"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 how a permanent member of the Cliniques universitaires Saint-Luc can submit a **clinical** research project to CEHF. This procedure is applicable to experiments performed at the Cliniques universitaires Saint-Luc in one or more of the following categories:

- Commercial experiment
- Non commercial experiment
- Prospective interventional
- Prospective non interventional
- Retrospective
- Human Body Material (HBM) and Residual Human Body Material (RHBM)
- Medical Need Program
- Compassionate use
- Innovating technique
- Transnational research

This procedure is structured as follows:

1 PROCEDURE'S OBJECT 1
2 PROCEDURE'S SCOPE 3
3 RESPONSIBILITIES AND AUTHORITIES 3
4 PROCEDURE'S REVISION 3
5 PROCEDURE'S DESCRIPTION 4
5.1 TO KNOW BEFORE SUBMITTING DOCUMENTS TO THE CEHF 4
5.2 LIST OF DOCUMENTS TO SUBMIT 4
5.2.1 Prospective studies (interventional and non-interventional) 4
5.2.1.1 Non commercial 4
5.2.1.2 Commercial 7
5.2.2 Retrospective studies 9
5.2.2.1 Non commercial 9
5.2.2.2 Commercial 10
5.2.3 Experimentations involving (Residual) Human Body Material ((R)HBM), including blood, but not intended for transfusion 10
5.2.3.1 Non commercial 10
5.2.3.2 Commercial 12
5.2.4 Compassionate use and medical need programs 12
5.2.5 Innovating techniques 12
5.2.6 Transnational research 13
5.3 ELECTRONIC SUBMISSION VIA THE DATABASE CLAIRE 13
5.3.1 Non-commercial studies 13
5.3.2 Commercial studies 13
5.3.2.1 Tab « ETUDE » 13
5.3.2.2 Tab « Logistique » 14
5.3.2.3 Tab «CE» 14
5.4 PAPER COPY OF THE DOCUMENTS 14
5.5 TIMING 15
5.6 FOLLOW-UP 16
5.6.1 Amendments 16
5.6.2 End of experiments 16
5.7 SPECIFIC QUESTIONS 16
5.7.1 Adding a new site 16
5.7.2 Financial agreements 17
5.7.3 IRB and FWA numbers 17
6 DEFINITIONS AND ABBREVIATIONS 18
6.1 ABBREVIATIONS 18
6.2 DEFINITIONS 18
6.2.1 Prospective studies (interventional and non-interventional) 18
6.2.2 Retrospective studies 19
6.2.3 Experimentations involving Residual Human Body Material (RHBM) 19
6.2.4 Primary and secondary use of HBM 20
6.2.5 Compassionate use and Medical Need Program 20
6.2.6 Innovating techniques 21
6.2.7 Transnational research 21
6.2.8 Recapitulative table (definitions and applicable laws) 22
7 REFERENCE DOCUMENTS 23
8 AAHRPP ACCREDITATION STANDARDS 23
9 LINKS INTRANET 23
10 LINKS INTERNET 23

2 PROCEDURE'S SCOPE

P_SCOPE

3 RESPONSIBILITIES AND AUTHORITIES

The sponsor identifies the leading Ethics Committee emitting the single and binding opinion for the country and that will condition all the experiment initiation. The Leading Ethics Committee must be part of the list of Ethics Committee with full agreement.

With respect to the GCP (4.4) and the Belgian law concerning experiments on human (May 7, 2004), it is the responsibility of the principal investigator to submit the project for opinion to the Ethics Committee. Under penalty of inadmissibility, the project is submitted simultaneously to the leading Ethics Committee (LEC) and to the non-leading Ethics Committee (NLEC) by the sponsor, via the investigators.
The investigator can delegate the submission practical arrangements to the CRCM.

When submitting an experiment not subject to a contract with a third party to the EC, the investigator is liable to inform by email (michel.vanhassel@uclouvain.be) the Head of the Clinical Research Unit of his plan to start an experiment and its potential financial implications.

The coordinator of academic studies and of the academic central locket :

- Brings support with regard to regulations to the academic sponsor and evaluates the institutional feasibility of the study in collaboration with the Head of the Clinical Research Unit ;
- Ensures that the submission file to the EC, prepared by the investigator or his/her study coordinator, is complete ;
- Submits to the EC the academic studies for which the files are complete

4 PROCEDURE'S REVISION

The procedure has been modified after

- The development of the database Claire to allow electronic submission of a research protocol to the Ethics Committee.
- The addition of new categories of submission (transnational, RHBM, innovating techniques…)
- The integration of central lockets in the submission process to the CE.

5 PROCEDURE'S DESCRIPTION

5.1 To know BEFORE submitting documents to the CEHF

- To identify the type of study that he is going to submit and the applicable laws, the investigator must refer to the list of definitions and to the recapitulative table at the end of the present procedure.

- For COMMERCIAL experiments, the investigator informs the CEHF, through the Document 1, if it has been chosen as leading or non-leading EC and provides contact information of the NLEC when applicable (see CEHF-DSQ-003, choice and agreements of ethics committees).

  It is essential that the investigator and/or the study coordinator(s) verify, before submitting to the CEHF :

  - **all documents (versions and dates, to mention in the document titles and in the footers of the protocols and ICFs) related to the clinical research project**
  - **the presence of all requested annexes.**

- For NON COMMERCIAL experiments, the principal investigator contacts the academic central locket (Guichetacademique-saintluc@uclouvain.be) as soon as he starts writing the protocol, for :
  - Evaluation of the feasibility of the study
  - Submission to the CEHF

- **The CEHF attributes an internal reference number to all clinical research projects. Please refer to this number for all subsequent correspondence/contacts.**

5.2 List of documents to submit

5.2.1 Prospective studies (interventional and non-interventional)

5.2.1.1 Non commercial

The principal investigator contacts the academic central locket (Guichetacademique-saintluc@uclouvain.be) as soon as he starts writing the protocol, for :

- Evaluation of the feasibility of the study

- Submission to the CEHF

Documents to submit are the following :

Document	Comment	Paper copy	Electronic copy	Ref doc
Acknowledgement of receipt of valid application	provided and completed by the investigator, must contain all the documents submitted to the CEHF. **The investigator checks the content and the conformity of the documents (versions and dates).** The investigator signs the document and submits it to the CEHF.	X	X	**CEHF-FORM-007**
Document 1	Filled in, dated and signed by the investigator and co-signed for information and approval by the Head of Clinical Service. It is necessary to mention the original title of the clinical research project (English or French), mentioned on the final protocol, along with the date of the protocol, its number and EudraCT number (if applicable). **We ask you not to modify the layout of this document**	**X**	**X**	**CEHF-FORM-003**
Project summary	1-2 pages maximum, in French and in understandable terms for the non-medical members of the EC. The summary should include a short description of the protocol, methods and exams related to the experiment	**X**	**X**	
Documents information and informed consent form	Mandatory in French (for other languages, please submit documents when applicable). Please use the national templates of ICF. Please mention version and date in the Document title and the footers.	**X**	**X**	**CEHF-FORM-023/024/025/026**
Full protocol and amendments (if applicable)	**Signed** by principal investigator. Please mention version and date in the Document title and the footers.	**X**	**X**	
CV dated and signed (< 2 years)	principal investigator and sub-investigators Saint-Luc		**X**	
Financial disclosure form	Principal investigator and sub-investigators Saint-Luc (for drug and medical device experiments only)		**X**	**AAHRPP-FORM-035**
Insurance	**Insurance certificate** of the commercial sponsor, attesting that the policy is conformed to the Law 7 May 2004. The insurance certificate of the sponsor specifies that he assumes, even without fault, the responsibility of damages caused to a participant and/or his successors, damages directly or indirectly related to the experiment (any contractual stipulation to limit this liability is deemed by law (art 29 par.1) (1 paper copy). The requested certificate is provided by :		**X**	**AAHRPP-FORM-003**

	1. The **academic sponsor** in case of sponsor external to Cliniques Saint Luc. **2. Insurance service** (please see contact list) of Saint-Luc when the sponsor of the experiment is member of Cliniques Saint-Luc. The certificate should be related to the copy of the e-mail confirming the protection (with reference to the protocol of the experiment) to the investigator, to which will be annexed the general insurance certificate. **3. University** when the sponsor of the experiment is UCL. 4. In case of absence of certificate of insurance company of the sponsor, the standard insurance certificate should be completed and provided by the company. For experiments sponsorised by Cliniques St Luc, please provide the insurance request form to inform the CEHF of the limit of validity of the insurance. For other non commercial experiments, the certificate must mention the limit of validity of the insurance and the study title.			
Financial terms	**Notification** of financial terms (or their absence) **or** financial agreement to be transmitted for evaluation to person in charge of the Unité Recherche Clinique (Medical Direction of Cliniques universitaires Saint-Luc), or to a member of his staff (please see contact list). - If there is a financial agreement, the non-signed version of the agreement is accepted at time of initial submission. - If the study doesn't have any financial issues, the Medical Direction should be informed as well through the notification provided to the person in charge of the Unité de Recherche Clinique.		**X**	
For drug/medical device experiments :				
CTA/FAMHP submission form	**Clinical Trial Application Form** (https://eudract.ema.europa.eu/eudract-web/index.faces) signed by principal investigator and provided by the sponsor Medical device experiments must be notified to FAMHP (the submission form will be provided to CEHF) : - Clinical studies with medical device without CE label		**X**	

	- Clinical studies with medical device with CE label but used in a different indication. **Application form to notify a clinical investigation with a medical device,** signed by the principal investigator and provided by the sponsor (see AAHRPP-SOP-008).			
CE label (medical device)	Please provide the CE label of the medical device to CEHF if available.	**X**	**X**	
Investigator's brochure	**If the drug/medical device is not registered :** the summary of pharmacologic and toxicologic data/description, use instructions (investigator's brochure provided by the sponsor)		**X**	
Scientific and public leaflets	**If the drug/medical device is registered in Belgium (even if not commercialized):** scientific instruction and public instruction as validated by the commission of drug authorization. These instructions can be provided by the sponsor		**X**	
CTA/FAMHP submission form	Confirmation that all medication tested in the experiment are provided by the sponsor. This information **must** be transmitted to the EC		**X**	

5.2.1.2 Commercial

Document	Comment	Paper copy	Electronic copy	Ref doc
acknowledgement of receipt of valid application	provided and completed by the promotor, must contain all the documents submitted to the CEHF. **The investigator or the study coordinator checks the content and the conformity of the documents (versions and dates).** The investigator or the study coordinator signs the document and submits it to the CEHF.	**X**	**X**	**CEHF-FORM-007**
Document 1	dated and signed by the investigator and co-signed for information and approval by the Head of Clinical Service. It is necessary to mention the original title of the clinical research project (English or French), mentioned on the final protocol, along with the date of the protocol, its number and EudraCT number (if applicable). **We ask you to not modify the layout of this document**	**X**	**X**	**CEHF-FORM-003**
Project summary	1-2 pages maximum, in French and in understandable terms for the non medical members of the EC. The summary should include a short description of the protocol, methods and exams related to the experiment	**X**	**X**	

Documents information and informed consent form	Mandatory in French (for other languages, please submit documents when applicable). Please use the national templates of ICF. Please mention the version and date in the Documents' titles and in the footers.	**X**	**X**	**CEHF-FORM-023/024/025/026**
Billing sheet	Payment of the fees by the sponsor will be realized upon receipt of the bill sent by the UCL and completed by the sponsor.	**X**	**X**	**CEHF-FORM-006**
Information sheet for a clinical research project submitted to the CEHF	This document is completed by the investigator and/or study coordinator and by the sponsor.		**X**	**CEHF-FORM-005**
Full protocol and amendments (if applicable)	**Signed** by principal investigator**.** Please mention the version and date in the Document title and in the footers.	**X**	**X**	
CV dated and signed (< 2 years)	Principal investigator AND sub-investigators Saint-Luc		**X**	
Financial disclosure form	Principal investigator and sub-investigators Saint-Luc		**X**	**AAHRPP-FORM-035 (template provided by the commercial sponsor is accepted)**
Insurance	**Insurance certificate** of the commercial sponsor, attesting that the policy is conformed to the Law 7 May 2004. The insurance certificate of the sponsor specifies that he assumes, even without fault, the responsibility of damages caused to a participant and/or his successors, damages directly or indirectly related to the experiment (any contractual stipulation to limit this liability is deemed by law (art 29 par.1). The certificate must indicate the end of validity of insurance and the protocol title.		**X**	**AAHRPP-FORM-004**
Financial agreement	Financial agreement to be transmitted for evaluation to person in charge of the Unité Recherche Clinique (Medical Direction of Cliniques universitaires Saint-Luc), or to a member of his staff (please see contact list). The non-signed version of the agreement is accepted at time of initial submission.		**X**	
For drug/medical device experiments:				
CTA/FAMHP submission form	**Clinical Trial Application Form** (https://eudract.ema.europa.eu/eudract-web/index.faces) signed by principal investigator and provided by the sponsor Medical device experiments must be notified to FAMHP (the submission form will be provided to CEHF) :		**X**	

	- Clinical studies with medical device without CE label - Clinical studies with medical device with CE label but used in a different indication. **Application form to notify a clinical investigation with a medical device,** signed by the principal investigator and provided by the sponsor (see AAHRPP-SOP-008).			
CE label (medical device)	Please provide the CE label of the medical device to CEHF if available.	**X**	**X**	
Investigator's brochure	**If the drug/medical device is not registered :** the summary of pharmacologic and toxicologic data/description, use instructions (investigator's brochure provided by the sponsor)		**X**	
Scientific and public leaflets	**If the drug/medical device is registered in Belgium (even if not commercialized):** scientific instruction and public instruction as validated by the commission of drug authorization. These instructions can be provided by the sponsor		**X**	
	Confirmation that all medication tested in the experiment are provided by the sponsor. This information **must** be transmitted to the EC		**X**	

5.2.2 Retrospective studies

5.2.2.1 Non commercial

Procedure for submission to CEHF : the investigator

- sends to the CEHF secretary a letter describing the retrospective study that he would like to initiate ;
- completes the simplified procedure submission form CEHF-FORM-009 and transmits it to the CEHF ;
- sends also the inform consent form (if applicable) ;
- sends his CV (and the coinvestigators' CVs, if applicable).

Document	Comment	Paper copy	Electronic copy	**Ref doc**
Description letter	Completed by the investigator : should describe the type of data to be collected, the rationale for the research and the modalities to	**X**	**X**	

	protect the data confidentiality. If applicable, an exemption to the consent process will be requested.			
Simplified submission document	Signed and dated by the principal investigator and the Head of Service. **Please do not change the lay out of the document.** The EC will notify his agreement and sign it.	**X**	**X**	**CEHF-FORM-009**
Investigator's resume (< 2 years)	Dated and signed		**X**	
Documents information and informed consent form	If no exemption requested. Mandatory in French (for other languages, please submit documents when applicable). Please mention version and date in Document title and footers.	**X**	**X**	

5.2.2.2 Commercial

Idem 5.2.2.1, but in addition :

Document	Comment	Paper copy	Electronic copy	Ref doc
Financial agreement	Financial agreement to be transmitted for evaluation to person in charge of the Unité Recherche Clinique (Medical Direction of Cliniques universitaires Saint-Luc), or to a member of his staff (please see contact list). The non-signed version of the agreement is accepted at time of initial submission.		**X**	
Financial disclosure form	Principal investigator and sub-investigators Saint-Luc		**X**	**AAHRPP-FORM-035 (template provided by the commercial sponsor is accepted)**

5.2.3 Experimentations involving (Residual) Human Body Material ((R)HBM), including blood, but not intended for transfusion

5.2.3.1 Non commercial

ICF : Informed Consent Form ; PC : Paper Copy ; EC : Electronic Copy

The investigator : transmits the documents according to the table below. For more details on documents to submit with the standard procedure, see 5.2.1.1. For a simplified submission, see 5.2.2.1. The investigator :

- Sends to the CEHF secretary a summary of the project or a protocol describing the study implying (R)HBM that he would like to initiate ;
- fills in the simplified procedure submission form CEHF-FORM-009;
- provides also all the documents that will be given to the patient (informed consent form if present).
- Provides his updated CV (and the coinvestigators' CVs, if applicable).

Type of HBM	Type of submission	Documents	PC	EC	Reference Doc
(a) Primary use of HBM, including blood (but not intended for transfusion) : sampling performed for the current study.	• It is a prospective interventional study. • Standard submission with informed consent and insurance.	AoR	X	X	CEHF-FORM-007
		Document 1	X	X	CEHF-FORM-003
		Summary	X	X	
		Protocol	X	X	
		ICF	X	X	
		CV of investigators		X	Dated and signed
		Insurance		X	
		Financial agreement		X	e-mail to URC
(b) Secondary use, for a new study, of material collected in the frame of another clinical study.	• Standard submission with informed consent and insurance. • The patient must be contacted to sign a new informed consent.	Same as just above.			
(c) Residual Human Body Material (RHBM), including residual blood. The investigator must check in Medical Explorer the absence of patient's refusal to use residual body material for research purposes.	• If no associated clinical data : Simplified submission.	Simplified submission form	X	X	CEHF-FORM-009.
		Summary or protocol (type of data, objectives, methods…)	X	X	Must describe measures to guarantee confidentiality.
		CV investigator		X	Dated and signed
		ICF	X	X	Preferred but not mandatory. Request of exemption in accompanying letter.
	• If associated clinical data are retrospective, i.e. already available at the time of final approval by the CEHF : Simplified submission.	Same as above. Please mark « Retrospective study » AND « RHBM » in Simplified submission form.			
	• If associated clinical data are prospectively collected, i.e. not yet available at the time of final approval by the CEHF : Standard submission with informed consent and insurance.	AoR	X	X	CEHF-FORM-007
		Document 1	X	X	CEHF-FORM-003
		Summary	X	X	
		Protocol	X	X	
		ICF	X	X	
		CV of investigators		X	Dated and signed
		Insurance		X	
		Financial agreement		X	e-mail to URC

(d) Urine, stool, tears, hair, sweat, nails, breastmilk	• These are waste. Only associated clinical data determine the type of study.	Documents to submit according to associated clinical data : • Retrospective associated clinical data : simplified submission. • Prospective associated clinical data : standard submission.

5.2.3.2 Commercial

Idem 5.2.3.1, but in addition:

Document	Comment	Paper copy	Electronic copy	Ref doc
Financial agreement	Financial agreement to be transmitted for evaluation to person in charge of the Unité Recherche Clinique (Medical Direction of Cliniques universitaires Saint-Luc), or to a member of his staff (please see contact list). The non-signed version of the agreement is accepted at time of initial submission.		**X**	
Financial disclosure form	Principal investigator and sub-investigators Saint-Luc		**X**	**AAHRPP-FORM-035 (template provided by the commercial sponsor is accepted)**

5.2.4 Compassionate use and medical need programs

The Royal Decree of 25 April 2014 (Royal decree modifying the Royal Decree of 14 December 2006 about drugs for human and veterinary use) has modified the way a medical need or compassionate use program can be submitted to Ethics Committee. **Indeed, the request must first be submitted to FAMHP who will provide the project to the designated Ethics Committee**.

This Royal Decree also states that requests can only come from applicant for authorization under the centralized procedure or the manufacturer, importer or sponsor as defined in the Law of 7 May 2004 related to experimentation on humans.

5.2.5 Innovating techniques

- Validated innovating techniques : the practitioner must
  - Inform the medical direction of the implementation of the innovating technique;
  - Notify the Ethics Committee of this implementation (electronic and paper copy of project and information document);

- Obtain oral or written consent from the patient;
- Report or index a paper copy in the medical record of the patient.

- Non-validated innovating techniques: the practitioner must submit the project (protocol, summary) as well as the informed consent documents to the Ethics Committee (electronic and paper copy). The Ethics Committee will decide if the Law on Human Experiment (Belgian Law dated May 7, 2004) applies.

5.2.6 Transnational research

They are the non-european international trials sponsored by Cliniques universitaires Saint-Luc. These studies must be submitted to the CEHF, even if no site in Belgium is involved. More detailed: see 208-AAHRPP-SOP-063 and 209-AAHRPP-FORM-081.

5.3 Electronic submission via the database CLAIRE

SUBMISSION OF A MEDICAL EXPERIMENT WHOSE INVESTIGATOR IS A MEDICAL DOCTOR BELONGING TO THE PERMANENT STAFF MUST BE PERFORMED ELECTRONICALLY.

5.3.1 Non-commercial studies

The academic central locket submits the study via the database CLAIRE

5.3.2 Commercial studies

The investigator or the study nurse records the study to submit to CEHF in the database CLAIRE.

5.3.2.1 Tab « ETUDE »

The following items must be completed :

- n° protocole
- n° Eudract for the trials with an IMP
- Acronyme
- Type: 2 scroll lists
- Service : scroll list
- CT Cancer : if applicable
- Phase : scroll list
- Nombre de patients prévus

- Titre
- Pathologie
- Molécule/matériel
- Fin assurance
- Investigateurs
- CRCM

5.3.2.2 Tab « Logistique »

- Encode the sponsor. If the sponsor (and his correct address) doesn't exist in the scroll list, please ask an employee of the CRU to record it in the sponsors' list.

5.3.2.3 Tab «CE»

- « Soumissions au CE » : add submission to the EC 
- Select the type of submission in the scroll list

- The reference number of the CEHF is automatically generated and reported in the tabs C.E. and Etude.
- Both the Ethics Committee and the person logged in Claire receive an automatic email referenced with the attributed submission number.
- The logged person sends the electronic version of the submission documents in reply to the email.
- The submission and the status history as well as the letters issued by the CEHF are readable in the tab C.E. of the related experiment.

5.4 Paper copy of the documents

The requested paper versions will be provided by the investigator or the CRCM to the Ethics Committee together with the copy of the issued email.

THE LEGAL START CLOCK FOR THE SUBMISSION REVIEW BY THE ETHICS COMMITTEE STARTS ONLY AFTER THE RECEPTION OF BOTH THE ELECTRONIC AND THE PAPER VERSION OF THE REQUESTED DOCUMENTS, AND WHEN THE FILE HAS BEEN VALIDATED AS COMPLETE.

- Address for the documents submission :

Président du Comité d'Éthique Hospitalo-Facultaire

Avenue Hippocrate 55.14

Tour Harvey – niveau 0

1200 Bruxelles

Tél. : 02/764.55.14

Fax : 02/764.55.13

E-mail : commission.ethique-saint-luc@uclouvain.be

5.5 Timing

- In most of experiments (phases II, III et IV), the LEC has to issue single opinion to the investigator **within 28 days maximum**.
- If the clinical research project submitted to the EC is complete, the LEC sends the acknowledgment of receipt within 3 days upon receipt.

- **Day 1 to Day 20 :** The NLEC can transmit their comments to the LEC within 20 days regarding the following points :
    i. qualifications of local investigators and collaborators
    ii. quality of installations
    iii. information and informed consent document

If modifications are requested by the LEC and/or by NLEC to the sponsor, the clock stops until receipt of modifications.

- **Day 21 to Day 25 :** the NLEC has 5 days to inform the LEC if he accepts or not the opinion of the LEC (no possibility of modifications). In case of no reaction from the LEC, the site can not start the experiment.
- **Day 26 to Day 28** : the LEC has 3 days to inform the principal investigator of the single opinion of the EC (copy to the NLEC, FAMHP).

N.B. :

- ***EC meetings are held every Monday***
- ***Documents have to be submitted to CEHF 12 days before the meeting***
- ***The secretary of CEHF is opened from Monday to Friday (10h-13h).***
- ***If possible, we ask to the sponsor to provide information by e-mail, in particular all documents related to SAE, SUSARs, CIOMS.***

5.6 Follow-up

5.6.1 Amendments

- All modification of the initial protocol (substantial or non substantial amendment) must be transmitted to the CEHF and a new approval should be requested if necessary (please see CEHF-SOP-015 amendment submission procedure).

5.6.2 End of experiments

- The CEHF **must** be informed of the end of the experiment as well as the number of recruited patients on an annual basis (CEHF-FORM-028 notification end of trial).

5.7 Specific questions

5.7.1 Adding a new site

- **When adding a new site to an experiment already on going, can the NLEC request modifications in the informed consent form?**

  No. If the NLEC of the new site agrees with the informed consent form, the site can participate to the experiment. If not, the site will not participate.

5.7.2 Financial agreements

- **Must the LEC have access to the financial agreements between sponsor, investigator and medical direction of each site where the experiment will take place and review these financial agreements?**

  Yes.

  The Law requires the EC to give its opinion, the EC reviews (Article 11 10 °) "the amounts and terms of any compensation / indemnity and compensation of investigators and participants, as well as relevant elements of each contract between the sponsor and the site ";

  The purpose of this requirement is to consider the safety of participants may be influenced by the financial aspects of the agreement between the sponsor and first handlers and this security brings transparency, especially between developers and experiment site (usually hospitals).

  It is necessary that the clinical research project submitted to the ethics committee of the single opinion contains the contracts that bind the promoter and manipulator and each experiment site.

  To examine these contracts, it is not necessary that the contract is already signed; the draft agreements can also be sent as long as the contracts (which must correspond to the draft agreement) are sent as soon as possible. The approval of the EC can be given if the final contract matches the project which has been sent initially.

5.7.3 IRB and FWA numbers

- **What are IRB and FWA numbers and are we affiliated?**

  These numbers refer to the registration of the EC to the Office for Human Research Protections (OHRP). The institution asserts that all clinical research experiments that take place are guided by Ethical Principles as defined in the Belmont Report and Helsinki's statement. This is required by the Department of Health and Human services and by American pharmaceutical industries performing clinical trials outside of USA.

  For cliniques universitaires Saint-Luc

  IRB:00001530 (expiration August 07, 2020)
  FWA:00003749 (expiration September 15, 2021)

6 DEFINITIONS AND ABBREVIATIONS

6.1 Abbreviations

CEHF : Comité d'Ethique Hospitalo-Facultaire Saint-Luc - UCL
CIOMS : Council for international organization of medical sciences
CU : compassionnate use program
CUSL : Cliniques universitaires Saint-Luc
EC : Electronic Copy
EC : Ethics Committee
FWA : Federal Wide Assurance
ICF : Informed Consent Form
IRB : Institutional Review Board
LEC : leading EC
MNP : Medical Need Program
NLEC : non leading EC
OHRP : Office for Human Research Protections
PC : Paper Copy
SAE: serious adverse event
SOP : standard operating procedure
SUSAR: suspected unexpected serious adverse reaction
UCL : Université catholique de Louvain
URC : Unité de Recherche Clinique

6.2 Definitions

6.2.1 Prospective studies (interventional and non-interventional)

Prospective interventional and non-interventional studies fall within the scope of the Belgian Law of 7 May 2004 on human experimentation. The participant must sign an informed consent, and the sponsor must subscribe to a "non-fault" insurance.

Prospective study : when the data are not yet available at the time of final approval by the CEHF.

Interventional study : when a supplementary effort is required from the patient (e.g. : additional blood tube during a standard blood sampling ; questionnaire, if falling out of current practice ; every other intervention).

Non-interventional study : when there is no intervention. It means in the following cases : questionnaires during a routine or standard medical visit, recording of medical data coming from standard of care, prospective collection of data in the medical file of the patient without any contact with the patient.

6.2.2 Retrospective studies

The retrospective studies do not fall within the scope of the Belgian Law of 7 May 2004 on human experimentation.

The art 3, §2 states: "*The present law is not applicable for studies purely retrospective on basis of data from the past available in the files of the patients, in medical files or administrative files or databases and for all that no new data relative to patients are obtained*".

These studies are not considered as experimentation on humans because it is based on the analysis of medical files and will not include any new questions for the participants nor prospective research of information from the participants. There is no direct interaction between investigator and participant.

In a retrospective study, the informed consent of the participant can be requested but it is also possible that an exemption is requested to the EC. The exemption's request to the informed consent can be justified by disproportionate efforts to obtain this consent, by the risk to wake of a painful past or ask a family about a deceased person. The CEHF evaluates validity and justification of the research and measures that are taken to guarantee privacy and confidentiality of the data.

6.2.3 Experimentations involving Residual Human Body Material (RHBM)

Studies on residual human body (biological) material are out of the scope of the Belgian Law on human experiments dated May 7, 2004.

The article 2, 23° specifies: "*Experiments on embryos in vitro, on human biological material or on corpses do not fall within the scope of this law"*.

The applicable law is the Belgian Law of December 19, 2008 on the acquisition and use of human body material intended for human medical application or for scientific research.

The residual human body material (RHBM) is the part of the human body material taken for the diagnosis or treatment of a donor which, after a sufficient part was kept for the diagnosis or for the donor treatment is redundant and could be destroyed.

Studies on RHMB are not experiments on the human person but correspond to the use of residual body (biological) material (material which is redundant and could have been destroyed) for research purposes. There is no interaction between the investigator and the subject.

The Ethics Committee evaluates the validity and the justification of the research. The EC also evaluates the measures taken to guarantee the confidentiality of the data collected and the absence of refusal expressed by the patient for the use of his residual human body material. However, when clinical data are associated to this material (i.e. when the investigator looks in the medical file of the patient or gathers information by the patient's treating physician in order to correlate the results of his analyses on the residual material to the clinical data of the patient), the investigation is in fact an experiment "on the human person". The associated clinical data may be

- Retrospective, i.e. already available at the time of final approval by the CEHF : this experiment is thus out of the scope of the Belgian Law on human experiments dated May 7, 2004.
- Prospective, i.e. not yet available at the time of final approval by the CEHF : this experiment is thus a prospective non interventional or interventional study. The investigator must therefore collect an informed consent by the patient and contact an insurance.

6.2.4 Primary and secondary use of HBM

Primary use of HBM: any use of human body material for which the donor specifically gave his consent in the context of the sampling. The material is collected specifically for the needs of the study. This sampling is not intended to establish a diagnosis or to treat. This acquisition takes place in a specific intervention, or *at the same time* as a sampling intended to establish a diagnosis or to treat. This acquisition corresponds to an interventional study.

Secondary use of HBM: human body material collected for a previous study and which will be used for a new study for which the patient did not give his consent. The patient must be contacted and sign a new informed consent for this new use.

6.2.5 Compassionate use and Medical Need Program

Compassionate use : provision, for compassionate reasons, of a drug which can be taken into account for the centralized procedure, to a group of patients suffering from a chronic disease, a disease which severely weakens health, a disease which is a threat to life, and if this disease can

not be treated satisfactorily with a drug available on the Belgian market and which is authorized for the treatment of this disease. The concerned drug must be under procedure for authorization on the market in accordance with art 6 of the European regulation or being under clinical trials. The concerned drug is therefore not yet authorized for any indications.

Medical need program: provision of a drug for human use in order to respond to medical needs for patients suffering from chronic disease, a disease which severely weakens health, a disease which is a threat to life, and if this disease can not be treated satisfactorily with a drug available on the Belgian market and which is authorized for the treatment of this disease. The concerned drug must have been under procedure for authorization on the market in accordance with art 6 of the European regulation but the indication for the treatment of this disease is not authorized or the drug is not yet on the market with this authorized indication.

6.2.6 Innovating techniques

An innovating technique is an invasive, diagnostic or therapeutic technique, introduced for the first time by a practitioner at the CUSL, hoping to improve the health care provided to the patient.

- The validated innovating technique has already been applied in an external service and has been published in a peer-review scientific journal. The medical direction must be informed of its implementation and the Ethics Committee must be notified. The patient must have provided an oral or written consent which must be reported in the medical record of the patient.
- The non-validated innovating technique : a practitioner willing to introduce in practice an innovating technique that he developed, must submit the project to the Ethics Committee who will decide if the Law on Human Experiment (Belgian Law dated May 7, 2004) will apply.

6.2.7 Transnational research

They are the non-european international trials sponsored by Cliniques universitaires Saint-Luc. These studies must be submitted to the CEHF, even if no site in Belgium is involved. More detailed: see 208-AAHRPP-SOP-063 and 209-AAHRPP-FORM-081

The sponsor of this type of international research assumes responsibility for the management of the whole research performed in Belgian and abroad centers. In general, all the procedures put in place for the human experiment at Cliniques universitaires Saint-Luc remain valid.

Nevertheless, he must care for the respect of the applicable legislation in each of the concerned centers as well as the protection of the vulnerable population with respect to applicable laws and customs.

The sponsor of a clinical research performed outside the European Community countries must follow the applicable laws and rules as well as the Good Clinical Practices and the declaration of Helsinki. The requirements in terms of “no-fault” insurance are country related. Therefore the sponsor will contact the manager of the CUSL insurance department. The designation of a national coordinator is strongly recommended to coordinates the legal requirements of a specific country. The sponsor is responsible for ensuring the same protection for participants abroad as in Belgium particularly concerning the local Ethics Committee review process, the translation and validation of patient information and informed consent forms, and the procedures linked to the clinical trial.

6.2.8 Recapitulative table (definitions and applicable laws)

Type d’étude	Loi	Commentaire
Prospective interventional	May 7, 2004 on human experiment	When data are not yet available at the time of final approval by the CEHF AND a supplementary effort is required from the patient (e.g. supplementary tube during a standard blood sampling ; questionnaire out of current practice ; every other intervention).
Prospective non interventioanl	idem	When data are not yet available at the time of final approval by the CEHF BUT there is no intervention, i.e. in the following cases : questionnaire during a routine visit ; recording of data from standard of care ; collect of data in the medical file without interaction with the patient.
Retrospective	8 December 1992 Act on the protection of private life with respect to the processing of personal data	When the data are already available at the time of final approval by the CEHF. Informed consent is preferred but request for exemption is possible if the effort to obtain the consent is unproportioned. No insurance required by law.
Residual human body material	December 19, 2008 on the acquisition and use of human body material intended for human medical application or for scientific research	The law concerns only the material (including blood, but not intended for transfusion). If there are associated clinical data, one of the above categories applies.

Compassionate use and Medical Need Program	Royal Decree of 25 April 2014 (Royal decree modifying the Royal Decree of 14 December 2006 about drugs for human and veterinary use)	Provision, under certain conditions, of a drug for human use but the drug is not yet on the market with this authorized indication.
Innovating technique	Internal rules of CUSL	Invasive, diagnostic or therapeutic technique, introduced for the first time by a practitioner at the CUSL, hoping to improve the health care provided to the patient. It is either validated or non-validated.
Tansnational research	Belgian laws, GCP and local customs.	Non-european international trials sponsored by Cliniques universitaires Saint-Luc.

7 REFERENCE DOCUMENTS

053 - CEHF-DSQ-002 - Check list submission new commercial experiment,
152 - CEHF-DSQ-003 – Ethics Committee agreement,
058 - CEHF-DSQ-011 – Check list submission new non commercial experiment,
054 - CEHF-FORM-003 - Document 1,
055 - CEHF-FORM-005 – Contact information submission CEHF,
CEHF-FORM-006 – Billing information CEHF,
057 - CEHF-FORM-007 - Acknowledgement of receipt of valid application,
133 - CEHF-FORM-014 – annual status – end of trial notification
061 - CEHF-SOP-015 - Amendment submission procedure

8 AAHRPP ACCREDITATION STANDARDS

I.6.B
II.2.C
II.2.D

9 LINKS INTRANET

10 LINKS INTERNET

P_EXTERNAL_LINKS

EUDRACT, GCP, Moniteur belge