Newsletter Ethics Committee Research UZ/KU Leuven
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Dear researchers and team

With this newsletter we try to help you in doing high-quality clinical and translational research with respect for the well-being and privacy of each patient and participant.
Ethics Committee Research UZ/KU Leuven

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1. Data Access Committee (DAC)

Research data obtained from human genome research is increasingly encouraged in the scientific community. Funders and journals now require researchers to share the research data underlying their study results through genome data repositories. Human genome data are considered sensitive personal data under the General Data Protection Regulation (GDPR). Genomic and genetic data are never considered “anonymous”. To address concerns about sharing human genomic data, genome data repositories employ a controlled access model. Controlled access aims to protect the rights and interests of research participants. These repositories entrust the access control to Data Access Committees (DACs), which are responsible for reviewing requests from third parties seeking access to genomic/genetic datasets.

To streamline the process, a single Data Access Committee called "DAC KU Leuven/UZ Leuven" has been formally established. The DAC KU Leuven/UZ Leuven will be supported by a dedicated DAC Office staffed by a research employee from EC Research UZ Leuven. The DAC Office can be reached at dac@uzleuven.be. The intention is to exclusively use this DAC (and not establish your own DAC) when referring to a DAC from UZ or KU Leuven.

The DAC will be organized as a working group under the Data Protection Board UZ Leuven (DPB), acting on behalf of the university and LRD when necessary. The DAC will include representatives from all relevant supporting services of KU Leuven/UZ Leuven, as well as domain experts for consultation and coordination.

The DAC has a meaningful and coordinating function, and the DAC Office supports the DAC administratively and serves as a point of contact for researchers in the following situations:

- When KU Leuven researchers submit data to EGA (European Genome-phenome Archive)
- When KU Leuven researchers receive requests from third parties to access their datasets with their own human genetic data
- When KU Leuven researchers request access to external genetic/genomic datasets in repositories (including EGA, NIHdbGAP)
- When KU Leuven researchers want to submit genetic/genomic data to a domain-specific database other than EGA

You can find more information about DAC on its website https://www.uzleuven.be/en/dac.

2. Including prison inmates as participants in clinical trials

The inclusion of prison inmates as participants in clinical trials requests careful consideration. In the absence of explicit legislation, the permissibility of their inclusion remains ambiguous. Nevertheless, there is no ethical justification for depriving inmates of the potential benefits of scientific research all together. After all, systematically excluding certain groups from research is ethically problematic. The following pertinent criteria and aspects can assist you in making an informed decision on whether or not to involve incarcerated individuals:

Detainees must be regarded as vulnerable subjects, i.e. individuals whose willingness to volunteer in a clinical trial could be unduly influenced by expectations of benefits from participation or by potential repercussions from higher-ranking individuals in the hierarchy for declining participation. Consequently, special attention must be given to the consent process, preferably involving an independent party such as a nurse or chaplain (rather than a guard). Alongside consent, it should be explicitly stated that detainees will not face any positive or negative consequences regarding their evaluation or length of detention based on participation or non-participation. These safeguards are necessary to ensure an independent and informed decision-making process.

Additionally, a distinction should be made between the individual detainee's right (with a specific health concern) to participate in a study and conducting research solely within the detainee population. The latter can be justified if the aim is to enhance detainees' health, care, detention conditions, or to gain insights relevant to these aspects. Furthermore, if an individual detainee is to be included in a study not designed exclusively for detainees, it is advisable to inform the relevant ethical committee accordingly.

Lastly, practical arrangements warrant attention. Due consideration should be given to the practical feasibility of the study and its follow-up (visits, examinations, etc.).

3. Requests for secondary use of (personal) data and/or samples

This text discusses the process at EC Research regarding requests for the secondary use of data and samples collected in prospective academic studies sponsored by UZ Leuven. We already have mentioned this information in the December 2020 newsletter of EC Research.

At EC Research, we regularly receive requests for secondary use of (personal) data and/or samples that have been collected in prospective academic studies with UZ Leuven as sponsor and which researchers now want to share with other research partners (academic and/or commercial) in the context of new scientific research projects.

The key points are:

1. Even if consent has been obtained from participants for data/sample sharing in new projects, EC Research approval is required and a new S-number will need to be registered in such case (see also point 4.).
2. The ICF given by the participants in the original prospective study (primary use) must have foreseen that (pseudonymised) data and/or samples collected within the study could be further shared with research partners (academic and/or commercial partners, inside and/or outside the EU, as the case may be).
3. EC Research will review whether the research question of the new research project(s) is in line with the research question(s) of the original study.
4. The role of UZ Leuven and the research partners in the new research project(s) shall be examined by EC Research. If the sponsor of the new research project(s) is not UZ Leuven, the new research project(s) cannot be set up as an amendment to the original study and will require a new S-number and approval by EC Research. The necessary contractual arrangements will need to be in place between UZ Leuven and the research partners to cover the envisaged secondary use of data and/or samples (such as a DTA or MTA/DTA or even a service agreement – templates can be found on CTC's website).

4. m-Path

m-Path is a platform to facilitate real-time monitoring and real-life interventions (https://m-path.io/landing/), built by researchers for researchers.

We would like to shed light on the classification of m-Path within the scope of the Medical Device Regulation (MDR).

As defined in Article 2 of the MDR, a medical device is any instrument, apparatus, appliance, software, implant, reagent, material, or other article intended for use in the diagnosis, prevention, monitoring, treatment, or alleviation of disease or injury. Importantly, this includes devices used for assessing the safety and efficacy of medical interventions.

However, it is essential to clarify that m-Path does not always fall under the MDR. When m-Path's sole purpose is data collection and it does not provide interpretation or function as an intervention, it typically does not fall within the scope of the MDR. In such cases, m-Path is considered a tool for data collection rather than a medical device under the regulation.
To summarize, m-Path may be considered a medical device when its use involves evaluating safety and efficacy. However, if it solely collects data without interpretation or intervention, it generally does not fall under the MDR's definition of a medical device.

5. Lay summary master's theses

As explained in our newsletters of July 2020 and October 2022, the sponsor (i.e. data controller) of a study needs to provide a description of the purpose/goal of the research in layman's terms (Art 13 and 14 GDPR) towards the study participants/data subjects (transparency). The sections under 'Research' in the GDPR questionnaire will automatically be included in Mynexuzhealth. Study participants will in this way be informed about the (prospective and retrospective) studies in which their data are being processed after they are flagged with the corresponding S-number in KWS. Given the importance of informing the patient about the use of their data, flagging in KWS is essential. The PI is responsible for flagging each patient with the right S-number whose data are processed in study.

All master's theses within the Biomedical Sciences Group must undergo an ethical review procedure. Every student preparing a master's thesis must complete a questionnaire that identifies the type of research. Each master's thesis is assigned an MP number. However, only an S number, and not an MP number, can be used to flag in KWS. Therefore, for these studies with use of retrospective UZ Leuven patient data directly submitted to the OBC, it is necessary to create an S number for master's theses in order to inform patients via Mynexuzhealth about the processing of their data for research purposes.
Every master's thesis submitted to the OBC must include a lay summary of the study. This lay summary is part of the protocol and needs to be reviewed and approved by the OBC. Once a master's thesis that processes data from UZ Leuven patients has been evaluated by the OBC and can be approved, EC will be informed by the OBC. Before the

OBC formally approves the study, EC will administratively assign an S number to the (by OBC already evaluated) master's thesis. EC will communicate this assigned S number to the OBC. The OBC will then communicate this S number to the student when sending the approval letter for the master's thesis.
The student is responsible for filling out the GDPR questionnaire. In this questionnaire, the 4th bullet should be marked: "KU Leuven will process data without UZ Leuven being a data controller or processor for the purpose of the study (e.g., KU Leuven acting as a sponsor)." The lay summary can be completed. Patients can be flagged in KWS with the S number afterwards, and the lay summary will be visible to the patient in Mynexuz.

6. Decision tree SMEC – EC

The Social and Societal Ethics Committee (SMEC) evaluates research for ethical approval in the humanities and the behavioral or social science research traditions. Also protocols in engineering, natural or life science may be submitted to the SMEC panel. More information can be found on the website (https://www.uzleuven.be/en/ethics-committee-research/smec).

SMEC is authorized to evaluate research proposals involving human participants to ethical review insofar as i) they do not fall under the Human Subject Experiments Act (i.e., the "Experiments Act" of May 7, 2004), ii) there is no involvement of UZ Leuven patients (data) and/or staff, and iii) the studies do not take place within the Health Sciences campus of UZ Leuven.

However, if, despite the study being eligible for submission to SMEC for the reasons mentioned above, the expertise of the members of EC Research better aligns with the subject of the study, it is advisable to submit the study here.

A decision tree has been established to help researchers at KU Leuven submit research projects to the most appropriate EC using a decision tree. A number of recommendations are made to assist researchers in their choice and give them an understanding of how the regulatory framework for ECs works.

This decision tree has been recently updated and can be found on our website: https://www.uzleuven.be/en/ethics-committee-research/smec

7. Complaints about clinical studies received by the ombudsman

The ombudsman provides EC Research with a list of complaints and questions they have received related to clinical studies. The complaints can be categorized into the following categories:

- Questions about compensation and invoices

Study participants complain about receiving an invoice for a procedure they supposed to be covered by the study budget. For participants in a study, it is not always clear which costs will be covered by the sponsor and which costs they are responsible for (such as standard of care procedures) . The information in the Informed Consent Form (ICF) should be explicit about this, and during the discussion of the ICF between the researcher and the participant, this aspect should be clarified verbally as well.

- Study team is not available for questions

The ombudsman is contacted multiple times because the contact number provided in the ICF is not reachable. Please ensure that the study team is easily accessible for questions.

8. Maintaining Ethical Standards beyond approval

While approval by an EC is a significant step in the research process, it is imperative to recognize that compliance with ethical standards does not end with the approval itself. Researchers play a crucial role in ensuring that their studies are conducted with the utmost integrity and in strict accordance with the approved protocols. Once a study is approved, it becomes the responsibility of the researcher to adhere to the protocol. It is essential to adhere to the study design, methods, and procedures as outlined in the approved protocol. Any significant changes must be submitted to EC with an amendment for further review and approval.

9. Procedure for medicinal products in compassionate use and medical need programs, urgent situations, off label use, samples and import

We referred to this procedure in our previous newsletter, you can find it here in Muzlidoc: https://wiki.uz.kuleuven.ac.be/pages/viewpage.action?pageId=774635289

10. BAREC Compensation guidance

The Belgian Association of Research Ethics Committees (BAREC) has issued a Guidance that provides recommendations for fair compensation of subjects for their participation in clinical research in Belgium ("Guidance"). You can find it on the website (https://barec.be/wp-content/uploads/sites/6/2023/11/BAREC-Guidance-on-Compensation-of-Clinical-Research-Participants-Version-21_11_2023.pdf) The objective of the Guidance is to present a common framework with practical guidance of interest to ECs, sponsors, investigators and participants involved in clinical research in Belgium.

As a general rule, all study-related expenses should be reimbursed or be compensated for (when a reasonable fixed lump-sum has been agreed upon). Compensation should be clearly reflected in the ICF (payment form, frequency, amount, timing,...).

Additional compensation, such as for time investment, inconvenience, or willingness to participate can be offered, but should be well-justified.
If the sponsor wants to include such compensations, these should be clearly justified in the application dossier to the EC which evaluates the acceptability of these costs in view of undue influence. If the EC agrees, compensation should be reflected in the ICF (payment form, frequency, amount, timing,...).
Patients or healthy volunteers have equal rights to compensation although expected therapeutic benefit can be taken into account.

11. UZ Leuven policy regarding source data/medical record sharing

Cf. https://gbiomed.kuleuven.be/english/ctc#4.%20Data%20protection

Please take note that in accordance with the present position of the Belgian Federal Agency for Medicines & Health Products (FAMHP), UZ Leuven does not permit remote source data verification by external parties. As such, medical records cannot be shared outside UZ Leuven in any other format (see exceptions below). If verification of medical data is needed, than this should be done on-site at the premises of UZ Leuven. Alternatively, the pseudonymized data can be reviewed through data fields in the (e)CRF and/or through data/parameter entry into an IxR System.

Permitted exceptions:
- Sharing of pseudonymized medical data for adjudication of safety events, provided that the requirement for adjudication is described in the EC-approved research protocol and informed consent.
- Sharing of pseudonymized radiology images for central reading, provided that the requirement for central reading of images is described in the EC-approved research protocol and informed consent.

We appreciate you understand that as a hospital, UZ Leuven has a responsibility and obligation to protect its patients' right to privacy. Moreover, the act of pseudonymizing records/reports involves a significant burden to our staff and carries an important risk of GDPR noncompliance/breach, which could result in significant fines for UZ Leuven.

Any deviations from the above requires the explicit approval from UZ Leuven's Board of Directors. Questions can be submitted to the Chief Medical Officer, Prof. Dr. G. Van Assche.

12. ICF template interventional study without investigational medicinal product (IMP)

For clinical trials with study drugs in adult patients, a separate ICF template is already available.
We are happy to announce the development of an Informed Consent Form (ICF) template tailored for interventional studies that do not involve medicinal products. This template is specifically designed for interventional studies that do fall under the Law of 7 May 2004 but do not fall under the category of clinical trials (which typically involve IMP's (investigational medicinal products).
This new ICF template is highly adaptable to a variety of scenarios, such as questionnaire-based studies, research involving additional procedures like blood sampling, scans, tests, comparison of techniques, and other interventions.
You can find the template (in English, French and Dutch) on our website.

13. Race and ethnicity in clinical trials with investigational medicinal products

The medical field has undergone significant changes in recent decades, including increased cultural and racial diversification in Europe and the United States due to migration. The number of clinical trials worldwide has also significantly increased, emphasizing the importance of diverse clinical trial populations, in order to optimally reflect the (diversity of) the target population. While clinical trials provide evidence for the efficacy and safety of medical treatments, certain subgroups may not be represented in the trial population, may be disproportionately affected or respond differently to medications. Therefore, it is crucial to have representative study populations that reflect the general population's diversity in terms of age, sex, race, ethnicity, age and lifestyle. Currently, there is a lack of diversity in clinical trials, leading to underrepresentation of i.a. racial minorities. Adequate reporting of race and

ethnicity can potentially contribute to better understanding of cultural, social, and biological differences, enabling the identification of population groups disproportionately affected by certain diseases, along with genetic information collected from study participants. Inclusion of diverse populations in clinical trials not only benefits research accuracy but also promotes fairness and equal care for all patients. Properly informing patients about the collection of sensitive data and addressing barriers, such as mistrust, language and lack of information/access, are important steps in ensuring diverse participation in clinical trials.

To address these concerns and promote ethical practices, we recommend that any clinical study considering the collection of race and ethnicity data should provide clear justifications for doing so, along with detailed plans on:

- HOW race and/or ethnicity will be DEFINED (including categorical definitions and categories),
- the MEASURES that will be taken to promote DIVERSITY in race and/or ethnicity in the study (including efforts to ensure access equity),
- HOW the information will be COLLECTED (with a strong recommendation for self-reporting, and the option to refuse collection on data of race and ethnicity),
- HOW this information will be handled in the ANALYSES (whether or not it will be tested as a covariate in dose-exposure-response models),
- assessing the POTENTIAL IMPACT on future patients (such as potential dosing stratification based on race or additional screening for certain racial groups if race is a risk factor for toxicity),
- MEASURES to AVOID, IDENTIFY, and ADDRESS DISCRIMINATION (including reporting statistical models and comparisons without race as a covariate, following the guidance provided by Hughes et al. 2022 CPT; 10.1002/cpt.2799).

By adopting these comprehensive recommendations, we ensure that ethical considerations regarding race and ethnicity are not limited to data collection alone but also encompass proactive steps to anticipate and address potential ethical challenges as medical treatments and recommendations reach the market.

It is crucial to communicate to patients the importance of voluntarily providing these sensitive data, and to ensure that individuals have the freedom to decide whether they wish to share such information. EC shall verify compliance with these principles in the ICF.

14. Qualtrics

Due to Qualtrics' new pricing policy, the campus license for Qualtrics will not be offered at KU Leuven anymore in the coming years. The campus license is being phased out after a transition period in the current academic year. The framework agreement for Qualtrics Research Core expired on 31 October 2023. To address short-term needs and allow time to find an alternative, a one-year contract extension with Qualtrics has been signed. Please be aware that the internal pass-through price for this license year will increase from €100 to €280 per license. Students will have access to Qualtrics only for the current academic year. Please consider this when promoting Qualtrics in classes or utilizing it for master's theses.

Starting from October 2024, Qualtrics will no longer be offered centrally at KU Leuven. It is important to note that students will no longer have access to Qualtrics. If you still want to continue using Qualtrics, you will need to purchase a single user license directly from Qualtrics, which is limited to 2500 responses. As a possible alternative for most use cases, KU Leuven has expanded the Limesurvey service.

15. Winter clock stop

Please be informed that there is a winter clock stop between 23/12/2023 and 07/01/2024. Submissions performed during this period, will have 08/01/2024 as a validation date.

We wish you a Merry Christmas and a happy 2024!