**DEFINITION[[1]](#footnote-1)**

Documentqui rassemble les informations relatives à l'étude : informations de base, justification, objectifs, résultats, conception, analyse pré-spécifiée, méthodologie, monitoring, sécurité et suivi, enregistrement des données de l'investigation clinique. Ce document est nommé plan d’investigation clinique ou protocole d’investigation clinique.

**INSTRUCTIONS D’UTILISATION**

* Ce document est un modèle de protocole basé sur les directives du règlement européen 2017/745[[2]](#footnote-2), les guidelines de l’AFMPS1, la Norme Internationale ISO[[3]](#footnote-3) et les bonnes pratiques cliniques de recherche (ICH GCP[[4]](#footnote-4)).
* Les parties proposées dans ce modèle doivent TOUTES figurer dans votre document final afin de répondre aux requis réglementaires. Si une partie n’est pas utilisée, une justification devra être ajoutée.
* Certains renseignements peuvent également être fournis dans d'autres documents qui doivent être référencés dans le protocole en annexes (brochure d’investigateur, consentement éclairé, contrat de recherche, plan statistique, plan de gestion des risques, plan de monitoring, etc).
* 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.
* Le texte en vert doit être adapté aux spécificités du protocole.
* 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
* Clinical Development phase
* Acronym
* Protocol identification (code or number)
* Name of test drug/investigational product.
* Eu Number = numéro européen d’identification généré lors de la création de l’étude sur le portail CESP (voir guichet central académique)
* Sponsor
* If not apparent from the title, a brief (one to two sentences) description giving design (parallel, cross-over, blinding, randomized) comparison, duration, 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 protocol

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 clinical investigation 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 investigations and the protection of patients.

I will ensure that the requirements relating to Regulatory Authorities and 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 Regulatory Authorities and EC 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 Regulatory Authorities and EC approval, except where necessary to ensure the safety of study participants.

Name Signature Date

Name Signature Date

1. Protocol synopsis

|  |  |
| --- | --- |
| Name of Sponsor/Company: | |
| Name of Device : | |
| Title of Study | |
| Indication | |
| Study centre(s) | |
| Publication (reference) | |
| Studied period (years):  (date of first enrolment)  (date of last completed) | Clinical Phase: |
| Objectives:  - Primary  - Secondary | |
| Hypotheses | |
| Study Design (Treatment Schema) | |
| Number of patients (planned and analysed) | |
| Endpoints :  - Primary  - Secondary | |
| Diagnosis | |
| Main criteria for inclusion (inclusion/exclusion criteria) | |
| Procedures : Schedule of assessments – Study Flowchart | |
| Duration of treatment : | |
| 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](#_Toc117604499)

[2. Signature page 5](#_Toc117604501)

[3. Protocol synopsis 6](#_Toc117604502)

[4. Schedule of activities 7](#_Toc117604503)

[5. List of abbreviations and definitions 10](#_Toc117604504)

[6. Ethics 11](#_Toc117604505)

[7. Identification and description of the investigational device 12](#_Toc117604506)

[8. justification for the design of the clinical investigation 12](#_Toc117604507)

[9. Benefits and risks 12](#_Toc117604508)

[10. Objectives and hypotheses 13](#_Toc117604509)

[11. Design of the clinical investigation 13](#_Toc117604510)

[11.1. General description 13](#_Toc117604511)

[11.2. Study subjects 13](#_Toc117604512)

[11.2.1. Description of population 13](#_Toc117604513)

[11.2.2. Recruitment procedures 14](#_Toc117604514)

[11.2.3. Participants eligibility 14](#_Toc117604515)

[11.2.4. Vulnerable subjects involved (if applicable) 14](#_Toc117604516)

[11.3. Informed consent process 14](#_Toc117604517)

[11.4. Procedures 14](#_Toc117604518)

[11.5. Monitoring plan 15](#_Toc117604519)

[12. Amendments 15](#_Toc117604520)

[13. Deviations from the clinical investigation plan (deviation, violation) 15](#_Toc117604521)

[14. Device accountability 16](#_Toc117604522)

[15. Adverse events, adverse device effects and device deficiencies 16](#_Toc117604523)

[15.1. Definitions 16](#_Toc117604524)

[15.2. Assessing, Recording, and Analyzing Safety Parameters 17](#_Toc117604525)

[15.2.1. Time Period and Frequency for Collecting AE and SAE Information 18](#_Toc117604526)

[15.2.2. Method of Detecting AEs and SAEs 19](#_Toc117604527)

[15.2.3. Follow-up of events 19](#_Toc117604528)

[15.2.4. Regulatory Reporting Requirements for SAEs or SADEs 19](#_Toc117604529)

[15.2.5. Pregnancy 19](#_Toc117604530)

[15.2.6. Laboratory Test Result Abnormalities 20](#_Toc117604531)

[16. Statistical design and analysis 20](#_Toc117604532)

[17. Data management 21](#_Toc117604533)

[17.1. Archiving 21](#_Toc117604534)

[17.2. Data Quality Assurance 21](#_Toc117604535)

[17.3. Data Management Responsibilities 21](#_Toc117604536)

[17.4. Data breach 22](#_Toc117604537)

[18. Finance and Insurance 22](#_Toc117604538)

[19. End, suspension or premature termination of the clinical investigation 23](#_Toc117604539)

[20. Publication policy 23](#_Toc117604540)

[21. Bibliography 23](#_Toc117604541)

[22. Appendix 23](#_Toc117604542)

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 Regulatory Authorities (RA) and/or Ethics Committee (EC) for formal approval to conduct the study. The decision of the RA and/or of the EC concerning the conduct of the study will be made in writing to the sponsor.*
* *The study will be conducted in accordance with legal and regulatory requirements (European Regulatory 2017/745, Belgian law of 22 Decembre 2020, 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 lead 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.*

1. Identification and description of the investigational device

* Brief description of the device.
* Details of the device manufacturer.
* Model or type name or number, including software version and accessories, if any, allowing full identification.
* Description of how to ensure traceability during and after the clinical investigation, e.g., by assigning lot numbers or serial numbers.
* Intended use of the device in the proposed clinical investigation.
* Population and indications for use of the device.
* Detailed description of the device, including all materials that will be in contact with tissue or body fluids. The description should detail all drug substances, human or animal tissues or their derivatives, or other biologically active substances and mention compliance with applicable national regulations.
* Summary of training and experience required for use of the device, taking into account risk assessment.
* Description of the medical or surgical procedures specific to the use of the device.
* References to the investigator's brochure and instructions for use.

The above information should also be provided, where possible, for the comparator where applicable.

1. justification for the design of the clinical investigation

* Assessment of the results of relevant preclinical trials/analyses and prior clinical investigations, if any, conducted to justify the use of the device in human subjects.
* References to literature and data relevant to the clinical investigation and serving as background information for the proposed clinical investigation.

1. Benefits and risks

* Expected adverse effects of the device.
* Risks associated with participation in the clinical investigation.
* Steps taken to control or mitigate the risks.
* Expected clinical benefits.
* Justification of the benefit/risk ratio

1. Objectives and hypotheses

* Purpose of the clinical investigation, statements regarding the clinical performance, efficacy or safety of the device under investigation to be verified.
* Objectives, primary and secondary, described in terms of "superiority", "non-inferiority" or "equivalence", if applicable.
* Scientific rationale and clinical relevance regarding magnitude of effects, margins of non-inferiority or limits of equivalence, if applicable.
* Primary and secondary assumptions, if any.
* Expected risks and adverse effects of the device, which should be evaluated.

The objective(s) should address the purpose of the clinical investigation and should relate to the hypotheses (if any) and corresponding endpoints relevant to the target population. The objectives of the clinical investigation should translate directly into the pre-specification andimplementation of the primary endpoint(s). Statements should be linked to eligibility criteria for the subject and users.

1. Design of the clinical investigation
   1. General description

* Type of clinical investigation to be conducted (e.g., randomized, blinded or open-label, parallel or crossover, multicenter, international), the control group (e.g., comparative statement and reversible treatment of a chronic condition), and the comparator, with rationale and justification for choice.
* Description of the development phases of the device.
* Number of medical devices and comparators (if any) used per subject.
* Follow-up provided and expected duration (total and per subject) of the study. Justification for the duration of follow-up is recommended.
* Details of measures taken to minimize bias
* Definition of the end of the clinical investigation.
  1. Study subjects
     1. Description of population
* Number of expected subjects
* 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
* Representativeness of the study population in relation to the target population
  + 1. Recruitment procedures
* 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
* Estimated time required to recruit the expected number of subjects
  + 1. Participants eligibility
* Inclusion criteria
* Exclusion criteria
* Procedures for withdrawal and/or replacement of subjects, if applicable
  + 1. Vulnerable subjects involved (if applicable)
  + Description of the vulnerable population to be included in the clinical investigation.
  + Description of the screening process to identify and protect vulnerable populations.
  + Description of the specific process for obtaining informed consent.
  + Description of the specific responsibility of the ethics committee.
  + Description of any medical care provided to subjects after the clinical investigation is completed.
  1. Informed consent process
* Procedure for informing the patient, for obtaining informed consent and for protecting vulnerable populations involved, if applicable.

The identity and participation of the subjects in the experimentation, will remain strictly confidential in accordance with the European General Data Protection Regulation of April 27, 2016 (in application since May 25, 2018), the Belgian law of July 30, 2018 on the protection of privacy with regard to the processing of personal data, as well as the law of August 22, 2002 on the rights of patients. 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 experimentation.

* 1. Procedures
* Clinical procedures and diagnostic tests used during the clinical investigation and any deviations from standard clinical practice.
* Activities performed by the sponsor's representatives.
* Any known or foreseeable factors that may compromise the results of the clinical investigation or the interpretation of the results. For example, any comparator or other device or drug used, and therefore any concomitant authorized or prohibited treatments, but also subject factors such as age, sex, lifestyle.
* The methods for considering these factors in the clinical investigation, for example by the choice of subjects, by the design of the clinical investigation (such as stratified randomization) or by the statistical analysis, should be described.
* The follow-up period of the clinical investigation must be adequate to demonstrate clinical performance, efficacy or safety over a period of time sufficient to represent a realistic trial of the device and to allow identification and assessment of the risks associated with any adverse effects of the device.
* The specific and appropriate medical care to be provided to subjects after completion of the clinical investigation, if any.
* Recommended follow-up of subjects after completion of the clinical investigation.

The extent and nature of follow-up activities for the successful completion of the investigation in accordance with the clinical investigation plan should be described and, in accordance with Section 72 of the MDR, should be based on the objective(s), methodology, and degree of deviation of the intervention from normal clinical practice. Overall, the study should be designed to minimize pain, discomfort, fear, and any other possible foreseeable risks to subjects. For this, a rationale in relation to the available preclinical data and the results of the clinical evaluation may be recommended.

* 1. Monitoring plan

Complete the document *AAHRPP-DSQ-023 Monitoring Plan* to plan the site monitoring

Site monitoring is conducted to ensure the human subject protection, study procedures, laboratory, study intervention administration, and data collection processes are of high quality and meet sponsor, GCP/ICH and regulatory guidelines.

General description of site monitoring: who will conduct the monitoring, at what frequency monitoring will be done, and what level of detail monitoring will be conducted.

1. Amendments

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 Regulatory Authorities and Ethic Committee having examined the initial protocol.

The clinical investigation plan must include a description of the procedures for amending the plan.

1. Deviations from the clinical investigation plan (deviation, violation)

* A statement that the investigator is not permitted to deviate from the clinical investigation plan. Except if to protect the rights, safety and well-being of human subjects under emergency circumstances may the investigator deviate without prior approval of the sponsor.
* Procedures for recording, reporting, and analyzing deviations from the clinical investigation plan.
* Reporting requirements and timelines.
* Corrective and preventive actions and criteria for disqualification of the principal investigator.

1. Device accountability

* Description of device accountability procedures.
* Procedures, specific materials and instructions for the safe return of devices under investigation, including potentially hazardous devices.

1. Adverse events, adverse device effects and device deficiencies
   1. Definitions

**ADVERSE EVENT (AE)**

An adverse event is any untoward medical occurrence, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational device.

**SERIOUS ADVERSE EVENT (SAE)**

A serious adverse event means any adverse event that led to any of the following:

* death,
* serious deterioration in the health of the subject, that resulted in any of the following:
  + life-threatening illness or injury,
  + permanent impairment of a body structure or a body function,
  + hospitalisation or prolongation of patient hospitalisation,
  + medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
  + chronic disease,
* foetal distress, foetal death or a congenital physical or mental impairment or birth defect

**adverse device effect (ADE)**

An adverse device effect is an adverse event (ADE) related to the use of an investigational device.

**serious adverse device effect (SADE)**

A serious adverse device effect is an adverse device effect that has resulted in any of the consequence characteristics of a serious adverse event

**device deficiency**

A device deficiency means any inadequacy in the identity, quality, durability, reliability, safety or performance of an investigational device, including malfunction, use errors or inadequacy in information supplied by the manufacturer

**incident**

An incident means any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect.

**serious incident**

A serious incident means any incident that directly or indirectly led, might have led or might lead to any of the following:

* the death of a patient, user or other person,
* the temporary or permanent serious deterioration of a patient's, user's or other person's state of health,
* a serious public health threat.

**serious public health threat**

A serious public health threat is an event which could result in imminent risk of death, serious deterioration in a person's state of health, or serious illness, that may require prompt remedial action, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time

* 1. Assessing, Recording, and Analyzing Safety Parameters

Complete the document *AAHRPP-DOE-023 Risk assessment form* to determine the risk of the trial

* Based on the risk profile of the study product.
* For adverse event reporting, the protocol specifies the adverse events or abnormal laboratory test results that are critical to the safety assessments and that the investigator should report to the sponsor
* For adverse event reporting, the protocol specifies serious adverse events that the investigator does not need to report immediately to the sponsor.
* Describe how decisions will be made regarding determining relatedness and grading severity
* Timelines for reporting by the principal investigator of all adverse events and device defects to the sponsor and, if applicable, to ethics committees and the regulatory authority.
* Details of the adverse event reporting process, including date of event, treatment, resolution, assessment of severity and relationship to the device under investigation, and related procedure.
* Details of the process for reporting device defects.
* List of foreseeable adverse events and expected adverse effects of the device, their likely impact, means of mitigation or treatment.
* Emergency contact information for reporting serious adverse events and serious adverse device reactions.
* **Adapt the text below to the protocol-specific reporting procedures** 
  + 1. Time Period and Frequency for Collecting AE and SAE Information

Adverse events, adverse device effects, device deficiency, incident (serious and non-serious) should be recorded on the CRF from the time the patient signed consent through **last patient visit.** Collect all non-serious adverse events (not only those deemed to be device-related) continuously during the study period.

For all adverse events, sufficient information should be obtained by the investigator to determine the causality, the severity and the seriousness of the adverse event.

The investigator and any qualified designees are responsible for detecting, documenting, and reporting events that meet the definition of an AE or SAE and remain responsible for following up on AEs that are serious, considered related to the study intervention or the study, or that caused the participant to discontinue before completing the study.

All SAEs, SADEs must be collected and require immediate (within 24 hours) notification from the time of signing the consent, including those thought to be associated with protocol-specified procedures, and within xxx days following discontinuation of patient. The investigator must report any SAE, SADEs that occurs after these time periods and that is believed to be related to study intervention or protocol-specified procedure.

In the event that the investigator does not become aware of the occurrence of a SAE, SADE immediately (eg, if an outpatient trial patient initially seeks treatment elsewhere), the investigator is to report the event within 24 hours after learning of it and document the time of his/her first awareness of the adverse event.

For reported death of a subject, whatever the cause could be, the investigator shall supply the sponsor with any additional information requested.

The investigator uses the standard  [Clinical Investigation Summary Safety Report Form](https://ec.europa.eu/health/sites/health/files/md_sector/docs/md_mdcg_2020-10-2_guidance_safety_report_form_en.xlsx?web=1) (see Appendix xxx) to submit the SAE or SADE to the sponsor. The investigator will submit any updated data to the sponsor or designee within 24 hours of updated information being available.

Investigators are not obligated to actively seek AEs, ADEs or SAEs, SADEs in former study participants. However, if the investigator learns of any SAE or SADE, including a death, at any time after a participant has been discharged from the study, and he/she considers the event reasonably related to the study intervention or study participation, the investigator must promptly notify the Sponsor.

* + 1. Method of Detecting AEs and SAEs

AEs, ADEs will be reported by the participant (or, when appropriate, by a caregiver, a surrogate, or the participant’s legally acceptable representative) or by the research team using the device.

AEs, ADEs can be spontaneously reported or elicited during open-ended questioning, examination, or evaluation of a participant. Care should be taken not to introduce bias when collecting AEs, ADEs and/or SAEs, SADEs. Inquiry about specific AEs, ADEs should be guided by clinical judgement in the context of known AEs, ADEs, when appropriate for the program or protocol.

AEs, ADEs including SAEs, SADEs occurring during at home period should be collected during in-clinic visits or during call with participants, and reported as early as possible (In the case of SAE or SADE, within 24 hours of learning of the event).

* + 1. Follow-up of events

Non-serious AEs or ADEs should be followed to resolution or stabilization, or reported as SAEs or SADEs if they become serious.

Follow-up is also required for non-serious AEs or ADEs that cause interruption or discontinuation of study intervention and for those present at the end of study intervention as appropriate.

* + 1. Regulatory Reporting Requirements for SAEs or SADEs

Prompt notification by the investigator to the Sponsor of SAEs or SADEs is essential so that legal obligations and ethical responsibilities toward the safety of participants and the safety of a product under clinical investigation are met.

An investigator who receives an investigator safety report describing SAEs or SADEs or other specific safety information (eg, summary or listing of SAEs) from the Sponsor will file it along with the Investigator’s Brochure.

The Sponsor or designee must report SAEs and SADEs to regulatory authorities (FAMHP) via the Clinical Investigation Summary Safety Report Form and sent to the R&D division of the FAMHP, either by e-mail to [ct.rd@fagg-afmps.be](mailto:ct.rd@fagg-afmps.be) or via the CESP, as desired.

* + 1. Pregnancy

If, following initiation of the study intervention, it is subsequently discovered that a participant is pregnant or may have been pregnant at the time of study exposure, including during at least for xx months after study product administration, the investigator must immediately notify the sponsor.

Follow-up information regarding the course of the pregnancy, including perinatal and neonatal outcome and, where applicable, offspring information, must be reported au sponsor. Protocol-required procedures for study discontinuation and follow-up must be performed on the participant.

* + 1. Laboratory Test Result Abnormalities

The following laboratory test result abnormalities should be captured on the CRF :

* Any laboratory test result that is clinically significant or meets the definition of an SAE
* Any laboratory test result abnormality that required the participant to have study intervention discontinued or interrupted
* Any laboratory test result abnormality that required the participant to receive specific corrective therapy

It is expected that, wherever possible, the clinical rather than laboratory term would be used by the reporting investigator (eg, anemia vs low hemoglobin value).

1. Statistical design and analysis

Use the document AAHRPP-DSQ-020 Statistical Analysis Plan (guideline) to complete this section

The description and justification of the statistical model and analysis of the clinical investigation should cover the following

* Analysis population (e.g., intention-to-treat [ITT], per-protocol [PP], and actual treatment [AT] analysis) and procedures considering the data set.
* Descriptive statistics of baseline, treatment, safety data, and, where appropriate, primary and secondary endpoints.
* Analytical procedures including measures of precision, such as confidence intervals, where appropriate.
* Significance and power of primary endpoint(s) and, if applicable, overall statistical verification strategy.
* Sample size calculation and justification considering:
* all relevant clinical data on the outcome variable and effect size, if applicable;
* expected outcome assumptions in treatment groups, if any;
* adjustments due to pre-planned interim analyses, if any
* the magnitude of detectable effects and the non-inferiority margin, which should be less than the magnitude of detectable effects and justified relative to the comparator effect, if applicable
* the allocation ratio used for randomization (e.g., 1:1, 1:2), if applicable
* the expected dropout rate, such as withdrawal, loss of sight, death (unless death is an endpoint).
* All statistical parameters and methods used to calculate the sample size or non-inferiority margin should be clearly stated.
* Exploratory and sensitivity analysis (e.g., to test the robustness of the results of the primary and secondary analyses to the different methods used to deal with missing data), if applicable.
* Procedures for reporting deviations from the original statistical analysis plan.
* In the case of multicenter clinical investigations, a strategy for managing potential imbalances in enrollment at different investigative sites.
* Strategy for pooling data, if appropriate.

1. Data management

* Methods for data entry and collection.

In accordance with Article 72 of the MDR, all information related to the clinical investigation must be recorded, processed, handled and stored by the sponsor or investigator, as the case may be, in such a way that it can be accurately reported, interpreted and verified, while preserving the confidentiality of the recordings and of the personal data of the subjects, in accordance with the applicable legislation on personal data protection. In addition, appropriate technical and organizational measures must be in place to protect the processed information and personal data from unauthorized or unlawful access, disclosure, dissemination, alteration or destruction, or accidental loss, especially when the processing involves transmission over a network.

* 1. Archiving
* Describe the methods for archiving the data (CRF, Informed Consent, Source document,…) N.B. according to Belgian law: data to be kept for a minimum of 20 years after the study is stopped: AR of 18 May 2006 article 24.
  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

Complete the document *AAHRPP-DSQ-021 Data Management Plan*

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 regulatory authorities and ethics committee serious data breaches : transgressions against the  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 [clinical tria](https://www.ema.europa.eu/en/glossary/clinical-trial)l.

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, suspension or premature termination of the clinical investigation

* 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 clinical investigation and a justification for this
* A description of the criteria for stopping parts or all of the clinical investigation
* Criteria and provisions for premature termination or suspension of the clinical investigation for the entire investigation or for one or more sites.
* Requirements for subject follow-up and continuing care, after termination or temporary suspension of the investigation, for follow-up of subjects who have withdrawn consent and for subjects who have been lost to follow-up.
* In addition, it should be clear in the clinical investigation plan that the competent authority will be informed of the end of the clinical investigation, and that a rationale will be provided in the event of temporary or early termination of the study.

1. Publication policy

This clinical investigation is registered on EU Clinical Trials Register (<https://www.clinicaltrialsregister.eu/ctr-search/search> ) and is available to the public.

The final report will be published on CUSL website (<https://www.saintluc.be/index.php/fr/recherche-clinique-etudes-academiques> ) one year after the end of the study.

Statement indicating the conditions and time frame under which the results of the clinical investigation will be published, including the role of the sponsor and the criteria for authorship.

1. Bibliography

List of bibliographic references related to the clinical investigation

1. Appendix

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

1. [AFMPS/FAMHP](https://www.afmps.be/fr/humain/produits_de_sante/dispositifs_medicaux/evaluation_clinique/etudes_a_notifier) Clinical investigations – Guidance on Dossier Content [↑](#footnote-ref-1)
2. [RÈGLEMENT (UE) 2017/745 DU PARLEMENT EUROPÉEN ET DU CONSEIL du 5 avril 2017 relatif aux dispositifs médicaux](https://eur-lex.europa.eu/legal-content/FR/TXT/HTML/?uri=CELEX:32017R0745&from=EN) [↑](#footnote-ref-2)
3. Norme internationale ISO 14155 : 2020 (F) [↑](#footnote-ref-3)
4. [ICH GCP E6 (R2) Guide de bonnes pratiques cliniques](https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf) [↑](#footnote-ref-4)