"Please do take into account that this is a translation of the original French version validated in the Quality Management System (QMS) of Cliniques universitaires Saint-Luc through the software Ennov GED. Therefore in case of doubt, differences, inconsistency or discrepancy in this English version, the French version shall prevail"

1 PROCEDURE'S OBJECT

This procedure describes the requirements for an investigator and for a sponsor of a **PROSPECTIVE INTERVENTIONAL EXPERIMENT** to submit an annual report to the Ethics Committee of the CUSL.

2 PROCEDURE'S SCOPE

P_SCOPE

3 RESPONSIBILITIES AND AUTHORITIES

Responsibilities of the commercial or non-commercial sponsor of clinical trial with a medicinal product:

- for each trial ***with a medicinal product***: submits **in due time** a Development Safety Update Report (DSUR) (106-AAHRPP-FORM-018) to the national competent authority and to the principal Ethics Committee. This requirement is specified in the Clinical Trial Agreement.
- continuously weighs anticipated benefits and risks of the clinical trial.
- informs the investigator concerning any new element which could influence the participants' safety during or after the end of the trial.

Responsibilities of the investigatorof any prospective interventional experiment :

- before the annual assessment date, provides the Ethics Committee (whether local or principal) of the CUSL (CEHF) with the annual report form of the experiment. This form is being filled in, signed and submitted by the investigator to the CEHF.
- provides the CEHF with the requested explanation.
- stops all research activities if requested by the CEHF.

- informs the sponsor of the CEHF decision.
- reports to participants any new element which could influence their safety during or after the end of the trial.

Ethics Committee (CEHF) responsibilities :

- receives and reviews the DSUR (if CEHF is principal EC) and the annual report (whether CEHF is local or principal)
- has the authority to stop an experiment performed at the CUSL if the benefit / risk balance is severely decreased.
- has the authority to stop temporarily the experiment performed at the CUSL if the annual report is not received within the timeframes.
- provides a written authorization to the investigator for continuing investigations.

4 PROCEDURE'S REVISION

5 PROCEDURE'S DESCRIPTION

PREAMBLE :

Duration of the Ethics Committee approval :

The approval of the principal Ethics Committee is valid for entire duration of the study. The date of approval is the date the conditions were determined to be met.

- Nevertheless, **for prospective interventional clinical experiments** the perpetuation of the approval for the CUSL is depending on the annual report provided by the principal investigator to the CEHF.

- CEHF can ask the investigator and/or the sponsor to send a progress report more often than annually. The clinical research projects that are subject to this kind of evaluation are protocols that present a higher risk for participants (typically, some protocols of Phase 1 studies, protocols with innovative therapies or particular medical devices). This request of more frequent evaluation is made on a case-by-case decision, after discussion about the protocol. This will be clearly notified in the initial CEHF opinion letter.

- The approval provided by the CEHF is valid for the duration of the experiment without any condition in retrospective studies or prospective non interventional studies (involving not more than minimal risk to participants).

Annual report submission date :

The annual assessment date is defined as one year (365 calendar days) after the protocol was approved by the ***Ethics Committee or the Leading Ethics Committee in multicenter studies***.

As reminder for this annual report, an email will be automatically generated and sent to the principal investigator and to the principal CRCM eleven and twelve months after the principal Ethics Committee approval date.

The CEHF review of this annual report **MUST** be performed within 365 + maximum 60 days (= 14 months) from the initial or past approval date. The prolongation of the approval will then begin the next day. In order to allow the evaluation of the received information within the timeframe, the annual report must be provided to the CEHF at the latest 15 days before the end of this 365 + 60 days (=14 months) period.

Example:

- The initial approval is provided by the principal Ethics Committee (whether CEHF or an external EC) on the 20th January 2014.

- The annual assessment date will be the 19th January 2015 (approval date + 365 days).

- An email will be automatically generated on December 19, 2014 and sent to the principal investigator and CRCM.

- Areminder will also be sent the 19th January 2015.

- The latest date for the annual report submission will be 5th March 2015 (20th January +45 days)

- The latest review date for the EC is 20th March 2015 (20th January +60 days).

This 365 days + maximum 60 calendar days fits to the accepted timelines for the DSUR submission to the regulatory authorities (ref: ICH guideline E2F on development safety update report: 2.2 Periodicity and DSUR data lock point).

PROCEDURE :

5.1 DOCUMENTS TO BE SUBMITTED TO THE ETHICS COMMITTEE OF THE CUSL BY THE INVESTIGATOR

5.1.1 CLINICAL TRIALS WITH MEDICINAL PRODUCT (COMMERCIAL OR NON COMMERCIAL)

5.1.1.1 DSUR : FOR ONE CLINICAL TRIAL : the sponsor sends a DEVELOPMENT SAFETY UPDATE REPORT (106-AAHRPP-FORM-018) containing the SAE and SUSARS' list and evaluating the safety of the participants to

- the competent authority
- the CEHF or the leading ethics committee in multicenter studies
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of the Member States in whose territory the clinical trial is being conducted and if ,the treatment of subjects is still ongoing in the Member State concerned until the last patient last visit (LPLV) or until the end of trial criteria as defined in the protocol are being reached.

- the reporting time frame for annual reports starts from the date of the first authorization of the clinical trial by a competent authority in any member state. The report should be submitted within 60 days of this cut-off date. In the case of short-term trials (less than 6 months), the safety report may be submitted within 90 days after the end of the trial (as part of the end of study report).
- the DSUR must be issued even if no patient is included in the trial.
- the sponsor can delegate the DSUR preparation to a third party.
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5.1.1.2 : ANNUAL REPORT FORM : The investigator will complete and sign the annual report form for the CUSL **in any case** even if another document is provided by the sponsor.

5.1.2 OTHER PROSPECTIVE INTERVENTIONAL EXPERIMENTS

5.1.2.1 : ANNUAL REPORT FORM : The investigator will complete and sign the annual report form for the CUSL.

DOCUMENTS TO BE PROVIDED TO THE CEHF FOR THE ANNUAL REVIEW

	Paper copy	Electronic copy	Provided by sponsor	Provided and signed by investigator
Annual report	X	X		X
ADDITIONNALLY FOR DRUG EXPERIMENTATION				
DSUR		X	X	

5.2 REVIEW BY THE ETHICS COMMITTEE :

5.2.1 ANNUAL REPORT RECEIVED BEFORE THE ANNUAL ASSESSMENT DATE (ON DUE TIME: 365 + 45 days):

5.2.2.1: After receipt and analysis of the report during the protocol analysis meeting, if CEHF has **no objection** for the continuing of the study, the investigator will be notified that the study has been reviewed and can be continued. The investigator will provide the sponsor with this advice.

5.2.2.2: Otherwise, the CEHF will send a mail to the investigator **asking for precisions** regarding the questions of the CEHF. The investigator will have the opportunity to answer the questions.

5.2.2.3: If CEHF thinks the **conditions are no longer met for the approval**, a temporary halt of recruitment or early termination can happen.

- The investigator is informed by letter and will immediately inform the sponsor. The investigator will still have the opportunity to respond in person or in writing.
- The EC informs the Medical Director of the CTC **AND** the Administrative Director of the CTC of the CUSL, the Belgian authorities, the principal Ethics Committee and the FDA if needed. In addition, all emitted mails are available (based on authorized access) via Claire Software and therefore also available.

5.2.2 ANNUAL REPORT NOT RECEIVED IN THE TIMEFRAME OF 365 + 45 DAYS :

- If the annual report is not received in the timeframe by the CEHF:

    - An email will be sent by the CEHF to the principal investigator : the protocol will be put on the agenda of the 14 days later meeting.

5.2.3 ANNUAL REPORT RECEIVED AFTER THE ANNUAL ASSESSMENT DATE (365 + 60 days):

- If the annual assessment date is reached before the conditions are reviewed and approved :

    - New enrollment of participants at the CUSL may not occur until a perpetuation of the approval is obtained.
    - All research activities must stop.
    - Interventions and interactions on current participants must stop, unless the EC finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants to continue participating. ***In that case, the principal investigator will justify the safety or ethical issues to the EC.*** Then, the participants still in the study will continue to receive all the guarantee for the clinical trial until they are dropped out.

- The investigator is informed by letter and will immediately inform the sponsor.

- The EC informs the Medical Director of the CTC **AND** THE Administrative Director of the CTC of the CUSL, the Belgian authorities, the principal Ethics Committee and the FDA if needed. In addition, all emitted mails are available (based on authorized access) via Claire Software and therefore also available.

6 DEFINITIONS AND ABBREVIATIONS

- DSUR = DEVELOPMENT SAFETY UPDATE REPORT
- CEHF = COMITE D'ETHIQUE HOSPITALO-FACULTAIRE SAINT-LUC UCL
- EC = ETHICS COMMITTEE
- CUSL = CLINIQUES UNIVERSITAIRES SAINT-LUC

7 REFERENCE DOCUMENTS

- 106-AAHRPP-FORM-018: Template Development Safety Update Report (DSUR)
- 133-CEHF-FORM-014: Annual status form

8 AAHRPP ACCREDITATION STANDARDS

– Element II.2.D

9 LINKS INTRANET

10 LINKS INTERNET

P_EXTERNAL_LINKS

ICH GCP 1996 –Directives 2001/20/CE et 2001/83/CE – Loi relative aux expérimentations sur la personne humaine 7/5/2004

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/09/WC500097061.pdf

http://ec.europa.eu/health/files/eudralex/vol-10/2011_c172_01/2011_c172_01_en.pdf

http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM294558.pdf

http://www.fagg-afmps.be/fr/humain/medicaments/medicaments_a_base_de_plantes/recherche_developpement/essais_cliniques/ : Circular 586

http://www.fagg-afmps.be/fr/binaries/Circulaire-593-2012-12_tcm291-208387.pdf