Seminar Series:

Facts and pitfalls of observational studies - How to plan and conduct HRO projects

Q&A from the session

“International multicenter HRO projects”

October 1, 2025

- Difference between the main project site being in Switzerland and the main site being European or extra-European?
    - Partially covered in part I <u>AND</u> in part II:
        - In general, neither in European countries nor extra-European countries there is a Human Research Act (HRA) that regulates non-clinical/ non-interventional human research, such as covered by the Human Research Ordinance (HRO) in Switzerland.
        - That means, if a Swiss site acts as Sponsor-Investigator/ Sponsor-Project Leader (= main site), then it cannot be expected, that aspects, such as the requirement for an Ethics approval, the categorization of the research project, are clear for all participating sites outside Switzerland
            - E.g. in Germany and Austria only clinical trials with medicinal products or medical devices are regulated by a real law
            - E.g. in other countries, a HRO research project could be categorized as interventional/ clinical trial with medical devices, which changes requirements completely (see example of part II of the session)
            - E.g. in Germany there are different types of ECs: ECs affiliated with the medical associations/ Ärztekammern of the different federal states/ Bundesländer (review/ judge only interventional clinical trials according to “Arzneimittelgesetz” und “Medizinproduktedurchführungsgesetz”) as well as institution-specific ECs, such as of an university, a hospital, etc. (review/ judge primarily other clinical trials and maybe non-interventional projects, such as observational studies and further use, according to Paragraph 15 der “Berufsordnung für Ärztinnen und Ärzte” like with only one vote by a “Lead Ethics Committee”)
        - So from a regulatory point of view, it can become very complicated/ challenging to start and conduct international multicenter HRO projects.

        - From the perspective of Data protection (e.g. in case of border crossing of data!):
            - It seems to be easier as long as sites are involved that have got a comparable data protection legislation (e.g. according to the GDPR/ DSGVO, such as countries in the European Union)
                - There is a so-called adequacy decision of the European Union dating January 2024, which has stated that Switzerland's data protection level is comparable to the level in the European Union – so transfer of data FROM a European country to Switzerland and vice versa (European countries count as safe countries in terms of data protection and data transfer, see DPO Annex 1) should not be a problem
            - It is more complicated with project partners in countries/ states without a comparable data protection legislation, such as many extra-European countries or the US (Cloud-Act) (see example part II of the session) – here get advice and

support by the responsible data protection office and/ or the Legal Department of the institutions

- What are the ethical requirements and issues in case of international multicenter projects?
  - Partially covered by the Thomas Gruberski during the presentation part I:
    - Independent how the project is handled abroad and if it requires an Ethics Approval in other countries, in Switzerland all research projects according to the HRO require a submission and an Ethics approval for all Swiss sites
    - Consider: in international multicenter projects ICFs might be required as country-specific ICFs and in more and different languages than the official languages in Switzerland!
    - Participants of HRO projects according to chapter 2 (and 4 and 5) or Data/ Sample donors in HRO projects according to chapter 3 need to be informed in the case, data are transferred abroad, in which countries and under which circumstances this will happen (e.g. identifying, pseudonymized or anonymized data)
      - Coded/ pseudonymized data for which the code list/ the key remains in the sending institution – it is not a problem
    - As pre-requisite for data sharing with other partners in other countries, Swiss Ethics Committees (sometimes even Scientific Journals) require listing of the recipient countries, the proof that participants/ donors were informed, as well as concluded Data Transfer Agreements (DTA) or Data Transfer Use Agreements (DTUA) or Material Transfer Agreements (MTA) with each of the foreign recipients/ project partners.

- When can data be sent to a foreign country without a necessary ethics approval?
  - If there is no Ethics approval required for a human research project, then the project is likely not in the scope of the HRA and the Ethics Committees in Switzerland are not responsible for a review/ judgement, e.g. projects for quality assurance, truly anonymized data, etc., **OR** the project is led abroad in another country and only data are shared/ transferred to a research partner/ institution in Switzerland
  - In this case, the controller institutions, e.g. the hospitals, universities, in which the data becomes or was collected, are fully responsible for the data
    - In most of the Swiss institutions/ hospitals a special governance commission or board or an institutional Ethics Committee exists and is responsible to check the projects concerning recipient countries, research partners, patient information, type of data (identifying, de-identified), contracts (DTA, DTUA, MTA) and the way of intended data transfer.

- E.g. an observational longitudinal study, low risk, academic, how would you manage monitoring? How would you address quality assurance?
  - Please see material of the HRO lunch session “Quality: Law, practice and common hurdles” in 2024: Quality: Law, practice and common hurdles - Tools & Resources
  - Partially answered by means of several specific examples also in part II of the session (please check the presentation (Pdf) or consult the video recording, provided on the webpage together with this Q/A document)

- In international multicentric HRO projects, is the sponsor or institution that initiated the project responsible for liability (or possibly insurance) at all participating centres? For example, if I participate in a research project in Switzerland with a sponsor based in Germany, is the institution in Germany liable?
    - Answered during the Q/A part of the session by Thomas Gruberski:
        - Although there is no HRA in other countries, it is common sense, that the sponsor is liable. So he/she has to provide the insurance, independent if he/ she is located in Switzerland or outside Switzerland.
        - So if an Ethics Committee, e.g. in Germany, decides that a non-interventional study or an observational study (such as projects according to HRO chapter 2) require an insurance, then an insurance has to be taken out by the sponsor of the project.
        - So, also if the sponsor is being situated in Switzerland, in which according to the HRA and the HRO the project would not require an insurance, it's up to the sponsor in Switzerland to organise an insurance.
        - Of course, it's always helpful, if foreign study/ project sites, that are involved in the study/ project help and say: listen, we have some experience with this insurance company or the other company that can make some recommendations.

- In international projects, must an (individual) protocol be submitted to the Ethics Committee (EC) in each country or even each institution involved? What aspects need to be considered in terms of coordination between the different parties?
    - See also question 1 (see above)
    - And yes, the protocol needs to be submitted to each EC of each country involved (maybe even to different institutional ECs in a country). Content-wise, it should be the same protocol that is handed in to the EC in Switzerland (even if ECs abroad do not understand the way of categorizing a non-interventional research project)
        - Country-specific differences (e.g. concerning data protection) should be addressed in one and the same master protocol

- If we want to join a German "Anwendungsbeobachtung"/Registerstudie, is it correct to submit the project as a HFV3 project in Switzerland, with an IC adapted to Swiss Legislation? My experience is, that this needs quite some amendments in the protocol as well as in the IC.
    - Suggestions made by moderator of the session:
        - If the Swiss site is indeed part of the overall research project and already collected routine data is being transferred and fed into the foreign registry, then in it would be an HRO3 project, i.e. a project under HRO chapter 3 (reuse).
        - If the Swiss site is part of the research project, but data is specifically being collected (not routine data) that will later be entered into the foreign registry, then it would most likely be a project under HRO chapter 2 (prospective data collection).
        - If the Swiss site is not part of the research project, but only already collected routine data is to be contributed to the foreign registry, then of course certain data protection requirements apply to the data transfer, but a submission to a Swiss Ethics Committee might not be necessary in that case.

- Question to Thomas Gruberski: You said that the GC in Basel only allows use of coded/ pseudonymized data. Is that hospital-specific, or does every GC in Switzerland only covers coded/ pseudonymized data?
        - Please see template of the national version of the General Consent (GC) on the swissethics webpage: General Consent

- It was shown that there were conditions in the ICF that need to be accepted to participate (like the data sharing). Can this also be done with further use? E.g. you can only participate if you allow further use (e.g. for a biobank)
    - Partially answered also in part I of the session:
        - In case of intended further use of research data from a research study according to ClinO, ClinO-MD or HRO chapter 2, 4, and 5, it is strongly recommended to obtain separate consents: one for participation in the study/ project and one for potential further use of the research data, i.e. for future research projects according to HRO chapter 3
            - It is not recommended to make participation in a study dependent on consent for further use, since participants may then not agree to participate in the actual study/ project
        - This also accounts for specific ICFs for research projects according to HRO chapter 3 (although here often data / samples are used from patients, that have agreed on the General Consent of an institution and these data / samples can always be used also for other future research projects according to HRO chapter 3).