SCTO
PLATFORMS

Online seminar on recent changes to the implementing Ordinances of the Human Research Act (HRA)

Monday, 28 October, 12.00-13.00

Information on participation:

Organised by the Regulatory Affairs Platform and the Education Platform.

Introduction

- Seminar prepared by SCTO Regulatory Affairs platform, with technical support from SCTO Education Platform
- **Questions**:
  - **during presentation**: in the chat (→ for moderated Q&A session at the end)
  - **during Q&A at the end**: by raising hand/unmuting
- Presentation will be **recorded**
- Video, slides & Q&A provided on the seminar website after the seminar
- Feedback poll at end → please fill in!

Introduction

How familiar do you already feel with the new ordinances?

→ please anwer the poll

Introduction

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Online Seminar

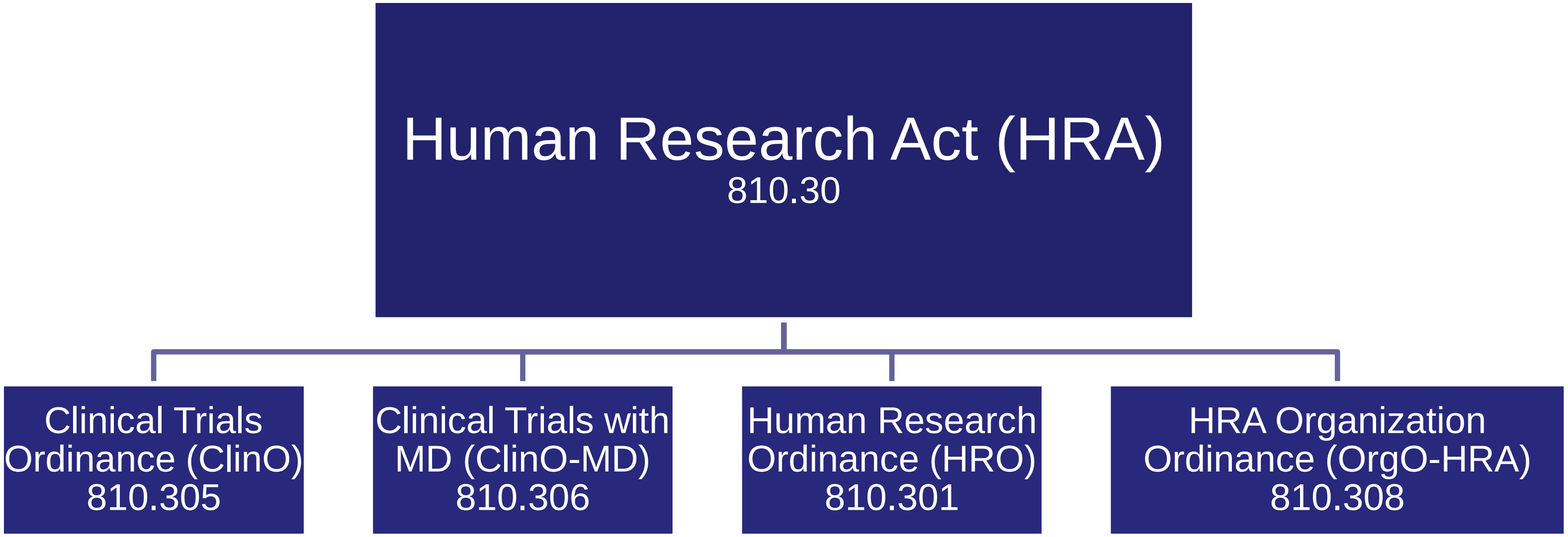
HRA ordinances – what has changed?

Speakers – Güliz Vanli Jaccard, Claudia Becherer

Agenda

Topics
Welcome
A brief history of HRA and its ordinances
Major changes to ClinO
Timelines
Major changes to HRO
Where to find extra information
Q&A

- Research involving human beings in Switzerland is regulated by the Federal Act on Research Involving Human Beings (Human Research Act, HRA) and the four associated ordinances.



Human Research Act (HRA)
810.30

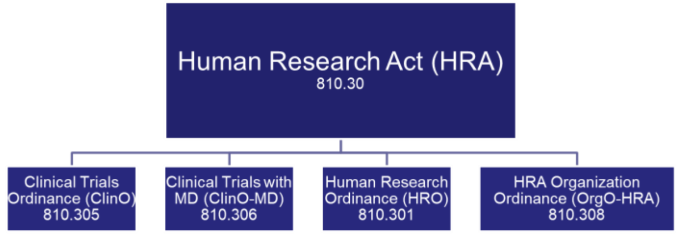
Clinical Trials Ordinance (ClinO)
810.305

Clinical Trials with MD (ClinO-MD)
810.306

Human Research Ordinance (HRO)
810.301

HRA Organization Ordinance (OrgO-HRA)
810.308

- HRA has been in force since January 1, 2014
- Federal Council ran a public consultation between 26 April 2023 – 16 August 2023
- SCTO with its CTU Network actively participated to this public consultation drawing its strong expertise in clinical research
- Federal Council approved the partial revisions on 7 June 2024
- The amended ordinances enter into force on 1 November 2024, except for the provisions on transparency, which enter into force on 1 March 2025.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10th Anniversary of the HRA this year! :

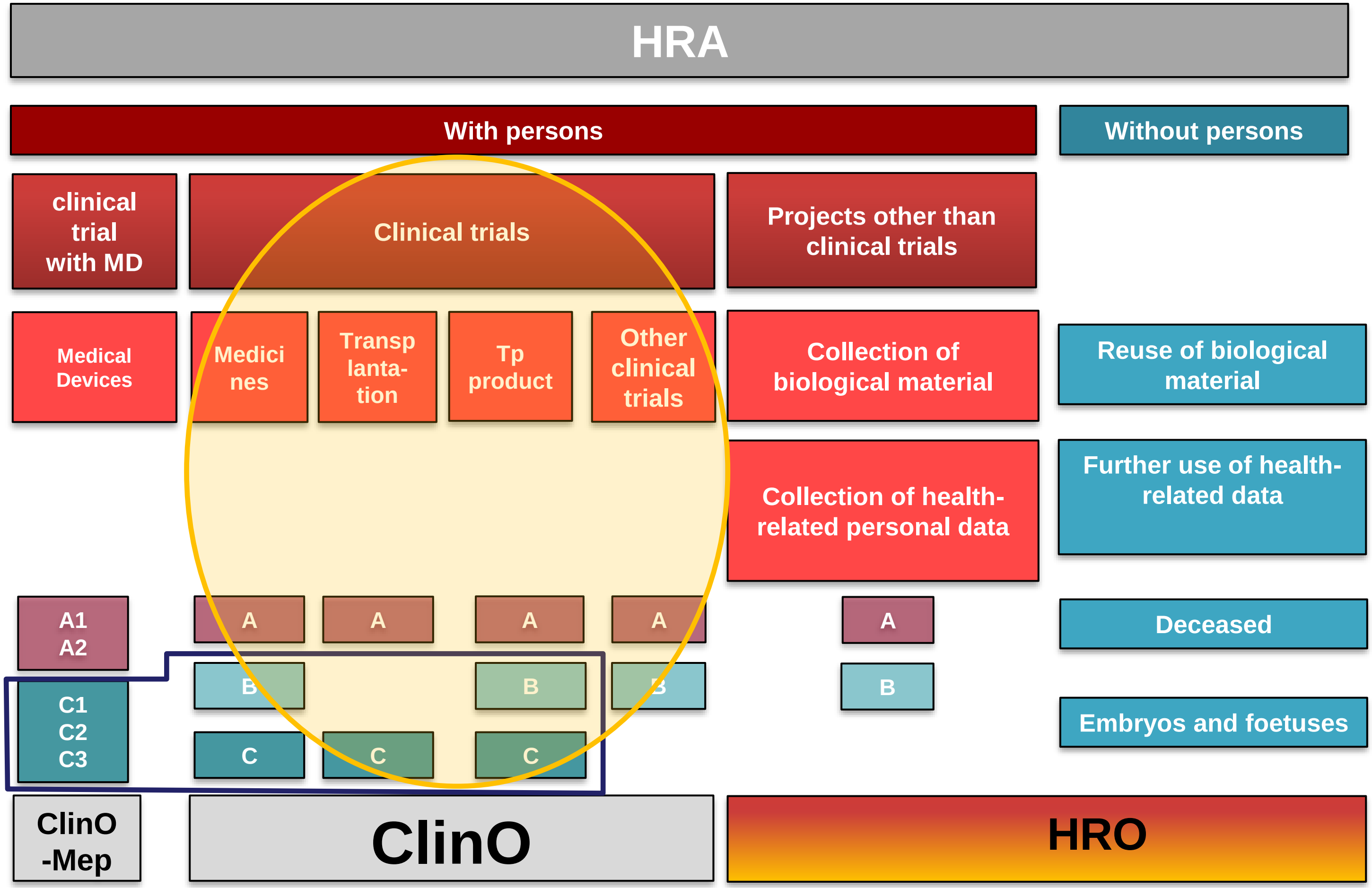
KOFAM: Ten Years of the Human Research Act – past, present and future
https://kofam.ch/en/research-on-humans/10-years-HRA

Revisions aimed to:

1. Promote a favorable framework for research
   - technical developments in the field of digitalization
   - better alignment with EU Clinical Trial Regulation (EU) No. 536/2014 = facilitated transnational research
2. Further improve the protection of participants
   - communication with the participants, and information provided to them are improved
   - inclusivity is improved, right to self determination is strengthened
   - requirement for transparency and retention of study data is harmonized with international regulations
3. Division of responsibilities between federal and cantonal authorities aligned with practice

Major Changes to ClinO

– Please note that we won’t be able to cover all modifications made on the HRA ordinances, for full compliance and detailed understanding, we encourage you to consult the original legal documents.



Major Changes to ClinO

Major Changes to ClinO

- Changes in the terminology and definitions
- "institute" is replaced by "Swissmedic"
- “health-related” in the definition of an intervention is removed
- definition of “intervention” is amended. It is defined as: **any measure** to which the participant is subjected and whose effects on this person are to be investigated
- term “Annual Safety Report (ASR)” was repealed as it is not commonly used internationally
- *New terms*
- investigational medicinal product and placebo are now defined
- surplus information and incidental findings are newly defined

Major Changes: ClinO Art. 4a

Inclusion of relevant group of people

Rationale: Research projects must include the groups of people relevant to the scientific question under study in order to obtain relevant conclusions from the results. However, in practice, this requirement is not always met, and it often happens that certain groups are underrepresented, such as women.

- *The sponsor and the investigator must ensure adequate representation of the relevant groups: particularly in terms of sex and age (provided that these groups are relevant to the scientific question).*
- *Intentional exclusion or underrepresentation of certain groups from a clinical trial must be explained and justified in the application documents submitted to the ethics committee.*

Major Changes: ClinO Art. 6

Professional Qualification

Rationale: Given the advances in digitization and the associated possibilities and risks in data processing, it is important that more attention is paid to data security and data protection of participants in trials.

- *investigator of a clinical trial must have appropriate knowledge and skills in data security and protection to comply with data protection provisions.*
- *another way for the investigator to ensure compliance with these provisions is to ensure they have the relevant expertise within the project team or by engaging specialists from the institution conducting the trial or externally.*

Major Changes: ClinO Art. 7

Information of the trial participants

- *para. 1 lit. 7e^{bis} : Surplus information may be obtained in certain clinical trials. If this is the case, participants must be informed about the significance of the information and the consequences of exercising their right to be informed or not. The purpose of this provision is to ensure participant's right to be informed or not.*
- *para. 1 lit. 7h^{bis}: Trial participants should be informed of the approximate date when the lay summary will be published in SNCTP and how to reach this information*.

Major Changes: ClinO Art. 7a

Information in case of genetic analyses

Rationale: In alignment with Federal Act on Human Genetic Testing (HGTA)

- *Participants should be specifically informed about presymptomatic or prenatal genetic test or analyses aimed at family planning are conducted as part of clinical trials which may have results related to the health of the participant or the embryo or fetus.*
- *a. participant must receive information on the purpose, type, and relevance of the genetic analysis*
- *b. the frequency and nature of the predispositions to the disease (anomaly)*
- *c. medical, psychological, and social consequences the analysis*
- *d. the impact genetic analysis results can also have on family members and their right* ***not*** *to know*
- *Participants should also be informed of the conditions under which they are required to communicate the results of the presymptomatic analyses to insurance companies*

Major Changes: ClinO Art. 7c

Informed consent form

- *researchers can now obtain consent from research participants electronically (so-called e-consent).*
- *Going to be covered in the HRO section*

Communication of results

Rationale: Participants have the right to be informed about their health (as well as the right not to know).

- *this applies to all information, targeted or surplus, resulting from the clinical trial analysis that meets current standards of analytical and clinical validity.*
- *in certain cases, the right of protection of life might precede the right not to know:*
- *a. the result in question may be subject to a legal obligation to communicate*
- *b. the result in question may lead to a health measure involving or implying informing the person concerned of the result*
- *c. the person concerned must be informed of certain results in order to protect the life and health of third parties, the legal representative of a person who is incapable of discernment is obliged to be informed of the results*

Major Changes: ClinO Art. 10-13

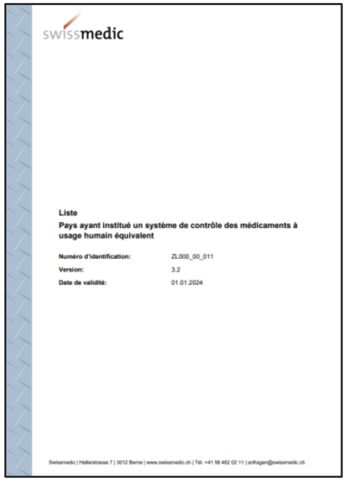
Liability coverage

- *Art. 10 exemption from liability: the extent of the damage and the criterion of acutely life-threatening disease are no longer relevant to liability exemption considerations, and have both been deleted*
- *Art.13 liability coverage must newly extend to damages occurring up to 20 years after the completion of the clinical trial (instead of the previous 10 years). With this change the legislation* is aligned *with the relevant new provisions of the Swiss Code of Obligations (CO Art. 60 para. 1bis)*

Major Changes: ClinO Art. 19

Categorization of clinical trials on medicinal products

- *certain clinical trials on medicinal products have been reclassified from “Category C” to “Category B”. The trials concerned are those involving:*
- *investigational medicinal products authorized in other countries with equivalent medicinal product control*
- *investigational medicinal products that are authorized in Switzerland and undergone low-risk (minor) modifications (listed exhaustively in Annex 2bis) are also categorized in B*



swissmedic

Liste

Pays ayant institué un système de contrôle des médicaments à usage humain équivalent

Numéro d'identification:	ZL000_00_011
Version:	3.2
Date de validité:	01.01.2024

Swissmedic | Hallerstrasse 7 | 3012 Berne | www.swissmedic.ch | Tél. +41 58 462 02 11 | anfragen@swissmedic.ch

Swissmedic publishes a list of countries with equivalent medicinal product control systems.
Quality of the medicinal products marketed in these countries is presumed established, and it does not need to be classified in category C.

Major Changes: ClinO Art. 23

Deadline for clinical trials

Rationale: Equivalent provision in Article 11 of the EU-CTR, with the aim to ensure that the application remains scientifically valid between submissions and that the participants do not participate to trials that no longer reflect the correct scientific knowledge

- *For category B and C studies, a deadline of two years is set for submission to the second approval authority after approval has been issued by the first authority. (A request for a deadline extension will be regarded as a substantial modification to the clinical trial. In the event of non-compliance with this deadline, the initial approval will lapse).*
- *For category B and C studies, a deadline of two years is set for the enrolment of the first participant after issue of the last approval obtained (A request for a deadline extension will be regarded as a substantial modification to the clinical trial. In the event of non-compliance with this deadline, the trial will be considered as interrupted).*
- *Note: For trials that are authorized under the old law, the two-year time limits apply from 1 November 2024*

Major Changes: ClinO Art. 38

First visit, end, premature termination, interruption, or resumption of the clinical trial

Rationale: Better alignment with EU-CTR on different notifications related to the status of a clinical trial

- *investigator must declare the first patient first visit to the EC within 30 days*
- *investigator must declare the end of the trial (in Switzerland) to the EC within 30 days*
- *in multinational studies, investigator must declare the global end of the trial to the EC within 90 days*
- *investigator must declare the premature termination, interruption or resumption of a clinical trial to the EC within 15 days (with justifications included in the declaration)*
- *for Category B and C clinical trials, such notifications and reports must also be submitted to Swissmedic*

Major Changes: ClinO Art. 39

Documentation of adverse events (AE)

- *In justified exceptional cases, the standardized documentation of some adverse events (if non-critical, meaning they are not significant for the evaluation of the trial's safety, must be detailed in the research protocol and subject to approval by the regulatory authorities) might be waived for Category C clinical trials*
- *Adverse events* ***critical to the safety evaluation*** *must always be documented in a standardized manner for Category B and C clinical trials*

Major Changes: ClinO Art. 40-41

Serious Adverse Events (SAE) and Suspected Unexpected Serious Adverse Reaction (SUSAR)

Rationale: Alignment with provision of the EU-CTR

- *Art. 40: a fatal serious adverse event occurring at a trial site in Switzerland need* ***no*** *longer be reported to the ethics committee within 7 days (unless it constitutes a SUSAR)*
- *Art 41: not only SUSARs with fatal consequences* ***but also*** *life-threatening SUSARs must be reported to the ethics committee (and to Swissmedic) within 7 days*
- *SUSAR reporting requirements continues after the completion of the trial in Switzerland (when the investigator or sponsor* ***becomes aware*** *of a SUSAR)*

Major Changes: ClinO Art. 45

Obligation of conservation

Rationale: Alignment with provision of the EU-CTR

- *the sponsor must retain all data related to clinical trial for a minimum of 20 years from the completion or premature termination of the trial.*
- *the investigator must retain all documents necessary for the identification and medical follow-up of participants, as well as all other original data, for at least 20 years from the completion or premature termination of the clinical trial.*

Major Changes: ClinO Art. 64-65

Registration

Rationale: Alignment with provision of the EU-CTR

- *certain information on the clinical trial must be published in BASEC in the national languages for the regions in which participant recruitment is envisaged (currently only one national language is required)*
- *Phase I clinical trials on medicinal products where the drug is administered exclusively to adults must also be registered before the start of the trial, however publication of certain business relevant details may continue to be delayed*

Major Changes: ClinO Art. 65a

Registration and Publication of Trial Results (takes effect on March 1, 2025)

Rationale: Alignment with provision of the EU-CTR, aimed at ensuring transparency in the field of clinical trials

- *sponsor must publish a summary of the results of the trial in an international registry within one year of the trial's completion or premature termination (If a study is interrupted for more than two years, it is considered prematurely terminated and results must also be published)*
- *a lay summary of the results of the trial - understandable to the general public, in the national languages used for recruitment - must also be published in BASEC. This must also be done within one year of the trial's completion or premature termination*

Timelines

Clinical trials that are approved under current law (before 1 November 2024);

- *the liability, liability coverage and retention duties for research projects under ClinO, ClinO-MD and HRO will continue to be governed, even after 1 November 2024, by the law currently in force*
- *the new notification, reporting and documentation duties for ongoing clinical trials under ClinO will apply from 1 November 2024 in principle. However, until 31 October 2025 researchers are allowed to fulfil these obligations under current law*
- *the two-year period until the application must be submitted to the second authorizing authority and the two-year period until the first participating person must be included into clinical trials according to the ClinO will only start to run from 1 November 2024*
- *the new rules for the categorization of a clinical trial with medicinal products can also be applied to trials that were approved under current law. Researchers have until 31 October 2025 to apply for an adjustment of the category in accordance with the new law if they so wish*

Timelines

Publication of the summary of results of clinical trials under ClinO

- *as mentioned earlier, the amended provisions on transparency will come into force from 1 March 2025. The duty to publish the summary of results within one year of completing a clinical trial under ClinO applies from 1 March 2025 for all trials that are completed after 1 March 2025. It does not apply to trials that are completed before 1 March 2025*

Major Changes to HRO

Disclaimer and Legend

Disclaimer:

“Not all details of the new regulation are listed, for example, the regulations in the area of research with radiopharmaceuticals are not addressed.”

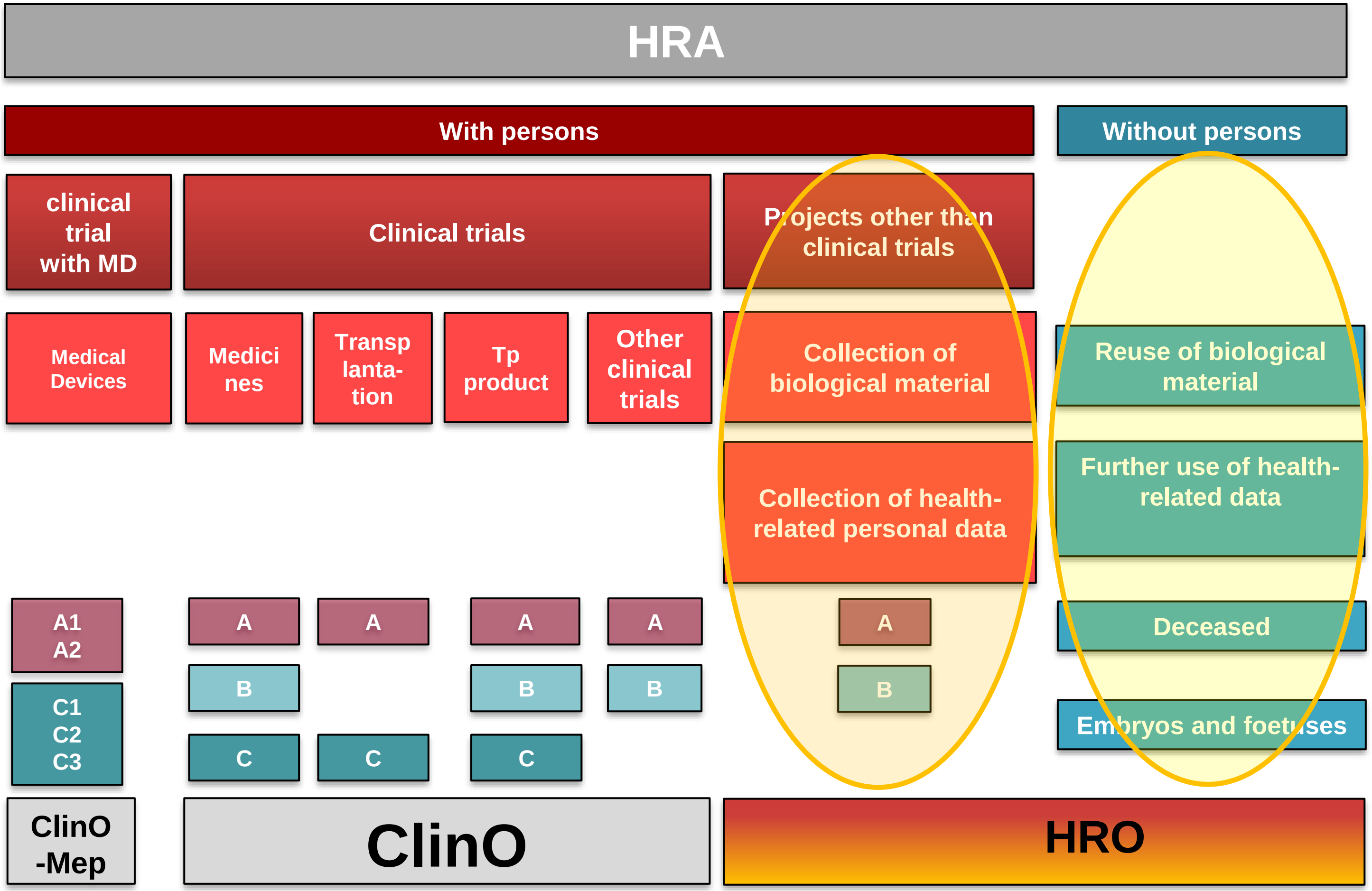
“No liability is taken for the correctness of the translation of documents and excerpts from Swiss national languages into English.”

Legend

▪ *A square is a citation from law or other offical document*

➢ *An arrow is an hint, an idea or an open question*

HRO-Projects



HRA

With persons

Without persons

clinical trial with MD

Clinical trials

Projects other than clinical trials

Medical Devices

Medicines

Transplantation

Tp product

Other clinical trials

Collection of biological material

Collection of health-related personal data

Reuse of biological material

Further use of health-related data

Deceased

Embryos and foetuses

A1 A2

C1 C2 C3

A | A | A | A | A

B | B | B | B

C | C | C

ClinO-Mep

ClinO

HRO

Agenda

- References to other ordinances
- Transition periods
- Main changes in particular paragraphs
- To-do list
- Where can I get information/support?

References

Reference to ClinO with regard to:

- Art. 3, Scientific integrity,
- Art 4, scientific relevance and
- Art.4a, inclusion of relevant persons

➢ Only changes with the new Art.4a, inclusion of relevant groups; those has been adressed in the first part by Güliz, protocol template are updated

Major Changes to HRO

Surplus information, Art 1a; Art 5a

(Überschussinformation, informations excédentaires, Informazioni sulle eccedenze)

- „Results, that are obtained within the framework of a research project but are neither necessary for the completion of the project nor for the study of the scientific issue"
- A good definition of it in protocol template: „*an incidental finding is information that is clinically relevant*"

  (*Zufallsbefund*, *découverte fortuite*, *reperto incidentale)*

Major Changes to HRO

Surplus information, Art 1a; Art 5a

- Participants **must** also **be informed** about possible incidental findings.

➢ ‘Further use’ of studies from the third chapter, not mentioned. This makes sense, since the participant is not seen by the researcher. The “initial informing investigator” is obliged to provide the participant with correct information.

➢ Handling of genetic data in insurance relationships, (Art. 42 - Art. 44 GUMG/LAGH), does apply to further use projects, too!

➢ Documentation about „right and will not to know“ is important.

Major Changes to HRO

Professional qualification - Data protection, Art. 4a

- The project leader must have *appropriate knowledge and skills in the areas of data security and data protection* or be able to *guarantee these by involving appropriate expertise*.

➢ How is this to be proven?

Major Changes to HRO

Art: 6a End of research project

- “…the end of the research project is deemed to be **the last collection** of collection **of personal data** relating to health or the last collection **of biological material** as part of a research project, unless otherwise provided for in the research plan”

➢ The clear definitions makes it easier to plan retention/archiving

Major Changes to HRO

- The clear definitions makes it easier to plan retention/archiving

Art. 5 Storage of biological material

- "…to do this, it must refer to nationally and internationally **recognised guidelines**;"

Art: 23a retention obligation

- The project leaders must store all data related to the research project for **at least ten years** after completion or cancellation of the research project.

Major Changes to HRO

Art: 18 Changes ("Amendments")

- "…changes to the research project *which concern* ***the goal*** *or the central topic of the research project are now* ***also applicable for category A studies***"

Major Changes to HRO

Anonymisation (Art.25)

Excerpt from the explanatory report:

- “As long as there is a key, encoded data cannot be considered anonymous, even if they appear to be anonymous to persons who do not possess the key.”
- Anonymisation must be carried out using a state-of-the-art method
- Processing steps must be documented
- Residual risk of re-identification must be described

➢ Anonymisation is a resource-intensive step that needs to be well planned. Caution is advised when transferring data and one is obliged to “anonymise correctly”.

Major Changes to HRO

Coding (Art.26)

from the explanatory report:

- “Biological material or health-related personal data are considered to be correctly coded if it is not possible, or only with a disproportionate amount of effort, to assign them to a specific person without access to the key or the source data.”
- For further us projects: The key must be in the possession of a person or organisational unit <u>that is not involved</u> in the research project (paragraph 2). The other person may, however, work in the same organisation.

➢ Who is keeping the key? Document it on the delegation log keep it up to date if person changes, including after the end of the data/material collection.

Major Changes to HRO

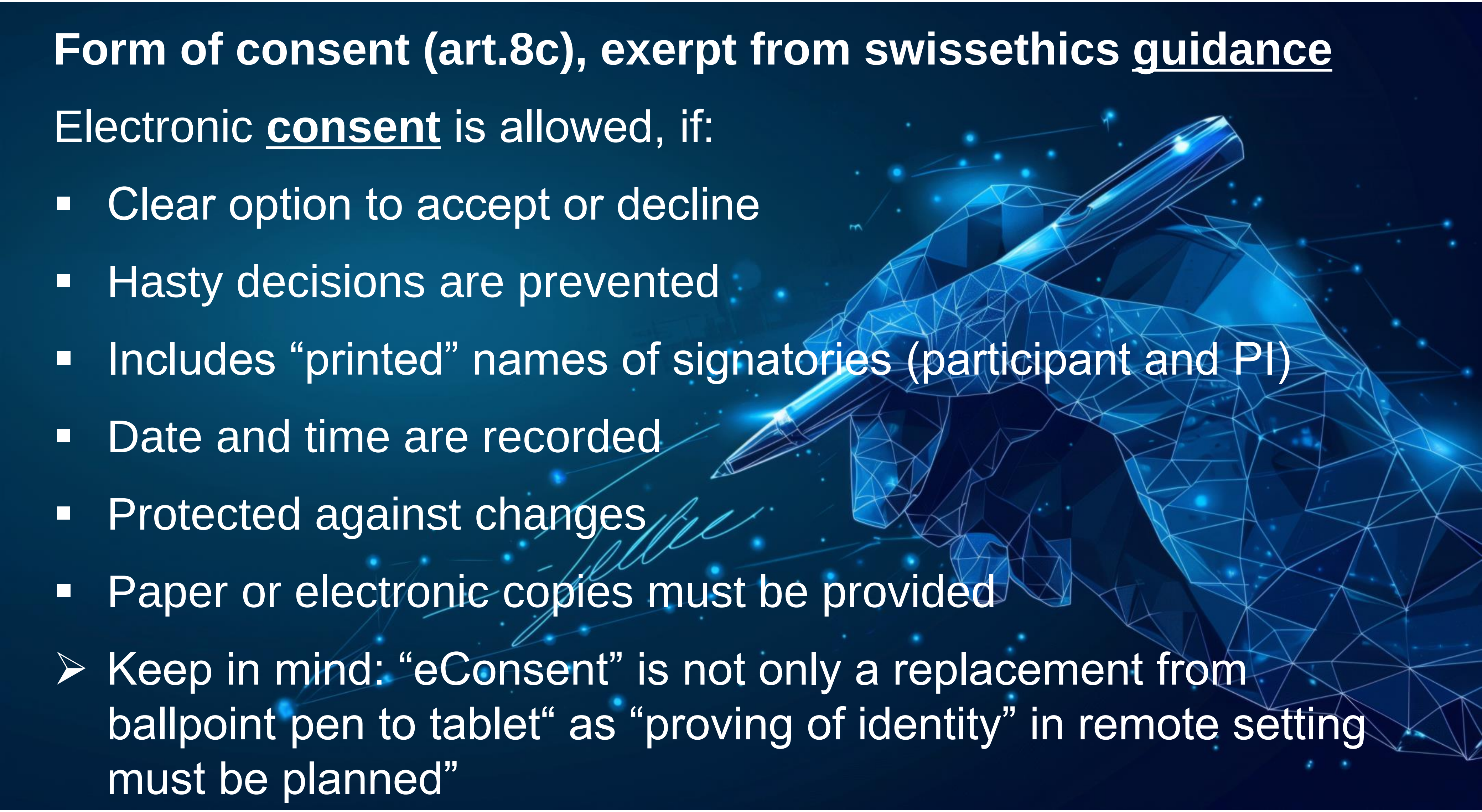
Form of consent (art.8c), exerpt from swissethics <u>guidance</u>

Remote **<u>consent</u> <u>process</u>** is allowed if:

- System comply with ICH-GCP
- Provided information comply with ICH-GCP
- Possibility to ask question
- For subjects with impairments or lack of familiarity with elect. devices the process must be appropriate
- If the process is interactive, it must be appropriate for intended audience

➢ Keep in mind: Same procedures like in real life – only transfer to remote setting! Check of identity must be planned!

Major Changes to HRO



Form of consent (art.8c), exerpt from swissethics <u>guidance</u>

Electronic **<u>consent</u>** is allowed, if:

- Clear option to accept or decline
- Hasty decisions are prevented
- Includes “printed” names of signatories (participant and PI)
- Date and time are recorded
- Protected against changes
- Paper or electronic copies must be provided

➢ Keep in mind: “eConsent” is not only a replacement from ballpoint pen to tablet“ as “proving of identity” in remote setting must be planned”

Transitional provisions

Storage/retention/„Archiving“; HRO Art. 48a and Liability HRO Art. 13, exerpt from presentation FOPH:

- „According to current law, the liability, securing and retention obligations for research projects are (still) governed by the HRO if they were approved before 07. June 2024.”

➢ No (further) transitional provisions, so approved projects do not have to be adapted to the new ordinance by 31 October 2025.

To Do

- **Check** wether you have **ongoing studies**, that have to be amended until 31. October 2025
- **Download** within the next 3 days the old versions of protocols/ICFs, generate in word via „comparison mode“ an track change version vs the new templates
- With this tc-versions, you could easier detect where you have to amend s.th.

- **Check** your **SOPs** and working instructions
- **Train** (and **document**) your study team to the changes
- **Communicate** changes to external sponsors (abroad)

Where can I get help and Information?

CTUs:

- **HUG-Geneva:** Presentation in French, November 11th, followed by a publication in bulletin in December
- **DKF-Basel:** Presentation in German, focusing project management an sponsor-oversight topics, November 12th
- Information Flyer available at Homepage, specific regulatory review of ongoing projects available (not free of charge)
- **CTU-Bern and CRC-Lausanne**: Help is always provided!
- **CTU-EOC:** Specific support and infos available on homepage
- **CTC-Zürich:** Event with the Cantonal Ethics Commission Zurich,Tuesday, 29 October 2024, event in German, registration via USZ website
- **CTU-St. Gallen:** Comparision document between the current and the upcoming ordinances (in German) (available upon request)

Where can I get help / Information?

SCTO:

- The Easy-GCS will be up-dated by end of year

SPCRC:

- National Congress for Study Nurses and Coordinators 2024

Sources of information

Swissmedic:

- general overview: Implementation of new ordinances
- Guideline Submission Clinical Trial Application Dossier
- Combined studies

Swissethics:

- excess information and incidental finding (Guideance)
- eConsent

Other:

- Fedlex, Compilation of laws
- https://dkf.unibas.ch/de/services/regulatorik/informationsblaetter/
- explanatory report (FOPH- only available in FR/IT/DE)

End of session

Thank you for participating!

Reminder:

- Video, slides & Q&A provided on the seminar website
- Unanswered questions will be covered in Q&A doc

Further questions:

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