Newsletter
Ethics Committee Research UZ/KU Leuven
Number 17 – April 2022

Dear researchers and teams

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.

We wish you all a happy Easter!

Ethics Committee Research UZ/KU Leuven

Members: Dominique Bullens, Ariel Alonso Abad, Pascal Borry, Guy Bosmans, Xavier Bossuyt, Simon Brumagne, Michèle Dekervel, Jean-Jacques Derèze, Erwin Dreesen, Lut De Groote, Theresia De Fraye, Jan de Hoon, Aernout De Raemaeker, Lia De Wilde, Céline Gillebert, Rik Gosselink, Walter Janssens, André Loeckx, Koen Luyckx, Ben Nemery, Marleen Renard, Angélique Rézer, Miet Schetz, Karin Sipido, Anne Smits, Mathijs Swaak, Anne Uyttebroeck, Annick Vanclooster, Marilien Vandeputte, Veerle Vanparys, Ben Van Calster, Bart Van der Schueren, Kristel Van Landuyt, Katelijne van Overwalle, Jan Verhaegen, Gregor Verhoef, Minne Casteels

Staff: Amber Bruijnes, Britt Keyaert, Monique Leys, Lian Rijkers, Ruth Storme, Indra Verhaeghe, Sofie Vervoort

1. Guidance on the use of electronic informed consent

In our Newsletter of November 2020, we informed you about the guidance on the use of electronic informed consent in interventional clinical trials. This guidance describes the methods and restrictions to be taken into account when using electronic methods to inform a potential participant about a clinical trial and/or to get the Informed Consent Form signed. Please always take this guideline into account when considering electronic consent in a clinical study.

We kindly remind you that all our previous newsletters can be found on our website.

2. Training General Data Protection Regulation (GDPR) and Medical Device Regulation (MDR)

On the EC website, different recordings can be found of training sessions, e.g. on GDPR and MDR given by the CTC's legal department to EC members: https://www.uzleuven.be/nl/ethische-commissie-onderzoek/opleidingsinformatie
This training can also be useful to you.

Recordings of topics as the Clinical Trial Regulation (CTR), Data Management and Artificial Intelligence can also be found on our website.

3. GCP training by e-learning

In a collaborative effort, the CTC's of all 7 Belgian academic hospitals have developed a GCP-e-learning. The training will be offered through the UZ leercentrum & KU Leuven Toledo and will substitute the face to face GCP training previously provided by Dr Ingrid Klingmann.
The training has been fully validated by TransCelerate and as such, successful completion of the knowledge assessment will result in an internationally recognized training certificate which remains valid for 3 years (or until the next GCP revision).
Please be reminded that evidence of GCP training is required for any experimentation under the Belgian Law, and is highly recommended for all clinical researchers and staff.

4. Initial submission

Please only submit clean versions for **initial** submissions (i.e. not for substantial modifications or amended documents following EC-remarks). For an initial submission versions with track changes will not be accepted.

5. Safety related events reporting to EC

Due to changes in legislation, the following rules currently apply with regard to safety reporting to the EC:

Fatal event in studies covered by the law of 7 May 2004

All deaths needs to be reported without delay to the sponsor (irrespectively of whether the death is related to disease progression, study procedure or is an unrelated event). Each death of a study subject in a clinical trial should be reported to the local and central EC, unless otherwise specified in the protocol. In our March 2018 newsletter, we specified how a fatality should be reported to EC for studies covered by the law of 7 May 2004. EC requires via mail:

- The S-number of the study
- The cause of death
- The suspicion whether the death is related to the study or not.

Please do not provide the name of the individual concerned.

Other safety events in studies covered by the law of 7 May 2004

The Investigator is responsible for ensuring that all safety events are recorded in the (e)CRF and reported to the sponsor. After informed consent has been obtained and after initiation of study-related interventions all SAEs as defined in the protocol must be reported to the sponsor within 24 hours of the trial staff becoming aware of the event. The immediate report shall be followed by detailed, written reports.

The sponsor will assess whether any relevant safety information that becomes available during the study should be reported ad hoc to the EC.

The sponsor has the obligation to, once a year throughout the clinical trial (or on request), submit a progress report to the EC's containing an overview of all SARs occurred during the reporting period and taking into account all new available safety information received during the reporting period.

On the website of CTC (https://gbiomed.kuleuven.be/english/ctc/, Toolbox, Standardised safety language) you can find protocol safety language to be inserted in the safety section of interventional protocols.

Pilot studies in preparation of the CTR (Clinical Trial Regulation)

We refer to the guidance for sponsors. On p. 6/36 is mentioned:

> Safety reporting will not be handled in the pilot. This means that the safety reporting documents (i.e. DSUR, SUSAR) must not be submitted to the National Contact Point (NCP) and that the current rules for submission to the FAMHP and to the EC issuing the single opinion have still to be followed.
>
> This means that for DSUR & SUSAR the procedure as described in CT-3 detailed guidance and circular letters 586 and 593 available on the FAMHP website (reporting according to the directive) and following the law of 7 May 2004 has to be followed. For pilot dossiers the "EC issuing the single opinion" is to be understood as the independent evaluating EC. This means that in the CTR pilot project, the College does not inform local ECs or sites about safety reporting. Submission to additional partners (investigators or local ECs) remains the responsibility of the sponsor.

Studies covered by the CTR

The safety aspects and SUSARs will be evaluated by the SaMS (Safety Assessment Member State). When Belgium is assigned as SaMS for an investigational medicinal product (IMP), FAMHP will coordinate the assessment of the safety reporting.
In article 44 of the CTR is mentioned that the responsible ethics committee is to be involved in the assessment of ASRs & SUSARs, if required per national law. In the Belgian legislation, this responsibility is **not assigned** to the ECs (recognized under the law of 7 May 2017).
Thus, for clinical trials approved under CTR, direct submission of safety reports is no longer required to EC Research and it is sufficient to submit SUSARs via EudraVigilance and DSURs via CTIS.

Studies covered by the MDR

Safety reporting in clinical investigations should be done in line with the requirements of the Regulation (EU) 2017/745 – Medical Device Regulation (MDR) Article 80.

Once Eudamed is available and fully functional, SAE reporting will have to be done through the Eudamed web form. Until then, as from May 26 2021 the new template for the Clinical Investigation Summary Safety Report Form should be used to report SAEs. Reportable events must be reported all at the same time to all national competent authorities where the clinical investigation is authorized to start or has commenced. In Belgium the completed SAE Reporting Form may be sent to the R&D division of the FAMHP by e-mail at ct.rd@fagg-afmps.be or through CESP.

For investigations approved under MDR reportable events do not need to be sent directly to the EC. For investigations approved under MDD and only approved by the EC, it is requested to continue to provide the SAE reporting directly to the EC and not to the FAMHP.

6. Answers to EC-remarks

After a remark letter has been sent by EC on a study, we ask you to take the following into account when submitting your response to these comments:

1. Please repeat each comment and formulate a response to it, or submit a cover letter with a response to all the above comments.
2. In addition to responding to the comments, the study documents (protocol, ICF) should also be updated.
3. Please provide answers in their entirety. Incomplete questions and answers will slow down the evaluation process.
4. To facilitate the review of the adapted documents, we ask that all changes made to the original version be marked with **track changes**.
5. Please always provide the modified version of a document with a (new) version number and a (new) version date (both in the file name and in the footer/header of the document itself) so that we can clearly indicate the finally approved version in our final advice.
6. New documents (not included in the initial submission file or not explicitly requested in the EC comment letter) have not been discussed by the members and therefore cannot be mentioned in the final favourable opinion. These documents can be submitted as modification as soon as the initial dossier is approved by EC.
7. A response to the comments is expected within 6 months. If comments remain unanswered for more than 6 months, the study will be administratively closed. Consequently, the research project must be resubmitted for an opinion from EC.

7. Case reports

A case report is a detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin) *(from NCI dictionary).*

Since many journals require EC/IRB advice for case reports, we recommend submitting them to EC Research directly via ec@uzleuven.be.

A template ICF can be found on our website. In addition to the ICF (without the patient's name), please also provide us with a brief explanation (covering letter) of the case description. The ICF can only be signed by the patient after EC submission and approval. Make sure that you do not provide the name of a patient to EC.

Also when you intend to write a case report in the context of a master's thesis, we recommend you to submit it directly to EC and, after approval, to enter the assigned S-number in SCONE.

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

Change of procedure for research with artificialised and extracted material (examples are already existing cell lines and in vitro models) when they are not used for genetic research -Change of the Belgian Law on HBM (of 19th December 2008). (Law of 23 February 2022 on provisions concerning human body material and embryos and gametes, published on 8th March)

The previous definition of transformation of HBM (Human Bodily Material) is replaced by 2 other definitions, i.e. *artificialised* and *extracted* material. Artificialised material is any HBM produced or cultivated outside of the human body. Extracted material is material that has been extracted from HBM and does not contain cells anymore. Both materials are now exempt from the biobanking requirements on condition that these materials are not used in genetic research purposes. Genetic research is defined as 'scientific research, without application on humans, that is performed on genetic material such as DNA, RNA, irrespective whether the genetic material was isolated from other body material or not'. 'Genetic research' as defined above by the authorities may limit the use of modern research methods and will be further explored in the BBMRI-ERIC ELSI workgroup and the biobank compendium workgroup.

For artificialised and extracted material, when they are not used for genetic research it suffices to submit the research project and its purpose to EC Research. The researcher is responsible for complying with all conditions (i.a. not being used for genetic research…) and confirms this in a (short) template we provide on our website (cf. highlighted below). If EC Research does not express any concern within 28 (calendar) days after receipt of the research project and the completed declaration, the research project can start and registration in a biobank is not needed anymore. It also implies that artificialised and extracted material, when they are not used for genetic research, can be imported and exported without the need to involve a biobank, can be used without consent of the donor, are not subject to traceability requirements (towards the donor) and are exempt from obligations to report incidental findings.

Other contractual and legal obligations concerning traceability and the correct use of HBM remain unchanged. For research involving new creation of artificialised/extracted material, the previous flow (including submission to biobank) still applies.

Template:
(Only if you tick all checkboxes, the adapted procedure will apply)

I confirm that HBM (Human Bodily Material) will be used in the scientific research project S….. and that

- □ only already existing artificialised/ extracted HBM will be used
- □ it will not be applied in humans (cf. def. in Art. 2 of the Law of 19th December 2008)
- □ no genetic research on the artificialised/ extracted HBM will be performed

Info

ec@uzleuven.be

www.uzleuven.be/ethische-commissie/onderzoek

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