



29 May | 12h00 - 13h00 | online seminar

Facts and pitfalls of observational studies

Quality: Law, praxis and common hurdles

In this seminar session, you will learn about «quality in a nutshell». We will start with the respective law and then give practical tips and examples on how to keep the quality of your project high.

Registration and more information:
sctoplatforms.ch/HRO-training-series

- **Questions :**
 - in the chat
 - by raising hand and unmuting after presentation
- Presentations will be **recorded** (Q&A won't)
- **Video, slides & Q&A [provided here](#)** after session
- **Feedback poll** at the end → please fill in!
- Please **mute** yourself during the presentation
- Certificate of attendance: **correct name** !



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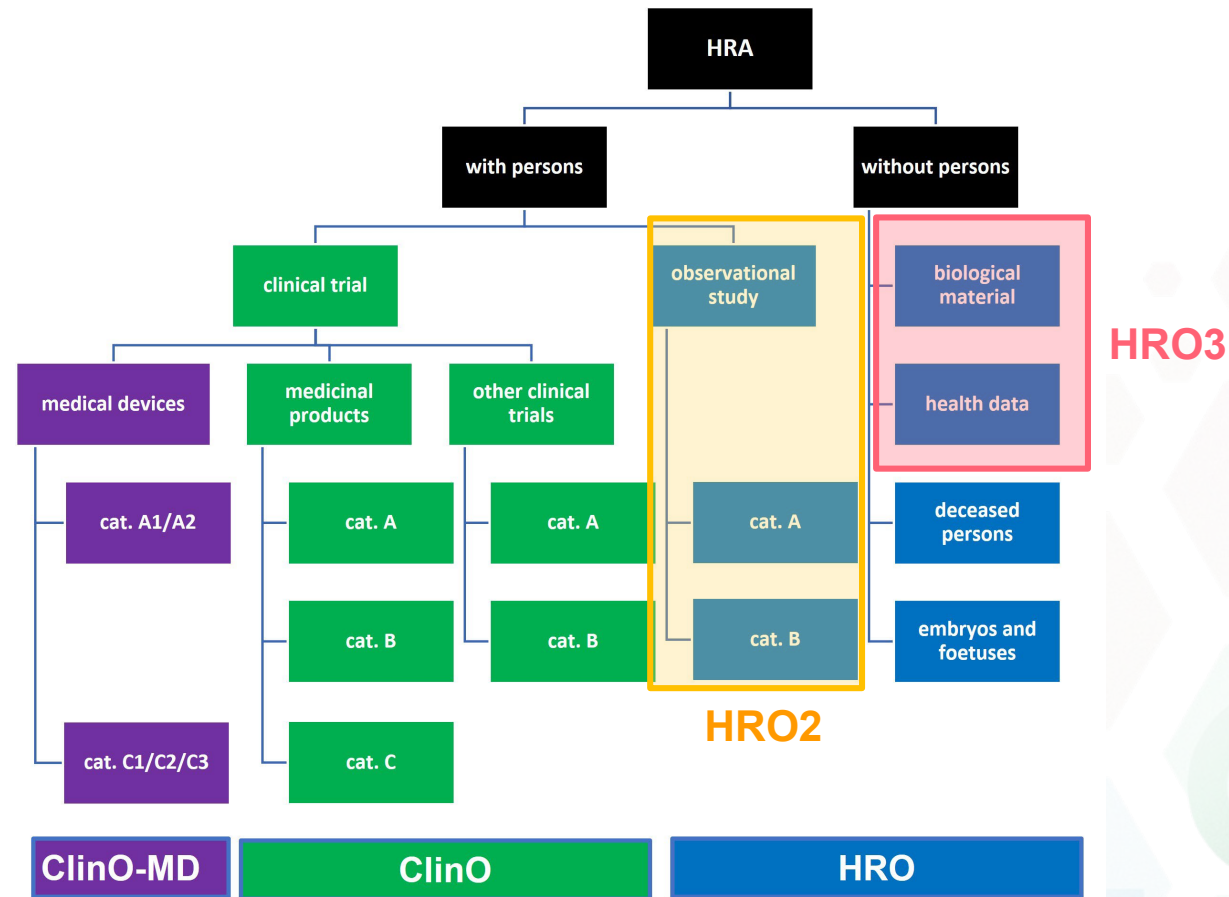
Quality: Law, practice and common hurdles

Quality criteria and quality management in HRO projects

May 29, 2024

Speaker: **Claudia Fila & Clara Landwehr Lardelli** (on behalf of contributors from the QM, DM, DRS, Monitoring unit - Clinical Trials Center (CTC) Zurich)

Research studies according to HRO

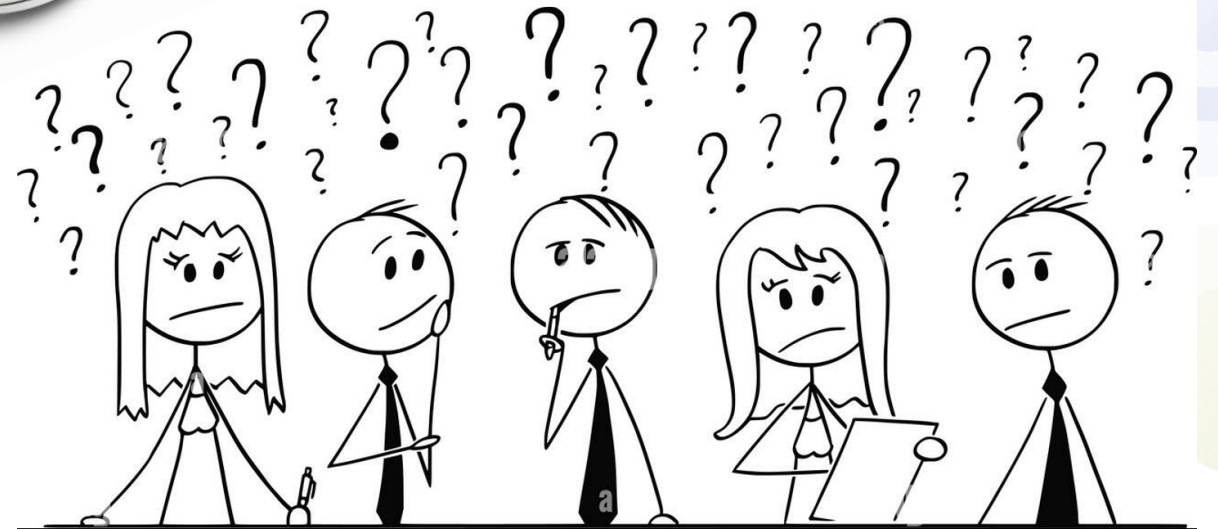


Quality / quality management in HRO projects

**Ordinance
on Human Research with the Exception of Clinical Trials
(Human Research Ordinance, HRO)**

of 20 September 2013 (Status as of 1 September 2023)

*The Swiss Federal Council,
on the basis of the Human Research Act of 30 September 2011¹ (HRA),
ordains:*



Quality guideline for HRO projects

- NO quality guideline such as ICH-GCP or ISO standards as for clinical / interventional studies
- BUT: general scientific requirements in the HRA apply to all types of human research studies, including HRO studies → one of which «SCIENTIFIC QUALITY»

HRA

Art. 10 Scientific requirements

¹ Research involving human beings may only be carried out if:

- the recognised regulations concerning scientific integrity are complied with, in particular with regard to the handling of conflicts of interest;
- scientific quality requirements are met;
- the recognised international Good Practice guidelines for research involving human beings are complied with; and
- the persons responsible have appropriate professional qualifications.

² The Federal Council shall specify which national and international regulations must be complied with.

HRO

Art. 2 Applicable provisions

The provisions concerning scientific integrity and scientific quality set out in Articles 3 and 4 of the Ordinance of 20 September 2013² on Clinical Trials (ClinO) apply *mutatis mutandis*.

ClinO

Art. 4 Scientific quality

The sponsor and the investigator of a clinical trial shall ensure scientific quality. In particular:

- they shall define a research question based on the current state of scientific knowledge;
- they shall use an appropriate scientific methodology; and
- they shall ensure the availability of the resources required for the clinical trial and provide the necessary infrastructure.

Scientific quality criteria for HRO projects

ClinO

Art. 4 Scientific quality

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- they shall define a **research question** based on the current state of scientific knowledge;
- they shall use an appropriate **scientific methodology**; and
- they shall ensure the **availability of the resources required** for the clinical trial and provide the **necessary infrastructure**.

HRO

Art. 4 Professional qualifications

- The project leader responsible for a research project must:
 - be entitled to practise independently the profession specifically qualifying him or her to conduct the research project in question;
 - have the training and experience required to conduct the research project in question;
 - be conversant with the legal requirements for research projects or be able to ensure compliance by calling in appropriate expertise.
- The other persons conducting the research project must have the professional knowledge and experience appropriate to the activities in question.

HRO

Art. 5 Storage of health-related personal data and biological material

- Any person who stores health-related personal data for research must take appropriate operational and organisational measures to protect it, and in particular:
 - restrict the handling of the health-related personal data to those persons who require this data to fulfil their duties;**
 - prevent unauthorised or accidental disclosure, alteration, deletion and copying of the health-related personal data;**
 - document all processing operations which are essential to ensure traceability.**
- Any person who stores biological material for research must, in particular:
 - comply with the principles set out in paragraph 1 *mutatis mutandis*;
 - ensure that the technical requirements are met for appropriate storage of the biological material;
 - make available the resources required for storage.

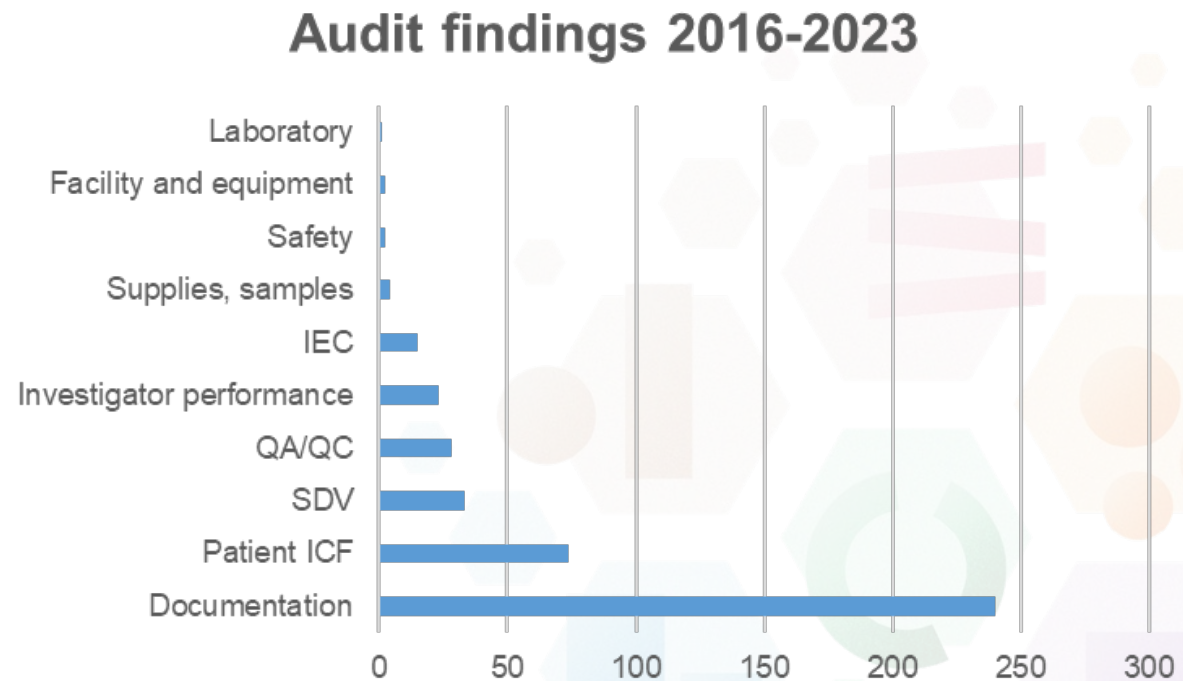
- **Research question** based on current scientific knowledge and **appropriate methodology**
- **Necessary resources** (professional study staff) and **infrastructure** (e.g. for appropriate storage and handling of data / samples as well as traceability of all operational steps)

System - and project -specific auditing



Typical problems / deviations in HRO projects – experiences from audits

2016-2023		
		In %
Documentation	240	57
Facility and equipment	2	0
IEC	15	4
Investigator performance	23	5
Laboratory	1	0
Patient ICF	74	18
QA/QC	28	7
Safety	2	0
SDV	33	8
Supplies, samples	4	1
	422	



Institution -specific guidelines for HRO projects

- Good Practice guidelines for research according to HRO at the University Hospital Zurich (USZ)
- Based on legal requirements and audit findings
- Provide many practical tips/ hints/ instructions aimed at ensuring high quality

Specific to HRO projects according chapter 2 (HRO2)

<p>USZ Universitäts Spital Zürich</p> <p>Dokumentenart: Richtlinie Geltungsbereich: Universitätsspital Zürich Zielgruppen: Alle Mitarbeitenden</p>	<p>Clinical Trials Center Erfassen durch: Regina Grossmann Autor: DFL_CTC_EX, Nicole Leisinger Gültig ab: 11.03.2022</p>
<p>Leitfaden zur Durchführung von Forschungsprojekten mit Erhebung von Daten und Entnahme von Proben (HFV2)</p>	
<p>Änderungshinweis: Migration der Erstausgabe vom 20.11.2020, die im Intranet USZ publiziert war ins DMS, sowie Aktualisierung und Präzisierung einzelner Kapitel.</p>	
<p>Gemäss SDI-Beschluss vom 23.09.2020 wurde bestimmt, dass die Forschung mit gesundheitsbezogenen Personendaten und/oder biologischem Material am Universitätsspital Zürich reguliert wird. Dazu tragen die Leitfäden HFV 2 und 3, kontrollierter Zugang zu den Daten und Proben sowie adäquate Vereinbarungen mit USZ-internen und USZ-externen Nutzern bei. Abweichungen von im Leitfaden beschriebenen Vorgehen müssen begründet werden.</p>	
<p>Referenzen:</p> <ul style="list-style-type: none"> • Bundesgesetz über die Forschung am Menschen (810.30) • Verordnung über die Humanforschung mit Ausnahme der klinischen Versuche (810.301) • Deklaration von Helsinki • Deklaration von Taipei • Bundesgesetz über den Datenschutz (235.1) • Gesetz über die Information und den Datenschutz IDG (170.4) 	

Specific to HRO projects according chapter 3 (HRO3)

<p>USZ Universitäts Spital Zürich</p> <p>Dokumentenart: Richtlinie Geltungsbereich: Universitätsspital Zürich Zielgruppen: Alle Mitarbeitenden</p>	<p>Clinical Trials Center Erfassen durch: Regina Grossmann Autor: DFL_CTC_EX, Nicole Leisinger Gültig ab: 15.06.2023</p>
<p>Leitfaden zur Weiterverwendung biologischen Materials und gesundheitsbezogener Personendaten für die Forschung (HFV Kap 3)</p>	
<p>Änderungshinweis: Erneute Anpassungen an die aktuellen Prozesse des Data Governance Boards sowie strukturelle Anpassungen.</p>	
<p>Gemäss SDI-Beschluss vom 23.09.2020 wurde bestimmt, dass die Forschung mit gesundheitsbezogenen Personendaten und/oder biologischem Material am Universitätsspital Zürich reguliert wird. Dazu tragen die Leitfäden HFV 2 und 3, kontrollierter Zugang zu den Daten und Proben sowie adäquate Vereinbarungen mit USZ-internen und USZ-externen Nutzern bei.</p>	
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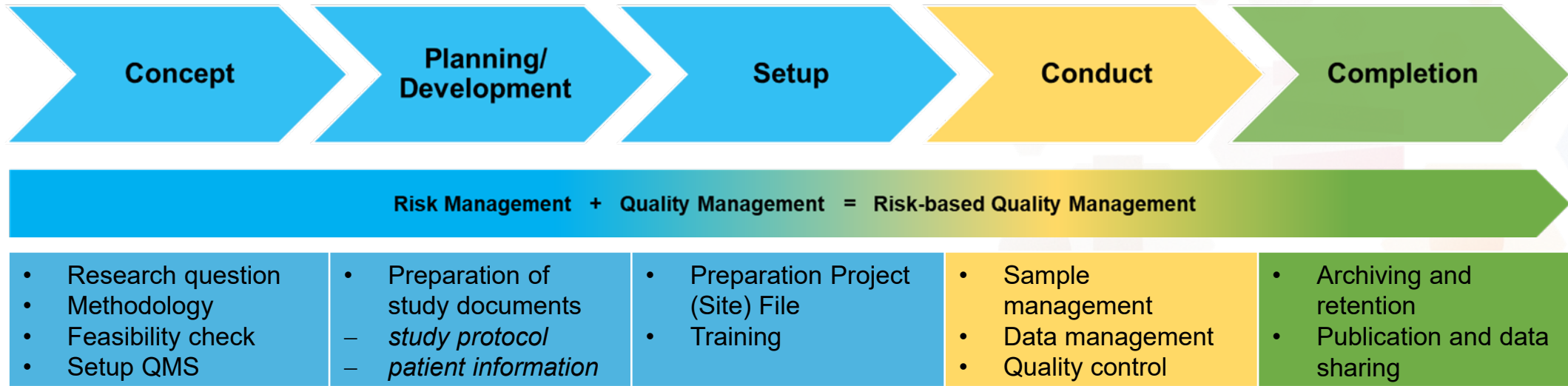
QM – independent of the type of human research

- Always risk-based
 - Risks for **participants/ patients** (indicated by the risk-based categorization) → risk for physical damage in HRO projects is zero or rather low, risk for data breaches and violation of privacy as high as in clinical/ interventional trials
 - Risks for **process/ procedure deviations** (depending on the complexity of a project and the extent of specifically vulnerable operational steps) → deviations may interfere with safety (**HRO2**), data protection, validity and quality of research data
- Affects aspects (processes, procedures) in all phases of a human research study → also of a HRO project



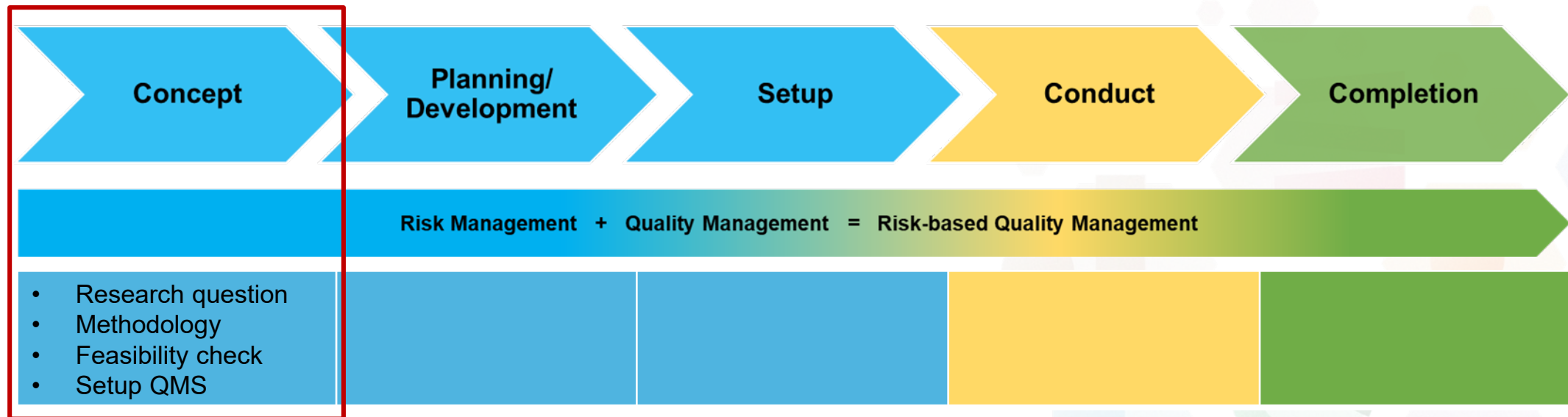
Aspects / activities affecting quality

- Along the different phases of a HRO project
- Exemplary excerpts from the guidelines



Aspects / activities affecting quality

- Along the different phases of a HRO project
- Exemplary excerpts from the guidelines



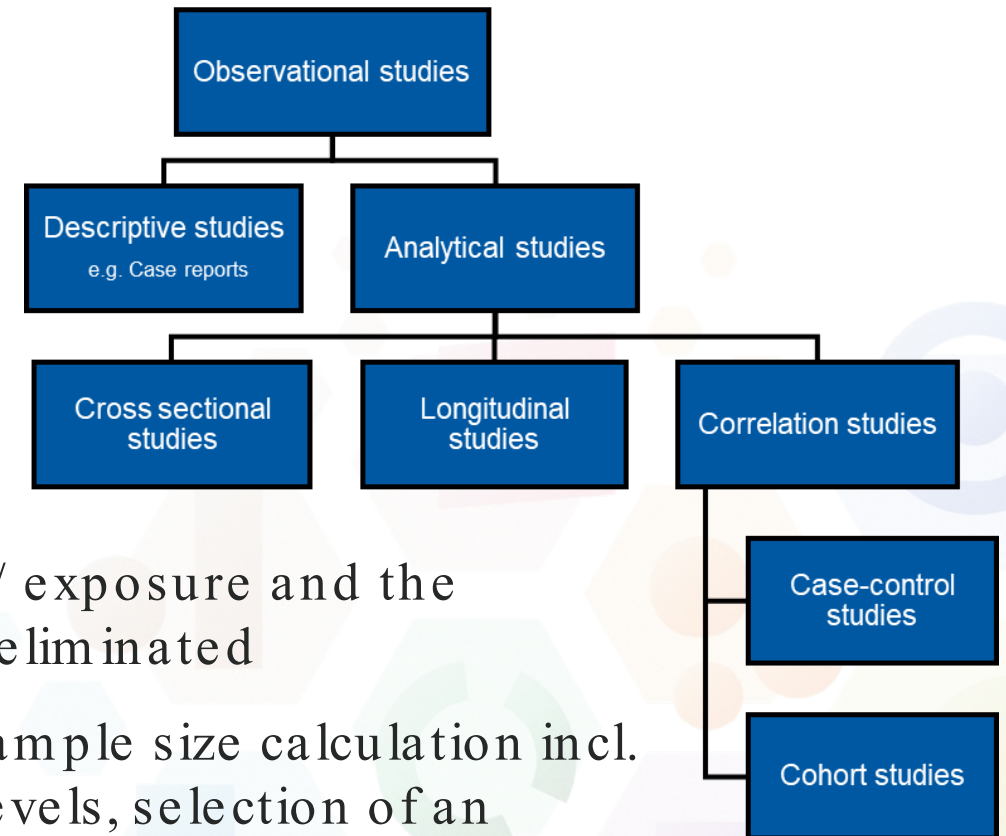
Generation of the research question

- Scientifically sound question (based on the current state of scientific knowledge)
- Make use of the **PECO** model (variant of the PICO model for non-interventional studies)
 - **4 criteria** to be included in a fully formulated research question
- Statement of hypotheses → facilitates conclusion at the end of the project

PICO FRAMEWORK			
P	I	C	O
Patient, Population or Problem	Intervention or Exposure	Comparison	Outcome
What are the characteristics of the patient or population? What is the condition or disease you are interested in?	What do you want to do with this patient (e.g. treat, diagnose, observe)?	What is the alternative to the intervention (e.g. placebo, different drug, surgery)?	What are the relevant outcomes (e.g. morbidity, death, complications)?

Usage of an appropriate scientific methodology / design

- Selection of an appropriate type of study
 - Descriptive / qualitative studies → endpoints may not be possible or needed
 - Analytical / quantitative studies → measurable / estimated endpoints by using tools → numerical results
 - **CAVE:** vulnerable to confounders !
 - Third-party-variables related to the risk factor/ exposure and the considered outcome → must be diminished / eliminated
- Early involvement of a **statistician/ biometrician** (sample size calculation incl. rationale, compensation for drop-outs, significance levels, selection of an appropriate statistical test, possibly interim analysis)

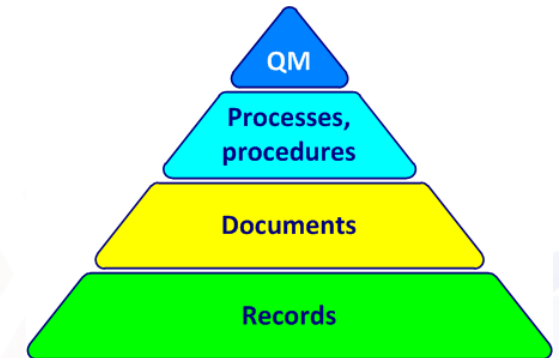


Feasibility check

- Number of **eligible participants/ patients/ data / sample subjects** (inclusion / exclusion criteria)
 - Statistically determined sample size meets recruiting capacity in case of **HRO2** studies
 - Does it require a multicenter project?
 - Statistically determined sample size meets availability of pre-existing health-related data / samples in case of **HRO3** studies (consent via General Consent (GC) can be an inclusion criterion)
 - Assessment → institutional versus federated query system (e.g. SPHN) ?
- Time schedule meets **available human resources/ man power**
- Budget planning meets **available financial resources** → possibilities for research funding, e.g.: <https://www.samw.ch/de/Foerderung.html>, <https://www.swissfoundations.ch/>

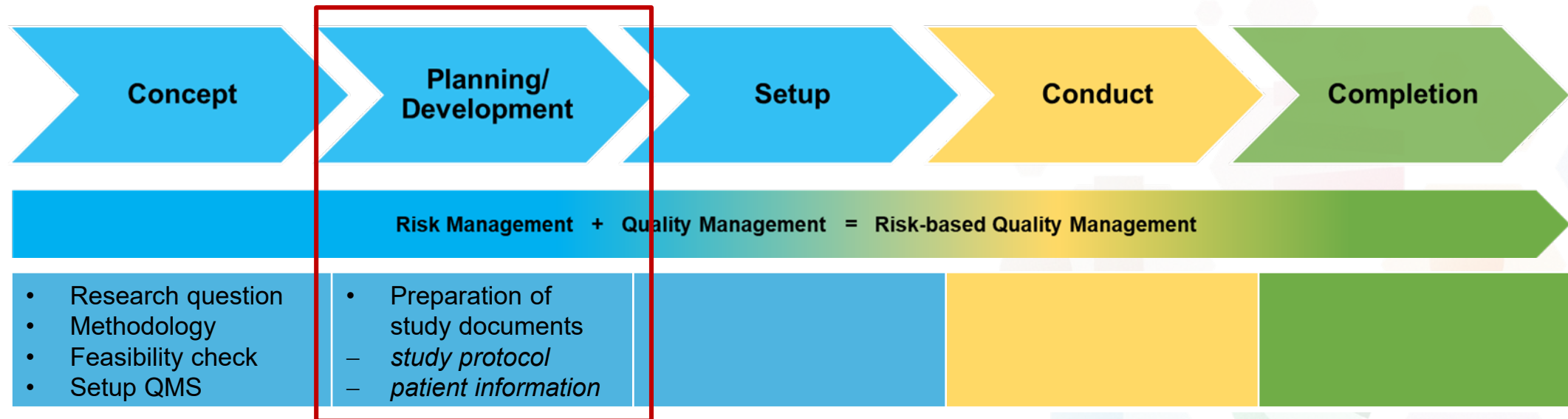
Developing a Quality Management System (QMS)

- A set of internal rules (collection of documented policies, processes / procedures and records)
 - Basis for training and knowledge transfer
- Electronic and / or paper -based
- No extensive QMS as for clinical trials, but **project -specific QMS** strongly recommended
- Descriptions of / instructions for processes / procedures in HRO projects typically **vulnerable to errors / deficiencies** : «*WHAT can WHEN and HOW go wrong ?*»
 - Responsibilities of the Project Leader (especially in IITs if Project Leader is Sponsor at same time)
 - Training and delegation of project-specific tasks to study staff
 - Patient information and obtaining consent (many different types / ways)
 - Various aspects in data / sample management (procurement, data / sample protection, data capture, data transfer to third parties, data / sample retention); various aspects in document / record management
 - Management of Safety related events (e.g. Serious Events (SEs) in **HRO2** projects)
 - Measures of quality control; maintenance of the QMS (adaptation / changes, version control, etc.)



Aspects / activities affecting quality

- Along the different phases of a HRO project
- Exemplary excerpts from the guidelines



Preparation of study documents – PROTOCOL (1)

- Make use of **STROBE**(**ST**rengthening the **R**eporting of **OB**servational Studies in **E**pidemiology) !
 - Initiative of an international consortium (epidemiologists, statisticians, researchers, editors) regarding reporting criteria in epidemiology
 - Describes **criteria** (checklists) for **protocol development of observational studies** (non-interventional research projects)

[STROBE - Strengthening the reporting of observational studies in epidemiology \(strobe-statement.org\)](http://strobe-statement.org)





































The screenshot shows the STROBE website homepage. At the top left is the STROBE logo, a red square with white diagonal lines. To its right is the text "STROBE" in red, followed by "Strengthening the reporting of observational studies in epidemiology" in black. Below this is a red navigation bar with white text for "Home", "Checklists", "Translations", "Publications", "Commentaries", "Contributors", and "Links". The main content area has a white background. The first section is titled "What is STROBE?" in red. Below it is a paragraph of text: "STROBE stands for an international, collaborative initiative of epidemiologists, methodologists, statisticians, researchers and journal editors involved in the conduct and dissemination of observational studies, with the common aim of **STrengthening the Reporting of OBservational studies in Epidemiology**." Below this is a line of text: "For STROBE-related entries in PubMed click [here](#)." The second section is titled "Aims and use of STROBE" in red. Below it is a paragraph of text: "Incomplete and inadequate reporting of research hampers the assessment of the strengths and weaknesses of the studies reported in the medical literature. Readers need to know what was planned (and what was not), what was done, what was found, and what the results mean. Recommendations on the reporting of studies that are endorsed by leading medical journals can improve the quality of reporting."

Preparation of study documents – PROTOCOL (2)

- Make use of swissethics protocol templates (see webpage)
 - Specific templates for HRO studies
 - Always use the **current template version** published on the swissethics webpage (regulatory up to date) → do **not** use an old protocol and adapt it !
 - **Never** use a protocol template for a clinical trial !
→ contains content and standard formulations for interventional studies that are not relevant for HRO studies

swissethics.ch/en/templates/studienprotokolle

Research projects with persons (HRO chap. 2) (Human research other than clinical trials)					
Project plan template: Research involving human subjects with the exception of clinical trials					
		English	2.5	updated: 05.02.2024	
Further use with consent (HRO chap. 3)					
Template for the submission of a project "further use with consent" according to HRA/HRO					
		Deutsch	4.0	updated: 25.10.2022	
					
		Italiano	4.0	updated: 25.10.2022	
					
					
					
					English
					4.0
					updated: 25.10.2022
Note: Use the template for the submission of a project "further use without consent" according to HRA Art.34/HRO in case there is no consent for some or for all the health-related personal data and/or biological material used in the research project.					
Further use without consent (HRO chap. 3)					
Template for the submission of a project "further use without consent" according to HRA Art.34/HRO					
		Deutsch	4.0	updated: 25.10.2022	
					
		Italiano	4.0	updated: 25.10.2022	
					
					English
					4.1
					updated: 25.10.2022
Research involving deceased persons					
Template for the submission of a project involving deceased persons, according to HRA/HRO					
		Deutsch	1.0	updated: 03.02.2024	
					
		Italiano	1.0	updated: 03.02.2024	
					
					Français
					1.0
					updated: 03.02.2024

Preparation of study documents – PROTOCOL (3)

- Templates contain **all essential protocol sections/ topics**
- For certain topics a **more detailed description** is expected, such as:
 - Recruitment, screening, patient information and informed consent procedure
 - Data / sample life cycle (data / sample procurement, data capture, data / sample protection, data / sample transfer / transport)
 - May be in form of a separate Data Management Plan / Sample Management Plan as protocol appendix in case of large, complex studies
 - Intended quality control measures
 - Safety Management in case of **HRO2** studies

Preparation of study documents – INFORMATION & CONSENT (1)

- Make use of appropriate swissethics protocol templates (see webpage) for HRO2 / HRO3 projects

swissethics.ch/en/templates/studieninformationen-und-einwilligungen

Research projects with persons (HRO chap. 2)	Further use of biological material and personal data (HRO chap. 3) / Biobanks																
<p>Study information for HRO-projects with persons, according to HRA/HRO chapter 2</p> <p>Template of swissethics for HRO with persons, according to HRA/HRO chapter 2 (neither ClinO nor HRO chapter 3 "further use")</p> <table> <tr> <td>  Deutsch</td> <td>3.2 updated: 25.11.2021</td> <td>  Français</td> <td>3.2 updated: 09.02.2024</td> </tr> <tr> <td>  Italiano</td> <td>3.2 updated: 25.11.2021</td> <td></td> <td></td> </tr> </table>	  Deutsch	3.2 updated: 25.11.2021	  Français	3.2 updated: 09.02.2024	  Italiano	3.2 updated: 25.11.2021			<p>Template for a patient information/informed consent according to HRA/HRO art. 28</p> <p>Template of swissethics for the further use of biological material and genetic personal data in uncoded form for a research project (art. 28 HRO)</p> <table> <tr> <td>  Deutsch</td> <td>2.1 updated: 07.04.2022</td> <td>  Français</td> <td>2.1 updated: 07.04.2022</td> </tr> <tr> <td>  Italiano</td> <td>2.1 updated: 07.04.2022</td> <td></td> <td></td> </tr> </table>	  Deutsch	2.1 updated: 07.04.2022	  Français	2.1 updated: 07.04.2022	  Italiano	2.1 updated: 07.04.2022		
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  Italiano	2.1 updated: 07.04.2022																
<p>Study information for relatives/parents/legal representatives (HRO)</p> <p>Template for writing the study information for relatives/parents//Eltern/legal representatives according to HRO</p> <table> <tr> <td>  Deutsch</td> <td>2.2 updated: 25.11.2021</td> <td>  Français</td> <td>2.2 updated: 25.11.2021</td> </tr> <tr> <td>  Italiano</td> <td>2.2 updated: 25.11.2021</td> <td></td> <td></td> </tr> </table>	  Deutsch	2.2 updated: 25.11.2021	  Français	2.2 updated: 25.11.2021	  Italiano	2.2 updated: 25.11.2021											
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  Italiano	2.2 updated: 25.11.2021																

Preparation of study documents – INFORMATION & CONSENT (2)

- Very different types for patient information and consent depending on the type of HRO project
 - **HRO2**: project -specific patient information leaflet with Informed Consent Form (ICF)
 - **HRO3**: project -specific patient information leaflet with Informed Consent Form (ICF) OR information with right to dissent OR General Consent (GC) OR surrogate consent by Ethics Committee (HRA Art. 34) – depending on:
 - Type of data (genetic data / samples versus non-genetic data)
 - Possibility for person identification (un-coded versus coded/ pseudonymized versus anonymized data / samples)
 - Possibility to contact data / sample subjects for obtaining consent (reasonableness)

Preparation of study documents – INFORMATION & CONSENT (3)

- Many institutions have a GC implemented (on swissethics webpage → template of HRA compliant national GC)

swissethics.ch/en/templates/studieninformationen-und-einwilligungen









General consent

Template general consent: for the general further use of coded personal data and coded material for research purposes.

As a researcher, you must ensure that the general consent is implemented in your institution before using it. As per the swissethics statement of 22 February 2019 on the general consent ([link](#)): "Every institution that uses the general consent is obliged to respect national and international norms and standards for the data banks (registries) and biobanks. In this way, the rights of donors who voluntarily participate in the research can be guaranteed.

The general consent can be used in principle for people who are capable of discernment. If a legal representative has to sign in the event of incapacity in the consent procedure, the patient himself has to agree again when he regains his capacity. More detailed information will be provided at a later stage on the specific requirements for the incapacity in the consent procedure and for children and adolescents." (See in particular the recommendations of unimeduisse of 12 January 2020 ([link](#))).

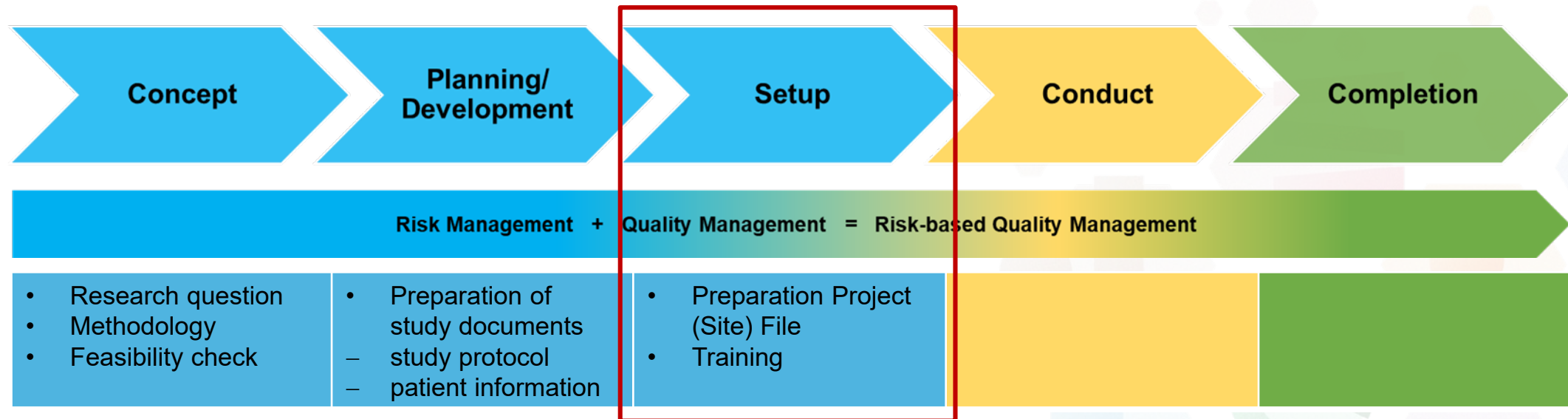
The institutions based in the cantons of Ticino, Vaud, Fribourg, Valais and Neuchâtel must consult with the competent Ethics Committee on the valid version of the Consent General before using it.

		Deutsch	2019/2_D			Français	2019/2_F
		Italiano	2019/2_I			English	2019/4_E updated: 19.04.2021

- Specific for the further use of already existing data / samples (residual material) from clinical routine / previous research studies in **HRO3** studies **ONLY**
- CAVE: GC cannot be applied for HRO3 projects with un-coded genetic data / samples (here always project -specific information and consent !)

Aspects / activities affecting quality

- Along the different phases of a HRO project
- Exemplary excerpts from the guidelines



Preparation of the Project (Site) File/ Folder

- Equivalent to the Trial Master File (TMF) and / or Investigator Site File (ISF) in interventional studies
- Should be prepared and maintained in a **similar manner**
- Content (all project -associated documents):
 - List of involved sites (in case of multicenter projects) and all involved Project Leader(s)
 - Approval by the Ethics Committee
 - Approved and signed project protocol
 - Contracts / agreements with collaboration partners, service providers and third parties
 - Licenses, e.g. of electronic systems or tools
 - All other approved study documents (blank of PatInfo / ICF, possibly GC, recruitment -supporting material)
 - Documentation of Serious Events (SEs) for **HRO2** projects (forms, list)
 - Signed original ICFs (excl. projects with GC or surrogate consent by the Ethics Committee)
 - Source data location list as well as filled -in and signed CRFs



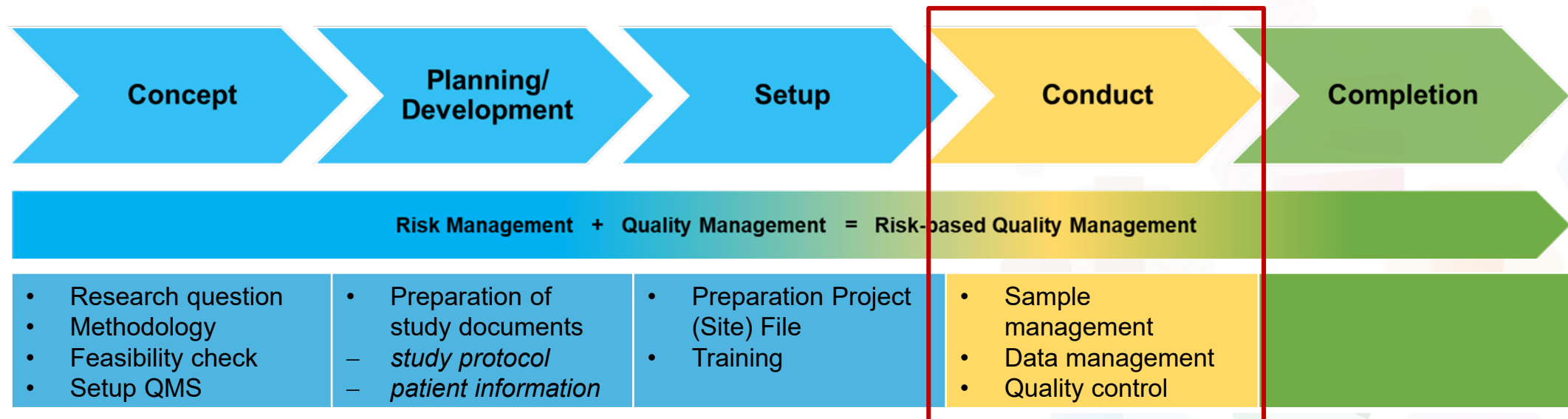
Training

- **General training** of study staff on the preparation, conduct and completion of a human research study (e.g. GCP courses if HRO-specific content is addressed or HRO -specific courses)
- **Study -specific training** on all relevant operating procedures (e.g. responsibilities, patient information / consent, sampling material, data collection / manual data extraction, data capture onto Case Report Form (CRF), handling of data management system, etc.)
- **Delegation** of project leader -specific responsibilities to study team members possible
 - Training on the specific tasks by the project leader → preparation of **training log** (incl. signatures)
 - Delegation of the specific tasks to trained study staff → preparation of **delegation log** (incl. signatures)



Aspects / activities affecting quality

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Sample Management

- Sampling of biological material and analysis (or storage in a biobank) in case of **HRO2** studies
- Collection of samples (removal from biobank) and analysis in case of **HRO3** studies
- According to Protocol or Sample Management Plan (or Standard Operating Procedure)
- Depending on:
 - **Type of material/ sample** (liquid versus solid, stable versus fragile, etc.)
 - Storage conditions (e.g. temperature log)
 - **Type of processing and analysis/ testing**
 - **Time point** of processing and analysis (perhaps preparation and interim storage in fridge / freezer OR long -term storage in a biobank)
- Management Systems: Biobanking Management Systems, e.g. CentraXX


Data Management (1)

- Generation / collection of source data
 - In case of **HRO2** studies (collection of data, by sampling biological material and direct/ subsequent analysis)
 - In case of **HRO3** projects with samples from a biobank and subsequent analysis
- Transfer / data capture from source document/ location into Case Report Form (CRF) →
paper-based versus electronic format

Data Management (2)

- Data extraction in case of **HRO3** studies
 - **Manually** (all kind of data formats → primarily unstructured data (e.g. text from reports, audio / video files)
 - If performed by members of the study team → work with un-coded data / samples
 - Data must be transferred/ captured onto the CRF / into the database
 - **Automated** (only structured data (e.g. lab data, imaging data) → various data sources → done by clinical data warehouse
 - Very efficient → data per time
 - HRO compliant process of coding/ pseudonymization and storage of key by project -independent entity
 - Encrypted data transfer
 - Readily formatted for data cleaning and statistical analyses
- CAVE: Respect local data / sample governance rules of the institution (e.g. at USZ by DGB)!

Data Management (3)

- Data management of collected / extracted data via:
 - GCP-compliant electronic data management system (e.g.  **REDCap**) with many advantages:
 - Electronic CRF with **easy-to-use plausibility checks**
 - **Access control** with personal login and password
 - **Role-based permission / user management** → users are assigned to specific roles that correlate with specific rights to fulfill certain tasks
 - **Audit trail** → tracking of access / input / modification / deletion / export of data, of change in roles / rights, of changes to forms / visit schedules
 - **Queries system** for quality control purposes
 - User-friendly and intuitive: eCRFs may be developed by study teams
 - Used by most of the Swiss academic CROs/ CTUs

Quality control (1)

- Monitoring of HRO projects **not mandatory** → but **risk -based** quality control («monitoring light») strongly recommended
- If research group/ study team has the experience and capacity (human resources) → **internal quality control** possible (e.g. by project -independent members of the study team)
- Well-defined and described processes (Standard Operating Procedures (SOPs), Working Instructions (WIs)) within a QMS require less quality control
- Focus on 3 aspects:
 - **1. Processes**
 - **2. Data Management**
 - **3. Project (Site) File/ Folder**

Quality control (2)

– Processes

- **Patient/ data / sample subject information / informed consent** process → verification of study-specific PICs or verification if General Consent (GC) available (20% - 50% of all participants)
- Process of **eligibility check** (inclusion / exclusion criteria)
- **Sample/ laboratory process flow** (e.g. blood sampling – transfer – analysis – storage)
 - Sample storage and management (accessibility of storage, storage conditions, temperature monitoring, documentation, e.g. temperature log)
- **Safety aspects** (applicable only for **HRO2** projects) → documentation and assessment of Serious Events (SEs)

Quality control (3)

– Data Management

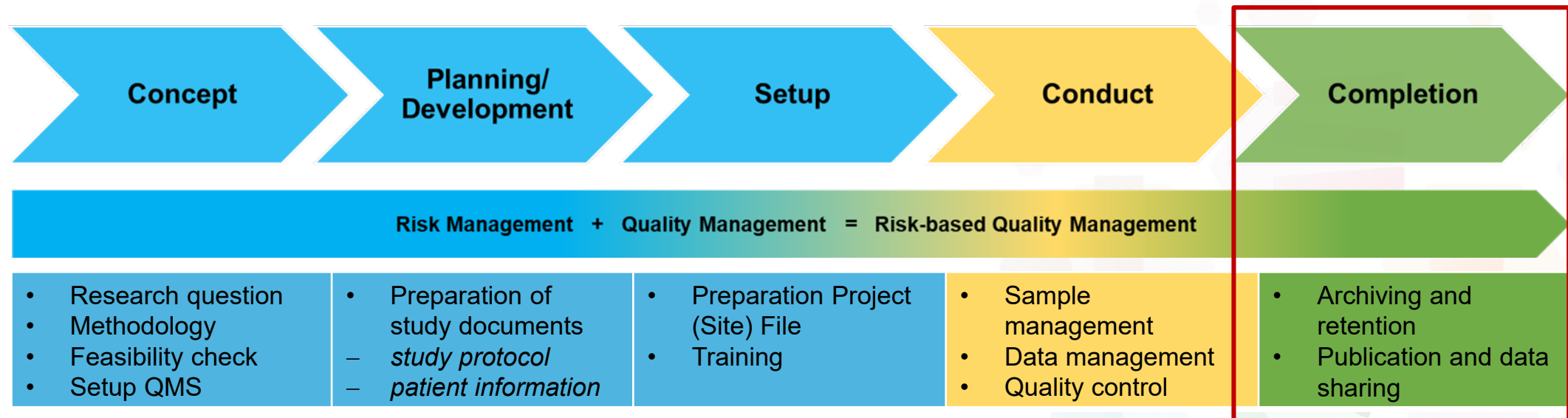
- Type of **data extraction** (automated versus manually, **HRO3**) and **data transfer** → according SOP / WI (validated)?
- **Review of the database** / Case Report Forms (CRFs) incl. usermanagement and roles
- **Source Data Verification** (SDV) → focus on primary endpoint
- **Central data monitoring** (check on plausibility, missing data, drop -outs)
- **Study progress/ completion status**
- **Query management** (questions asked, questions answered?)
- If no possibility for internal / external quality control (e.g. due to budget constraints) → at least certain measures, such as Double Data Entry, 4-eyes-entry, etc., recommended

Quality control (4)

- **Project (Site) File/ Folder**
 - Standard Operating Procedures (**SOPs**) and Working Instructions (**WIs**) in place (primarily for critical process steps)
 - Check on **protocol compliance**
 - Incl. compliance to Data Management Plan (steps of the whole data life cycle)
 - **Essential documents** , such as approvals (e.g. CEC,possibly CISO, possibly DGB) and contracts
 - Review of **running logs** in case of changes (e.g. temperature log)
 - **Study team** (training / delegation log, contact form), qualification and trainings

Aspects / activities that affect quality

- Along the different phases of a HRO project
- Exemplary excerpts from the guidelines



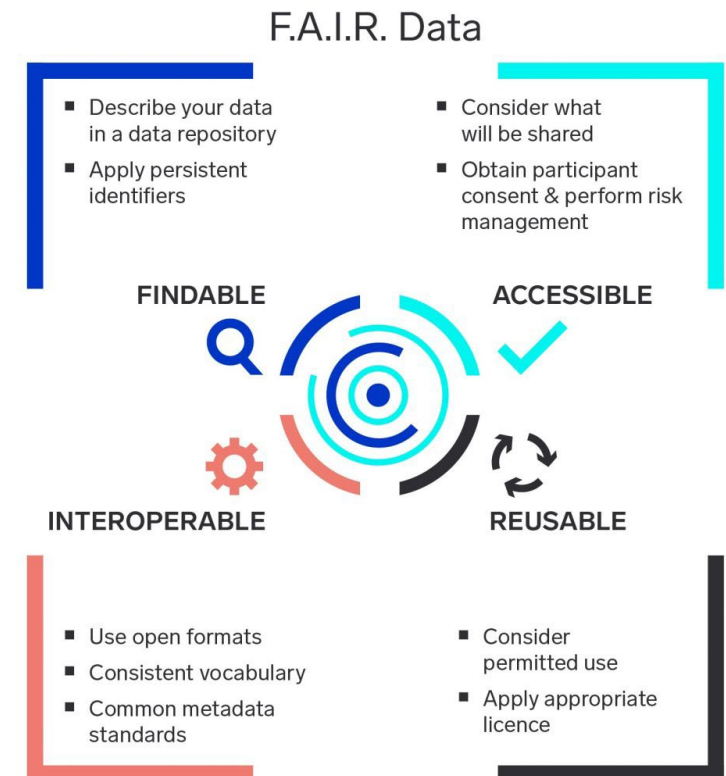
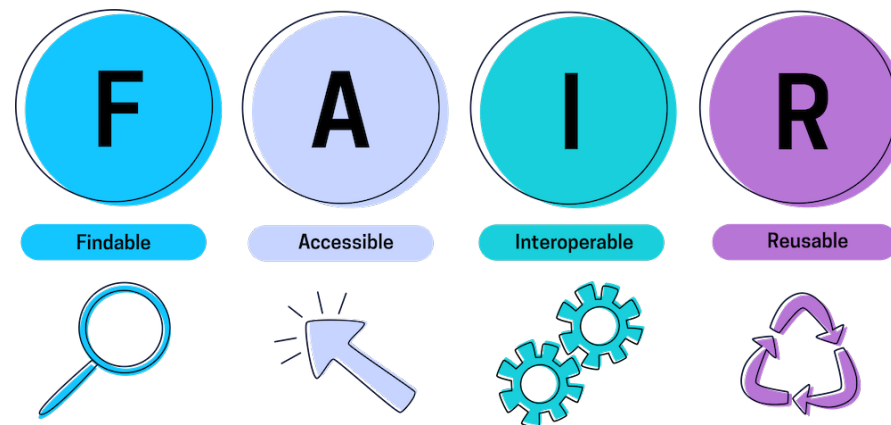
Archiving / retention

- NO minimum retention period defined by law
- Responsibility remains with the Sponsor/ Sponsor -Project Leader
- Statement of the retention period in the protocol recommended for all HRO projects (Ethics Committee accepts a period of **10 years**)
 - **Obligatory statement** in case of **HRO3** studies with requested surrogate consent by the Ethics Committee (HRA Art. 34)
- **Infrastructure:**
 - **Adequate facility** (access-controlled, measures to avoid unintentional or premature destruction (no fire, water, theft), data must be available within reasonable period of time)
 - **Index of archived documents** (paper-based and / or electronic, storage location and responsible person) must be available
 - **Destruction** after archiving period must be documented (involved staff, date, signature)



Publication / Data sharing

- Often required by journals or funding bodies: open access incl. open research data (de-identified raw data, but NO source data incl. person -identifying data)
 - To ensure reproducibility of the study findings
- Appropriate science-specific long term repositories
- Prerequisite: FAIR principles



Summary

- Recognized GCP guidelines for clinical/ interventional trials
→ do not apply to research projects according to HRO
- Defined scientific quality requirements in Swiss legislation (HRA, HRO) → inspired by GCP → do also apply to HRO projects
- For successful completion of HRO projects → QM measures required throughout the entire project procedure / in all phases of the project
- Appropriate QM in HRO projects → apply typical GCP principles → adapt in terms of extent and intensity to the nature of HRO projects (risk, complexity, individual challenges)
- Get yourself trained to specific requirements of HRO projects in courses / educational events tailored to the criteria of research according to HRO



**Take
home message*

Thank you for your attention!

Questions / Answers



APPENDIX: Q/A part

- Data Management WITHOUT GCP -compliant data management system (1)

➤ Expectations by the Ethics Committee

7.2 Data recording and source data

Describe how project data is recorded, e.g. with paper Case Report Forms (CRF) or an electronic Case Report Form (eCRF) such as secuTrial® or Redcap®. Efforts should be made not to use any software, like Microsoft Office software's (e.g. Excel), that do not have an audit trail and do not guarantee data privacy and data reliability, as changes can be made in an uncontrolled manner. If a software without audit trail is used nonetheless, describe how data quality and data traceability throughout the research project is guaranteed.

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

If paper CRFs are used, describe how data is transferred to an electronic database for later analysis. An electronic database is recommended.

Source: Excerpt from the swissethics project protocol template

APPENDIX: Q/A part

- **Data Management WITHOUT GCP -compliant data management system (2)**
- MS Excel → is not built with the level of permission and access management, no role assignment, no audit trail, no queries system
 - If still used: protected cloud system that combines controlled access and user rights with tracking of changes at file / document level, and using the feature/ mode «track change» (to provide a certain level of traceability)
 - how to do → see e.g.: [Track changes in a Shared Workbook - Microsoft Support](#) and [How to Use Track Changes in Excel - YouTube\[1353949028\]](#) (https://www.youtube.com/watch?v=Itz8v_z7ha4)
 - **CAVE:** Any other electronic solution with / without controlled access management and audit trail → check if compliant with local information security requirements at the institution

- **Next series : already in preparation** 😊
 - Topic idea? Send it to verena.golz@usb.ch
 - Further concerns? Let us know!
- Additional projects concerning HRO knowledge in the making



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Thank you for participating!

Further questions : Verena.Golz@usb.ch

