SCTO PLATFORMS

8 May | 12h00 - 13h00 | online seminar

Facts and pitfalls of observational studies

Registries and biobanks: Background, obstacles, and practical views

This seminar session gives insights about common pitfalls when working with large sets of clinical patient data and biological samples. We will look at practical tips for planning projects and research questions, up to regulatory requirements and real-life examples.

Registration and more information:

sctoplatforms.ch/HRO-training-series

General information

- **Questions**:
  - in the chat
  - by raising hand and unmuting after presentation
- Presentations will be **recorded** (Q&A won't)
- **Video, slides & Q&A will be provided** after the session
- **Feedback poll** at the end → please fill in!

REC

- **Speakers:**

  Claudia Becherer
  (Teamleader Regulatory Affairs, DKF Basel)

  Sina Hansen, PhD
  (Scientific Officer Coordination & Project Management, DKF Basel)

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Facts and pitfalls of observational studies: Registries, cohorts and biobanks

Sina Hansen & Claudia Becherer

DKF Basel

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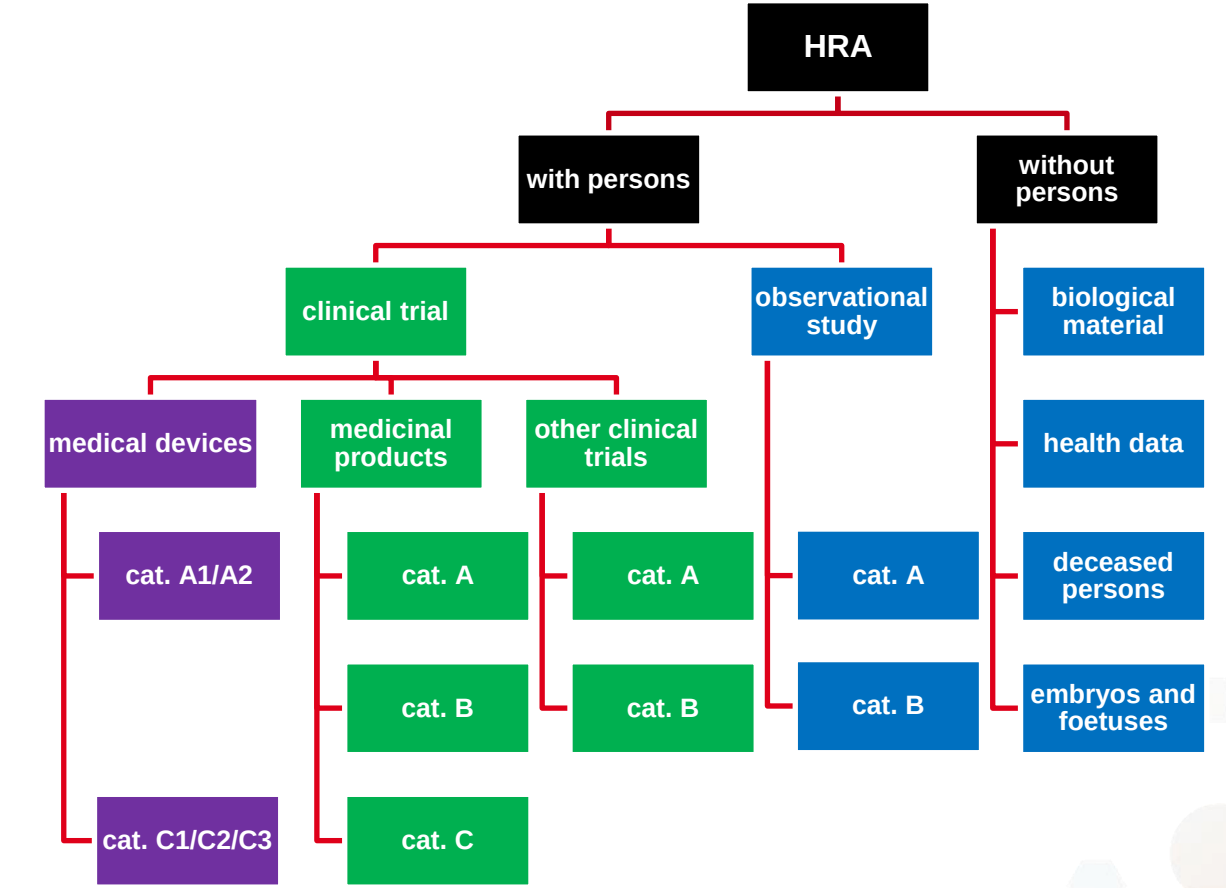
Regulatory & ethical aspects

Legal Situation in Switzerland



HRA Human Research Act
ClinO-MD Ordinance on Clinical Trials with Medical Devices
ClinO Ordinance on Clinical Trials with the Exception of Clinical Trials of Medical Devices
HRO Human Research Ordinance
According to Ch. Seiler, EK Bern

Data Protection Act

Anonymised biological material

Anonymously collected and anonymised health-related data

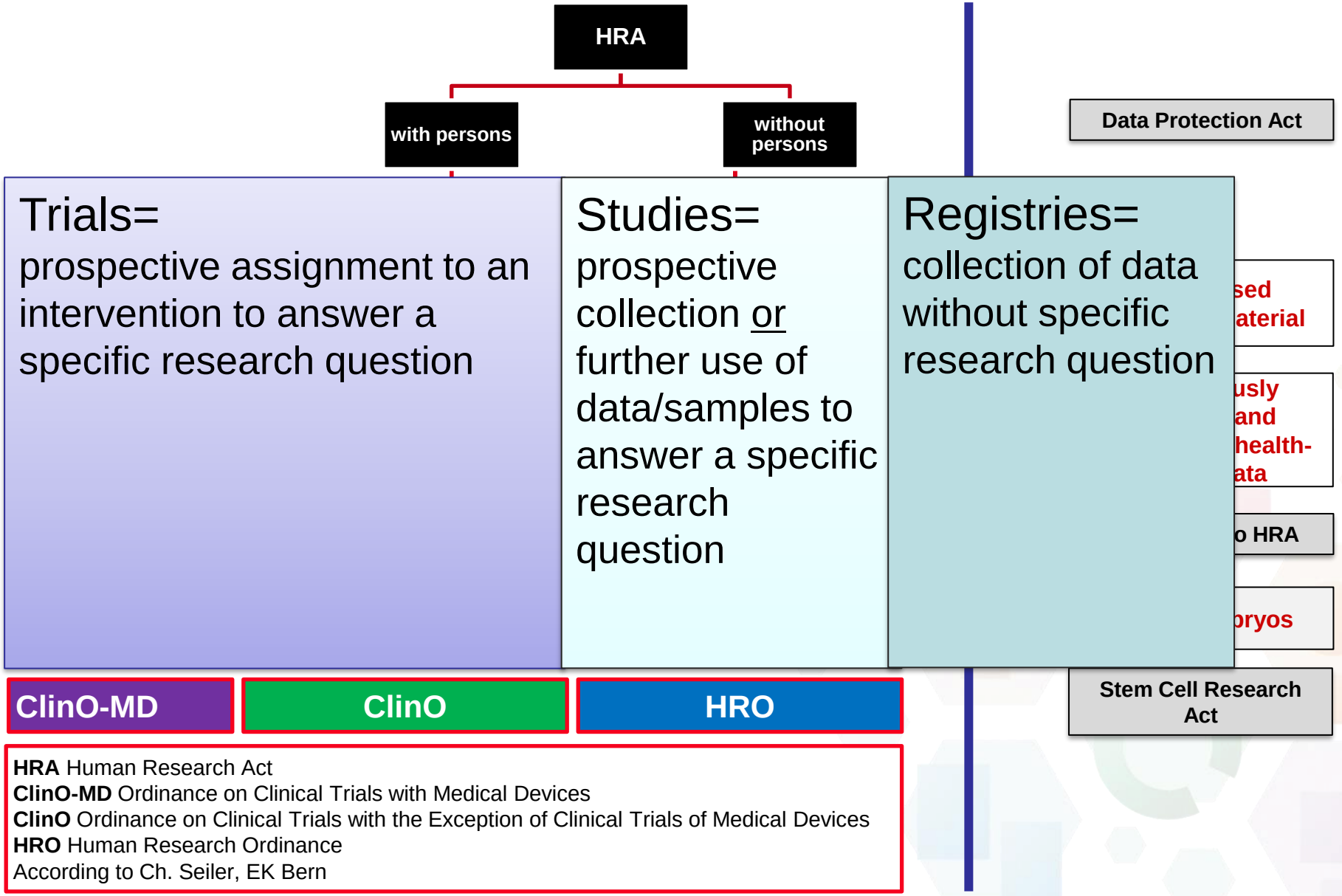
not subject to HRA

In vitro embryos

Stem Cell Research Act

Regulatory & ethical aspects

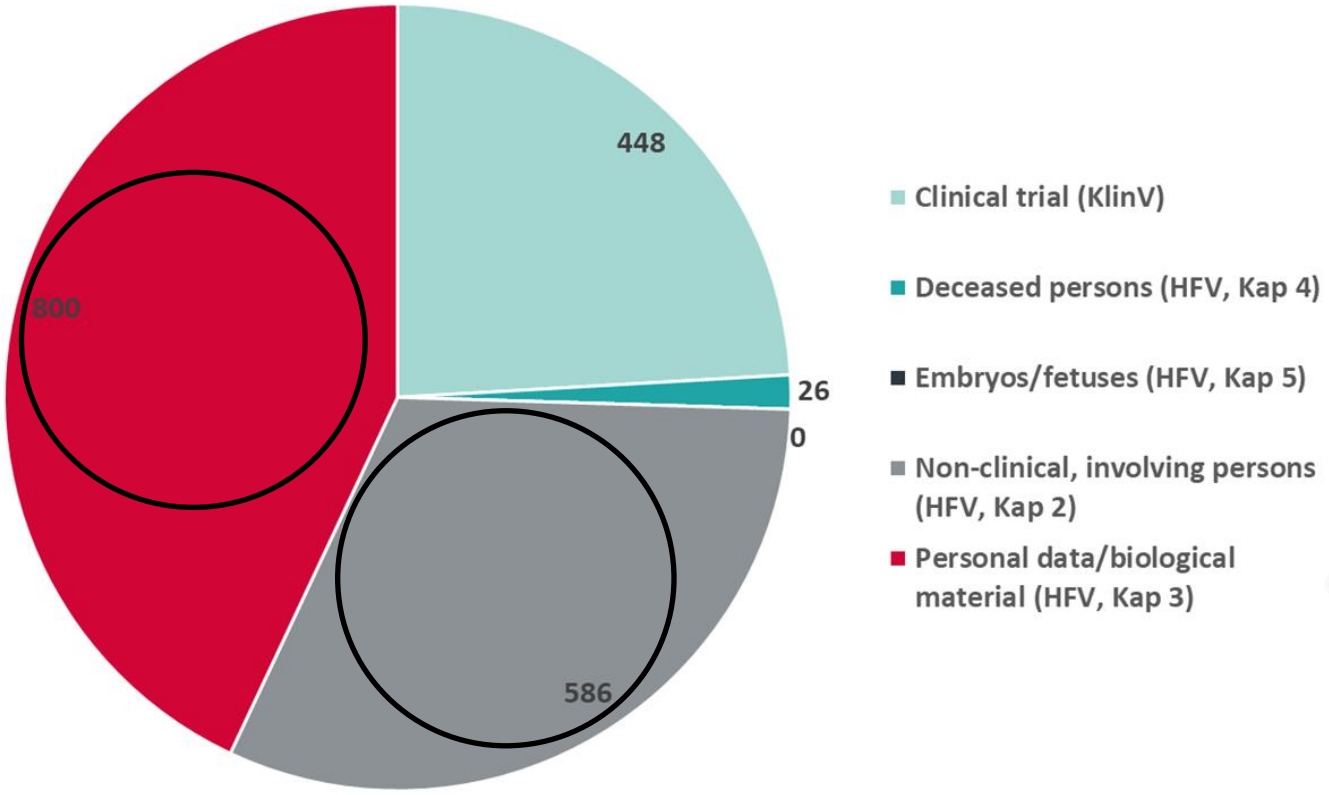
Legal Situation in Switzerland



Regulatory & ethical aspects

EC Submissions & Situation in Switzerland

Number of projects 2022 in Switzerland acc. to RAPS-Registry -> 1`860



Partly Cohorts and Registries

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Regulatory & ethical aspects

Main differences between trials, cohorts and registries

	Clinical Trial	Cohort/Registries
Research Question	1	-/1/ ∞
Recruitment Target	1	Open/ ∞
Ethics-Approval	1	-/1/ ∞
Data Sources	eCRF	CDHW/eCRF
Statistical Analysis	1	1/ ∞

Regulatory & ethical aspects

Overview

What was the basis for the following slides?

- Questions we received in advance
- Questions from our daily consulting work
- Issues we have worked on the past for different projects

These topics were worked out in a "Bingo" I like to play with you!

Afterwards two case studies, one from Switzerland and one from abroad, presented by my colleague Sina.

Regulatory & ethical aspects

Most common questions

BINGO

Difference cohort vs registry?	Approval Swissmedic?	Approval Ethic Committe?
Endpoint? Case Number?	Retrospective? Prospective?	Routine Data? Additional Data?
Only Data? Samples?	Art. 34?	Upcoming changes?

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Regulatory & ethical aspects

Most common questions

BINGO

Difference cohort vs registry?		

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Regulatory & ethical aspects

Most common questions

Registry:

- specific health related problem or intervention
- Standardized documentation without specific research question at start
- epidemiological correlations, quality assurance, economic evaluation
- Guiding principles for registries in human research (swissethics-Homepage)

Cohort:

- section of population
- observed with specific research question over a defined time period
- determine differences in the occurrence of the respective target disease

Data Repositories:

- provide data sets for further use from completed projects

Regulatory & ethical aspects

Most common questions

BINGO

	Approval Swissmedic?	

Regulatory & ethical aspects

Most common questions

Requirement of an Swissmedic approval

- "Swissmedic verifies whether the quality and safety of the test product is guaranteed"
- In general, the therapeutic products to be observed in a registry are authorized for the Swiss market
- No Swissmedic Approval is needed!

More information: https://www.swissmedic.ch/swissmedic/en/home/humanarzneimittel/clinical-trials.html

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Regulatory & ethical aspects

Most common questions

BINGO

		Approval Ethic Committe?

Regulatory & ethical aspects

Most common questions

Requirement of Ethic Committee approval

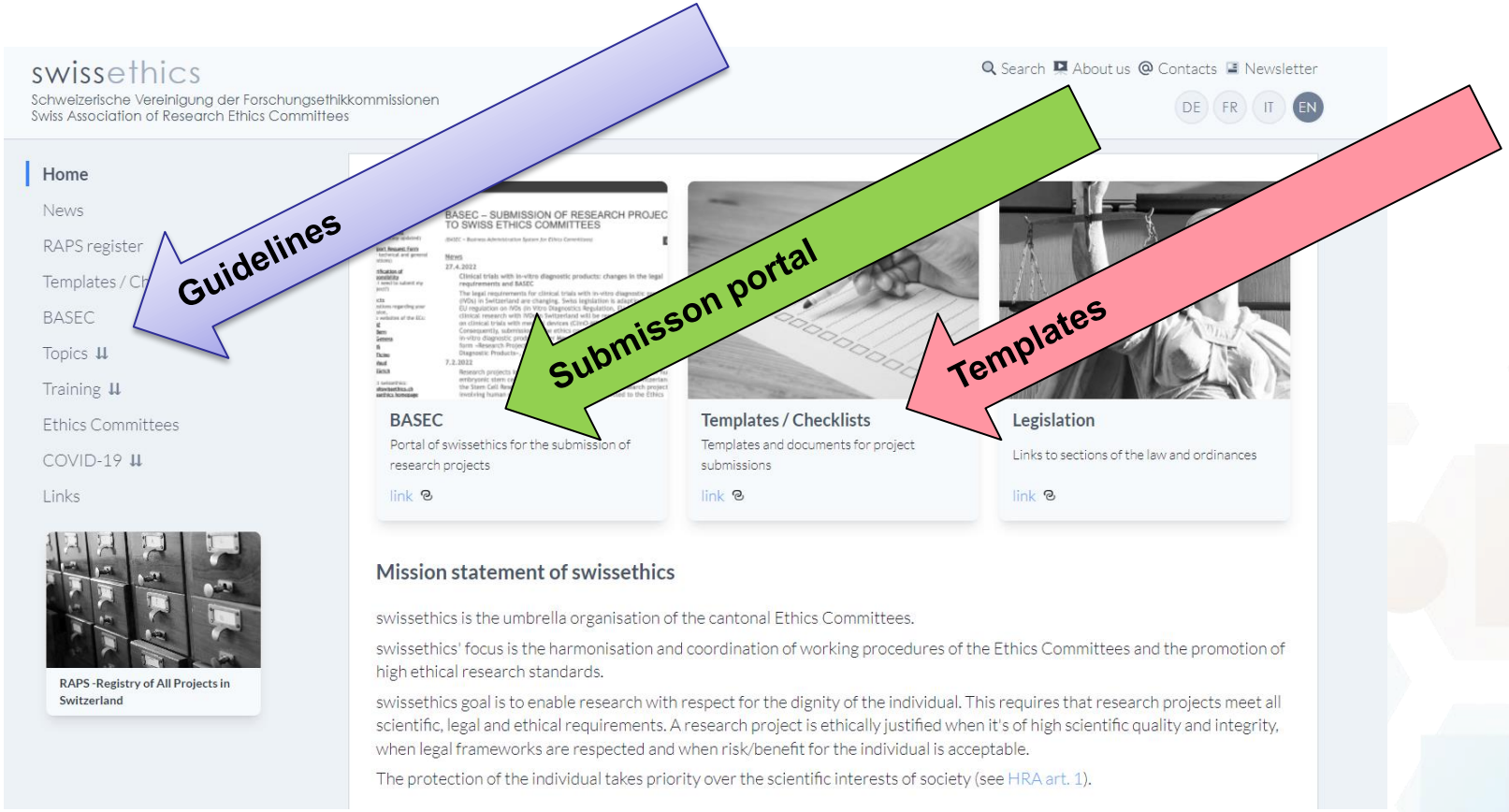
- Approves “Research: method-driven search for generalizable findings ….with regard to Human health”
- Research questions to be answered in a project in which material or data is collected and (re-) used
- Approval necessary!

Regulatory & ethical aspects

Most common questions

swissethics homepage

= Association of all Swiss Ethics Committees



Documentation

- **Study protocol**
- **Informed Consent Form**
  (Study information, patient/participant info, General Consent) from actual project or the project of origin
- **Further documents given to participants:**
  recruitment documents such as flyers, advertisements, …
  diaries, questionnaires …
- **Data Collection Form** ((e)CRF)
- **Contracts** with sponsors/financier/other centres
- **Regulatory framework**
  DTUA, MTA, Biobank Regulations, …
- **CV** of the project leader
- **Cover Letter** (please use it to describe any special circumstances so that Ethics Committee has a chance to become aware of it)

More information: http://swissethics.ch

Regulatory & ethical aspects

Most common questions

BINGO

Endpoint? Case Number?		

Regulatory & ethical aspects

Most common questions

Ethic Committee with regards to “Endpoint and case number”

- To answer a research question an exact case number is necessary
- Start of collection is often done before the exact question is formulated
- “Storage for research purposes” is already regulated in the ordinances
- We therefore recommend a submission even without a specific research question/case number
- Ethics Committee provide you feedback for your data collection

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Regulatory & ethical aspects

Most common questions

First submission

subsequent submissions ∞

Regulatory & ethical aspects

Most common questions

BINGO

	Retrospective? Prospective?	Routine Data? Additional Data?
Only Data? Samples?		

Regulatory & ethical aspects

Most common questions

“retrospective” and “prospective”

- Both is possible, depends on what you need to answer the research question
- General Consent covers both – but is the outcome you need systematically collected?
- For additional collection you must ask patients permission beforehand, but than both is covered (medical history and observation for future consultations)
- For all kind of use you need an ethics approval

Regulatory & ethical aspects

Most common questions

“Additional data vs routine data”

- With “THE FIRST QUESTION” (data acquisition) out of routine an ICF is necessary:
- If the question “How do you do today?” is asked to patient systematically, the answer is documented and evaluated for you study protocol – it is research, and you need an ICF and EC-approval for it!
- The general consents at Swiss hospitals are not congruent - check for each institution!
- The institution's Data Governance Board should be consulted before obtaining the data

Regulatory & ethical aspects

Most common questions

“only data” and “biomaterial”

- Both is possible…
- If a General Consent is established it covers the further use of left over samples
- Additional sampling needs always an ICF
- Sampling and logistics is an additional workload
- Storage requires capacities and biobank regulation

Regulatory & ethical aspects

Most common questions

BINGO

	Art. 34?	

Regulatory & ethical aspects

Most common questions

“Art. 34”

- if the data subject has not been properly informed of use of data and/or material, there is no objection of the individual and the interests of the research prevail the Ethics Committee may give *“substitute consent”*
- the *explanatory reports* providing guidance to the HRA speak of “specific research questions” and “concrete cases” -> n=1
- this means that if a cohort/registry is established in accordance with Art. 34, all resulting research questions must be approved in accordance with Art. 34 (including arguments as to why the disproportionality still exists)

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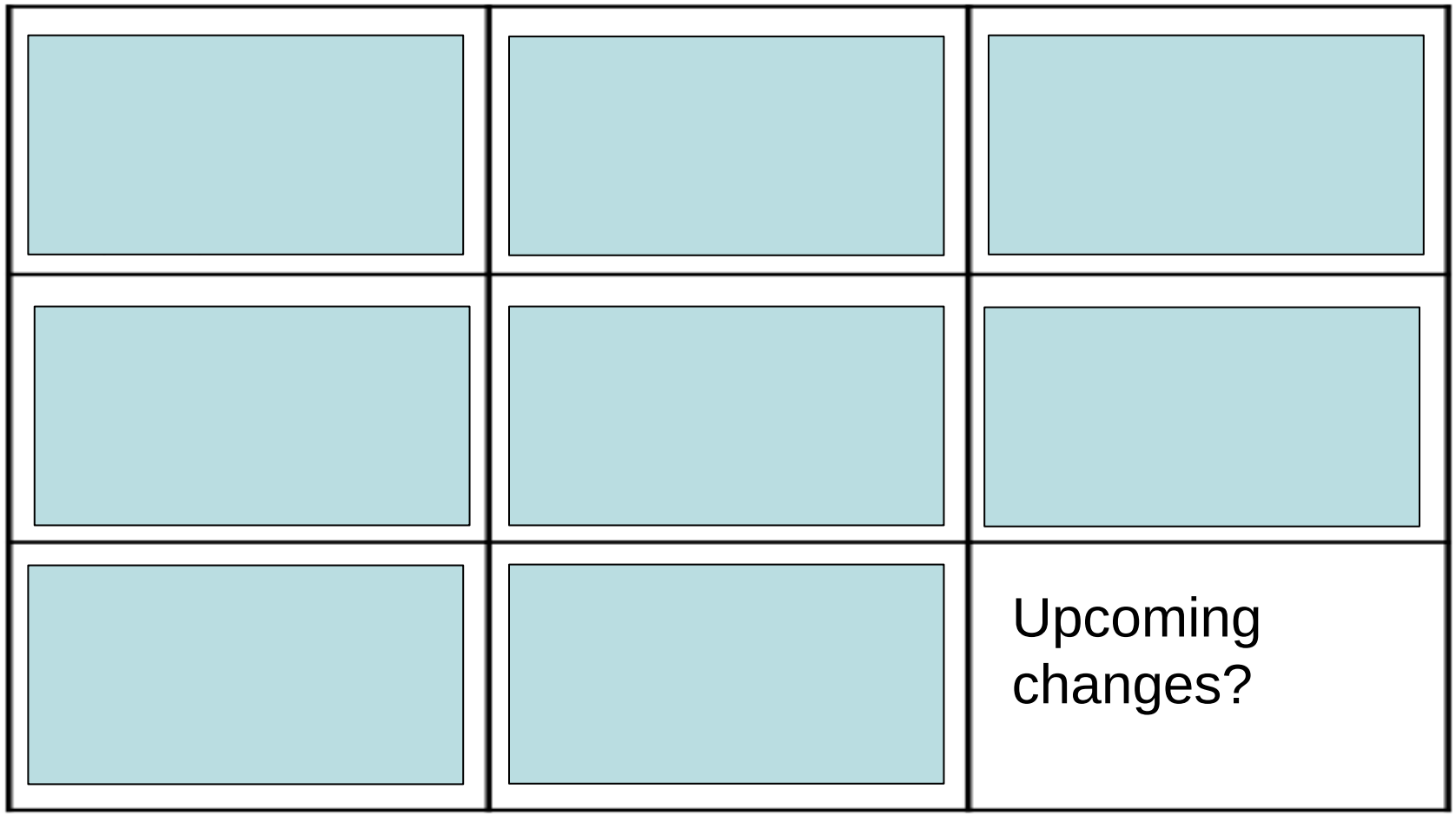
Regulatory & ethical aspects

Most common questions

BINGO



Regulatory & ethical aspects

Most common questions

“upcoming changes to new ordinances”

- Ordinances have been undergoing consultation
- Upcoming changes to be expected early 2025
- Not entirely clear what will come in force….
- 3 major changes:
- eConsent
- Anonymization (according to the current state of the art, done by trained personnel, processing steps needs to be documented)
- Detailed information on “excess information” (incidental findings) and “planned publication of results” to patient and in protocols

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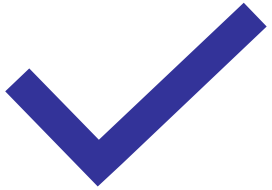
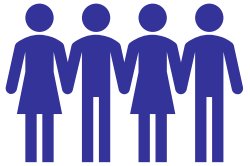
First Input from practice

After a lot of theoretical input



Some more input



From the cohort we gained a lot of experience over the last 11 years

Introduction to Swiss Multiple Sclerosis Cohort (SMSC)

- Swiss but worldwide one of largest and best documented MS cohorts: 1721 patients with median 7 years follow-up
- 13'287 standardised documented visits
- 8'316 evaluated brain MRIs
- 297'000 biosamples
- >20 ongoing integrated research projects
- ongoing high ranked publications
- Since 2024 a clinical trial is embedded
- NCT02433028

“what we have learned”

- A “treasure” is being built up that needs continuous care and attention
- Become multicentric is not easy as every centre has its own routine, especially important for sampling/shipment
- More frequent updates on “minor changes” to the ethics committees
- We developed based on swissethics-template a “SMSC further use template”
- More details (data protection) in the ICF (?)
- Streamlined organization and good communication makes changes easier to implement (e.g. “PI changes")

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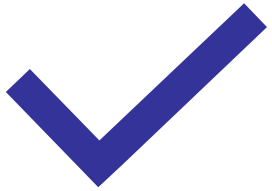
Second input from practice

After an Swiss-specific input



Some more input

But international!

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IRASPEN
International Rare And Severe Psoriasis Expert Network

The International Rare And Severe Psoriasis Expert Network (IRASPEN) - A Prospective Registry With Genotype-Phenotype Correlation

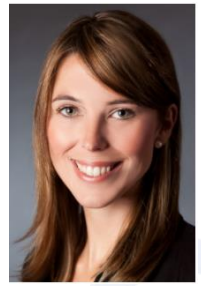
Project Leader: Prof. Dr. med. Dr. sc. nat. Alexander Navarini
University Hospital Basel

Co- Project Leader: PD Dr. med. Julia-Tatjana Maul
University Hospital Zürich

Global Project Manager: Ivana Cvijetić, MSc

Site Start Up: Sina Hansen, PhD

Study physician: Tatjana Steybe



Funded by Boehringer Ingelheim

Project design

Multicenter, non-interventional study with prospective collection of data and biological material

=> HRO category A

Minimum 180 patients (> 6 months)
Up to 360 healthy relatives (parents, older siblings)

Project design

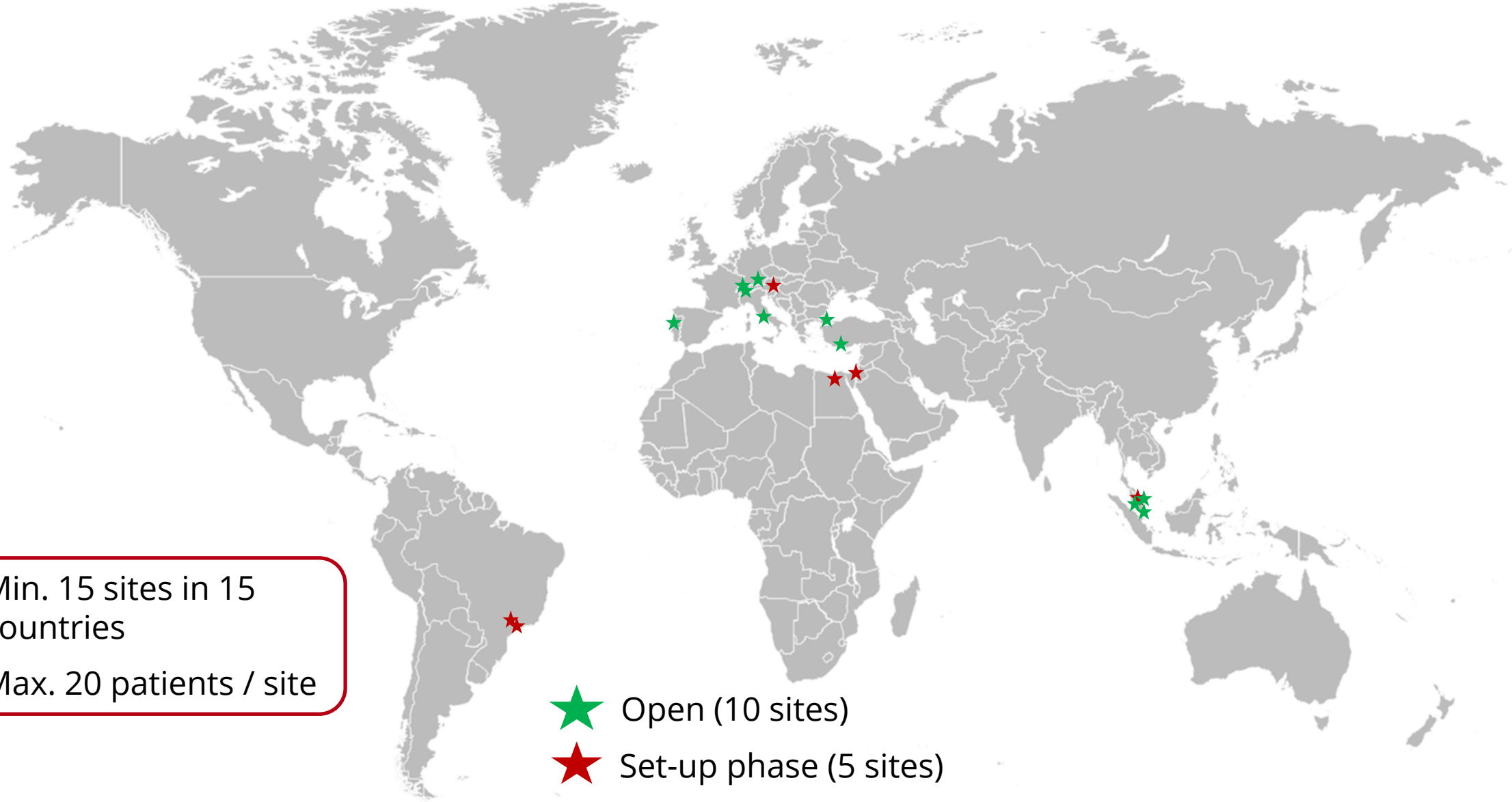
V1	V2	V3	V4	V5	V6	V7	V8	Flare
Baseline	week 12	week 24	week 52	week 104	week 156	week 208	week 260	Up to 4
	+/- 30 days							Flexible

Schedule of Assessments:

8 visits over 5 years & flexible flare visits

- Medical examinations
- Collection of Patient Reported Outcomes
- Flare dependent collection of skin biopsies (twice) and blood samples (three times) for genetic analysis
- Kits provided for biosample collection
- Central sample analysis in Basel
- Biobanking of «left over» samples

Project design



- Min. 15 sites in 15 countries
- Max. 20 patients / site

★ Open (10 sites)

★ Set-up phase (5 sites)

Challenges

15 countries - 15 regulations

Questionnaire licenses

Genetic analysis

… just an observational study?
Quick and easy?

All age groups & healthy relatives & lots of languages

Biosample kit import & sample export

Study agreements

Clinical routine

Study-specific insurance

Image source: https://www.spreadshirt.de/shop/design/felliges+mammut+i+comic+tiere+i+elefant+geschenk+untersetzer-5c98083d2225090d703ea7cc?sellable=Zb5EbYran1Fx4NJoDalg-996-32&view=D1

Other learnings

Feasibility check is necessary

=> Are potential sites equipped to conduct the registry?

- Indicate age groups of patients
- Facilities and staff to collect, process and store biological samples
- CRO support required
- Any approvals beyond ethics required?
- Yearly resubmissions/ reportings?

Other learnings

Invest in data quality

- Don’t overload the visits
- Electronic CRF
- Worksheets
- Regular central data monitoring
- Reimbursement only after eCRF completion

Other learnings

CROs are very helpful, still be mindful

- Local expertise and language skills
- Sometimes mandatory (mainly outside of Europe)
- Often focused on clinical trials (agreements, safety, monitoring)

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In a Nutshell

- Think about what you «really» need
- Plan resources long term and conservative
- Biosample logistics is work-intensive
- Invest in data quality

Image source: https://pixabay.com/de/

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Questions?

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Next HRO lunch session

27 March	Ethics approval: Insights from the ethics committees
17 April	Data governance and protection: How to navigate the regulatory jungle
8 May	Registries and biobanks: Background,obstacles and practical views
29 May	Quality: Law, praxis and common hurdles

More information and registration:
sctoplatforms.ch/HRO-training-series

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SCTO Symposium, June 11

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Thank you for participating!

Further questions: Verena.Golz@usb.ch