GENERAL INFORMATION CONCERNING THE CONTRACT MANAGEMENT

Preliminary notice:

The approval of the principal investigator for performing the experiment must be obtained by the sponsor prior to any contract negotiation.

Contract review process:

A commercial central desk is now in charge of the initial submission of commercial studies and is the single access path to the Ethics Committee: as soon as the center has been selected, the requested documents described below and practical information must be provided by email to: guichetcommercial-saintluc@uclouvain.be . The commercial central desk transfers all the completed documents to the contracts, finances and reporting (CoFi) team.

To speed up the process of contract review we invite you to strictly respect the following steps described on our website: https://www.saintluc.be/en/research/ctc-contract-management.php

1 : FILL IN THE CONTRACT SET-UP QUESTIONNAIRE AVAILABLE ON OUR WEBSITE : https://www.saintluc.be/en/research/ctc-contract-management.php

2 : SEND THE FOLLOWING DOCUMENTS BY EMAIL TO guichetcommercial-saintluc@uclouvain.be .

- **The contract set-up questionnaire**
- **The complete study protocol with a flow chart**
- **The patient information sheet and the informed consent form**
- **The selected draft of the agreement**
- **A budget proposal**

3 : THE COMMERCIAL CENTRAL DESK TRANSFERS ALL THE COMPLETED DOCUMENTS TO THE CONTRACTS, FINANCES AND REPORTING TEAM (COFI).

Please take into account that the contract review time can be accelerated when an already validated template is proposed:

- **Either the commercial template validated by the Belgian academic hospitals**
- **Either a master agreement already negotiated between your company and the Cliniques universitaires Saint-Luc**
- **Either a recent (<1 year) contract validated by the Cliniques universitaires Saint-Luc**

NEVERTHELESS, TO DECREASE THE REVIEWING TIME, THE SPONSOR/CRO IS ADVISED TO TAKE ALREADY INTO ACCOUNT THE REGULATORY AND FINANCIAL ISSUES DETAILED IN THIS DOCUMENT BEFORE THE « COFI » TEAM WILL PROCESS THE CONTRACT PROPOSAL.

The COFI team is composed of:

Dr M. Van Hassel : Head of the COFI	michel.vanhassel@uclouvain.be	+32 2 764 15 10
Mme C. Janssens de Bisthoven	clementine.janssens@uclouvain.be	+32 2 764 15 15
Mr S. Livolsi	san.livolsi@uclouvain.be	+32 2 764 23 10
Mme M. Masson	marie.masson@uclouvain.be	+32 2 764 15 74
Mr P. Mourlhou	paul.mourlhou@uclouvain.be	+32 2 764 76 24
Mme P. Stevaux	pauline.stevaux@uclouvain.be	+32 2 764 12 42

The Cliniques universitaires Saint-Luc have been awarded full accreditation for its human research protection program by the Association for the Accreditation of Human Research Protection Programs (AAHRPP), an independent and non-profit organization. Considered the “gold seal” for human subject protection, AAHRPP accreditation signifies that an organization follows rigorous standards for ethics and quality. Therefore, the regulatory section of the agreements must fulfill the GCP and the local legislation declined in an AAHRPP approved wording.

The contract management must be carried out before the protocol submission to the Ethics Committee. The contract final draft must be provided for the Ethics Committee submission. The contract signatures will be initialized after the Ethics Committee has approved the experiment. The sponsor is requested to provide us with the Leading Ethics Committee approval as soon as it is issued.
Agreements must be signed at least by 3 parties: sponsor, principal investigator and (on behalf of the institution) Prof Jean-Louis Vanoverschelde, Medical Director.

Documents to be provided (electronic versions):

- **The complete study protocol with a flow chart**. The investigator will define in regard of the flow chart what is to be considered as "standard of care" or not. This information must also be reported in the participant's information form (CUSL internal procedure related to the Belgian Law dated 10 April 2014 art.46 as well as ICF templates from the FAHMP).
- **The patient information sheet and the informed consent form**
- **Drafts of the agreements** (word version)
- A **budget proposal** with detailed items (per visit fee- overhead included, VAT excluded) of the different topics (data management, investigator fee, technical assessments, additional fees such as start-up etc) to be covered. Any information transmitted in relation to the protocol must be paid for. The principal investigator budget proposed must not include the fees accounted for in the additional contracts.

Practical information to be provided at the initial submission:

- Principal investigator
- Number of patients to be recruited locally
- IMP or medical device – other
- IMP : phase

- Which medication /device is provided by the sponsor
- Material provided by sponsor: ECG, oxymeter, …?
- Specific requirements for the experiment: technical training required, IT training (software, hardware)…
- Type of CRF
- Planned initiation visit date
- Planned start of the study
- Estimated duration of recruitment
- Estimated study end (LPLV)

Additional fees to the main contract:

Start-up fee: 3.000€ (for interventional trials) A reduced start-up fee of 600€ is applicable for observational, retrospective or phase 4 studies.	This fee is independent of the patient recruitment. It covers the time spent by the investigator and by the study coordinator before the study starts and the access badges to the patients' files. The payment **must** be made upon signature of the agreement.
Archiving fee : 150€/box (if not organized by the sponsor) for 20 years	(size : 488 mm x 304mm x 379mm)
Audit fees: 150€/h for the PI and 60€/h for the study coordinator	In case of CRO or sponsor driven audit
Administrative amendment fee: 250€, protocol amendment involving budget: 500€	For each amendment to the investigator agreement sent for signature and requested by the sponsor.
Patient travel fees	What is foreseen? Vouchers are preferred.
Screen failures	

Particular fees such as long lasting trials, transfer of material from other sites etc	To be discussed per protocol.

Additional services :

Separate agreements (or exhibits to the main contract) must be drawn up with the different technical departments involved in the trials. They must also be signed at least by 3 parties: the sponsor, the representative of the concerned department and (on behalf of the institution) Prof Jean-Louis Vanoverschelde, Medical Director.

Negotiation is carried out with the contact person of each service: CoFi contact should be informed of the status.

		Contact	**Responsible signature**
Laboratory	Central or Local lab: if local lab is used, for which tests:	pierre.wallemacq@uclouvain.be soumaya.wasmine@uclouvain.be	Prof. P. Wallemacq, Laboratory referent for clinical research
	Lab materials provided (dipsticks …): if applicable, please describe		
Pathology	requested material	alessandra.camboni@uclouvain.be anne.mourin@uclouvain.be	Prof A Jouret-Mourin
Radiology	contact the referent person	muriel.decooman@uclouvain.be	The referent

		(commercial studies in oncology except haematology) valerie.rosseels@uclouvain.be (other commercial studies) perrinne.triqueneaux@uclouvain.be (non-commercial studies)	radiologist for the requested exam
Nuclear Medicine	contact the referent person	francois.jamar@uclouvain.be	Prof F. Jamar
Pharmacy	contact the referent person	pharmaetudes-saintluc@uclouvain.be	Mrs D. Wouters - Head of Pharmacy
	Medication provided by the sponsor?		
Cardiology	contact the referent person	virginie.donnay@uclouvain.be christophe.beauloye@uclouvain.be	Prof C. Beauloye
Rheumatology	contact the referent person	isabelle.Faille@uclouvain.be bernard.lauwerys@uclouvain.be	Prof B. Lauwerys

SPECIFIC mandatory regulatory requirements for the Clinical Trial Agreements: (AAHRPP ELEMENTS IN YELLOW MUST BE TAKEN INTO ACCOUNT)

TITLE	ELEMENT	TYPE OF SENTENCE
Parties	Sponsor or CRO and Cliniques universitaires Saint-Luc	Cliniques universitaires Saint-Luc ASBL**,** Avenue Hippocrate 10, 1200 Bruxelles, registered to the BCE with the n° 416.885.016, legally represented by the Medical Director
Term of the agreement	Subject of the trial	
	Effective date = date of the last signature	
	Total number of patients to be included Number of patients locally expected	
Regulatory pre condition	Compliance with the protocol, Helsinki declaration, GCP, Belgian laws, European directives and ethics committees. IND or IDE experiments are also regulated by the FDA regulation.	
Responsibilities	**Sponsor responsibilities** **AAHRPP Element I.8.D.:** Before initiating research, the Organization has a written agreement with the Sponsor about plans for disseminating findings from the research and the roles that Researchers and Sponsors will play in the publication or disclosure of results.	- *Sponsor will publicly register a protocol summary in* ***Clinicaltrials.gov.*** *(or equivalent)* - *The SPONSOR shall provide the investigator with the following:* - *The protocol;* - *All necessary documentation to allow the proper performance of the trial, including but not limited to Investigator's Brochure, the Study Product Monograph.* - *A copy of the trial insurance certificate;* - *A copy of the approval and feedback from the central Ethics Committee;*

		- *A copy of the notification to the Competent Health Authority;* - **ONLY IMPS STUDIES:** *The sponsor will be responsible for ensuring that any Suspected Unexpected Serious Adverse Reaction (SUSAR) are appropriately reported to the relevant health authorities and ethics committees according to applicable laws and regulations.*
	Investigator and center responsibilities	*- The Principal Investigator agrees that he is primarily responsible for all aspects of the trial, and for the full conduct and the quality of all protocol related treatments given in his own institution.* *- The Principal Investigator is responsible for the submission to his ethics committee.* *- In the event that the Principal Investigator ceases to be involved in the Trial for whatever reason, the center agrees to notify SPONSOR immediately. Within thirty (30) days after such notification the SPONSOR and center shall agree a successor acceptable to both parties.* *- It is the responsibility of center to ensure that all work performed by its employees, agents, contractors and/or the representatives is done in compliance with the protocol,*
Recruitment-Communication	**AAHRPP Element I.8.D.:** Before initiating research, the Organization has a written agreement with the Sponsor about plans for disseminating findings from the research and the roles that Researchers and Sponsors will play in the publication or disclosure of results.	*- The SPONSOR and the Ethics Committee must approve, in writing, the text of any communication soliciting patients for the study before placement, including but not limited to, newspapers and radio advertisements, direct mail pieces, internet advertisements or communications and newsletters. Such communications must comply with applicable laws and guidelines.*

		- Information published in Clinicaltrials.gov (or equivalent) can be publicly disclosed.
	Participant's consent	*-The Principal Investigator shall obtain from each subject legally signed written informed consent prior to the first trial specific procedure, in compliance with applicable regulations and guidelines and any modifications thereof.*
Study data	Data transmission	*- Principal Investigator agree to provide Sponsor periodically and in a timely manner with all trial results and other data called for in the protocol on properly completed (written or electronic) case report forms.* - Timing for data entry in eCRF: 5 working days; queries : 2 days; Data base lock/query : 24 hours
	Data property	- The SPONSOR is owner of the study data (data collected in relation to the study). *- The sponsor may utilize the data in any way it deems appropriate, subject to and in accordance with applicable privacy and security laws and regulations and the terms of this agreement.*
Monitoring	**AAHRPP Element III.2.A :** The investigator permits monitoring and auditing by the sponsor and inspection by the appropriate regulatory authority.	. Subject to the provisions of this agreement, ***SPONSOR's appointed monitors shall have the right to access and use the medical records*** during the term of this Agreement and thereafter.
	AAHRPP Element I.8.B: In studies where Sponsors conduct research site monitoring visits or conduct monitoring activities remotely, the Organization has a written agreement with the Sponsor that the Sponsor promptly reports to the Organization findings that could affect the safety	- ***Available for I8B, I8C and I8E*** *:During and for a period of [specify a period of time appropriate to the specific study, for example, at least two years after the completion of the study; or specify a triggering event, for example completion of data analysis], [the sponsor] shall promptly (or in a timely manner appropriate to the level of risk involved) report to the investigator*

	of participants or influence the conduct of the study.	*any information that could directly affect the health or safety of past or current study subjects or influence the conduct of the study, including but not limited to the study results and information in site monitoring reports and data safety monitoring committee reports as required by the protocol. In each case, the investigator and [the organization] shall be free to communicate these findings to each study subject and the IRB.*
	AAHRPP Element I.8.C: When the Sponsor has the responsibility to conduct data and safety monitoring, the Organization has a written agreement with the Sponsor that addresses provisions for monitoring the data to ensure the safety of participants and for providing data and safety monitoring reports to the Organization. At a minimum, data and safety monitoring reports should be sent annually, so they can be considered by the IRB at the time of continuing review.	
Results notification	**AAHRPP Element I.8.E:** When participant safety could be directly affected by study results **after the study has ended**, the Organization has a written agreement with the Sponsor that the Researcher or Organization will be notified of the results in order to consider informing participants.	
Continuing review	**AAHRPP Element II.2.D:** The IRB or EC has and follows written policies and procedures to conduct reviews by the convened EC.	**Only for IMPS studies:** *In the case of clinical trial with a medicinal product and if our Ethics Committee is the Leading one for Belgium: according to the applicable legislation, the Development Safety Update Report (DSUR) will be established by the Sponsor and the last version will be transmitted to the Ethics Committee via the investigator within 364 days (or more*

		frequently if requested by the EC) after the protocol approval by the Leading Ethics Committee and each year thereafter. A delay of 45 days will be authorized. If not provided beyond this period, the Ethics Committee will stop the research except if safety or ethical issues prevent it.
Audit, inspection		*The Contractor shall provide, and shall ensure that any member of the Study Team and (where applicable) any Collaborator undertake to provide, all reasonable cooperation to the Sponsor or representatives and assistance at all times during the term of this Agreement to carry out an audit of the Contractor's or (where applicable) any of its Collaborators' compliance with this Agreement (including all activities, performance, security and integrity in connection therewith), and Contractor's Quality Management System. In this respect, Contractor shall ensure, during business hours and upon giving reasonable prior notice, free access of Sponsor's auditors to Contractor's and (where applicable) any of its Collaborators' facilities and Study Sites, and all relevant information, data and records relevant to the Study, including the trial master file, taking into account Collaborator's and Collaborator's facilities and Study Sites' procedures for access.*
Emergency medical treatment for patients experiencing SAE or AE	**AAHRPP Element I.8.A:** The Organization has a written agreement with the Sponsor that addresses medical care for research participants with a research-related injury, when appropriate.	**INVESTIGATOR RESPONSIBILITY : MEDICAL CARE TO THE PARTICIPANTS :** *« The participating site and investigator will ensure adequate resources and staff for the study and will ensure medical care of the subjects. ».* **AND** **SPONSOR RESPONSIBILITY: *RESEARCH-RELATED***

		INJURY. *[The sponsor] shall be responsible for payment of the actual and reasonable medical expenses incurred in diagnosing and treating any injury, illness, or adverse reaction of a study subject that results from the administration of the study drug [or device] in accordance with the protocol or the proper performance of any Protocol procedure.* **AND** **NO-FAULT INSURANCE :** In accordance with the article 29 of the Belgian Law relating to experiments on humans dated May 7, 2004, SPONSOR shall assume, even without fault, the responsibility of any damages incurred by a Study Patient and linked directly or indirectly to the participation to the Trial, and shall provide compensation therefore through its insurance.
Confidentiality	Sponsor's confidential information	*The INVESTIGATOR agrees that all information and/or material which is or has been designated by Sponsor to be of a confidential and/or proprietary nature in the confidentiality agreement signed by both parties, pertaining to the business of Sponsor which is disclosed to the INVESTIGATOR by Sponsor prior to or during the term of this Agreement will be treated by the INVESTIGATOR as being confidential and will not be disclosed by the INVESTIGATOR either during the term of this Agreement or thereafter unless such information:* *a) is or becomes publicly known otherwise than through the fault of the INVESTIGATOR; or* *b) is made known to the INVESTIGATOR by a third party; or* *c) was already known by the INVESTIGATOR as evidenced by*

		written documentation prior to disclosure by ITEOS; or *d) is independently developed by employees of the INVESTIGATOR prior to the date of disclosure who have not had access to the information disclosed by Sponsor or to the Project results; or* *e) is required by lawful instruction of a court or government or administrative tribunal.*
	Participant's confidential information	SPONSOR guarantees the confidentiality of all information that might reveal the identity of the patient in respect of the Belgian privacy law (law of 8 December 1992 relative to the protection of private life).
Use of names, patent and intellectual property rights	**AAHRPP Element I.8.D:** Before initiating research, the Organization has a written agreement with the Sponsor about plans for disseminating findings from the research and the roles that Researchers and Sponsors will play in the publication or disclosure of results.	**Use of names:** *Neither Parties shall use the other's names or the names of the other's employees in any advertising or sales promotional material or in any other way without the prior written consent of the other.*" **Patent:** *The sole and exclusive right to any inventions, discoveries or innovations, whether* ***patentable*** *or not, arising directly or indirectly in the performance of the protocol and trial under this agreement and arising out of the use of the xxxx, shall be the property of the pharmaceutical company named xxx. Principal Investigator and center will promptly notify xxx, in writing of any such inventions. At the request and expense of xxx, Principal Investigator and participating center will cause to be assigned to xxx all right, title and interest in and to any such invention and provide reasonable assistance to obtain patents, including causing the execution of any assignment or other documents.* **Intellectual property:**

		The INVESTIGATOR will acquire no rights of any kind whatsoever with respect to any information, know-how, Project materials, compounds and/or compounds derivatives ("XXX Materials") provided by the Sponsor to the INVESTIGATOR under the terms of this Agreement. In consideration of the fees paid to the INVESTIGATOR for the Project, the Sponsor shall have the right to use any results, including any reports, generated by the INVESTIGATOR that are derived from a Project. *Sponsor acknowledges, however, that the INVESTIGATOR owns, licenses or controls pre-existing intellectual property such as standard operating procedures, screening protocols, testing materials and laboratory methodologies that are used by INVESTIGATOR to perform a Project and not developed solely for or provided by the INVESTIGATOR ("INVESTIGATOR Intellectual Property"). INVESTIGATOR may, whether alone or in conjunction with third parties, develop improvements, processes and methods that improve the INVESTIGATOR's Intellectual Property which can be used by the INVESTIGATOR at any time without disclosing Sponsor' confidential information or Sponsor' Materials ("Improvements").*
Publication rights	**AAHRPP Element I.8.D:** Before initiating research, the Organization has a written agreement with the Sponsor about plans for disseminating findings from the research and the roles that Researchers and Sponsors will play in the publication or disclosure of results.	**A: SPONSOR ROLE:** *If the Study is part of a multi-centre study, the INSTITUTION and the INVESTIGATOR agree, that the first PUBLICATION shall be a joint publication based on the analysis of the consolidated data from all participating centers, as described in the Protocol by the SPONSOR's statisticians, and not by the INVESTIGATOR(S) or the INSTITUTION* **B : INVESTIGATOR ROLE:** *The SPONSOR supports the exercise of academic freedom and*

		recognises the INSTITUTION's and the INVESTIGATOR's interest in making publications and presentations relating to the Study in scientific journals, at symposia, professional meetings or otherwise.
Insurance	Investigator has a malpractice insurance	*The investigator will maintain a medical professional liability and general liability insurance.*
	Sponsor has a no-fault insurance according to Belgian law	*In accordance with the Belgian Law relating to experiments on humans dated May 7, 2004, SPONSOR shall assume, even without fault, the responsibility of any damages incurred by a Study Patient and linked directly or indirectly to the participation to the Trial, and shall provide compensation therefore through its insurance.*
Liability		**Indemnification of investigator by sponsor:** *Investigator involved in the study will be indemnified by sponsor. Sponsor hereby agrees to indemnify the investigator, subject to the limitation below, from and against any and all loss, cost, damage claim or action (including reasonable attorney fees) provided :* *- the conduct of the investigator is not negligent* -…. **Indemnification of sponsor by investigator : (same sentence can apply for indemnification of investigator by sponsor: *each party shall indemnify defend and hold harmless the other*)**
Termination	Termination by both parties	*No addition to or modification of this Agreement shall be effective unless made in writing and signed by both parties. The Parties may terminate this Agreement upon thirty (30) days written notice sent by registered mail, to the other for any reason. If the Sponsor exercises this early termination right, the Sponsor agrees that it*

	Breach of contract Liquidation Bankrupcy Force Majeure Adverse Drug Reaction	*will pay the INVESTIGATOR for all portions of the Project actually performed up to the date of termination. If INVESTIGATOR exercises this early termination right, then it will refund any monies paid to it for the portions of the uncompleted Project.* *Either Party shall have the right to terminate this Agreement immediately upon written notice, in the event:* • *Of a material breach committed by the other Party which, if capable of being remedied, is not remedied for a period of thirty (30) days following the date of receipt of a written notice specifying the nature of the breach; and/or* • *The other Party committing numerous breaches of its duties or obligations under this Agreement which collectively constitute a material breach of this Agreement; and/or* • *The other Party is dissolved or liquidated, files or has filed against it a petition under any bankruptcy or insolvency law, makes an assignment for the benefit of its creditors or has a receiver appointed for all or substantially all of its property, or experiences an event analogous to any of the foregoing in any jurisdiction in which any of its assets are situated; and/or* • *Such Party is the non-defaulting Party, in case a force majeure event continues in effect for a period of more than three (3) months and/or* *Either Party shall have the right to terminate this Agreement immediately upon written notice, in the event of a noticed Adverse Drug Reaction.*
General provisions	Governing law	*This Agreement shall be construed and interpreted in accordance with the laws of Belgium, excluding its conflicts of law*

		provisions... The competent court shall be the courts of Brussels. (where the work is being performed).
	Resolving dispute	*In the event of a dispute between the PARTIES relating to the validity, interpretation or execution of the present agreement, which could not be resolved amicably, the PARTIES agree to attempt to resolve their dispute through the use of mediation in accordance with the mediation rules of BMediation. Mediation will begin no later than 15 days after the request for mediation notified by a PARTY to the other PARTY [IES] and the duration of mediation may not exceed 60 days, unless expressly agreed by the PARTIES. The mediation cost will be share equally between the PARTIES. In the event of failure of mediation, only the courts of Bruxelles will be competent.*
Terms of payment	**AAHRPP Element III.1.E:** Researchers and Research Staff must recruit participants in a fair and equitable manner. The following are prohibited in your research site or allowed under certain circumstances and which describe the circumstances will be assessed by the Ethics Committee on a case to case basis: - Payment arrangements in exchange for referrals of prospective participants ("finder's fees" or "referral fees") are allowable at your research site. - Payment arrangements designed to accelerate recruitment that are tied to the rate or timing of enrolment ("bonus payments").	

	The recruitment modalities must be approved by the Ethics Committee.	
	Invoice and payment request: A payment request of the services rendered during the reference period will be agreed by both parties. An invoice based upon this document will be issued by us and sent to your attention. The contract must reflect this provision by the following wording (or re-phrase):	"*The sponsor will send every three months a payment request form to the center with a summary of all reported visits or services rendered during the reference period. Upon agreement with the payment request form, the center will draw up an invoice at the attention of the sponsor. The sponsor will pay within 30 days after receipt of the invoice. Amounts due under this agreement are net of all taxes. VAT if applicable will be charged on top of the fees mentioned in this agreement and according the VAT directive".* *If the payment request is provided by the center : "Such [PO – payment request] will be deemed to be approved if no objection has been raised by [the other party – the Sponsor – CRO – Company Name] within a period of fifteen (15) calendar days".*
	Following invoicing data is needed:	- Corporate name -VAT number - Billing address - Mailing address - Contact name and e-mail
Signature page	Signed by Medical Director on behalf of Cliniques universitaires Saint-Luc AND by the principal investigator or the medico-technic department AND the sponsor or the CRO	APPROVED by the sponsor/CRO and by the medical director. ACKNOWLEDGED by the investigator

Access to the institutional procedures for sponsors/CRO:

A quality system is in place and covers all the process of a clinical research as well as the Ethics Committee performance. Applicable procedures are available to sponsors/CRO upon request to the clinical research quality manager. Only the French version of the documents related to the biomedical research quality system have been validated. An English translation is available upon request to the quality manager for clinical research.

Mrs Carole Dekelver: QAM Clinical Research at the CUSL	carole.dekelver@uclouvain.be	+32 2 764 23 99
Ethics Committee	commission.ethique-saint-luc@uclouvain.be	+32 2 764 55 14