

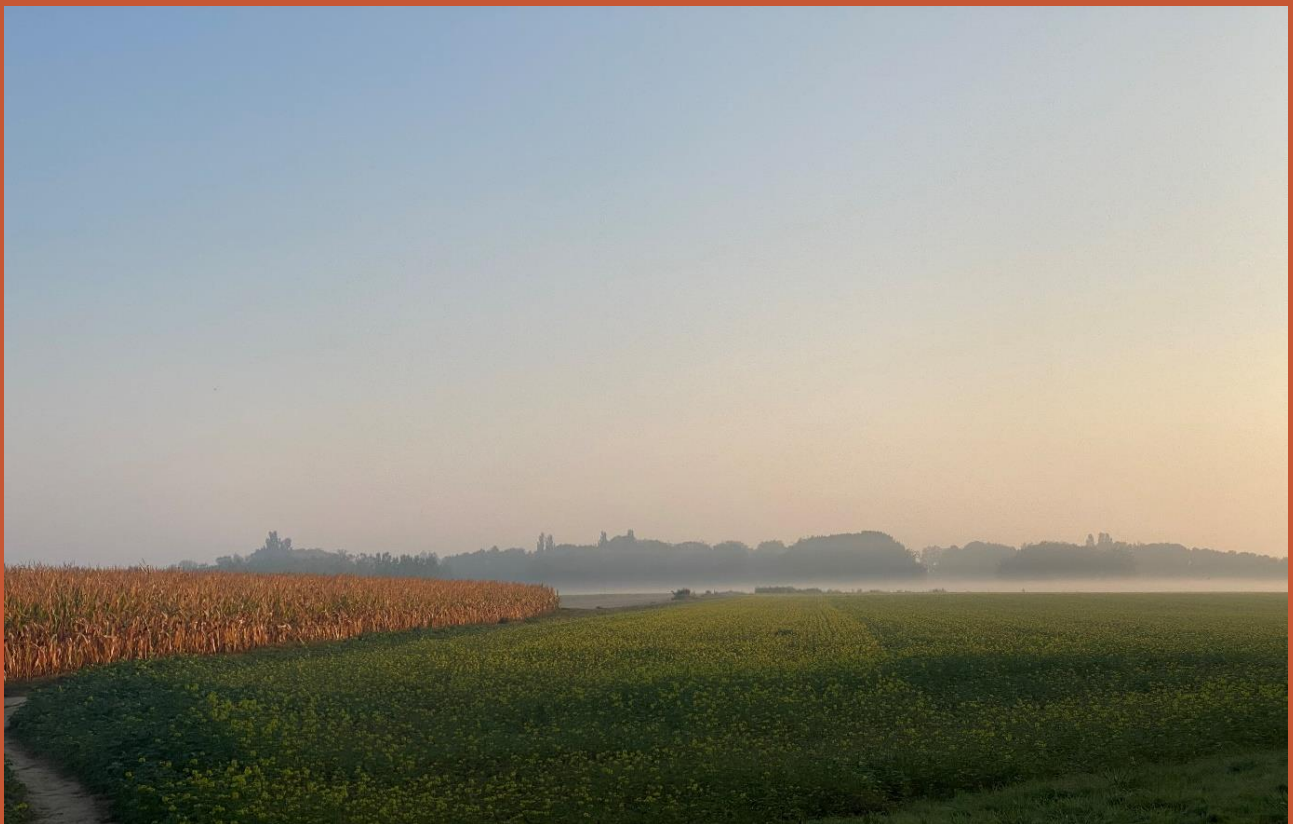
Dear researchers and teams

With this newsletter we would like to support and help you in doing high-quality clinical and translational research with respect for the well-being and privacy of each patient and volunteer.

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, Lut De Groote, Theresia De Fraye, Jan de Hoon, Aernout De Raemaeker, Lia De Wilde, Stefanie Goris, André Loeckx, Koen Luyckx, Ben Nemery, Eva Puttevils, Marleen Renard, Angélique Rézer, Miet Schetz, Karin Sipido, Anne Smits, Mathijs Swaak, Josse Thomas, Anne Uyttebroeck, Liliane Vandergeeten, Marilien Vandeputte, Veerle Vanparys, Ben Van Calster, Kristel Van Landuyt, Katelijne van Overwalle, Jan Verhaegen, Gregor Verhoef, Minne Casteels

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1. Guidance on the use of electronic informed consent

A [guidance on the use of electronic informed consent in interventional clinical trials](#) in Belgium is available. This guidance document is developed by a working group consisting of representatives of BAREC (Belgian Association of Research Ethics Committees), pharma.be (the Belgian association of the innovative (bio)pharmaceutical industry) and patient organizations, and was coordinated by the CT-College at the FPS Health, Food chain safety and Environment.

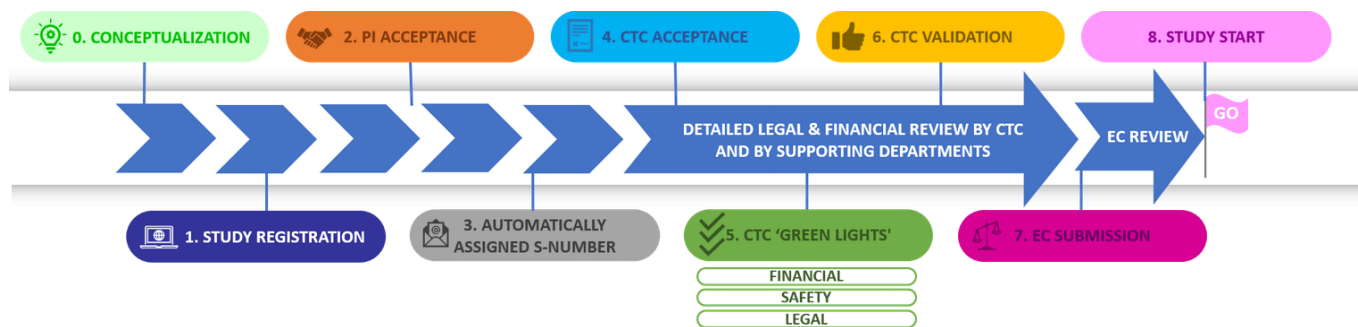
In general, the electronic Informed Consent Form (e-ICF) must at least provide the same information as the paper version. The use of interactive videos and multimedia components may make the information of the ICF more digestible. Some restrictions, however, should be taken into account and are mentioned below. These restrictions are also valid for the re-consent process.

Please note that this is a guidance and a trial site always has the right to refuse an electronic information process.

<p>Informing participant</p> <ul style="list-style-type: none"> - Preferably in person, at the trial site via personal face-to-face interview - May occur via video conference, not via a phone call. <p>In that case: participant has to declare in writing that he/she has understood the information given via the video conference and has had the opportunity to ask questions. A statement must be <u>added</u> to the consent part of the ICF</p>	<p>Signing</p> <p>Use advanced or qualified electronic signatures (eIDAS regulation). Signatures via e-ID or itsme® are qualified electronic signatures.</p> <p>OR</p> <p>Use a finger or a stylus or biometric e-signature, under the condition that it allows to prove that the person making the electronic signature was indeed the participant</p> <p>The participant has the freedom to choose to give his/her consent by signing electronically (via e-ICF) or by signing a paper version of the (e-)ICF.</p>
<p>Submission dossier</p> <p>All information needs to be provided in order to allow the evaluating EC to assess the e-ICF (format and content, including logos, images, photos, colours, videos, link to the web-based presentations, etc.) and/or method to obtain e-signature</p>	<p>GDPR compliant</p> <p>The sponsor will not be able to trace the identity of the participant.</p>

2. Flow from conceptualization until study start

In our previous newsletter, we informed you that as of July 1st, the clinical trial center (CTC) will no longer accept study applications by e-mail. From that date, study applications must be submitted electronically via the website: <https://www.uzleuven.be/nl/clinical-trial-center> (“registreer nieuwe klinische studie”). We would also like to show you visually the administrative flow to start a study, from conceptualization until study start, with involvement of CTC and EC.



The flow is also explained in more detail on the website of the CTC: <https://www.uzleuven.be/nl/clinical-trial-center/flow-opstart-klinische-studie>

We would like to highlight, as shown above, that a study can only be submitted to EC Research **after CTC validation**. Please await this confirmation (which you will receive by e-mail) before submitting the study to EC

3. Case reports

Since many journals require EC/IRB advice for case reports, we recommend submitting them to EC Research.

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.

4. Flow study evaluation when EC Research acts as local EC

When a multicenter clinical study is submitted under the Experiments Law of 7 May 2004 and not within CTR (Clinical Trial Regulation), the Ethics Committee can act either as a "central" EC or as a "local" EC. A multicenter experiment is an experiment conducted in accordance with a single protocol, but in different locations and by several researchers.

We hereby present the evaluation flow of a study when EC Research acts as a **local** EC for experiments not evaluated within CTR:



In the case of a multicenter experiment, the request (with identical documents) for an EC opinion is directed at the same time to the Ethics Committee responsible for giving the single opinion (= central EC) and to the ethics committees associated with the sites where the experiment would take place.

1. Study submitted, validated and discussed at EC meeting

EC Research checks the submitted documents. A dossier will be validated once all documents are correctly included as per guideline/requirements of submitting a dossier to EC.

2. An advice to the central EC is sent

After discussing the study at the EC meeting, EC Research gives its advice to the central EC.

3. Central EC approves the study

The central EC approves the study and sends its approval letter to EC Research.

4. EC Research asks approved documents to study team/sponsor

We ask for an answer to our comments passed on by EC Research to the central EC as well as the latest documents approved by the central EC with track changes.

5. Ratification of the approval from the Central EC

Upon receipt of the above documents, EC Research can ratify the EC approval of the central EC and the study at UZ Leuven can be started.

Currently each EC has its own internal procedure to evaluate and approve multicenter studies (e.g. some local ECs will ratify the Central EC's positive advice prior to study start at their site while other local ECs will not provide a ratification) as there is no (legal) guidance to adhere to. BAREC is working on a harmonized process flow which should be applied by all EC's in Belgium for multicenter studies, except for "pilot-studies" (studies evaluated within CTR), retrospective studies and studies with human body material. Once this process flow is finalised, it will be communicated in the subsequent EC Research newsletter.

5. Recruitment and inclusion employees UZ Leuven in a clinical study

EC often notices in academic studies that employees of the study team will be included when a healthy control group is needed.

EC Research recommends not to recruit participants in a study through a hierarchical superior. Participation should be completely voluntary, there should be no pressure from superiors. The same concern applies to recruitment of a PI's own students.

EC would rather propose to publicly advertise that healthy controls are sought for this study, without focusing on employees. They do not have to be excluded, but there should be a wider recruitment. Please always submit the recruitment material for EC-approval.

More information about recruitment and recruitment material can be found on [our website](#).

6. Statistical Analysis Plan

EC would like to stress the importance of a scientifically valid protocol, including clear research questions and objectives, description of primary and secondary endpoints/outcome. An **endpoint/outcome** variable is a characteristic of the patient that will be measured during the study. Typically, the **objectives** of a study are statements regarding the main outcome. For instance, the main endpoint/outcome of study may be patient survival at 1 year, defined as 1 if the patient was alive 1 year after finishing the treatment and zero otherwise. The main objective of the study can then be formulated as, for instance: "To demonstrate that the proportion of patients that have survived at 1 year is larger in the experimental group than in the control group."

A description in the protocol about the number of participants (sample size) that will be included and why this number was chosen, is very important. The sample size calculation is typically based on a statistical procedure (test, confidence interval, model, etc.). Basically, one calculates the sample size necessary to assess the main objective of the study through the use of a statistical test or model. There should be a **clear correspondence between the sample size of the study, the main objective and the analysis** of the data. The model/tests used to calculate the sample size will define the main analysis that will be carried out with the data of the study. When describing the sample size calculation one should clearly state the outcome used, the statistical test or model employed, the level of significance, the power, as well as the effect size

and the estimates for all necessary parameters. One should also state how the estimates of the parameters used in the sample size calculation were obtained.

The statistical analysis plan should obviously contain the test/model used for the sample size calculation. It should also contain a description of any other analysis that will be carried out. It is important to clearly state which analysis will be confirmatory (analysis carried out to assess the objectives of the study main and/or secondary) and which ones will be merely descriptive. It is strongly advisable to do so for each study objective separately, rather than merely including a generic list of statistical tools. The analysis plan should include information on how missing data will be handled.

Exploratory studies may not require a rigorous statistical formalism but their findings will have to be interpreted with extreme caution. Essentially, these studies generate hypotheses that will need to be tested in further confirmatory studies. The exploratory nature of a study should be clearly stated in the protocol and any subsequent publication. Please also clearly state the method of participant sampling.

EC would like to direct you to the following website of the “Leuven Biostatistics and statistical Bioinformatics Centre (L-BioStat)”: <https://gbiomed.kuleuven.be/english/research/50000687/50000696>.

To all researchers of the Group Biomedical Sciences, L-BioStat offers consultation to provide statistical advice on various methodological and statistical aspects of the research project. Free advice is provided through scheduled one hour consulting appointments. Further, it also offers in-depth collaborative consulting, including analysis of data, writing of a statistical report and incorporation of the results in (an) article(s).

You can also discuss/collaborate with colleagues from several departments in KU Leuven with extensive biostatistical expertise, both in Biomedical Sciences as in the other groups.

7. Submission of a project to the UZ/KU Leuven Biobank

All human body material that is collected and/or used for scientific research after November 1st 2018, or that is intended to be used, must meet the criteria imposed by the Law of December 19th 2008 and the related Royal Decree of January 1st 2018. Consequently, all studies or projects in which human body material is collected, stored or used at UZ/KU Leuven (including VIB-KU Leuven) must be approved by the UZ/KU Leuven Biobank. For this purpose, your file must be submitted to wbb@uzleuven.be. This is also valid for historical collections of human body material that were collected before November 1st 2018, and of which the material is, or will be intended for use in scientific research.

For new start up studies/projects, this submission to the biobank should be done after obtaining an S-number by the Clinical Trial Center and before submission to the EC research. Without approval of the biobank, your dossier will not be valid for EC research.

For historical collections, the biobank approval can be given retrospectively, considering that adjustments are subject to additional evaluation by EC research, in order to bring the collection in line with the current legal framework concerning human body material and GDPR.

If you have any questions about this, you can find more information on <https://www.uzleuven.be/nl/biobank-0> or contact the biobank (wbb@uzleuven.be or 016/34 61 93).

8. General Data Protection Regulation: implications on the ICF

When an amendment to a study is submitted, EC invites you to also update the Informed Consent Forms (ICF's) to GDPR.

The GDPR is the European General Data Protection Regulation that came into force in all European organisations on 25th of May 2018. This Regulation has additional implications for the collection and use of personal data in clinical research.

Additional information on GDPR should be provided to participants who have been included in an experiment before or after 25 May 2018 and where new personal data are collected after 25 May 2018. The ICF should therefore be adapted accordingly. EC refers to the ICF templates, available on our website, in which the paragraphs relating to GDPR are listed and can be reproduced.

The following elements are important to be mentioned in the ICF:

- Which data will be collected;
- Sponsor being identified as data controller (“verwerkingsverantwoordelijke”);
- Contact details of the Data Protection Officer (DPO) of the study site;
- The right to submit a complaint to the Data Protection Authority;
- Retention period of the data (25 years);
- A statement that the GDPR and Belgian law related to GDPR will be respected.

As stated in a previous newsletter, in case of amendments to the information provided to the participants (ICF), it is strongly advised to use an **ICF addendum** for **participants already included in the study**. The ICF addendum lists only the changes or new information which is clearer to the participant than an amended ICF where changes are highlighted.

When inclusion is still ongoing, the use of the amended ICF is required for *new participants*.

9. Studies using human body material from deceased persons: EC Research

All studies using human body material must be notified and approved by EC Research, including studies on deceased persons. Furthermore, from a legal point of view, all studies using human body material with a relevant purpose for scientific research (cf. Art 8, §1, 2° of the Law on body material) must be submitted to a recognized EC, i.e. EC Research.

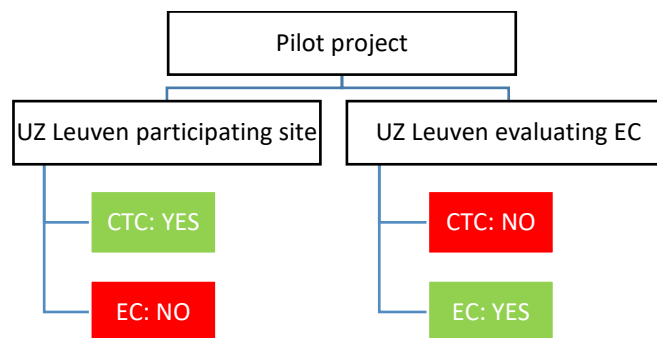
EC Research can ask EC Care for advice on certain issues, but this exchange of opinions will be done internally. As a researcher, you submit your file in one place (i.e. EC Research).

10. Clinical Trial Regulation and pilot projects

In 2021 or later, the European regulation will apply to all interventional clinical trials with medicines (CTR 536/2014). The objective of the CTR is to simplify and harmonize the submission and evaluation process of clinical trials applications across Europe. When the CTR applies, a study cannot be evaluated by the EC of a participating site. The study will be evaluated by an **independent EC**, selected by the CT College.

As a preparatory step before the implementation of the CTR, several EC's are already involved in **pilot projects**. Via the pilot projects, we can gain experience with the new regulation, with UZ Leuven as participating trial center as well as evaluating EC.

We would like to draw your attention to this scheme:



When UZ Leuven is a participating site in a pilot project, the study must be submitted to the Clinical Trial Center (CTC) but it will not be evaluated by EC Research. EC Research only receives minimal information about the study and about the evaluation by another EC. When the study team has questions about these studies, we encourage to discuss these with the sponsor of the study.

11. Contact

EC Research can be reached by telephone between 10 am and 11 am or preferably by email via ec@uzleuven.be. This email address should also be used for new applications.

The email address ec-submission@uzleuven.be will **not** be used anymore.

Please be informed there will be a **winter clock stop** between 18/12/2020 and 04/01/2021. Submissions performed during this period, will have 04/01/2021 as a validation date.

Information

ec@uzleuven.be

www.uzleuven.be/ethische-commissie/onderzoek

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