**DEFINITION**

Un protocole de recherche clinique est un document décrivant le(s) objectif(s), la conception, la méthodologie, les aspects statistiques et l’organisation d’une expérimentation. Le terme protocole recouvre le protocole original ainsi que ses versions successives et ses modifications (Art 2,22° Loi 7 Mai 2004[[1]](#footnote-1))

**INSTRUCTIONS D’UTILISATION**

* Ce document est un modèle de protocole basé sur les directives des bonnes pratiques cliniques de recherche (ICH GCP E6 R2[[2]](#footnote-2)).
* Il doit être utilisé pour l’écriture du protocole dans le cas d’une expérimentation prospective interventionnelle, non médicamenteuse et ne portant pas sur un dispositif médical.
* Les parties proposées dans ce modèle peuvent être adaptées en fonction de vos besoins.
* Certains renseignements peuvent également être fournis dans d'autres documents qui doivent être référencés dans le protocole en annexes (par exemple, consentement éclairé).
* Le texte en rouge qui correspond aux instructions d’utilisation doit être retiré, ainsi que cette première page.
* Le texte en noir doit être conservé.
* Vous pouvez modifier les styles de titres et de mise en page. N’oubliez pas de mettre à jour la table des matières.
* Chaque version de protocole doit être numérotée et datée en pied-de-page.
* Le protocole doit être écrit en anglais.
* Format final : PDF

1. Title page

The title page should contain the following information:

* Protocol title
* Acronym
* Protocol identification (code or number)
* Sponsor
* If not apparent from the title, a brief (one to two sentences) description giving design, duration, procedures, and patient population
* Name and affiliation of principal investigator (address and phone number)
* Name and affiliation of coordinating investigator(s) (address and phone number)
* Name of the Sponsor including the name of Responsible medical head and address and phone/fax numbers
* Name and title of the person(s) authorized to sign the protocol and the protocol amendment(s) for the sponsor or Institution (principal Investigator, sub investigators)
* Identification and full contact details of the centralized laboratory and/or any other centralized medico-technical service
* Version and date of protocole

Version History

| **Version** | **Approval Date** |  | **Changes** |
| --- | --- | --- | --- |
| 1 |  | Original |  |
| 2 |  | Amendment |  |
| 3 |  | Amendment |  |
| 4 |  | Amendment |  |

1. Signature page

**SPONSOR REPRESENTATIVE**

Name Signature Date

**INVESTIGATOR (S)**

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

Name Signature Date

1. Protocol synopsis

|  |
| --- |
| Name of Sponsor/Company: |
| Title of Study |
| Study centre(s) and site(s) principal investigator(s) |
| Publication (reference) |
| Studied period :  (planned date of first enrolment)  (planned date of last completed) |
| Objectives:  - Primary  - Secondary |
| Hypotheses |
| Study Design |
| Number of patients (planned and analysed) |
| Endpoints :  - Primary  - Secondary |
| Main criteria for inclusion (inclusion/exclusion criteria) |
| Procedures : Schedule of assessments – Study Flowchart |
| Statistical Considerations |

1. Schedule of activities

Insert the study flowchart

Table des matières à mettre à jour

Pour que vos titres soient repris dans la table des matières, vous devez utiliser des styles de titres configurés dans le document. Utilisez les titres proposés dans la barre d’outils du document Word ou créez vos propres styles de titres.

Table of contents

[1. Title page 2](#_Toc106382320)

[2. Signature page 5](#_Toc106382321)

[3. Protocol synopsis 6](#_Toc106382322)

[4. Schedule of activities 7](#_Toc106382323)

[5. List of abbreviations and definitions 9](#_Toc106382324)

[6. Ethics 10](#_Toc106382325)

[7. Background Information and Scientific Rationale 11](#_Toc106382326)

[7.1. Medical Background 11](#_Toc106382327)

[7.2. Rationale 11](#_Toc106382328)

[8. Objectives 11](#_Toc106382329)

[8.1. Primary 11](#_Toc106382330)

[8.2. Secondary 11](#_Toc106382331)

[8.3. Endpoints 11](#_Toc106382332)

[9. Investigational plan 12](#_Toc106382333)

[9.1. Design 12](#_Toc106382334)

[9.2. Description of population 12](#_Toc106382335)

[9.3. Strategies for participant recruitment 12](#_Toc106382336)

[9.4. Participants eligibility 12](#_Toc106382337)

[9.4.1. Inclusion criteria 12](#_Toc106382338)

[9.4.2. Exclusion criteria 13](#_Toc106382339)

[9.4.3. Withdrawal 13](#_Toc106382340)

[10. Study interventions and procedures 13](#_Toc106382341)

[10.1. Method of assigning participant to interventions groups 13](#_Toc106382342)

[10.2. Sample lab collection 13](#_Toc106382343)

[10.3. Prior and concomitant therapy 13](#_Toc106382344)

[10.4. Protocol Deviations 13](#_Toc106382345)

[10.5. Data Quality Assurance 14](#_Toc106382346)

[10.6. Data Management Responsibilities 14](#_Toc106382347)

[10.7. Data breach 14](#_Toc106382348)

[10.8. Statistical Analysis 14](#_Toc106382349)

[10.9. Protocol Amendements 15](#_Toc106382350)

[11. Finance and Insurance 15](#_Toc106382351)

[12. End of study 15](#_Toc106382352)

[13. Dissemination of Results and Publication Policy 16](#_Toc106382353)

[14. Archiving 16](#_Toc106382354)

[15. Study Report 16](#_Toc106382355)

[16. Literature References 16](#_Toc106382356)

[17. Appendix 16](#_Toc106382357)

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. Background Information and Scientific Rationale
   1. Medical Background

Literature Revue: (references listed)

* The name and description of the study intervention(s)
* 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
* Justification of the study considering the current knowledge: a summary of findings from nonclinical studies that have potential clinical significance, and a summary from relevant clinical studies
* Benefits expected for the research
* Perspectives for the scientific community, the hospital, the public health.
  1. Rationale
* Description of the selected study population
* Statement of the hypothesis
* A summary of the known and potential risks and benefits, including an assessment of the expected benefits and risks

1. Objectives

*Goals are broad statements of what the proposal hopes to accomplish. They create a setting for the proposal. Specific objectives are statements of the research question(s). 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

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 to procedures (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
* Other protocol-specific details, such as centralization of evaluations (e.g., central laboratory or central reading center for clinical scans)
* Interim analysis plans
  1. Description of population
* Patient population studied

a description of the groups and subgroups of participants, including, if applicable, groups of participants with specific needs, e.g., age, gender, participation of healthy volunteers, participants with rare and ultra-rare diseases

* Number of patients planned
  1. Strategies for participant recruitment

Consider where subjects will be recruited and how (consultation, advertising,…); detailed description of the recruitment and informed consent process, particularly in cases where participants are unable to give informed consent

* 1. Participants eligibility

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.

If individuals of a specific gender or age group are not included or are underrepresented, an explanation of the reasons and justification for these non-inclusion criteria

* + 1. Withdrawal

Provide a list of reasons for which subjects may be discontinued from the study. Also note that subjects may withdraw voluntarily from participation in the study at any time. Describe the efforts to follow subjects who withdraw from the study.

1. Study interventions and procedures

Refer to the Schedule of activities (Study Flowchart)

The schedule must include clinic visits (screening, study period, follow-up visits), all contacts (e.g., telephone contacts) and all study interventions and procedures to be done during the protocol.

The protocol should specify the time that each phase of the project is likely to take, along with a detailed month by month timeline for each activity to be undertaken.

* 1. Method of assigning participant to interventions groups

The specific methods used to assign patients to interventions groups, to screen and randomize eligible patient, perform subsequent assignment should be described.

* 1. Sample lab collection

A description of the arrangements for complying with applicable rules for the collection, storage and future use of biological samples from clinical trial participants, if applicable, unless provided in a separate document

* 1. Prior and concomitant therapy

Medication allowed before and during the study

Drug interactions with study interventions and effect on study endpoints

* 1. Protocol Deviations

All important deviations related to study inclusion or exclusion criteria, conduct of the study, patient management or patient assessment should be described and justified in protocol and/or in the final report, as appropriate

* 1. Data Quality Assurance
* Quality assurance and quality control systems implemented to assure the quality of the data (If none were used, this should be stated).
* Documentation of methods used in Appendix (e.g. monitoring, …)
* Audit procedure if any
  1. Data Management Responsibilities

The protocol should provide information on how the data will be managed, including data handling and coding for computer analysis, monitoring and verification.

Instructions concerning the recording of study data on case report forms (CRF) :

* Name of used CRF – REDCap is required for clinical trials sponsored by CUSL
* Describe how data will be collected
* Refer to the CRF user manual

A description of the procedures for identifying data that are considered source data and are to be entered directly into the case report forms

Procedures for collecting data on participants who have withdrawn from treatment or the clinical trial, and for replacing and following up on these participants.

* 1. Data breach

A description of the measures taken to comply with the rules in force relating to the protection of personal data, and in particular the technical and organizational arrangements that will be applied to prevent unauthorized access, disclosure, dissemination, modification or loss of the information and personal data processed

A description of the measures that will be applied to guarantee the confidentiality of the information and personal data of the participants

A description of the measures that will be applied in the event of a data security breach, in order to mitigate the possible adverse effects

The Sponsor or designee must report to ethics committee, serious data breaches : transgressions against the [study](https://www.ema.europa.eu/en/glossary/clinical-trial) protocol or the regulation that are likely to significantly affect the safety and rights of a subject or the reliability and robustness of the data generated in the study.

* 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. 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 subjected at first opinion of the promoter of the study. After agreement by the promoter, these amendments will then be submitted to the opinion of the Ethic Committee having examined the initial protocol.

1. Finance and Insurance

Describe financing and insurance arrangements:

* Insurance without fault (Law of 7 May 2004)
* Financial agreement between the Sponsor, the investigator and the Institution to which it belongs :
  + Specific information to trials without direct individual benefit
  + Data protection
  + Conflict of interests

Details of the research funding and any cost which will be incurred should be detailed in the protocol, along with any per-participant or per-site payments.

Information about legal responsibilities and insurance must also be outlined.

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

A clear and unambiguous definition of the end of the study concerned and, if it is not the date of the last visit of the last participant, an indication of the estimated date of the end of the study and a justification for this

A description of the criteria for stopping parts or all of the study

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

Secure archiving of all documentation of the experiment (CRF, Informed Consent, Source document,…) during at least 20 years. Specify who archives, where and access conditions.

Data to be kept at least 20 years after the trial termination according to the Belgian legislation: RD 18 May 2006 art.24

1. Study Report

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

1. Literature References

List of bibliographic references related to the clinical investigation

1. Appendix

* Patient information and consent form
* Laboratory values and agreement
* Laboratory technics
* CRF / questionnaires
* Other

1. [Loi du 7 Mai 2004](http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=fr&la=F&cn=2004050732&table_name=loi) relative aux expérimentations sur la personne humaine [↑](#footnote-ref-1)
2. [ICH GCP E6 (R2) Guide de bonnes pratiques cliniques](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf) [↑](#footnote-ref-2)