Deze template dient enkel te worden gebruikt voor prospectieve interventionele studies met producten die geen IMP zijn of MD studies die onder de MDR art 82 vallen ("EC only" of "Separate opinion FAGG and EC"). Indien de studie valt onder art 62 van de Medical Device Regulation verwijzen we u naar de CIP-template. Indien de studie valt onder de EU Clinical Trial Regulation No 536/2014 (CTR) verwijzen we u naar de 'Protocol Template Interventional study with IMP_CTR'.

Begeleidende tips voor gebruik van deze template

- Deze template dient als startpunt voor het uitschrijven van een studieprotocol. De secties die hierin worden opgesomd kunnen aangepast of verder aangevuld worden naargelang de vereisten voor de studie.
- Tekst in het blauw dient als voorbeeldtekst. U kan de tekst aanpassen of verder aanvullen naargelang de vereisten voor de studie.
- Tekst in een kader geeft toelichting bij de inhoud van enkele secties. Deze kaders moeten verwijderd worden bij het uitschrijven van het protocol.

Study Protocol

Study Title:
Study Acronym:
Protocol Version and Date:
Registry Number:
Investigational Product or Medical Device:
Sponsor:
Coordinating/Principal Investigator:

PROTOCOL SIGNATURE PAGE

I agree:

- to assume responsibility for the proper conduct of this study
- to conduct the study in compliance with this protocol and any future amendments
- not to implement any deviations from or changes to the protocol without prior review and written approval from the Ethics Committee, except where necessary to eliminate an immediate hazard to the subjects, or for administrative aspects of the study (where permitted by all applicable regulatory requirements)
- that I am thoroughly familiar with the appropriate use of the investigational drug/medical device, as described in this protocol
- to ensure that all persons assisting me with the study are adequately informed about the investigational drug/medical device and their study-related duties and functions as described in the protocol
- that I am aware of and will comply with the current good clinical practice (GCP) guidelines and ethical principles outlined in the Declaration of Helsinki
- to conduct the study in accordance with all applicable laws and regulations

Printed name _____ Signature _____ Date _____

Table of Contents

1 Sponsor/Coordinating Investigator Information

Sponsor:
Principal Investigator:
Subinvestigator(s):
Coordinating Investigator *if applicable*:
Statistician :
Laboratory(ies) *if applicable*:
Pharmacy *if applicable*:
Study Coordinator:
Study site(s) and co-investigator(s) *if applicable*:

2 List of Abbreviations

3 Protocol Version History

Version N°	Version Date	Summary of changes

4 Trial Registration/Protocol Summary

Information	
Objectives:	
Study population:	
In- and exclusion crite-ria:	
Factors of interest / Data to be collected:	
Endpoints:	
Target sample size:	
Statistical considera-tions:	

5 Background and Rationale

Licht bondig de achtergrond en wetenschappelijke relevantie van het geplande onderzoek toe. De lezer dient voldoende inzicht te krijgen in het onderzoeksdomein van dit project. Beschrijf de motivatie om dit onderzoek uit te voeren en licht het doel van het onderzoek toe.

5.1 Overview of Disease Pathogenesis with Relevant Literature

5.2 Epidemiology

5.3 Current Treatments

5.4 Study Rationale

5.5 Rationale for Study Design

5.6 Rationale for Dose and Regimen

6 Study Objectives and Endpoints

Licht bondig de doelstellingen en eindpunten (kwantitatieve metingen die door de doelstellingen worden vereist) van het onderzoek toe. Beschrijf duidelijk de onderzoeksvragen en/of onderzoekshypothesen.

6.1 Primary Objectives

6.2 Secondary Objectives

6.3 Endpoints

7 Research Methods

Licht bondig het onderzoeksdesign en de rationale hiervoor toe. Licht toe hoe de toewijzing van een studiedeelnemer aan een groep gebeurt in geval van randomisatie.

7.1 Study Design

7.2 Study Population

7.2.1 Inclusion Criteria

7.2.2 Exclusion Criteria

7.2.3 Contraception / Pregnancy Avoidance Measures

7.3 Study Duration for Subjects

7.4 Group Allocation & Blinding *(if applicable)*

8 Study Assessments and Procedures

Geef een overzicht van de procedures per visite weer in een tabel. Ter aanvulling kan een schematisch diagram toegevoegd worden. Geef gedetailleerd weer welke data zullen worden gecollecteerd en geef daarbij aan of deze studie-specifiek zijn of deel uitmaken van de standaardzorg. De paragrafen 8.3.1 t/m 8.3.5 hieronder zijn voorbeelden.

8.1 Schedule of Activities

8.2 Study Assessments/Interventions per Visit

8.2.1 Screening

8.2.2 Treatment Period

8.2.3 Follow Up Period

8.2.4 End of Study Visit

8.3 Detailed Study Assessments

8.3.1 Physical Examination

8.3.2 Vitals Signs

8.3.3 Laboratory Testings

8.3.4 Efficacy Assessments

8.3.5 Safety Assessments

9 Interventions/Treatment

9.1 Treatments Administered

9.2 Product/Device Characteristics

9.3 Storage, Packaging and Labelling

9.4 Dosing Regimen

9.4.1 Dose Administration

9.4.2 Dose Modifications and Dose Delay

9.4.3 Treatment Interruption and Treatment Discontinuation

9.5 Treatment Compliance & Accountability

9.6 Blinding & Unblinding Procedures

10 Data Collection and Management

Beschrijf hoe de data zullen worden verzameld, gecontroleerd op kwaliteit en verwerkt voor de studieanalyse. Motiveer de keuze van de steekproefgrootte (sample size).

10.1 Monitoring

The investigator must make all trial documentation and related records available in case a monitoring visit or audit by the Sponsor is requested. Also in case of regulatory inspections all trial documentation should be made available to the inspector(s). All participant data must be handled and treated confidentially.
The Sponsor's monitoring frequency will be determined prior to the start of the trial. A monitoring plan will be generated detailing the frequency and scope of monitoring for the trial. Throughout the course of the trial the monitoring plan can be adjusted as necessary.

10.1.1 Composition of a Data Monitoring Committee (if applicable)

10.2 Data Collection

An Electronic Data Capture system "***add name of the system in the text***" will be used for data collection. The system is validated and access to all levels will be granted/revoked by the Sponsor representative. Trial data should be entered within reasonable time after the subject attended the visit. Corrections/modifications will be automatically tracked by an audit trail detailing date and time of the correction and the name of person performing the correction.

10.3 Database Management and Quality Control

10.4 Statistical Considerations and Data Analysis

Geef een uitleg over de gebruikte methode (procedure) en/of data-analyse strategie in relatie tot de gestelde onderzoekshypothesen. Leg mogelijke ethische implicaties van de geplande methodologie uit.

11 Safety Monitoring and Reporting

Geef de definitie van een AE en een SAE volgens de GCP-richtlijnen. Geef aan hoe deze AE's en SAE's zullen verzameld, nagekeken en gerapporteerd worden alsook de periode van collectie voor iedere studiedeelnemer. Indien van toepassing kunnen instructies meegegeven worden voor de opvolging van specifieke, reeds gekende nevenwerkingen.

11.1 Adverse Events

11.1.1 Definitions

For IMP studies: An adverse event is any untoward medical occurrence in a patient or clinical investigation subject participating in a clinical trial. It includes any unfavourable and unintended sign, symptom or disease temporally associated with the trial procedures, whether or not considered to be related to the trial procedures.

For Medical Device studies: 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.
Note:

a) This definition includes events that are anticipated as well as unanticipated events
b) This definition includes events occurring in the context of a clinical investigation related to the investigational device, the comparator or the procedures involved

11.1.2 Reporting

11.1.3 Laboratory Test Abnormalities

11.2 Serious Adverse Events

11.2.1 Definitions

For IMP studies: Any untoward medical occurrence that at any dose:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity,
- Is a congenital anomaly/birth defect

Or

- other important medical condition (ICH 2EA)

For Medical Device studies: Any adverse event that led to any of the following:

a) Death,
b) 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,
   - Hospitalization or prolongation of patient hospitalization,
   - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment of a body structure or a body function,
   - Chronic disease
c) Foetal distress, foetal death or a congenital physical or mental impairment or birth defect.

Medical and scientific judgement should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition above. These should also be considered serious.

11.2.2 Immediate Reporting

11.3 Suspected Unexpected Serious Adverse Reactions (SUSAR)

11.3.1 Definitions

An adverse reaction is any untoward medical occurrence in a patient or clinical investigation subject participating in a clinical trial including any abnormal sign, symptom, or disease temporally associated with the participant's involvement in the research, whether or not considered to be related to the research.

Serious if:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity,
- Is a congenital anomaly/birth defect

Or

- Other important medical condition (ICH 2EA)

Medical and scientific judgement should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition above. These should also be considered serious.

11.3.2 Immediate Reporting

11.4 Device Deficiencies

11.4.1 Definitions

Any inadequacy in the identity, quality, durability, reliability, safety or performance of an investigational device, including malfunction, user errors or inadequacy in information supplied by the manufacturer.

11.4.2 Immediate Reporting

11.5 Procedures for Handling Special Situations

11.5.1 Overdose Management

11.5.2 Pregnancy

11.6 Annual Safety Report

12 Ethical Considerations

12.1 Ethical Conduct of the Study

12.1.1 Declaration of Helsinki

The trial will be performed in accordance with the Declaration of Helsinki, the conditions and principles of Good Clinical Practice, the protocol and applicable local regulatory requirements and laws.

12.1.2 Ethics Committee

Before the start of the trial or implementation of any amendment, approval of the trial protocol and amendments, informed consent forms and other relevant documents will be obtained from the applicable ethical committee(s).

12.2 Informed Consent

Each participant shall provide Informed Consent before performance of any study-related activities. The IC form that is/are used must be approved by reviewing EC and be in a language that the participant can read and understand. The ICF should be in accordance with current ICH and GCP guidelines and with applicable local regulations.

12.3 Study Data Protection

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

12.4 Subject Identification

The participant identification will be treated as confidential and will be filed by the investigator in an identification log. This log is kept at the participating site and shall not be copied. In all reports and communication between the site and the Sponsor the participant shall be identified with a participant study number.

13 Insurance

UZ Brussel/VUB is, as Sponsor of the trial, responsible for ensuring appropriate general/product liability insurance and as required in accordance with applicable laws and regulations, country-specific liability insurance coverage for claims made by a trial subjects for injury arising from the subject's participation in the trial.

14 Reporting and Dissemination

The data and information collected during this trial will be reported in a clinical trial report and/or a publication in a scientific/medical journal. Reporting of trial results will be performed according to local regulations.

Data collected within the UZ Brussel or VUB as an employee or (PhD) student of the VUB are owned by the UZ Brussel VUB. For the correct authorship rules we refer to the International Committee of Medical Journal Editors:
https://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html

15 Finance and Conflict of Interest Statement

Investigators and study team members will provide the Sponsor with sufficient, accurate financial information in accordance with local regulations to allow the Sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities/ethics committee. Any update of information on financial interests should be disclosed during the course of the study.

16 Tables and Figures

17 References