Newsletter
Ethics Committee Research UZ/KU Leuven
Number 18 – October 2022

Dear researchers and teams

We hope you all had a nice summer!
With this newsletter we hope to assist 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. EC member call

The composition of EC is legally defined. A majority of the members should be physicians. The composition should ensure expertise in the main research areas and the members need to be experts in their domain.

EC is continuously looking for physicians with expertise to share their knowledge in EC. If you are interested, please contact the Chair, prof. Minne Casteels.

2. Annual progress reports

In several EC newsletters, we have highlighted the importance of submitting an annual progress report.
If the study is not completed within a year after initial approval, an annual progress report needs to be provided to EC Research UZ/KU Leuven according to ICH-GCP.
If a study was approved more than 12 months ago or when it has been more than 12 months since an annual progress report was submitted to EC Research UZ/KU Leuven, we will send the PI and the contact persons for that study, a reminder to provide us with an update and submit the annual progress report via ec@uzleuven.be

In the absence of a progress report, the study is considered closed; a progress report is considered as an extension of the EC approval.

The template used for this annual progress report can be found at our website.

If the study can be considered as closed (end of the study), we invite you to specify the date of termination of the study. The end of the study should be defined in the study protocol. Most frequently, the end of the study is defined as the date of the last visit of the last subject. Therefore, the end of recruitment is not the end of the study. EC should be notified within a period of 90 days after the end of the study. When a EudraCT-study (clinical trial) is completed, an additional Annex III form (End of trial form) must be submitted within these 90 days.
Within one year of the study being completed, a Clinical Study Report (CSR) containing the results should also be sent to EC. If a publication is available, it can be used as CSR.

3. CTC Office

Investigators and study teams are invited to schedule a proactive consultation with CTC staff on specific questions and/or challenging or innovative aspects of an existing or planned clinical research project. The CTC Office initiative is meant to promote project quality, increase project success rate and facilitate smooth study start-up through collaborative sharing of knowledge, expertise and best practice.
You can schedule an appointment through the scheduling tool to obtain project specific answers and guidance

with regards to study start-up, legal matters, complex partnerships, study set-up & organization, data management, monitoring, safety reporting, cost estimates, etc.

If there are EC-related questions, a member of EC staff can be invited during this appointment. EC can participate *ad hoc* in the CTC office, but we would like to indicate that this does not imply that we can give advice more rapidly when the study is submitted. The advice given during the CTC office meeting cannot substitute the advice of the plenary EC Research in which the EC-members will take a final decision.

4. Training (Tuskegee syphilis study) – teaching by history

This year marks the 50th anniversary of the uncovering of the Tuskegee syphilis study. This study was a clinical study conducted between 1932 and 1972 in Tuskegee, by the United States Public Health Service. 400 Afro-American sharecroppers were studied to observe the natural progression of untreated syphilis up to their eventual death by the disease. None of the infected men were treated with penicillin despite the fact that, by 1947, the antibiotic was widely available and had become the standard treatment for syphilis. Instead of treating the subjects of the study with penicillin and concluding it or establishing a control group to study the drug, the scientists in charge of the Tuskegee experiment hid the information on penicillin from the subjects in order to continue studying how the disease spread and eventually led to death.

This experiment aroused controversy and led to changes in the legal protection of the patients involved in clinical studies. Subjects involved in this experiment did not give their informed consent; they were not informed of their diagnosis.

This YouTube video explains the uncovering, the story and lessons from the Tuskegee syphilis.

5. ACT EU initiative of the European Commission

The European Commission (EC), the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) have published the 2022-2026 work plan of the initiative Accelerating Clinical Trials in the EU (ACT EU).

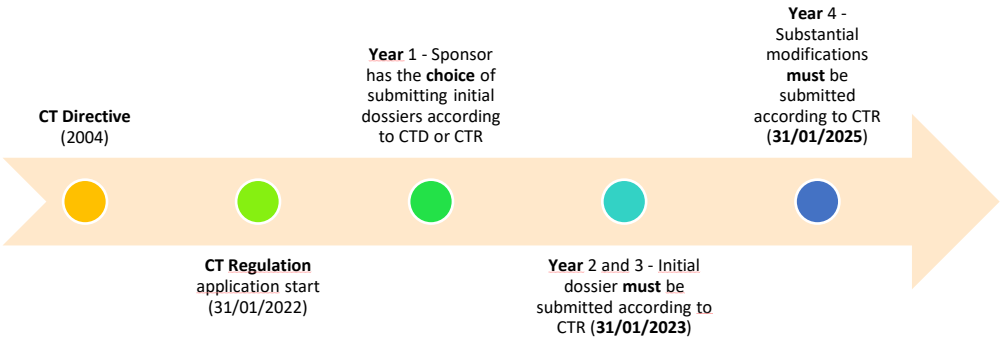
The aim of ACT EU is to further develop the EU as a focal point for clinical research, promote the development of high-quality, safe and effective medicines, and to better integrate clinical research in the European health system. The work plan highlights key focus areas such as innovation in clinical trials, robust methodologies and collaboration across stakeholders. You can find more information on EMA's website.

6. Clinical Trial Regulation (CTIS)

On 31 January 2022 the Clinical Trials Information System (CTIS) went live, as mandated by the EU Clinical Trials Regulation (CTR). From that date, clinical trial sponsors can register their trial in CTIS. CTIS will become the single entry point for submitting clinical trials information in the EU with the highest standards of safety for participants and increased transparency of clinical trial information.

Until 31 January 2023, sponsors will have the choice of submitting initial clinical trials according to the old (*Clinical Trial Directive*) or the new (*Clinical Trial Regulation*) legislation. From 31 January 2023, new initial studies must be submitted according to the CTR.

For the next two years, from 1 February 2023 to 31 January 2025, clinical trials approved under the old legislation will also be able to continue under the rules of that legislation until the end of the clinical trial or until the transition of the clinical trial to the new legislation. As of 31 January 2025, modifications must also be submitted via CTIS, i.e. studies must then be conducted entirely in accordance with the CTR.



7. Decentralised Clinical Trials

Clinical trials of medicines have made rapid advances when it comes to digitalisation and decentralisation. By this is meant the use of digital tools (electronic consent, electronic consultations, electronic data collection systems, direct to patient shipment, wearables and other medical devices, etc.), which reduce the need for patients to attend physical appointments at a hospital unit compared to a traditional clinical trial (decentralised clinical trials, DCT).

An EU DCT project group has been launched and a recommendation paper on the use of decentralised elements in clinical trials is under discussion. The recommendation paper is planned to be published in the fourth quarter of 2022. This recommendation paper was created as part of one of the priority actions of the ACT EU initiative of the EC, see above.

This recommendation paper aims to provide recommendations for sponsors and investigators regarding the use of decentralized elements in clinical trials with investigational medicinal products (IMP). This will be the first step in a harmonized and transparent EU approach to decentralized elements in clinical trials, while ensuring the necessary level of patient's safety, protection of rights and dignity, and the reliability of data.

We remind investigators that they should cautiously judge (and accept or not accept) the acceptability and feasibility of any decentral elements in a protocol.

8. Change of procedure for research with artificialised and extracted material when they are not used for genetic research

As mentioned in our previous newsletter, there is an adapted procedure in place for research with artificialised and extracted material, when they are not used for genetic research.

In this adapted procedure, it is sufficient to submit your research project and its objectives to EC Research (after registration at CTC). If EC has not expressed any objections within 28 calendar days after receipt of the research project and the filled-in statement available on our website , the scientific research can be started. A submission to the Biobank UZ/KU Leuven is not necessary, nor a registration of this MLM.

If it concerns artificialized/ extracted HBM produced in Belgium after 18 March 2022 you need to confirm that

□ the traceability towards the donor is lifted

□ the donors have been informed of the possible production of the artificialized/ extracted HBM and the potential consequences thereof (art. 10, §5, 2nd indent of the Law of 19 December 2008 (HBM Law)) including the lifting of traceability of the material.

For artificialized/ extracted HBM (especially which is made in-house), the researcher should always consider whether it is appropriate to select this flow, as this would make future genetic research inadmissible.

For research involving new production of artificialized/extracted HBM, the standard flow in accordance with the HBM Law (including submission to biobank) still applies.

9. Flagging patients in (retrospective) studies

As explained in our newsletter of July 2020, 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. This way of informing

patients is of utmost importance in retrospective studies as retrospective studies do not fall within the scope of the Belgian law on experiments and hence no ICF is required pursuant to said law. However, in accordance with UZ Leuven policy, registration at the CTC (including completing the GDPR questionnaire) and submission to EC is required in order to allow for a privacy check by the EC. Flagging study participants with the corresponding S-number in KWS is therefore also required in case of retrospective studies.

IT has reported in several studies that very few patients whose data are used in a retrospective study, were flagged 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.

10. Serious breach in clinical trials

The Clinical Trial Center (CTC) has published a new SOP on Project risk & issue management (mandatory for interventional studies with IMP and/or IMD), non-binding (but recommended) for other types of studies.

In the SOP the topic "Serious breaches in the context of CTR" is described.

In article 52 of the CTR is mentioned:

> "…'Serious Breach' means a breach likely to affect to a significant degree the safety or rights of a subject, or the reliability and robustness of the data generated in the clinical trial."
>
> "…The sponsor shall notify the concerned Member States about a serious breach of this Regulation or of the version of the protocol applicable at the time of the breach, through the EU portal without undue delay and not later than seven days of becoming aware of that breach."

The serious breach should be reported without undue delay and at latest within 7 calendar days of the Sponsor becoming aware of a serious breach.

ec@uzleuven.be

www.uzleuven.be/ethische-commissie/onderzoek

Telephone: 016 34 86 00 (between 10am and 11am)