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| --- | --- | --- |
|  | Clinical study protocol with questionnaire (Template) | Clinical trial Center |
| AAHRPP-DSQ-027\_EN | Version 2.0 | Application date :02/04/2024 |

*DELETE THIS PAGE IN THE FINAL VERSION OF YOUR DOCUMENT*

**DEFINITION**

A clinical research protocol is a document describing the objective(s), design, methodology, statistical aspects and organization of an experiment. The term protocol covers the original protocol as well as its successive versions and modifications (Art 2,22° Law May 7, 2004[[1]](#footnote-1))

**INSTRUCTIONS D’UTILISATION**

* This document is a protocol template based on the Good Clinical Practice guidelines for research (ICH GCP E6 R2[[2]](#footnote-2)).
* It should be used when writing a protocol for prospective experiments with questionnaires.
* The sections proposed in this template can be adapted to suit your needs.
* Some information may also be provided in other documents, which should be referenced in the protocol as appendices.
* The red text corresponding to the instructions for use should be removed, as should this first page.
* Text in black should be retained.
* Text in green should be adapted to your study.
* You can modify the title and layout styles. Don't forget to update the table of contents.
* Each protocol version must be numbered and dated in the footer.
* This document is available in English and French.
* Final format: PDF

Protocol Title

|  |  |
| --- | --- |
| Acronym / Protocol code | Fill in |
| Protocol version and date | Fill in |
| Sponsor | Cliniques universitaires Saint-LucBelgium |
|  |  |
| Investigator-Sponsor | Name and contact details |

The information contained in this document is the property of the Sponsor/ Investigator-Sponsor and may not be reproduced, published or disclosed to others without written authorization of the Sponsor/ Investigator-Sponsor.

Version History

| **Version** | **Approval Date** |  | **Changes** |
| --- | --- | --- | --- |
| 1.0 |  | Original |  |
| 2.0 |  | Amendment  |  |
| 3.0 |  | Amendment |  |
| 4.0 |  | Amendment |  |

1. Signature page

**INVESTIGATOR-SPONSOR**

 Name Signature Date

**SITE PRINCIPAL INVESTIGATOR**

I agree to conduct this study in accordance with the design and specific provisions of this protocol and will only make changes in the protocol after notifying the sponsor.

I understand that I may terminate or suspend enrolment of the study at any time if it becomes necessary to protect the best interests of the study subjects.

I agree to personally conduct or supervise this study and to ensure that all associates, colleagues, and employees assisting in the conduct of this study are informed about their obligations in meeting these commitments.

I will conduct the study in accordance with the protocol, Good Clinical Practice, the Declaration of Helsinki, and the moral, ethical and scientific principles that justify medical research. The study will be conducted in accordance with all relevant laws and regulations relating to clinical experimentation and the protection of patients.

I will ensure that the requirements relating to Ethics Committee review and approval are met.

I agree to maintain adequate and accurate records and to make those records available for audit and inspection in accordance with relevant regulatory requirements including the provision of direct access to data and source documents.

I agree to promptly report to the Ethics Committee any changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without Ethics Committee approval, except where necessary to ensure the safety of study participants.

 Name Signature Date

1. Protocol synopsis

1 page max

|  |  |
| --- | --- |
| Title of Study  |  |
| Acronym / Protocol code |  |
| Sponsor | Cliniques universitaires Saint-Luc |
| Investigator-sponsor |  |
| Department / Study centre(s) and site(s) principal investigator(s) |  |
| Pathology |  |
| Rationale / Literary references |  |
| Objectives | * Primary:
* Secondary:
 |
| Study Design |  |
| Number of patients  |  |
| Main criteria for inclusion (inclusion/exclusion criteria) |  |
| Total study duration: * date of planned first enrolment
* date of planned last completed
 |  |
| Study procedures  |  |

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1. List of abbreviations and definitions
2. Ethics
* *This protocol, any protocol amendments, informed consent form and other relevant documents (eg. recruitment advertisements) will be submitted to the Ethics Committee (EC) for formal approval to conduct the study. The decision of the EC concerning the conduct of the study will be made in writing to the sponsor. All correspondence with the Ethics Committee will be retained in the Investigator File.*
* *The study will be conducted in accordance with legal and regulatory requirements (Belgian law of 7 May 2004, Belgian law for Patient rights 22 August 2002, Private life GDPR 2018), as well as the Guidelines for Good Clinical Practice (International Conference on Harmonization 1996), and the last version of Declaration of Helsinki (World Medical Association).*
* *All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. This consent form will be submitted with the protocol for review and approval by the EC. The formal consent of a subject, using the EC-approved consent form, will be obtained before that subject is submitted to any study procedure. This consent form must be signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent. The written informed consent document should be prepared in the language of the potential patient population.*
* *The identity of the participant will remain kept confidential according to the General Data Protection Regulation of 27 April 2016 (in application on 25 May 2018), to the Belgian law of 30 July 2018 on the protection of natural persons with regard to the processing of personal data and the Belgian patient’s right law (22 August 2002). Personal data will be coded. Subjects will not be identified by name or in any other recognizable way in any of the records, results or publications related to the experiment.*
1. Objectives

An objective is the purpose for performing the study in terms of the scientific question to be answered. Express each objective as a statement of purpose (e.g. to assess, to determine, to compare, to evaluate) and include the general purpose (e.g. efficacy, effectiveness, safety) and/or specific purpose (e.g. effect of an intervention on disease incidence, disease severity, health behavior).

Objectives should be simple (not complex), specific (not vague), and stated in advance (not after the research is done). After statement of the primary objective, secondary objectives may be mentioned.

* 1. Primary
	2. Secondary
	3. Endpoints

A study endpoint is a specific measurement or observation to assess the effect of the study variable (study intervention). Study endpoints should be prioritized and should correspond to the study objectives and hypotheses being tested.

Always specify the timepoint (of measurement) along with the endpoint concerned, especially when it is possible to be measured more than once during the study.

The primary endpoint(s) should be clearly specified and its importance and role in the analysis and interpretation of study results should be defined. The primary endpoint is the basis for concluding that the study met its objective. Generally, there should be just one primary endpoint that will provide a clinically relevant, valid, and reliable measure of the primary objective.

The primary endpoint should be a clear, unarguable, quantitative measure of effect that will be the focus of the primary analysis and will drive the choice of sample size.

1. Background Information and Scientific Rationale
* Scientific explanation to define the issue : Discussion of important literature and data that are relevant to the study and that provide background for the study (literature revue with references listed)
* Justification of the study considering the current knowledge: bibliographical references and previously obtained results or data related to the study and serving as a basis for it
* Benefits expected for the research
* Perspectives for the scientific community, the hospital, the public health.
1. Investigational plan
	1. Design

Definition of the characteristics of the biomedical research by standard terms

* Experimentation type
* Monocenter or multicenter (national or international) ; number of centers
* With or without direct individual benefit
* Method of assignment (randomization, stratification)
* Number of study groups
* Study configuration : parallel groups or cross-over
* Approximate time to complete study enrollment
* Expected duration of subject participation
* Methods for collecting data for assessment of study objectives
* Interim analysis plans
	1. Study interventions

The schedule must include clinic visits and all contacts (e.g., telephone contacts) to be done during the protocol.

* 1. Description of population
		1. Patient population studied
* Number of patients planned
* Characteristics of the subjects to be included: age, sex, weight, size, race, medical history, biological parameters, definition of the pathology and the enumeration of its characteristics.
* Rationale for gender and age distribution of participants
* Justification for inclusion of participants unable to give informed consent or other special populations such as minors
	+ 1. Inclusion criteria

Provide a statement that subjects must meet all of the inclusion criteria in order to be eligible to participate in the study and then list each criterion.

* + 1. Exclusion criteria

Provide a statement that all subjects meeting any of the exclusion criteria at baseline will be excluded from study participation and then list each criterion.

* + 1. Withdrawal

Subjects are free to withdraw from participation in the study at any time. A subject must be discontinued from the study if he or his legal representative withdraws consent.

An investigator may withdraw a subject from the study for the following reasons: add a list of reasons why subjects may be withdrawn from the study.

In all cases, the reason why subjects are withdrawn must be recorded in detail in the electronic Case Report Form (eCRF) and in the subject’s medical records. The gathered subject data should be taken into account in the analysis of the study data.

A subject will be considered lost to follow-up if he or she fails to return for [Fill in] scheduled visits and/or is unable to be contacted by the study site staff.

The following actions must be taken if a subject fails to return for a required study visit: Adjust the actions below if they do not fit the design of your study.

* The site will attempt to contact the subject and reschedule the missed visit within [Fill in] and counsel the subject on the importance of maintaining the assigned visit schedule and ascertain if the subject wishes to and/or should continue in the study;
* Before a subject is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the subject (i.e. three telephone calls and a certified letter to the subject’s last known mailing address or local equivalent methods). These contact attempts should be documented in the subject’s medical record or study file;
* Should the subject continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.
	1. Strategies for participant recruitment
		1. Recruitment process

Detailed description of the recruitment process :

* How will potential participants be identified?
* What resources will be used for recruitment? (Describe the format of the resources, e.g. paper or electronic and how these will be presented to potential participants e.g. in consultation, by telephone, by post, via a display, via social media, ...)
* Who will be approaching potential participants and who will be obtaining informed consent? (Describe the professional role and whether there is a prior clinical relationship with potential participants)
* Will identification of potential participants involve access to identifiable information? If yes, describe what measures will be in place to confirm that access to this information will be lawful
	+ 1. Informed consent process

Information related to the study is provided to patients or their legal representative by the investigator during the consultation, according to the requirements pertaining to consent covered by ICH-GCP (E6).

There are also informed they could withdraw their consent at any time during the study without any consequence. This point is written in the informed consent form.

Patients or their legal representative receive the patient information and consent form and have time to think about their participation to the study. They have the opportunity to ask questions to the investigator (by email, phone or in consultation).

The investigator makes sure they have understood the information. They sign and date the informed consent form simultaneously with the investigator.

Patients or their legal representative receive a copy of the signed informed consent form.

In case of electronic consent with electronic questionnaire, explain

* the process used to inform participants and send them questionnaires (The researcher must contact the patient to inform them and obtain their e-mail address before sending the link to the questionnaire). Contact may be made by a member of the research team (not specifically the principal investigator) during a consultation, by telephone or by post. The contact must be documented.
* the process used to collect participants e-consent
* the data de-identification process
* the importance of participants traceability

You must use REDCAP to provide electronic consent and electronic questionnaire to participants. The information document must be clear and complete + a consent option, separate from the questionnaire if answers to the questionnaire are anonymous. In that case, the software used must be configured so as not to allow the link to be made between the consent and the questionnaire. For the content of the information document, the researcher can draw inspiration from the consent template (CEHF-DOE-141 or CEHF-DOE-093). In case of anonymous answers, explain in the information document (and during contact with the participant) that the identity provided at the time of consent cannot be linked to the answers to the questions and that the answers will remain anonymous.

Electronic consent form :

* One box to tick: "I have read the information and have had the opportunity to ask all my questions".
* A second box: "I agree to participate".
* A field for entering the consenting person's first and last name

Remark: The participant’s legal representative is the person designated by a written mandate dated and signed by both parties to represent the rights and defend the interests of the participant. If there is no legally designated person, the legal representative would be, in order, the cohabitant (spouse, legal or effective), the adult child, the father or mother, the adult brother or sister.

* 1. Protocol Amendements

If amendments to the protocol (modifying sense or objectives or modifying the undergone constraints or the risks incurred by the subjects) turn out to be necessary, they will be submitted to the opinion of the Ethic Committee having examined the initial protocol.

* 1. Protocol Deviations

Any significant deviations from the study inclusion or exclusion criteria, study conduct, patient management or evaluation will be described and justified in the final report and communicated to the Ethics Committee, as appropriate.

1. Data management
	1. Data Quality Assurance

All study data will be handled in accordance with the law on General Data Protection Regulation (GDPR) and institutional rules [Belgian law dated on 20 July 2018 and 22 Aug. 2002].

The collection and processing of personal data from subjects enrolled in this study will be limited to those data that are necessary to fulfil the objectives of the study. These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations.

Appropriate technical and organizational measures to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or alteration must be put in place. Sponsor and site personnel whose responsibilities require access to personal data agree to keep the identity of subjects confidential.

The informed consent obtained from the subject includes explicit consent for the processing of personal data and for the investigator/institution to allow direct access to his or her original medical records (source data/documents) for study-related monitoring, audit, Ethics Committee review and regulatory inspection. This consent also addresses the transfer of the data to other entities, if applicable.

Privacy and confidentiality of data generated in the future on stored samples will be protected by the same standards applicable to all other clinical data. The investigator will ensure that the confidentiality of subjects' data will be preserved. On CRFs or any other documents, the subjects will not be identified by their names, but by their study number. Documents that identify the names of participants against their study number will be maintained by the investigator in strict confidence.

Monitors, auditors and other authorized agents will be granted direct access to study subject’s original medical records for verification of clinical study procedures and/or data, without violating the confidentiality of the subjects, to the extent permitted by the law and regulations. In any presentations of the results of this study at meetings or in publications, the subjects’ identity will remain confidential.

* 1. Statistical Analysis
* Reasons for the sample size selected, statistical power of the study, level of significance to be used
* Describe planned analyses, comparisons and statistical tests
* Reasons for excluding subject from an analysis
* Planned monitoring of the results
* Frequency and nature of interim analyses
	1. Data handling and record keeping

Subjects who are included in the study will be assigned a unique study number. On all documents submitted to the sponsor, patients will only be identified by their study number. The subject identification list will be safeguarded by the site. The name and any other directly identifying details will not be included in the study database.

An electronic case report form (eCRF) will be used in REDCap software. The eCRF will be completed for subjects who have signed the informed consent. This eCRF will include specific pages for inclusion and exclusion criteria, and for reporting each visit. The investigator will review, approve and validate each completed eCRF; the investigator’s signature (validation) serving as attestation of the investigator’s responsibility for ensuring that all data entered on the eCRF are complete, accurate and authentic.

All data will be processed according to the principles that the European General Data Protection Regulation (GDPR) imposes, which is in force since 25 May 2018.

1. Who will responsible for the processing of personal data?

Complete. In general, it is the investigator-sponsor

2. Who is Data Protection Officer for the processing?

The institutional DPO could be reached by this email address : rgpd@saintluc.uclouvain.be

3. The purpose of the processing:

Scientific research

4. The legal basis of the processing:

Consent, but this can be withdrawn

4. Who are potential recipients of the personal data?

All researchers involved in this clinical study or in research projects that use materials original from this clinical study. Staff involved in monitoring and ethical evaluation and people from competent authorities. Subcontracted parties that perform analysis on study-related data or materials.

5. It is possible that the personal data will be viewed by people who are in countries that do not use the same standards as the EU in terms of legal protection of data. In that case, we guarantee that the conditions of European and Belgian legislation on the protection of personal data will be respected.

6. The storage period:

Study-related documents will be stored for at least 20 years, data included in the medical file for 30 years.

* 1. Case Report Form

An electronic data capture (EDC) system, i.e. REDCap, will be used for data collection. Data reported on each eCRF should be consistent with the source data. If information is not known, this must be clearly indicated on the eCRF. All missing and ambiguous data will be clarified.

The eCRFs will be developed, based on the protocol. The final eCRF design will be approved by the Investigator-sponsor.

All data entries and corrections will only be performed by study site staff, authorized by the principal investigator. Data will be checked and any errors or inconsistencies will be clarified. The principal investigator must verify that all data entries in the eCRF are accurate and correct.

REDCap is provided and maintained by Vanderbilt University; a license for use was granted to the CUSL. REDCap is a web-based system.

* 1. Data storage

The data is accessed through a web browser directly on the secure REDCap server. The server is hosted within the Cliniques universitaires Saint-Luc campus and meets hospital level security and back-up requirements.

* 1. Access to data

Direct access will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit study-related monitoring, audits and inspections.

Login in REDCap is password controlled. Each user will receive a personal login name and password and will have a specific role which has predefined restrictions on what is allowed in REDCap. Any activity in the software is traced and transparent via the audit trail and log files.

1. Insurance

The experimentation is covered under the Belgian Law of May 7, 2004 by a no-fault insurance (type of coverage: liability insurance).

Policy holder:

Cliniques universitaires Saint-Luc

Avenue Hippocrate, 10

1200 Brussels

Issuer of the certificate of insurance:

MS Amlin Insurance SE

Boulevard du Roi Albert II, 37

1030 Brussels

N° de police : LXX00259

1. End of study
	1. For an individual subject

The subject has completed the study if he or she has completed all of study procedures, including the last visit or the last scheduled procedure, as described in this protocol.

* 1. For the whole study

Overall, the end of the study is reached when the last study procedure for the last subject has occurred: last subject, last visit (LSLV).

As soon as the whole study has ended (cfr the definition above), the Investigator-sponsor shall notify the Ethics Committee in a timely manner according to the regulatory requirements (within 90 days after the end of the study, or if the study had to be terminated early, this period must be reduced to 15 days and the reasons should clearly explained).

1. Dissemination of Results and Publication Policy

The protocol should specify not only dissemination of results in the scientific media, but also to the community and/ or the participants, and consider dissemination to the policy makers where relevant. Publication policy should be clearly discussed- for example who will take the lead in publication and who will be acknowledged in publications, etc.

This study is registered on Clinicaltrials.gov (<https://clinicaltrials.gov/> ) and is available to the public.

1. Archiving

Essential clinical study documents are kept at least 20 years after the study termination according to the Belgian legislation: RD 18 May 2006 art.24.

Source documentation are kept for 30 years, according to the Belgian legislation (Art 35 Belgian Law of 22 April 2019).

Specify who archives, where and access conditions.

1. Study Report

Deadline of writing final report, who will draft it and to whom it will be transmitted.

1. Litterature References

List of bibliographic references related to the clinical investigation

1. Appendix
* Questionnaires
1. [Law of May 7, 2004](http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=fr&la=F&cn=2004050732&table_name=loi) on human experimentation [↑](#footnote-ref-1)
2. [ICH GCP E6 (R2) Good](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf) clinical practice guideline [↑](#footnote-ref-2)