption Standard encrypted) to the ISPM. All data and files are then imported at the ISPM into the secure MEMDoc database and deleted from the transport device.
g) At the ISPM, signed Informed Consents forms, withdrawals, CRFs, and further documents or data mediums containing identifying or medical information are stored in a locked personal filing cabinet of the project manager or data manager of the SRDR at ISPM) are digitalized and archived electronically in the secure MemDoc database.

7 Finances

7.1 Responsibilities

a) The Executive Office manages the finances. The SRDR Director and the President of the Steering Board need to approve the allocation of funds.
b) The Steering Board members actively support the Executive Office for fundraising.

7.2 Income

The SRDR covers its funding requirements as follows:

a) Grants from not-for-profit organizations

b) Contributions for research from public funds and from the bodies entrusted with the research funding
c) Contributions of pharma companies
d) Other revenues
e) Contribution of the ISPM (salary of the SRDR Director and the leader of SwissRDL plus all general IT- and administrative support, all infrastructure such as rooms, photocopiers, fax, phones, etc.)
f) Matching-Funds from the University Hospitals to perform the following tasks (non-exhaustive list):
    - Coding affected patients using Orphacode
    - Obtaining informed consent from the patients
    - Data preparation for data transfer
    - Creation of interfaces for the transfer of data to the SRDR
    - Internal information campaigns
    - Participation in meetings with SRDR

7.3 Allocation of funds

The funds are allocated based on the cost estimates in connection with the research programs and the SRDR. Expenses to be met from the funds are:

a) Salaries of the SRDR Team members at the ISPM.
b) Expenses incurred by the meetings of the Steering Board and by the presentation of the research findings at national or international events.
c) The development and hosting of the database.
d) Consumables, like laptops, printing costs, or the website.
e) Other expenditure in connection with the realization of the statutory aims of the SRDR.

7.4 Liability

The assets of the organization are the sole guarantor for the liabilities of the organization. Members who have resigned or been expelled shall have no claims on the organization's assets.

7.5 Transparency

The annual final revision is presented to the Steering Board.

8 Final provisions

8.1 Entry into force

This Agreement shall enter into force on the day it is accepted and adopted by the Steering Board and the SRDR Director.

8.2 Amendments to this agreement

Steering Board resolutions regarding a full or partial amendment to this agreement require a two-thirds majority of the members of the Steering Board to be adopted. This includes decisions about the organization of the SRDR (e.g., the inclusion of a new group of stakeholders), the fusion with another registry, or changes concerning data deletion/transfer.

8.3 Termination of this Agreement

a) The Steering Board and the ISPM, represented by the actual SRDR Director, may terminate this Agreement at any time by giving a 12 month prior written notice unless a material breach of this Agreement by one of both parties occurs.
b) The provisions concerning Confidentiality, Data protection, and Publications shall survive the Agreement’s expiration.

8.4 Dissolution of the SRDR Steering Board

a) The dissolution of the Steering Board may only be agreed upon by a two-thirds majority of the members present at an extraordinary meeting of the Steering Board summoned explicitly and solely for the purpose of passing a resolution to this end.
b) After the dissolution of the Steering Board, the Executive Office with the database remains at the ISPM under the lead of the SRDR Director.

8.5 Dissolution of the SRDR Executive Office

a) An interruption or termination of the SRDR has to be reported to
   - Any sponsor such as the FOPH, in accordance with the applicable guidelines of the sponsor
   - has to be reported to the KEK-BE within 90 days.
b) The respective sponsor decides how to proceed with the remaining assets.
c) If applicable, a copy of the database shall pass to the new Executive Office as soon as all legal aspects are met (e.g., ethic approval and DTUA).
d) Principle investigators of projects conducted in the context of the SRDR decide whether the additional data collected for the project shall remain at the ISPM or be transferred to the new Executive Office.

9 Appendixes

9.1 Appendix I: Ancillary Study and IC of SRDR

Under the following conditions, an Ancillary Study can use the patient information and the informed consent of SRDR and does not need separate ethical approvals

- The Ancillary Study aligns with the SRDR research protocol approved by the local ethics committee
- Aims of Ancillary Study are included in the aims of SRDR
- No interventions or assessments are done during the Ancillary Study
- Additional data are already available from medical records and not specifically collected during the Ancillary Study
- SRDR stores data and provides data maintenance and security
- Mode of financing corresponds to SRDR

9.2 Appendix II: Members of the Steering Board and their substitutes

As of 08.04.2022

- President: Prof. Dr. med. Matthias Baumgartner, University Children's Hospital Zurich (Substitute: Vice-President)
- Vice-President: Agnes Nienhaus, kosek (Substitute: Christine Guckert, kosek)
- SRDR Director: Prof. Dr. med. Claudia Kühni, University of Bern (Substitute: PD. Dr. Anne Tscherter, University of Bern)
- Dr. med. Loredana D'Amato Sizonenko, Hôpitaux Universitaires de Genève (HUG), Coordinatrice Orphanet Suisse (Substitute: Martin Arles, project manager Orphanet)
- Prof. Dr. med. Hans H. Jung, University Hospital Zurich (Substitute: Prof. Dr. med. Felix Beuschlein, University of Hospital Zurich)
- Prof. Dr. med. Jean-Marc Nuoffer, Center for rare diseases, University Hospital, Inselspital Bern (Substitute: Marlies Morf, Center for rare diseases, University Hospital, Inselspital Bern)
- Dr. Adrian Spörri, SwissRDL, University of Bern
- Dr. med. dent. Alfred Wiesbauer, ProRaris (Substitute: Therese Stutz, ProRaris)
- Dr. med. Andreas Wörner, University Children's Hospital Basel (UKBB) (Substitute: Prof. Dr. med. Emanuel Christ University Hospital Basel (USB))
- Dr. med. Christel Tran, Centre hospitalier universitaire vaudois (CHUV)

9.3 Appendix III: Members of the Council of the Steering Board

As of 08.04.2022

- Prof. Dr. med. Matthias Baumgartner, University Children's Hospital Zurich
- Agnes Nienhaus, kosek
- Prof. Dr. med. Claudia Kühni, University of Bern
- Dr. Adrian Spörri, SwissRDL, University of Bern
- Dr. med. dent. Alfred Wiesbauer, ProRaris
- Dr. med. Loredana D'Amato Sizonenko, Hôpitaux Universitaires de Genève (HUG)

9.4 Appendix IV: List of Data Providers

non-exhaustive list

- AllKids
- H+ (Hospitals of Switzerland)
- Participating disease-specific registries
- Physicians treating patients with rare diseases in private practice

- SwissPedNet
- Centres for Rare Diseases
- University Hospitals
- Non-University Hospitals
- Reference Centres for specific rare diseases

9.5 Appendix V: Core Data Set

X = entry mandatory; O = entry mandatory if a specific condition is met

	Variable	Description	Mandatory
Patient Information			
1. Personal Information			
	Patient ID	Clinic-specific code in Switzerland	X
	Date of Birth	dd.mm.yyyy	X
	Sex	-Female -Male -Other -Unknown	X
	First name		X
	Last name		X
	Street name		X
	Street number		
	Zipcode		X
	City		X
	Country		X
	Phone		
	E-mail		
	Correspondence Language	-German -French -Italian -English -Other -Unknown	X
2. Legal Representative			
	Relationship	Parents, legal custodians, etc.	
	First name		
	Last name		
	Street name		
	Street number		
	Zipcode		
	City		
	Country		
	Phone		
	E-mail		
3. Informed Conse			
	Information date	Date on which patient has been informed by the e.g., the clinic	X
	Consent status	-Consent signed -Consent refused	

	Variable	Description	Mandatory
		-No signature/no refusal within 6 weeks -Consent withdrawn	X
	Date of signature/ refusal/ withdrawal	dd.mm.yyyy	X
	Level of withdrawal	-stop medical data collection -stop being contacted for questionnaire surveys or nested studies -keep minimal data set only -unknown	O
4. Patient Status			
	Vital status	-Alive -Dead -Lost to follow-up -Unknown	
	Date of death	dd.mm.yyyy	
Clinical Information			
1. Classification			
	ORPHAcode		X
	Name of diagnosis	Information is automatically fetched from Orphanet.	
	ORPHA-Link	Information is automatically fetched from Orphanet.	
	ORPHAcode status	Information is automatically fetched from Orphanet.	
	Classification level	Information is automatically fetched from Orphanet.	
	Type of disorder	Information is automatically fetched from Orphanet.	
2. Diagnosis Information			
	Date of diagnosis	-dd.mm.yyyy -unknown	X
	Date valid until	dd.mm.yyyy if a diagnosis is not valid anymore, the date until the diagnosis was valid	
	Type of diagnosis	-confirmed -suspected	X
	Diagnostic method	-Molecular genetics -Biochemistry -Histology -Clinical -Imaging -EEG -Newborn Screening -Prenatal -Cytology -Antibody Status -Other	X

	Variable	Description	Mandatory
		-Unknown	
	Specify other diagnostic method		O
	How many genes or chromosomes are affected	-1 -2 -3 -unknown	O
	Affected gene or chromosome		O
	Used nomenclature		O
	Diagnosed mutation(s)		O
	Mutation carrier	-Symptomatic -Presymptomatic	O
3. Disease History			
	Disease-related symptoms (past or current)	-yes -no -unknown	X
	Age at first occurrence of symptoms	-Antenatal -Newborn (0-4 weeks) -First year of life (> 4 Weeks - 1 yr.) -Toddler (1 - 5 yrs.) -Schoolchild (6 - 12 yrs.) -Adolescent (13 - 17 yrs.) -Adult (> 18 yrs.) -unknown	O
	Year of first symptoms occurrence		
	Month of first symptoms occurrence	-January -February -March -April -May -June -July -August -September -October -November -December	
	Date of first contact with specialized center	dd.mm.yyy	
Registered in another Registry			
	Type of the registry	-National registry -International registry -Other -Unknown	
	Other type of registry	specify	
	Name of registry		
	Patient's registry ID		
	Biosample available for research	-Yes -No	

	Variable	Description	Mandatory
		-Unknown	
	Name of biobank	Link or name of the biobank where th biological sample is stored	
Treating Institution			
	Name of treating clinic/ hospital/ private practice	automatically generated	
	Name of treating department	automatically generated	

9.6 Appendix VI: Minimal Data Set

X = entry mandatory; O = entry mandatory if a specific condition is met

	Variable	Description	Mandatory
Patient Information			
1. Personal Information			
	Year of Birth	yyyy	X
	Sex	-Female -Male -Other -Unknown	X
2. Informed Consent			
	Information date	Date on which patient has been informed by the e.g., the clinic	X
	Consent status	-Consent signed -Consent refused -No signature/no refusal within 6 weeks -Consent withdrawn	X
	Date of signature/ refusal/ withdrawal	dd.mm.yyyy	X
	Level of withdrawal	-stop medical data collection -stop being contacted for questionnaire surveys or nested studies -keep minimal data set only -unknown	O
3. Patient Status			
	Vital status	-Alive -Dead -Lost to follow-up -Unknown	
	Year of death	yyyy	
Clinical Information			
1. Classification			
	ORPHAcode		X
	Name of diagnosis	Information is automatically fetched from Orphanet.	
	ORPHA-Link	Information is automatically fetched from Orphanet.	
	ORPHAcode status	Information is automatically fetched from Orphanet.	

	Variable	Description	Mandatory
	Classification level	Information is automatically fetched from Orphanet.	
	Type of disorder	Information is automatically fetched from Orphanet.	
2. Diagnosis Information			
	Year of diagnosis	-yyyy -unknown	X

9.7 Appendix VII: List of authorities and tasks

Table 1 Authorities and tasks of the Steering Board, the Executive Office, and SwissRDL

Steering Board	Council of Steering Board	Executive Office	SwissRDL
General			
1. Define the objectives of the SRDR 2. Protect the interests of the SRDR 3. Periodical check of the objectives, the datasets, the procedures, and this agreement 4. Approve working groups and groups of experts for specific rare diseases. 5. Elect the Council of the Steering Board	1. Together with SB a) define the objectives of the SRDR b) protect the interests of the SRDR c) periodical check of the objectives, the datasets, the procedures, and this agreement 2. Define and form working groups and groups of experts for specific rare diseases.[2]	1. Operational lead 2. Organize meetings, phone conferences, board meetings	1. Technical lead
Legal issues			
1. Revise and approve a) this agreement between SB and EO/ISPM b) DTUA c) agreements for data sharing, dissemination, and authorship.[1]	1. Together with SB, revise and approve a) this agreement between SB and EO/ISPM b) DTUA c) agreements for data sharing, dissemination, and authorship.[1] 2. Revise and approve[2] a) agreements/contracts with the third parties[3] b) ethics application and amendments	1. Revise and approve this agreement between SB and EO/ISPM 2. Develop and revise agreements for a) DTUA b) agreements for data sharing, dissemination, and authorship.[1] c) agreements/contracts with the third parties[3] 3. Prepare and revise ethics application and amendments	1. Data storage, security, and backup 2. Regulation of access

[1] e.g., PIs of Ancillary Studies, media, patient organization, industry

[2] The Council of the Steering Board consults the Steering Board as needed

[3] e.g., pharma industry, patient organization, foundations, FSO, COO, SPHN

Steering Board	Council of Steering Board	Executive Office	SwissRDL
Database and data collection			
1. Shared with CSB, revise and approve a) code book b) data base model c) procedures for data entry and data transfer d) procedure of data linkage with routine data e) procedures for self-notification and validation 2. Promote the participation of data providers through their networks	1. Shared with SB, revise and approve a) code book b) data base model c) procedures for data entry and data transfer d) procedure of data linkage with routine data e) procedures for self-notification and validation 2. Promote the participation of data providers through their networks	1. Shared with SwissRDL define, develop and revise: a) code book b) data base model c) procedures for data entry and data transfer d) procedures for data linkage with routine data e) procedures for self-notification and validation 2. Coordinate and support data collection 3. Coordinate new modules (disease-specific registries and ancillary studies) 4. Check data quality 5. Archive documents	1. Shared with SwissRDL define, develop and revise: a) code book b) data base model c) procedures for data entry and data transfer d) procedures for data linkage with routine data e) procedures for self-notification and validation
Finances			
1. Shared with CSB and EO develop long-term funding strategy 2. Approve annual financial reports of EO 3. Acknowledge[4] reports for funding institutions	1. Shared with SB and EO develop long-term funding strategy 2. Approve annual financial reports of EO 3. Revise and approve reports for funding institutions	1. Shared with SB and CSB develop long-term funding strategy 2. Prepare annual financial reports 3. Prepare and revise reports for funding institutions 4. Manage budget, funds, and personnel	1. Assist in fundraising 2. Report operating costs to EO

[4] To accept, recognize, confirm, or admit the existence or truth of something.

Steering Board	Council of Steering Board	Executive Office	SwissRDL
Communication and Dissemination			
1. Relate with other organizations which pursue similar objectives 2. Acknowledge[4] a) communication with official bodies b) reports for partners, authorities, and general public c) annual report 3. Shared with the EC and EO: a) Present the SRDR to the public/medical professional and in international collaborations and conferences b) Communicate with partner organizations, media, organizations, official bodies, industry, and patients and families	1. Relate with other organizations which pursue similar objectives 2. Define communication with official bodies as needed 3. Revise and approve a) reports for partners, authorities, and the general public as needed b) annual report 4. Shared with the SB and EO: a) Present the SRDR to the public/medical professional and in international collaborations and conferences b) Communicate with partner organizations, media, organizations, official bodies, industry, and patients and families	1. Develop and maintain the SRDR website 2. Inform data providers 3. Prepare and revise a) reports for partners, authorities, and general public b) annual report 4. Shared with SB an EC: a) Present SRDR to the public/medical profession and in international collaborations and conferences b) Communicate with partner organizations, media, organizations, official bodies, industry, and patients and families 5. Answer questions from patient organization and patients 6. Prepare and revise the annual report	1. Together with EO: develop the SRDR website

[4] To accept, recognize, confirm, or admit the existence or truth of something.

Steering Board	Council of Steering Board	Executive Office	SwissRDL
Research			
1. Shared with CSB a) Decide on establishment of scientific board b) Define SRDR research questions c) Revise and approve internal research projects (applications, analysis, publications) 2. Shared with CSB and EO: a) Define procedures for research applications, data sharing, and publication rules b) Coordinate and conduct scientific projects (applications, analysis, publications) c) Provide letters of support	1. Shared with SB a) Decide on establishment of scientific board b) Define SRDR research questions c) Revise and approve internal research projects (applications, analysis, publications) 2. Shared with SB and EO: a) Define procedures for research applications, data sharing, and publication rules b) Coordinate and conduct scientific projects (applications, analysis, publications) c) Provide letters of support	1. Keep track of all new and ongoing research projects 2. Prepare and revise internal research projects (applications, analysis, publications) 3. Shared with SB and CSB: a) Define procedures for research applications, data sharing, and publication rules b) coordinate and conduct scientific projects (applications, analysis, publications) 4. Keep track of all new and ongoing research projects	1. Support research projects as needed
Data sharing and inquiries			
1. Shared with CSB: a) Control and assist inquiries b) Define data sharing and publication rules	1. Shared with SB: a) Control and assist inquiries b) Define data sharing and publication rules	1. Evaluate, answer and control inquiries 2. Deliver on request of the SB and CSB data-sets for research projects and to third parties	1. Deliver on request of the SB, CSB, and EO data-sets for research projects and to third parties

Steering Board	Council of Steering Board	Executive Office	SwissRDL
Operation of registry			
N/A	N/A	1. Setup quality management 2. Perform quality controls	1. Technical operation of the registry 2. Data base administration 3. Development of a) registry software b) automatic data transfer c) semi-automatic data transfer d) self-notification web platform 3. Central data monitoring
Support			
N/A	N/A	1. Support for general inquiries about registry 2. Administrative support of a) CSB and SB b) working groups c) Experts for rare disease specialities	1. First level support for external partners 2. User management 3. Offer webinars to registry users 4. Second level support, IT issues, support for web services 5. Train data providers

Table 2 Authorities and tasks of the supporting bodies

Data Provider Board	Patient Board
General	
1. Support collaboration with stakeholders, governmental and private 2. Express an opinion on the strategic organization of the registry, such as data collection 3. Express an opinion on clinical developments 4. Can request to build a working group on specific topics	1. Support collaboration with stakeholders, governmental and private. 2. Express an opinion on the strategic organization of the registry, such as patient recruitment 3. Express an opinion on clinical developments 4. Can request to build a working group on specific topics
Legal issues	
1. Are informed and consulted as needed about a) ethics application and amendments b) Standard of DUTA c) Regulation for data sharing, dissemination, authorship.[1]	1. Are informed and consulted as needed about: a) ethics application and amendments
Database and data collection	
1. Are informed and consulted as needed about a) code book b) procedures for data entry and data transfer 2. Promote the participation of clinics/private practices through their networks	1. Are informed and consulted as needed about a) procedures for self-notification and validation 2. Promote the participation of patients through their networks
Finances	
1. Assist in fundraising as needed	1. Assist in fundraising as needed
Communication and Dissemination	
1. Increase awareness of the SRDR in the organization of the data provider	1. Increase awareness of the SRDR in the community of patients 2. Support and advise the EO in developing promotional material and patient brochures 3. Assist in the communication of study results in an accessible language
Research	
1. In the frame of working groups: a) Support research collaboration with other data providers b) Identify and advise on research topics relevant to rare diseases	1. In the frame of working groups: a) Identify and advise patients on relevant research topics b) Advise clinical outcome assessments (COA), including patient-reported outcome (PRO) c) User-testing of forms, procedures, and PRO tools d) Assist in reviewing research proposals as needed

[1] e.g., PIs of Ancillary Studies, media, patient organization, industry

Table 3 Approval of requests for funding, contracts, and allocation of funds

Approval	Steering Board	President	Vice President	SRDR Director
Request for funding		x	x	x
Contracts		x	x	x
Allocation of funds		x	x	x

9.8 Appendix VIII: Stakeholder

non-exhaustive list

- ANQ: Nationale Verein für Qualitätsentwicklung in Spitälern und Kliniken)
- COO: Cantonal Compensation Office
- FMH: Foederatio Medicorum Helveticorum
- FOPH: Federal Office of Public Health
- FSO: Federal Statistical Office
- GDK: Schweizerische Gesundheitsdirektorenkonferenz
- Obsan: Gesundheitsobservatorium obsan
- SAMW: Schweizerische Akademie der medizinischen Wissenschaften
- SAQM: Schweizerische Akademie für Qualität in der Medizin
- SBP: Swiss Biobanking Plattform
- SCTO: Swiss clinical trial organisation
- SBP: Swiss Biobank Plattform
- SIB: Swiss Institute of Bioinformatics
- SPHN: Swiss Personalized Health Network
- SULM: Schweizerische Union für Laboratoriumsmedizin
- SwissPedNet: Swiss Research Network of Clinical Pediatric Hub
- unimedsuisse

9.9 Appendix IX: Working Groups

As of 06. December 2021

1. ORPHA Coding
    a. Formed: 06. June 2021
    b. Lead Marlies Morf, University Hospital Bern,
    c. meets once per month
    d. The executive Office attends the meetings of this working group