**APPENDIX.4**

**Clinical Trial**

**Appendix I -** Protocol Template for IST (**I**nvestigator **S**ponsored **T**rial)

**PREFACE TO THIS PROTOCOL TEMPLATE**

***What is the Protocol template structure?***

This protocol template is based on the Standards of the International Council for Harmonization’s E6 (Revision 2) “Good Clinical Practice” (ICH-E6 GCP), Section 6 (Clinical trial protocol and protocol amendment (s)).

***How To Use This Template?***

The content of a trial protocol should generally include all the sections as listed in the protocol template. It is important to incorporate all sections of the template into your protocol and to do so in the same order. If a particular section is not applicable to your trial, please retain it, but indicate that it is not applicable by writing “N/A” under the section heading.

Version control is important to track protocol development, revisions, and amendments. It is also necessary to ensure that the most recently updated and IRB approved version of a protocol is used by all staff conducting the study. **With each revision, the version number and date located in the header of each page should be updated**. When making changes to an approved and “final” protocol, the protocol amendment history should be maintained.

Site specific information may be provided on separate protocol page(s), or addressed in a separate agreement, and some of the information listed below may be contained in other protocol referenced documents, such as an Investigator’s Brochure.

*Instructions are provided in Orange Italic*. Please ensure to delete them in your final version.

**<Title>**

*This title should include, where possible, information on the participants, condition being evaluated, and intervention(s) studied.*

**Protocol Number: <Number>**

**Protocol Acronym: <Acronym>**

**National Clinical Trial (NCT) Identified Number: <Number, once assigned by CT.gov>**

**Principal Investigator:** **<Principal investigator>**

**Sponsor: <Sponsor name, if applicable>**

*“Sponsor” indicates an institution, foundation, or individual who takes responsibility for and initiates a clinical investigation; often times this is the university with which the Principal Investigator is affiliated.*

**Grant Title: <Grant Title>**

**Funded by: <QNRF, IRF, sponsor…>**

**Clinical Trial Protocol Version, Date: v.<x.x>, <DD Month YYYY>**

*All versions should have a version number and a date. Use an international date format (e.g., 20 April 2020).*

*For the initial submission of a protocol to the IRB, indicate “Not applicable; this is the first version of the protocol.” For any subsequent amendment being submitted to the IRB, add details of the specific changes that are being implemented in the amendment.*

**Confidentiality Statement**

This document is confidential and is to be distributed for review only to investigators, potential investigators, consultants, study staff, and applicable independent ethics committees or institutional review boards. The contents of this document shall not be disclosed to others without written authorization from Sidra Medicine.

**INVESTIGATOR’S SIGNATURE**

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study shall be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable to Qatar regulations and ICH guidelines, as described in the Confidentiality statement above.

Principal Investigator or Clinical Site Investigator:

|  |  |  |  |
| --- | --- | --- | --- |
| Signed: |  | Date: |  |
|  | Name: | | |
|  | Title: | | |

Investigator Contact Information  
Affiliation:

Address:

Telephone:

Email:

*[For multi-site studies, the protocol should be signed by the clinical site investigator who is responsible for the day to day study implementation at his/her specific clinical site.]*

|  |  |  |  |
| --- | --- | --- | --- |
| Signed: |  | Date: |  |
|  | Name: | | |
|  | Title: | | |
|  | Affiliation: | | |

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**List of Abbreviations**

*All abbreviations used throughout the protocol must be defined, please add or delete as appropriate.*

|  |  |
| --- | --- |
| **AE** | Adverse Event |
| **CRF** | Case Report Form |
| **DSMB** | Data Safety Monitoring Board |
| **DSMP** | Data Safety Monitoring Plan |
| **GCP** | Good Clinical Practice |
| **EDC** | Electronic Data Capture |
| **ICF** | Informed Consent Form |
| **IP** | Investigational Product |
| **IRB** | Institutional Review Board |
| **ITT** | Intention to treat |
| **MOPH** | Ministry of Public Health |
| **PHI** | Protected Health Information |
| **PI** | Principal Investigator |
| **REDCap** | Research Electronic Data Capture |
| **SAE** | Serious Adverse Event |
| **SUSAR** | Suspected Unexpected Serious Adverse Reaction |
| **TMG** | Trial Management Group |
| **TSC** | Trial Steering Committee |
| **UP** | Unanticipated Problem |

**Clinical Trial Synopsis**

**\* Study General information**

**Full Title:** *Enter the full title*

**Protocol Number:***Enter Protocol number*

**Clinical Phase:** *I, II, III, or IV*

**Principal Investigator (PI) name:** *Enter**Name of PI*

**PI phone #:** *Enter**PI contact details*

**PI email address:** *Enter**PI email address*

**PI department:** *Enter PI department*

**\* Study Rationale:** *Brief explanation for rationale for design*

**\* Study Objectives**

**Primary Objective:** *Include primary outcome measures and method by which outcomes shall be determined.*

**Secondary Objectives:** *Include secondary outcome measures and method by which outcomes shall be determined.*

**\* Study Criteria**

**Inclusion Criteria** *Enter inclusion criteria*

**Exclusion Criteria** *Enter exclusion criteria*

**\* Study Population**

**Study Population:** *Include a brief description such as health status (e.g., healthy volunteers or HIV-positive), gender, age, etc.*

**Sample Size:** *N=* *(If more than one cohort also indicate sample size per cohort)*

**Accrual Ceiling:** *Include sample size plus an estimate for screening failures. (Ex. This study shall enroll 50 subjects and screen up to 100 subjects).*

**\* Study Duration**

**Study Duration:** *Provide the total length of time participants shall be on study (intervention + follow-up), include a projected end date.*

**Accrual Period:** *Length of time to completely enroll the study.*

**\* Study Design** *Provide an overview of the study design, including description of study type (e.g., double-blind, placebo-controlled, open label, dose-finding, randomized), study arms, sample size and schedule of interventions (e.g., vaccine administration*

**\* Study Agent/**

**Intervention Description** *Include name, dose, duration frequency, and route of administration, if applicable*

**\* Efficacy** *Explain how efficacy shall be measured*

**\* Safety** *Specific safety concerns, general plan for monitoring safety, and reporting events*

1. **General Information**

*This section should provide general information of the clinical trial.*

* 1. **Protocol information**

*Please provide information on the protocol title, protocol identifying number, acronym and date. Any amendment(s) should also bear the amendment number(s) and date(s).*

* 1. **Sponsor and monitor details**

*Please provide information including name and address of the sponsor and monitor (if other than the sponsor).*

* 1. **Protocol signing details**

*Please provide information including name and title of the person(s) authorized to sign the protocol and the protocol amendment(s) for the sponsor.*

* 1. **Sponsor's medical expert details**

*Please provide information including name, title, address, and telephone number(s) of the sponsor's medical expert (or dentist when appropriate) for the trial.*

* 1. **Investigators details**

*Please provide information including name and title of the investigator(s) who is (are) responsible for conducting the trial, and the address and telephone number(s) of the trial site(s).*

* 1. **Physician details**

*Please provide information including name, title, address, and telephone number(s) of the qualified physician (or dentist, if applicable), who is responsible for all trial-site related medical (or dental) decisions (if other than investigator.*

* 1. **Other departments details (if applicable)**

*Please provide information including name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.*

1. **Background Information**

*This section should give background and details about previous research with disease and investigational product(s), device(s) or procedure(s).*

* 1. **Background information**

*Please provide background information on the disease being researched.*

* 1. **Name and description of the investigational product(s) or device, or procedure used (as applicable)**

*Please provide background information on the investigational study product, or device including the mechanism of action, summaries of nonclinical and clinical studies, nonclinical and clinical pharmacokinetics, major route of elimination, safety profile, and the rationale for the starting dose and regimen chosen. Please include information on the metabolism of the investigational study product in humans and its potential for product interactions, if available. For medical devices, provide a description of each important component, ingredient or element, property, and principle of operation of the medical device. Describe, if applicable, any anticipated change(s) in the medical device during the course of the clinical study. If no changes to the device are anticipated, state this.*

*For the procedure, please provide background information on the procedure used, including summary from previous studies, information and any important previous studies findings or details.*

* 1. **Summary of findings from nonclinical studies**

*Please provide a summary of findings from nonclinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.*

* 1. **Summary of the known and potential risks and benefits, if any, to human subjects.**

*Please discuss why the risks to subjects, if any, are reasonable in relation to the anticipated benefits and/or knowledge that might reasonably be expected from the results.*

* 1. **Background for Investigational Product (IP), device or procedure**

*Please provide information including description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).*

* 1. **Compliance**

*Please provide a statement that the trial shall be conducted in compliance with the protocol, GCP and the applicable regulatory requirement(s). An example is provided below.*

The clinical investigation shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

The clinical investigation shall comply with the relevant national regulations in Qatar (MOPH) and shall not begin until required approvals from ethical committee (IRB) have been obtained. Additional requirements imposed by the ethical committees shall be followed. The clinical investigation shall be conducted in accordance with this protocol.

* 1. **Study Population**

*Please provide a description of the population to be studied.*

* 1. **Literature**

*Please include references to literature and data that are relevant to the trial.*

* 1. **Correlative Studies Background**

*Please provide background information on each planned correlative study including the biologic rationale and hypothesis as well as the relevant preclinical and clinical (if available) data. If this trial includes no correlative studies, this section should be deleted.*

1. **Trial Objectives and Purpose**

*This section should present a detailed description of the objectives and the purpose of the trial and describe the specific aims for the study.*

* 1. **Primary Objectives**

*Please insert primary protocol objectives.*

*Example (Ex.): To assess the efficacy of XXXX, in subjects with XXX disease.*

* 1. **Secondary Objectives**

*Please insert secondary protocol objectives.*

*Ex. To assess the safety of XXXX, in subjects with XXX disease.*

* 1. **Exploratory Objectives**

*Please insert any exploratory objectives, if applicable*

*Ex. To assess the exploratory safety of XXXX, in subjects with XXX disease.*

1. **Trial Design**

*This section should present the scientific integrity of the trial and the credibility of the data from the trial depend substantially on the trial design. A description of the trial design, should include:*

* 1. **Endpoints**

*Please provide a specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.*

*“Ex.:*

*Co-primary endpoints:*

* *Reduction in weight of 15 kg (assumed equal on average to 15 %) or more at one year.*
* *Remission of diabetes (HbA1c <48 mmol/mol) at 1 year.*

*Secondary endpoints:*

* *Quality of life*
* *Physical Activity*
* *Serum Lipids, Liver function tests, Urea & Electrolytes, plasma glucose*
* *Programme acceptability”.*
  1. **Study Design**

*Please provide a description of the type/design of trial to be conducted (e.g. double-blind, placebo-controlled, parallel design) and a schematic diagram of the study design, procedures, and stages.*

*This section should provide a visit-by-visit listing of all the procedures that shall take place at each visit. If the study shall have multiple procedures in one day (e.g. blood draws for a PK study) then the timing of each of these should be included.*

*If subjects are being randomized, please be sure to include the randomization instructions/procedures.*

*Ex. “Eligible subjects shall be randomly assigned to XXXX or placebo treatment groups in a 1:1 ratio using a computer-generated randomization scheme developed by the data manager”.*

* + 1. Schedule of Evaluations (diagram, flowchart or table)

*Please create a schedule of study-related events diagram/flowchart/table (if applicable) that outlines the activities and procedures to be followed at each visit. A sample diagram and a sample table are provided below and should be altered per study requirements.*

*It should be provided a description of the type/design of trial to be conducted (e.g., double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.*

*An example is provided below*.

*Example 1: Diagram A, study overview.*

**Screening**

All maternal admissions 23- 32+6 weeks GA (Gestational Age)

LDR/PSCU

**Exclusion**

• Congenital anomalies

• Major cardiac defects

• Placenta abruption or previa, hemorrhage

*Note: Partial abruptions are not excluded*

• Monochorionic twins

• Cord prolapse

• Hydrops

• Bleeding Accreta

• Fetal or maternal risk (i.e. compromise)

• Parents declined study

• Unlikely to return for 2 yr FU

**Inclusion**

• Delivered 230 - 326 weeks GA

• No known major congenital

anomalies

• Multiples (unless mono- chorionic) randomized to same group

• Antenatal consent

**2 Year FU**

**Data Collection**

Through Discharge

**Randomize**

At Delivery

**ARM 1**

**N=600**

**ARM 2**

**N=600**

**Total N=1200**

GA 23 – 32+6)

*Example 2: Table B, study procedures.*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Pre-Study | Wk  1 | Wk  2 | Wk  3 | Wk  4 | Wk  5 | Wk  6 | Wk  7 | Wk  8 | Wk  9 | Wk  10 | Wk  11 | Wk  12 | Off Study |
| *Product Administration* |  | X |  | X |  | X |  | X |  | X |  | X |  |  |
| Informed consent | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Demographics | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Medical history | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Concomitant meds | X | X----------------------------------------------------------------------------------------------X | | | | | | | | | | | |  |
| Physical exam | X | X |  | X |  | X |  | X |  | X |  | X |  | X |
| Vital signs | X | X |  | X |  | X |  | X |  | X |  | X |  | X |
| Height | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Weight | X | X |  | X |  | X |  | X |  | X |  | X |  | X |
| CBC w/diff, platelets | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Serum chemistrya | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| EKG (as indicated) | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Adverse event evaluation |  | X --------------------------------------------------------------------------------------------X | | | | | | | | | | | | X |
| Outcome Evaluation | X | i.e., Tumor measurements are repeated every *[# weeks]* weeks. Documentation (radiologic) must be provided for patients removed from study for progressive disease; Sustained virological response (SVR) [ Time Frame: 24 months ] | | | | | | | | | | | | Xc |
| Radiologic evaluation | X | Radiologic measurements should be performed every *[# weeks]* weeks. | | | | | | | | | | | | Xc |
| B-HCG | X |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Other tests, as appropriate |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Other correlative studies |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| a: *Albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, LDH, phosphorus, potassium, total protein, SGOT[AST], SGPT[ALT], sodium.*  *b: Serum pregnancy test (women of childbearing potential).*  *c: Off-study evaluation.* | | | | | | | | | | | | | | |

* + 1. Screening Visit

*Please provide a list in bulleted form of all screening procedures. An example is provided below.*

*Ex. “Screening procedures:*

* *Informed consent*
* *Medical history*
* *Medication history*
* *Physical exam”*
  + 1. Treatment Phase

*Please provide a list in bulleted points of all the necessary study procedures performed in every visit, as applicable. Examples are presented below.*

*Visit 1 (baseline/randomization)*

* *Randomization*
* *Medical history*
* *Medication history*
* *Physical exam*
* *Vital signs*
* *Concomitant medication*
* *Adverse Events...”*

*Visit 2/3/4... (± X day(s))*

* *Medication history*
* *Physical exam*
* *Vital signs*
* *Concomitant medication*
* *Adverse Events”*
  + 1. General Concomitant Medication and Supportive Care Guidelines

*Please state guidelines for use of concomitant medications or any additional appropriate supportive care medications or treatments. Include a discussion of known and possible risks associated with concomitant use. Include medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.*

*Whenever a concomitant medication or study product is initiated or the dose changed, investigators must review the concomitant medications’ and study products’ most recent package inserts, investigator's brochure, as well as updated information from protocol to obtain the most current information on drug interactions, contraindications, and precautions.*

*Ex: “Provide a list of selected concomitant medications or reference where the complete list can be viewed.”*

* 1. **Measures**

*Please include a description of the measures taken to minimize/avoid bias, including:*

*(a) Randomization.*

*(b) Blinding.*

*If subjects are being randomized, please be sure to included randomization instructions/procedures.*

*Ex. “Eligible subjects shall be randomly assigned to XXXX or placebo treatment groups in a 1:1 ratio using a computer-generated randomization scheme developed by the data manager. “*

* 1. **Study treatment**

*Please provide a description of the trial treatment(s) or device(s) or procedure(s), and the dosage and dosage regimen of the investigational product(s), device (s), or procedure (s). Also include a description of the dosage form, packaging, and labelling of the investigational product(s) or device(s).*

*Ex.: “Treatment shall be administered on an inpatient/outpatient basis. Reported adverse events and potential risks are described in Section 8. Appropriate dose modifications for Investigational product are described in Section 6”.*

* 1. **Study duration**

*Please provide the expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.*

*In this section, please describe the duration of study therapy.*

*Ex.: “In the absence of treatment delays due to adverse event(s), treatment may continue for (# cycles) or until one of the following criteria applies:*

* *Disease progression,*
* *Intercurrent illness that prevents further administration of treatment,*
* *Unacceptable adverse event(s),*
* *Patient decides to withdraw from the study, or*
* *General or specific changes in the patient’s condition render the patient unacceptable for further treatment in the judgment of the investigator”.*
  + 1. Duration of Follow Up

*Please describe the duration of study follow up.*

*Ex: “Patients shall be followed for #weeks/months/years after removal from study or until death, whichever occurs first. Patients removed from study for unacceptable adverse events shall be followed until resolution or stabilization of the adverse event”.*

* 1. **Subject discontinuation**

*Please provide a description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial. Please provide reasons for discontinuation from therapy.*

* 1. **Accountability for IP**

*Please provide the accountability procedures for the investigational product(s), device(s) or procedure(s) including the placebo(s) and comparator(s), if any.*

*The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product(s). These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product(s) and trial subjects. Investigators should maintain records that document adequately that* *the subjects were provided the doses specified by the protocol and reconcile all investigational product(s) or device(s) received from the sponsor.”*

* 1. **Randomization codes**

*Provide the maintenance of trial treatment randomization codes and procedures for breaking codes if applicable.*

*A study in which a number of similar subjects are randomly assigned to 2 (or more) groups to test a specific drug, treatment or other intervention is classified as randomized controlled trial. One group (the experimental group) has the intervention being tested, the other (the comparison or control group) has an alternative intervention, a dummy intervention (placebo) or no intervention at all.*

*Randomization as a method of experimental control has been extensively used in human clinical trials and other biological experiments. It prevents the selection bias and insures against the accidental bias. It produces the comparable groups and eliminates the source of bias in treatment assignments. Finally, it permits the use of probability theory to express the likelihood of chance as a source for the difference of end outcome. The groups are followed up to see how effective the experimental intervention was.*

* 1. **Source data**

*Provide the identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered to be source data.*

*Study data must be initially captured using one or more of the following methods: on paper source documents, in electronic medical records or other electronic databases (e.g., central laboratory database), and/or in Electronic Data Capture (EDC) systems. Please note that GCP requires that the protocol describes instances when the EDC acts as the source document.*

* 1. **Trial Committees (as applicable)**

*Please describe the committee that have oversight on the trial, as applicable.*

* + 1. Trial Management Group (TMG)

*Please provide a description of the TMG shall be detailed including all the information, responsibilities and guidelines. An example is provided below*.

Trial Management Group (TMG) shall consist of the PI, Co-Investigators, trial coordinator, research nurse, recruiting physicians and pharmacy representative and statistician *(please add or remove as applicable)*. TMG shall hold weekly meetings commencing two months prior to the commencement of the trial, which shall continue until recruitment and data analysis is completed. TMG meetings shall be chaired by the PI and minutes shall be recorded and maintained as part of trial documentation. TMG meetings shall discuss the week by week progress of the trial, with the aim of early identification of any risk to the trial or subjects, and shall also review and report any adverse events to the Trial Steering Committee (TSC) and Data Safety Monitoring Board (DSMB).

* + 1. Trial Steering Committee (TSC)

*Please provide a description of the TSC shall be detailed including all the information, responsibilities and guidelines. An example is provided below*.

TSC shall consist of (*number of) XX* Physicians with experience in leading clinical trials, who shall be independent of the Investigating team, employing departments and the funding body. TSC shall monitor trial progress and conduct every month, starting from two months before the commencement of the trial until recruitment and data analysis completed. and provide advice on scientific credibility. The TSC shall consider and act, as appropriate, upon the recommendations of the Data Safety Monitoring Board (DSMB) or equivalent, and ultimately carries the responsibility for deciding whether a trial needs to be stopped on grounds of safety or efficacy.

DSMB and TSC shall jointly ensure subject safety by monitoring the maintenance of patient confidentiality and review of adverse events.

|  |  |
| --- | --- |
| **Trial Steering Committee** | |
| *Dr. XXX* | *Hospital XXX* |
| *Dr. XXX* | *Hospital XXX* |
| *Dr. XXX* | *Hospital XXX* |

* + 1. Independent Data Safety Monitoring Board (DSMB) (as applicable)

*Please provide a description of the DSMB shall be detailed including all the information, responsibilities and guidelines. An example is provided below*.

An independent Data and Safety Monitoring Board (DSMB) has been established for the *XXX* trial. The terms of reference for this committee shall include performance of interim data analysis, periodic examination of emerging external evidence in relation to “*Drug Name/Device Name/Procedure Name”,* and monitoring of adverse events, compliance with the trial protocol, and progress of recruitment. The DSMB shall develop their own charter for the conduct of these and other activities.

The trial shall be monitored by a Data and Safety Monitoring Board (DSMB). The primary responsibilities of the DSMB are to 1) periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy, and 2) make recommendations concerning the continuation, modification, or termination of the trial.

The DSMB shall be composed of experts, fully independent of any ties to the trial, the sponsor, or any other activity or entity that might affect their objectivity. The members of the DSMB serve in an individual capacity and provide their expertise and recommendations. Two Senior “*Department XXX*” Physicians with expertise in Procedural sedation and not involved in this trial, shall be part of the DSMB Committee. Additional experts are members with clinical and statistical experience, and members with expertise in ethics and the specific disease area.

Timing and purpose of the DSMB meetings:

Initial meeting - shall be held soon after IRB approval of the project (and before the start of the trial) to review the research protocol, informed consent, and trial related documents.

[Second meeting – A second meeting shall be held after the enrollment of first XX subjects and meeting report shall be submitted to IRB.](webextlink://Second%20meeting%20–%20A%20second%20meeting%20will%20be%20held%20after%20the%20enrollment%20of%20first%2020%20subjects%20and%20meeting%20report%20will%20be%20submitted%20to%20IRB.)

Further meetings of the DSMB shall be held on a quarterly basis to evaluate the progress of the trial, including periodic assessments of data quality and timeliness, recruitment, participant risk versus benefit, performance of the trial site, and other factors that can affect trial outcome.

Issues relating to the general conduct and progress of the trial shall be discussed including adverse events and toxicity issues, accrual, demographic characteristics of subjects, comparability of groups with respect to baseline factors, protocol compliance, site performance, quality control, and fulfillment of documentation.

A formal report containing the recommendations for continuation or modifications of the trial shall be prepared by the DSMB Chairperson after each DSMB meeting and shall be sent to the DSMB members for review and approval. DSMB recommendation shall be given to all co-investigators and copies shall be submitted to the IRB.

Confidentiality of subjects is maintained by hiding their identity and coding them. The DSMB shall review data only by masked trial groups.

* 1. **Data and Safety Monitoring Plan (DSMP)**

*In this section, please include a written plan of the measures that shall be taken to ensure the safety of clinical research subjects and protect the validity and integrity of research data. The following questions should be addressed as a part of the DSMP and must be incorporated into your Sidra Medicine IRB application:*

* *Description of the proposed monitoring entity (i.e. Sidra Medicine DSMB, Independent Medical Monitor) and rationale for choosing the specified monitoring entity. If you are using an independent medical monitor or study monitoring committee/group, please specify their qualifications.*
* *Describe the data/events that shall be captured and submitted to the monitoring entity. Specify what data shall be collected during the course of the study to assess both safety and efficacy.*
* *Describe what adverse events may cause the subject to terminate protocol treatment. Specifically, describe treatment stopping rules for an individual patient and with what frequency?*
* *How often shall the monitoring entity review data/events (i.e. annually, semi-annually, etc.)?*
* *Describe the complete study stopping rules (criteria for study suspension and potential study termination). If there are no defined stopping rules, please provide a rationale. Also, state any specific triggers for action.*
* *All dose escalation trials are required to define dose limiting toxicities, rules for escalation of dose, and criteria for stopping the trial and defining the Maximum Tolerated Dose.*
* *How shall the monitoring entity’s comments/review be disseminated? (e.g. Submitted to the IRB at the time of continuing review and submitted to participating sites upon receipt of review comments).*

1. **Selection and Withdrawal of Subjects**

*This section should provide details for subject selection and subject withdrawal.*

* 1. **Subject inclusion criteria.**

*Please detail all the inclusion criteria for the inclusion of the subjects. An example is provided below.*

*Ex.:*

* *“Written informed consent*
* *Men and women aged 20–65 years*
* *T2DM of duration 0–6 years (diagnosis based on 2 recorded diagnostic-level tests, HbA1c and/or blood glucose).*
* *HbA1c≥48 mmol/mol at the last routine clinical check, within last 12 months if on diet alone*
* *HbA1c≥43 mmol/mol if on treatment with oral hypoglycemic agents*
* *Body Mass Index (BMI) >27 kg/m2 and <45 kg/m2”*
  1. **Subject exclusion criteria.**

*Please detail all the exclusion criteria for the inclusion of the subjects. An example is provided below.*

*Ex.:*

* *“Current insulin use*
* *Recent routine HbA1c ≥108 mmol/mol*
* *Weight loss of >5 kg within the last 6 months*
* *Recent eGFR <30 ml/min/1.73 m2*
* *Substance abuse*
* *Known cancer*
* *Myocardial infarction within previous 6 months*
* *Severe heart failure defined as equivalent to the New York Heart Association grade 3 (NYHA)*
* *Learning difficulties*
* *Current treatment with anti-obesity drugs*
* *Diagnosed eating disorder or purging*
* *Pregnant/ considering pregnancy*
* *Patients who have required hospitalization for depression or are on antipsychotic drugs*
* *People currently participating in another clinical research trial*
* *People with contraindications for MR scanning”.*
  1. **Subject withdrawal criteria (i.e., terminating investigational product treatment/trial treatment) and procedures specifying:**

*Please detail all the withdrawal criteria for the subjects. An example is provided below.*

*(a) When and how to withdraw subjects from the trial/ investigational product treatment.*

*(b) The type and timing of the data to be collected for withdrawn subjects.*

*(c) Whether and how subjects are to be replaced.*

*(d) The follow-up for subjects withdrawn from investigational product treatment/trial treatment.*

*An example is provided below.*

Participants who withdraw from the intervention protocol, or who fail to return for follow-up assessments, shall continue to have data collected from their routine diabetic clinic/GP visits, unless they specifically withdraw consent for this. Data analysis shall use best available follow-up weights (closest within a window of ±3 months from routine attendances) and end of study diabetes status for participants who discontinue the formal weight management programmed. (Drug intolerance, diet intolerance or poor compliance shall be recorded: these patients shall be included in ITT analysis).

1. **Treatment of Subjects. Investigational Product (IP), Medical Device, or procedures (as applicable)**

*This section applies to* ***clinical trials******using investigational product (IP), Medical Devices or new procedures,*** *as applicable.*

* 1. **Pharmaceutical/Medical Device/Procedures information**

***For IPs, p****lease describe the treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, instructions for reconstitution or storage instructions, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial. Also indicate if any special handling is* ***required****.*

***For Medical Devices****, please describe the device and use.*

***For Procedures****, please describe the procedure and rational.*

* 1. **Availability**

***This section is only applicable for IPs and medical devices.***

*Please summarize the information for Investigational Product/medical device, supplied to investigators by Pharmaceutical Company/other as applicable.*

* 1. **Product Ordering**

***This section is only applicable for IPs and medical devices.***

*Please include ordering instructions (i.e. contact person/office at Sponsor, telephone and fax number). Add as appendices, where applicable, copies of product order form. Indicate time necessary to fill order and expected time after order is placed that study product shall arrive.*

* 1. **IP Accountability**

***This section is only applicable for IPs.***

*Product Inventory Records – The investigator, or a responsible party designated by the investigator, shall maintain a careful record of the inventory and disposition of all agents received from Sponsor on an IP Accountability Record Form, if applicable.*

*Please note, if multiple products are being utilized in the research protocol, include product information, availability, ordering and accountability as necessary.*

* 1. **Procedures for monitoring subject compliance.**

***This section is only applicable for IPs and medical devices.***

*Please detail how the investigational product shall be monitored and subject compliance statements.*

1. **Assessment of Efficacy**

*This section should provide all the details to evaluate the efficacy of the investigational product(s), device(s) or procedure(s). An example is provided below.*

The primary goal of most clinical trials is an evaluation of the efficacy of the drug being evaluated. Therefore, it is important to understand if study outcomes are a true reflection of a drug's "real-life" effectiveness. Clinical trials generally evaluate three types of outcomes: subjective, objective, and health-related. Clinical trials that use subjective measures as endpoints usually evaluate outcomes such as symptom scores, the need for rescue medication, and quality-of-life measures. The majority of clinical trials rely on objective measures to test the efficacy of the disease medications.

Occasionally, studies shall include an assessment of health outcomes, either as a primary or secondary measure, during the course of the study. Commonly measured health outcomes include a reduction in need for rescue medications, a reduction in the need for emergent disease care, a reduction in hospitalizations, and a reduction in deaths. Studies designed to assess impact of treatment regimens on morbidity and mortality remain a high priority, as do studies designed to predict response to current disease related therapies.

* 1. **Specification of the efficacy parameters.**

*Please list and describe all study procedures and evaluations to be done as part of the study to support the determination of efficacy, as per the primary and secondary objectives outlined in this protocol. Discuss the sequence of events that should occur during the screening process and any decision points regarding participant eligibility. Include the time frame prior to enrollment within which screening procedures/ evaluations must be performed (e.g., within 28 days prior to enrollment). If a separate screening protocol is developed, describe how the screening protocol shall be used to identify participants for this study. In addition, discuss any special conditions that must be achieved during the enrollment and/or initial administration of study intervention. Include the procedures for administering the study intervention and follow-up procedures after administration (e.g., assessment of vital signs), as well as any specifics about subsequent follow-up visits, and unscheduled visits. Also, note if a specifically qualified person (e.g., physician, psychologist) should be performing any of the assessments. Include any definitions used to characterize outcomes (e.g., criteria for determining occurrence of acute myocardial infarction, characterization of a stroke as thrombotic or hemorrhagic, distinction between transient ischemic attack and stroke), should be explained fully.*

*For participants that may discontinue or withdraw early, it is important to capture the rationale during the final visit.*

*Provide justification for any sensitive procedures (e.g., provocative testing, deception). In addition, note where approaches to decrease variability, such as centralized laboratory assessments, are being employed. The specific timing of procedures/evaluations to be done at each study visit are captured in Section 6, Schedule of Activities and the time points of these procedures do not need to be included here. In addition, indicate where appropriate, that procedures/evaluations shall be performed by qualified personnel.*

* 1. **Methods and timing for assessing, recording, and analyzing of efficacy parameters.**

*This section may include a list and description of the following procedures/evaluations, as applicable:*

* *Physical examination (e.g., height and weight, organ systems, motor or vision assessment, or other functional abilities). If appropriate, discuss what constitutes a targeted physical examination.*
* *Radiographic or other imaging assessments. State the specific imaging required and, as appropriate, provide description of what is needed to perform the specialized imaging. Details describing how to perform the imaging in a standard fashion and equipment specifications.*
* *Biological specimen collection and laboratory evaluations. Include specific test components and estimated volume and type of specimens needed for each test. Specify laboratory methods to provide for appropriate longitudinal and cross-sectional comparison (e.g., use of consistent laboratory method throughout study, use of single, central laboratory for multi-site studies). If more than one laboratory shall be used, specify which evaluations shall be done by each laboratory. If such compliance is not required, a brief discussion should be included explaining why this is the case. In addition, discussion should include whether any laboratory tests (e.g., diagnostics) that shall be used are being developed concurrently or are commercially available. Special instructions for the preparation, handling, storage, and shipment of specimens should be briefly explained in this section.*
* *Special assays or procedures required (e.g., immunology assays, pharmacokinetic studies, flow cytometry assays, microarray, DNA sequencing). For research laboratory assays, include specific assays, estimated volume and type of specimen needed for each test. If more than one laboratory shall be used, specify which assays shall be done by each laboratory. Special instructions for the preparation, handling, storage, and shipment of specimens should be briefly explained in this section.*
* *Administration of questionnaires or other instruments for patient-reported outcomes, such as a daily diary.*
* *Procedures that shall be completed during the study as part of regular standard of clinical care.*

*Include in this section a discussion of the results of any study specific procedures that shall be provided to participant (e.g., radiographic or other imaging or laboratory evaluations). Address when endpoints shall be assessed with respect to dosing of rescue medication, if applicable.*

1. **Assessment of Safety**

*This section should provide information and instructions about safety management, definitions and reporting about Adverse Event (AE), Serious Adverse Event (SAE) and Unanticipated Problem (UP).*

*Please list and describe all study procedures and evaluations to be done as part of the study to monitor safety and support the understanding of the study intervention’s safety or that are done for other purposes (e.g. screening, eligibility, enrollment).*

*For more information see the MOPH “Guidelines on Reviewing and Reporting Unanticipated Problems Involving Risks to Subject or Others and Adverse Events”.*

Safety reporting is an integral and critical part of the clinical trial process. The objective of collecting safety data is early detection of important safety signals, protecting patients from unnecessary risks, and developing the safety profile of the drug, device or procedure contributing to its benefit-risk assessment.

* 1. **Adverse Events (AEs)**

*Please define AEs and address the responsibilities on investigators for reporting AEs.*

* + 1. AE Definition

*Please detail the definition for AE. An example is provided below.*

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

* + 1. Assessment of AE

*Please describe the method of AE assessment and severity. An example is provided below.*

The AEs assessment is based on the evaluation of their relevance and significance to the study, including an aggregate analysis of other occurrences of the same (or similar) event, before they can be determined to be an unanticipated problem involving risk to human subjects.

*Please describe the method of grading an AE for severity.*

*For example, many toxicity tables are available for use and are adaptable to various study designs.*

*An example is provided below.*

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines shall be used to describe severity.

* **Mild** – Events require minimal or no treatment and do not interfere with the participant’s daily activities.
* **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
* **Severe** – Events interrupt a participant’s usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term “severe” does not necessarily equate to “serious”.]
  + 1. AE Reporting

*Please describe the methodology for AE reporting procedures, including timeframes. An example is provided below.*

If the investigator determines that an adverse event is not an unanticipated problem, but the monitoring entity subsequently determines that the adverse event does in fact represent an unanticipated problem (for example, due to an unexpectedly higher frequency of the event), the monitoring entity should report this determination to the investigator, and such reports must be promptly submitted by the investigator to the IRB, the institution head, the funding body, and Department of Research at Qatar Ministry of Public Health.

AEs and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.

* 1. **Serious Adverse Events (SAEs)**

*Please define SAEs and address the responsibilities on investigators for reporting SAEs.*

* + 1. SAEs definition

*Please detail the definition for SAE. An example is provided below.*

An adverse event (AE) or suspected adverse reaction is considered "serious" (SAE) if, in the view of either the investigator or sponsor appears 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
* results in a congenital anomaly/birth defect; or based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

Adverse events that are unexpected, related or possibly related to participation in research, and serious are considered to be the most important subset of adverse events representing unanticipated problems because such events always suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized and routinely warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects.

* + 1. SAE Assessment

*Please describe the method of SAE assessment and causality. An example is provided below.*

Causal relationship shall be assessed for the intervention and procedures: The PI (or another delegated medically qualified doctor from the trial team) shall assess each SAE to determine the causal relationship and the Trial Management Group (if applicable) can also provide this assessment where necessary:

|  |  |  |
| --- | --- | --- |
| **Relationship** | **Description** | **Reasonable possibility that the SAE may have been caused by the intervention?** |
| Unrelated | There is no evidence of any causal relationship with the trial/intervention | No |
| Unlikely | There is little evidence to suggest there is a causal relationship with the trial/intervention (e.g. the event did not occur within a reasonable time after administration of the trial medication). There is another reasonable explanation for the event (e.g. the participant’s clinical condition, other concomitant treatment). | No |
| Possible | There is some evidence to suggest a causal relationship with the trial/intervention (e.g. because the event occurs within a reasonable time after administration of the trial medication). However, the influence of other factors may have contributed to the event (e.g. the participant’s clinical condition, other concomitant treatments). | Yes |
| Probable | There is evidence to suggest a causal relationship and the influence of other factors is unlikely. | Yes |
| Definite | There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out. | Yes |

* + 1. SAE Reporting

*Please describe the methodology for SAE reporting procedures, including timeframes. Further details should be included, including a description and a flow chart of when events are reported to various oversight and regulatory groups, and what study staff are responsible for completing and signing off on the SAE reports, and who shall receive notification of SAEs. An example is provided below.*

Based in MOPH guidelines, all serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique code numbers assigned to the trial subjects rather than by the subjects' names, personal identification numbers, and/or addresses. The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority (MOPH) and the IRB.

A completed SAE form for all events requiring immediate reporting should be submitted via email to the IRB and MOPH within 48 hours of knowledge of the event.

A separate form must be used to report each event, irrespective of whether or not the events had the same date of onset. The PI is responsible for reporting unanticipated problems involving risk of harm to subjects or others and Serious Adverse Events (SAEs) to IRB using Sidra IRB “Serious Adverse Event From” and to submit it through the IRBNET portal.

In addition, the SAE should be reported in DATIX system (Sidra web-based incident reporting and risk management software) as soon as possible.

* 1. **Unanticipated Problems (UPs)**

*Please define UPs and address the responsibilities on investigators for reporting UPs.*

* + 1. UPs Definition

*Please detail the definition for UP. An example is provided below*

The Qatar Ministry of Public Health considers unanticipated problems, in general, to include any incident, experience, or outcome that meets all of the following criteria:

* unexpected in terms of nature, severity, or frequency as given in the IRB approved research protocol and informed consent document.
* there is a reasonable possibility that it is related or possibly related to participation in the research; and
* suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized.
  + 1. UPs Reporting

*Please describe the methodology for UPs reporting. An example is provided below.*

Upon becoming aware of any other incident, experience, or outcome (not related to an adverse event) that may represent an unanticipated problem, the investigator should assess whether the incident, experience, or outcome represents an unanticipated problem by applying the criteria described above.

If the investigator determines that the incident, experience, or outcome represents an unanticipated problem, the investigator must report it promptly to the IRB, the institution head, the funding body, and Department of Research at Qatar Ministry of Public Health (MOPH), in addition, it should be reported to DATIX as soon as possible.

Unanticipated problems that are serious adverse events (SAE) should be reported within 1 week of the investigator becoming aware of the event. Any other unanticipated problem should be reported within 2 weeks of the investigator becoming aware of the problem. However, the reporting processes may vary from one protocol to another especially for multinational clinical trials - depending on the sponsor and the reporting timelines specific to the national regulations of the sponsor. However, in all cases, a flow of information should be maintained between the different parties involved.

1. **Statistics**

*This section should cover all the details about statistics management.*

* 1. **Statistical methods**

*Please include a description of the statistical methods to be employed, including timing of any planned interim analysis.*

*The statistical methods used for the research project objectives/hypotheses (e.g. t-test, chi-squared, multivariate modelling) must be sufficiently detailed. If conducting a randomized controlled research, you should state whether methods shall include an “intention to treat” (ITT) analysis, per protocol analysis, or both. An ITT analysis is preferred as it compares all subjects in the groups to which they were originally randomly assigned (despite withdrawal, treatment failure or cross-over). Consultation with a statistician is strongly recommended.*

* 1. **Number of subjects planned to be enrolled**

*Please include the number of subjects planned to be enrolled. In multicenter trials, the numbers of enrolled subjects projected for each trial site should be specified. Reason for choice of sample size, including reflections on (or calculations of) the power of the trial and clinical justification.*

*A sample size or power calculation should be performed. This calculation is used to estimate the number of subjects required to answer your primary research hypothesis with an accepted power. Conversely, it also allows you to estimate what power can be achieved with a limited number of participants. This number is calculated by specifying the magnitude of the effects that are expected (i.e. informed and clinically significant), variability of the measurements and the acceptable degree of type I and II errors. You need to specify the assumptions made for the calculation. It is recommended that you consult with a statistician for this section. Also keep in mind the estimated recruitment rate and whether you need to adjust for anticipated non-responders and losses to follow up.*

* 1. **Level of significance**

*Please include the level of significance to be used.*

* 1. **Termination criteria**

*Please include the criteria for the termination of the trial to be used for statistical analysis.*

* 1. **Procedure for not available data**

*Please details the procedure for accounting for missing, unused, and spurious data.*

* 1. **Procedures for reporting deviations**

*Please include the procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).*

* 1. **Subject selection**

*Please detail the selection of subjects to be included in the analyses (e.g., all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects).*

1. **Direct Access to Source Data/Documents**

*This section should confirm that the investigator(s)/institution(s) shall permit trial-related monitoring, audits, IRB review, and regulatory inspection(s), providing direct access to source data/documents. The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) shall permit trial-related monitoring, audits, IRB review, and regulatory inspection(s), providing direct access to source data/documents. An example is provided below*.

Study data must be initially captured using one or more of the following methods: on paper source documents, in electronic medical records or other electronic databases (e.g., central laboratory database), and/or in Electronic Data Capture (EDC) systems. Please note that GCP requires that the protocol describes instances when the EDC acts as the source document.

If paper CRFs are used, it should be provided support for initial data capture by providing source document templates. These are tools that can be used to create an initial data record that is able to be easily matched to the data collection instrument. Often these templates are created from the CRF.

**Monitoring and Inspection by Health Authorities**

*This trial shall be monitored in accordance with the ICH Guidance on GCP (ICH Topic E6(R2)) The clinical trial monitor shall visit the trial site at regular intervals. An example is provided below*.

The sponsor shall permit, representatives of the Sponsor’s quality assurance unit or a designated organization (as applicable), the monitor, IRB, as well as MOPH, to inspect all trial-related documents and other materials at the site, including the regulatory binder, completed CRFs, ICFs, and the patients’ original medical records/files. Audits may be conducted at any time during or after the trial to ensure the validity and integrity of trial data.

1. **Quality Control and Quality Assurance**

*This section should describe the Quality Control and Quality Assurance related to the trial, and include for example information related to:*

*“Clinical site study staff 1) completing checklists to confirm the appropriateness of each subject’s informed consent process; 2) conducting systematic comparison of the electronic or paper, if applicable) clinical data to the medical records; 3) reviewing the contents of the Essential Documents Binder and documenting the results of the review”.*

1. **Ethical and Regulatory Aspects**

*This section should describe the ethical considerations related to the trial. Examples are provided in each section.*

* 1. **Ethical Review**

*This section should describe information related to ethical review. An example is provided below.*

The study protocol, patient information and consent form, Investigator’s Brochures and Addenda, any written instructions to be given to the patient, available safety information, patient recruitment procedures (e.g., study website), information about payments and compensation available to the patients and documentation evidencing the investigator’s qualifications shall be approved by the IRB/EC per local regulations prior to study start. The written approval should identify all documents reviewed by name and version.

Changes in the conduct of the study or planned analysis shall be documented in a protocol amendment. The investigator must submit and, where necessary, obtain IRB/EC and/or Sponsor approval for all subsequent protocol amendments and changes to the ICF or changes of the investigational site, facilities, or personnel. The investigator should notify the IRB/EC of protocol deviations or SAEs occurring at the site and other AE reports received from the Sponsor in accordance with local procedures.

Safety updates shall be prepared by the Sponsor or its representative as required, for submission to the relevant IRB*.*

* 1. **Responsibilities of the Principal Investigator**

*This section should cover all the PI responsibilities. An example is provided below.*

The Principal Investigator (PI) is responsible for conduct of the trial at his/her site. He/she shall ensure that the trial is performed in accordance with the clinical trial protocol and the approved protocol amendments; the current version of the Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Patients), ICH Good Clinical Practice (ICH Topic E6 GCP); and applicable Health Authority requirements and national and state laws. In particular, the investigator must ensure that only patients who have given their written informed consent are included into the trial.

The PI has primary responsibility for protecting the rights and welfare of human subjects in research. The PI’s primary responsibilities also include the following:

* Delegation of Authority
* Oversight of the Research Team
* Knowledge of Human Research Protection Standards
* Evaluation of Adequacy of Resources
* Training Requirements
  1. **Patient Information and Informed Consent**

*This section should cover all the detailed information about Informed Consent. An example is provided below.*

An unconditional prerequisite for a patient’s participation in the trial is his/her written informed consent. The patient’s written informed consent to participate in the trial must be given before any trial-related activities are carried out. Adequate information must therefore be given to the patient by the investigator before informed consent is obtained. In addition to providing this written information to a potential patient, the investigator shall inform the patient verbally of all pertinent aspects of the trial. The language used in doing so must be chosen so that the information can be fully and readily understood by lay persons.

The ICF must be signed and personally dated by the patient (or the patient’s legally authorized representative) and investigator. The signed and dated declaration of informed consent shall remain at the investigator’s site and must be safely archived by the investigator so that the forms can be retrieved at any time for monitoring, auditing, and inspection purposes. A copy of the signed and dated information and ICF should be provided to the patient, or their legally authorized representative, before participation in the study.

Whenever important new information becomes available that may be relevant to the patient’s consent, the written patient information sheet and any other written information provided to patients shall be revised by the Sponsor or designee and be submitted again to the IRB for review and favorable opinion. The agreed upon, revised information shall be provided to each patient in the trial for signing and dating. The investigator shall explain the changes to the previous version to the patient. Case history or clinical records for each patient should document the informed consent process and that written informed consent was obtained using the revised ICF for continued participation in the study.

* 1. **Health Authorities**

*This section should describe information related to Health Authorities. An example is provided below.*

The clinical trial protocol and any applicable documentation (e.g., patient information, and ICF) shall be submitted to the Ministry of Public Health by the Sponsor in accordance with the local regulations.

1. **Data Handling and Record Keeping**

*This section should describe data handling and record keeping. Examples are provided in each section.*

* 1. **Data Collection**

*This section should describe all the related details for Data Collection. An example is provided below.*

The data collection plan for this study is to utilize [please complete] CRF system (ex. REDCap) to capture all treatment, toxicity, efficacy, and adverse event data for all enrolled patients.

The CRF is the primary data collection instrument for the trial. The clinical site shall keep CRFs current to enable the monitor to review the patients’ status throughout the course of the trial. To maintain confidentiality, only the study number, patient number, patient initials, and date of birth shall identify the patient on the eCRF. All data requested on the eCRF must be supported by and be consistent with the patient’s source documentation.

Source documents are the original documents, data, records and certified copies of original records of clinical findings, observations and activities from which the patient’s eCRF data are obtained. These can include, but are not limited to, hospital records, clinical and office charts, laboratory, medico-technical department and pharmacy records, diaries, microfiches, ECG traces, copies or transcriptions certified after verification as being accurate and complete, photographic negatives, microfilm or magnetic media, X-rays, and correspondence. All missing data must be explained. The investigator shall sign and date the patient CRF casebook indicating that the data on the CRF have been assessed. Each completed CRF shall be electronically signed and dated by the PI, once all data for that patient is final.

* 1. **REDCap (if applicable)**

REDCap (Research Electronic Data Capture) is a free data management software system that is fully supported by SIDRA MEDICINE. It is a tool for the creation of customized, secure data management systems that include Web-based data-entry forms, reporting tools, and a full array of security features including user and group based privileges, authentication using institution LDAP system, with a full audit trail of data manipulation and export procedures. REDCap is maintained on CTSC-owned servers that are backed up nightly and support encrypted (SSL-based) connections.

* 1. **Regulatory Binder and Archiving**

*This section should cover all Regulatory Binder Management.*

*Please refer to procedure “PRO- Preparation of Regulatory Binder for Clinical Trials”.*

1. **Financing and Insurance**

*This section should describe financing and insurance, if not addressed in a separate agreement. An example is provided below*

For IST Sidra Medicine sponsored clinical trials involving the use of medicinal product(s), device(s) or procedure(s) and introducing medium to high risk to the patients as determined by the Risk Assessment Category Tool (RACT), the sponsor must contract a guarantee (e.g. insurance) to ensure medical cost coverage of patient for trial related AEs.

For low-interventional IST involving the use of medicinal product(s), device(s) or procedures and introducing minimal risk (as determined by the RACT assessment tool), Sidra shall provide care to patients suffering AEs arising from the participation to the clinical trial free of charge at Sidra. If the needed care cannot be provided to those patients at Sidra, Sidra shall arrange and pay for their care at other hospitals in Qatar, such as at Hamad Medical Corporation (HMC).

1. **Publication Policy**

*This section should describe publication policy statement and plans for publication and authorship rules (as below), if not addressed in a separate agreement. An example is provided below*.

The trial shall be registered on ClinicalTrial.gov prior to the randomization of the first participant. Attempts shall be sought to publish protocol, all results, positive, neutral, as well as negative, in a peer-reviewed international journals. Authorship shall be determined according to the International Committee of Medical Journal Editors. Attempts shall be made to publish a list of all investigators with their contributions in all publications.

1. **Appendices**

*This section should detail all the additional appendices as appropriate, such as (please add or delete as applicable)*

* Patient/ Parent information leaflet
* Informed Consent form
* Assent form
* Questionnaire
* Data Sheet
* Applicable tables
* Any important appendix for the trial