Newsletter
Ethics Committee Research UZ/KU Leuven
Number 13 – April 2021

Dear researchers and teams

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

We wish you all a happy Easter!

Ethics Committee Research UZ/KU Leuven

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1. ICF templates for studies with UZ Leuven sponsor

On our website, you can find different informed consent form (ICF) templates (in Dutch, French and English) for each type of study:

- EudraCT study
- Interventional non-EudraCT study
- Non-interventional non-EudraCT study

For each type of study, EC, together with the Clinical Trial Center (CTC), has now prepared a specific ICF when UZ Leuven is the sponsor (and thus data controller) of the study.
These versions contain modifications in the confidentiality section, insurance section,... specifically for studies with UZ Leuven as sponsor. We strongly recommend to use this template.

In addition to the templates mentioned above, EC also has an ICF template available for a case report. This version will be updated in the coming weeks.

2. Annual progress report

The submission of an annual progress report to EC according to ICH GCP is mandatory after ethical approval.
A template, in Dutch and English, is available on our website.

3. Protocol written in the present tense

As you all know, EC approval must be obtained before the start and completion of the study. We understand that a protocol is sometimes written in the past tense in order to efficiently proceed to a publication, but this is not recommended and is confusing for the members of EC. We invite you to write and submit protocols to EC in the present tense.

4. Qualification Principal Investigator (PI)

An informative CV is very important to evaluate the suitability of the investigator.

In January 2022, the European regulation will apply to all interventional clinical trials with medicines (CTR 536/2014). When the CTR applies, a study cannot be evaluated by the EC of a participating site. When UZ Leuven is a participating site in a study , the study will be evaluated by an independent EC (which may not know your expertise) and not by EC Research. A comprehensive and well prepared CV gets even more important then.

A few highlights for a good and clear CV:

- Diplomas have to be listed and the most important trial experience should be documented.
- GCP training should be documented (in the CV or by a GCP certificate), mentioning the name of the certifying organisation and the date; it should not be older than three years.

A CV template developed by the EU Commission is available on our website.

5. Medical Device Regulation (MDR)

As of May 26, 2021, the European Regulation (EU) 2017/745 on Medical Devices (MDR) comes into force. The MDR introduces a major update of the regulatory framework in the European Union and brings about several changes to the scope of investigations that must be submitted for approval, the submission processes for clinical investigations and their substantial modifications, submission dossier contents and safety reporting.

All clinical investigations need to follow a regulatory pathway with the involvement of the Ethics Committee (EC) and/or Belgian competent authority (FAHMP). Depending on the status of the investigational medical device, the submission procedure can be different. The different process flows and regulatory pathways are depicted in this figure:

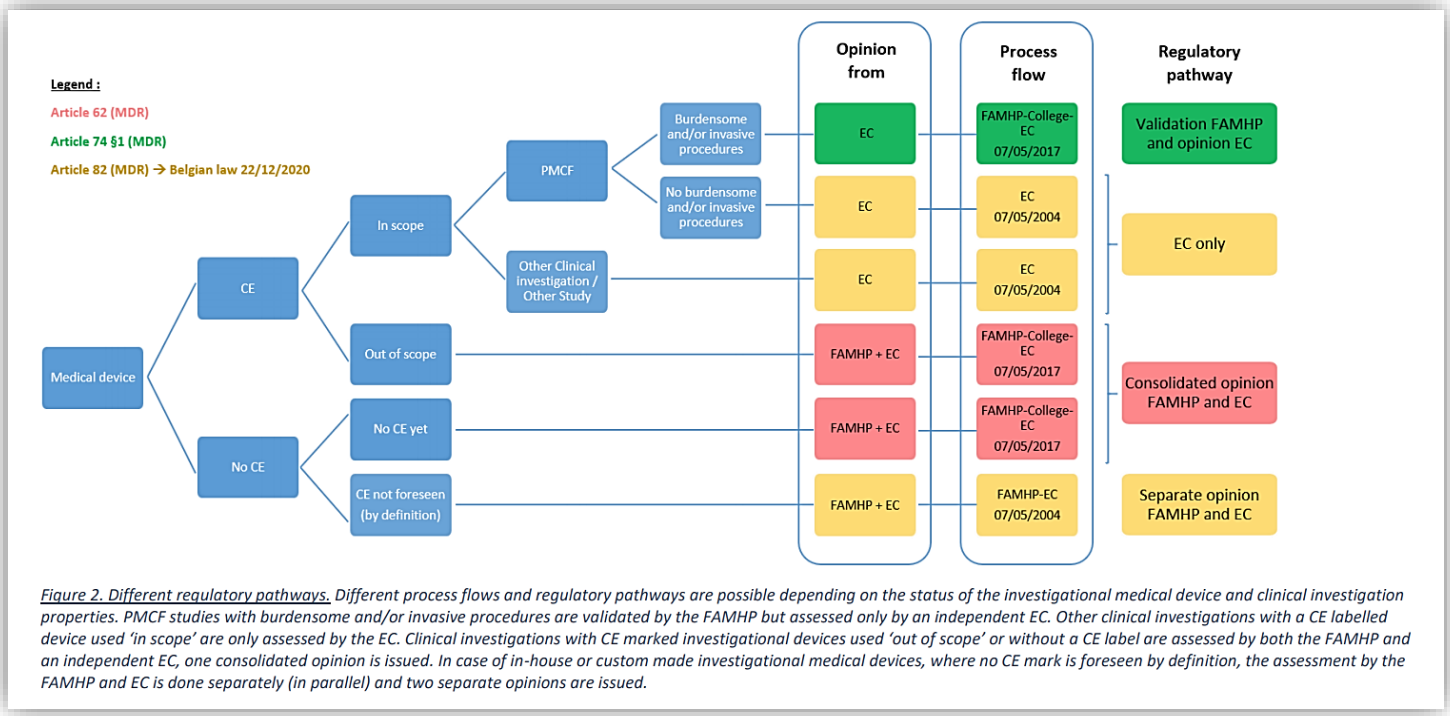

Figure 2. Different regulatory pathways. Different process flows and regulatory pathways are possible depending on the status of the investigational medical device and clinical investigation properties. PMCF studies with burdensome and/or invasive procedures are validated by the FAMHP but assessed only by an independent EC. Other clinical investigations with a CE labelled device used 'in scope' are only assessed by the EC. Clinical investigations with CE marked investigational devices used 'out of scope' or without a CE label are assessed by both the FAMHP and an independent EC, one consolidated opinion is issued. In case of in-house or custom made investigational medical devices, where no CE mark is foreseen by definition, the assessment by the FAMHP and EC is done separately (in parallel) and two separate opinions are issued.

We refer to the **FAHMP guideline** "*Submission Processes of Clinical Investigations according to MDR in Belgium*" (available on the website of the FAHMP) which aims to provide guidance for the different submission processes for clinical investigations under the new regulation from a national point of view.

We thank our colleagues Michèle and Dorien from the CTC for their instructive presentation in order to guide you (and us) through this (very complex) process.

See **intranet UZ Leuven**, https://wiki.uz.kuleuven.ac.be/pages/viewpage.action?pageId=450853793.

6. Retrospective studies

For the definition of a retrospective study, we refer to the Law of 7 May 2004: a retrospective study is a study based on data from the past already available in existing patient files, medical files or administrative files and to the extent no new data will in any way be collected for the purpose of such study (cf. article 3, §2 of the Law of 7 May 2004).

We would like to highlight:

- In the case of retrospective studies, please always indicate the end date of the data collected; this date must of course be in the past.
- The head/staff of the clinical department or the responsible care program must be informed and concur with this study; this is the PI's responsibility.
- When using data in retrospective research, collegiality and respect for the work and input of colleagues contribute to good collaboration. We therefore invite you to involve in such retrospective research the colleagues who have given intellectual input in your research (as co-researcher, co-author). Contacting the treating physicians will also help to avoid the same patients being published more than once in case studies (case reports and case series).
- Concerning statistics in retrospective studies:
  - Please always mention the planned sample size in the protocol
  - A retrospective study with a small sample size could often be seen as an exploratory study. 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.
- On the intranet page of the CTC (https://wiki.uz.kuleuven.ac.be/display/ctc/Documenten) you will find a link to a new protocol template for a retrospective study when UZ Leuven is the sponsor.
- If data will be shared with third parties, a data transfer agreement (DTA) must be in place containing GDPR language.

7. Rewarding study participants

- Be sufficiently specific about the conditions for obtaining this reward (e.g. Only when completing the whole study? What if the study is stopped prematurely?).
- A raffle among study participants warrants special conditions according to Belgian law and is not allowed.

8. Data management

The PI should take the appropriate measures to ascertain that the data collection is auditable, and this is his/her final responsibility.
Reference is made to the ICH-GCP E6(R2) guideline:
4.9. Records and Reports
ADDENDUM 4.9.0. The investigator should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry and should be explained if necessary (e.g. via an **audit trail**).
4.9.3. Any change or correction to a **CRF** should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an **audit trail** should be maintained); this applies to both written and electronic changes or corrections

9. And sorry for the many do's and don'ts

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