|  |  |
| --- | --- |
| **Short Project Title** |  |
| **Chief Investigator Name:** |  |
| **Student Name PI (if applicable)** |  |
| **University Faculty** |  |
| **IRAS Number** |  |
| **Date** |  |
| **SU Sponsorship No** | RIO |
| **NHS REC Number** |  |
| **Sponsor** | **Swansea University** |

**Study Summary** (complete the table above and below)

|  |  |
| --- | --- |
| **TITLE** |  |
| **SHORT TITLE** |  |
| **Protocol Version Number and Date** |  |
| **Methodology** | Type of study: single-blind, double-blind, randomised controlled, cross-over, etc. |
| **Study Duration** | Estimated duration for the main study protocol (e.g. from when all approvals have been received (REC, MHRA and R&D) to when the last subject/patient recruited has completed all study processes) |
| **Study Centre** |  |
| **Objectives** | Brief statement of key primary objectives |
| **Number of Subjects/Patients** | Number of Subjects/Patients expected to be recruited for the whole study. |
| **Main Inclusion Criteria** | Include the main disease /area to be researched and the **key** inclusion criteria |
| **Statistical Methodology and Analysis** | Describe briefly the statistical methodology to be used in the study |

|  |  |
| --- | --- |
| List of Content | Page No. |
| 1. Introduction |  |
| 1. Background |  |
| 1. Rationale |  |
| 1. Design and Objectives |  |
| 1. Sample and Recruitment |  |
| 1. Informed Consent Procedures |  |
| 1. Study Areas |  |
| * Laboratory Assessments (if applicable) |  |
| * Radiology Assessments (if applicable) |  |
| * Medical Device (if applicable) |  |
| 1. Safety Reporting |  |
| 1. Statistical Considerations |  |
| 1. Data Handling |  |
| 1. Publication Policy |  |
| 1. References |  |
| 1. Appendices |  |

1. **Introduction**

**The Introduction (as detailed below with the accompanying sub-headings) acts as the starting point for outlining the background and justification for the research, with clear concise objectives that have scientific merit and that relate to previous literature.**

2 Background

Discussion of research topic including historical background, study population, disease type and treatment, including current standard of care.

3 Rationale

A summary of known and potential risks and benefits to human subjects along with justification with regards to treatment period, which is supported by the literature with regards to the disease or condition, treatment for this indication.

**4** **Design and Objectives**

Objectives

Primary Objectives/Secondary Objectives to be outlined as defined by the Primary/Secondary Endpoints which are also to be listed here.

Research Design

A very brief overview as to the main elements of the study with regards to the design: phase, blinded/unblinded, placebo-controlled, parallel-group, cross-over, treatment plan and regime.

**5. Sample and Recruitment**

* Please note that the sample size for the study needs to be statistically evaluated.
* Statistical calculations should be included alongside estimated accrual numbers.
* Include a description that outlines the type of participant to be studied.
* Describe how the participants will be selected for the study e.g. from outpatient clinics, referring physicians or use of advertisements.
* State how the participant will be contacted and whether any vulnerable groups be used.

Inclusion Criteria

A set of criteria that determines that the patient is eligible to participate in the study. Include:

* Informed Consent (Additional measures have to be implemented if incapacitated adults are used)
* Age
* Disease Type
* Life Expectancy
* Specific parameters if applicable
* Anything that is relevant/specific to the trial/procedure
* Screening test results/parameters

Exclusion Criteria

A set of criteria that determines that the patient is ineligible to participate in the study. Include:

* Any inclusion criteria not met
* Cumulative doses of concomitant drug
* Participation in other trials
* Previous Treatments
* Allergies
* Other malignancies/past medical history

6 Informed Consent Procedures

* It is the responsibility of the Investigator, or appropriately GCP trained person delegated by the Investigator as documented in the site delegation log, to obtain written informed consent from each subject prior to any participation/study specific procedures.
* This should follow adequate explanation of the aims, methods, anticipated benefits and potential hazards of the study. If a Senior Research Nurse or other qualified persons will be taking consent, please state clearly in this section.
* The patient should be given ample time to consider giving their consent for the study. It is felt that 24 hours gives sufficient time for the patient to consider their participation within the study and give informed consent. If for any reason, less than 24 hours is to be given, please document why this is the case along with justification for this decision.
* The date that the Patient Information Sheet (PIS) is given to the patient must be documented within the patient’s notes to ensure that sufficient time is given **(minimum 24 hours)**.
* The Investigator (or other qualified person) must explain to the potential participant that they are free to refuse any involvement within the study or alternatively withdraw their consent at any point during the study and for any reason.
* All subjects that are actively enrolled on the study will be informed of the updated information and given a revised copy of the PIS/ICF in order to confirm their wish to continue on the study.

Further guidance can be found at: <http://www.nres.npsa.nhs.uk/applications/guidance/#InformedConsent>

7 **Study Area**

Screening Procedures

Detail any study specific screening procedures that the patient will undergo prior to their entry/eligibility into the study. Ensure that all patients that undergo screening are logged into a screening log associated with the study and that it is documented who is authorised to complete this task.

Schedule for participant Outline all treatments/interventions that the participant will undergo at each visit during their participation within the study.

Schedule of Assessment (in Diagramatic Format)

Please use a table format to detail the schedule of assessments that the participant will undergo at each visit.

Follow up Procedures (if applicable)

If any follow up procedures are required/applicable for this study, ensure that they are documented in this section. If the tests are standard they should be listed, although documented as standard care. Include the exact timeline in which the patient will be followed up and the frequency of the follow up.

**Laboratories** (if applicable)

## Central/Local Laboratories

Outline the laboratories that will be used and which tests/analysis will be conducted at each laboratory. Indicate clearly which tests will be performed by Swansea Bay UHB laboratories and which will be performed at external laboratories. Describe which tests will be performed as standard of care and which will be performed on additional samples taken specifically for the study.

## Sample Collection/Labelling/Logging

Describe how and where the collection of the sample from the patient will be recorded. Describe how the sample(s) will be labelled, including all identifiers to be used (e.g. study ID, name, D.O.B, hospital number) that will be used for each laboratory (N.B. samples should be pseudo-anonymised or fully anonymised wherever possible when sent to external laboratories). Where samples will be labelled differently for each laboratory please describe fully.

## Sample Receipt/Chain of Custody/Accountability

A full chain of custody record should be maintained to provide evidence of the sample journey from collection to final storage (or fully used in analysis) Describe how the sample journey from collection from the patient to the laboratory will be recorded. If the sample has a number of transit points between laboratories, please describe how the full journey will be recorded. Chain of custody records should be retained in the study file.

Describe the arrangements that have been made with the laboratories to notify the study team of any sample integrity problems.

If there is an intention to transfer samples to external laboratories, include a statement to that effect in this section.

## Sample Analysis Procedures

Describe an overview of the test methodology(ies) to be used for all sample analyses.

## Sample Storage Procedures (if applicable)

State how and where (named laboratory) the samples will be stored if not be tested immediately and describe the required storage conditions including minimum and maximum temperature range. Describe the reason for sample storage before analysis if the samples cannot be tested immediately.

## Sample Retention

Samples may be held after the end of study date for quality checking or verification of the research data. This should be for a defined period of time as set out in the protocol and should be for no longer than 12 months. This storage does not require a HTA licence **and does not allow for research to be conducted on the samples during the 12 month storage period**. Please state clearly if the samples will be retained for this purpose and the location of storage.

* If samples are to be retained for further research in line with patient consent then they must be held under a HTA licence once the end of study declaration has been submitted or another application to NHS REC made before the end of study declaration is submitted.
* Please state whether the intention is for the samples to be retained under the HTA licence and the location of storage
* Consider whether the research and laboratory teams have the required staff and storage resources for long-term retention and ongoing compliance with the Human Tissue Act for such storage.

**Radiology Assessments** (if applicable)

Full detail of radiological assessments is to be included here. If any radiological/imaging assessments are to be included, please give more detail with regards to the intervention here. If this includes what is considered to be above standard care an ARSAC (Administration of Radioactive Substances Advisory Committee) licence may be required. For further guidance consult the imaging department.

Further guidance can be found at:

<http://www.nres.npsa.nhs.uk/applications/guidance/#ionisingrad>

<http://www.arsac.org.uk/>

**Medical Devices** (if applicable)

MHRA classification In vitro, CE Marking, Risk Assessment. Make and Model and Manufacture Company.

End of Study Definition

State the parameters that mark the end of the study, i.e. the trigger to inform the REC that the study has been completed.

Subject Withdrawal

State under what circumstances participants will be withdrawn e.g. intolerable toxicity, intercurrent illness, subject withdrawing consent.

**8. Safety Reporting**

|  |  |
| --- | --- |
| General Definitions |  |
| Adverse Event (AE) | An AE is any untoward medical occurrence in a subject to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporarily associated with study activities. |
| Serious Adverse Event (SAE) | An SAE fulfils at least one of the following criteria:   * Is fatal – results in death (NOTE: death is an outcome, not an event) * Is life-threatening * Requires inpatient hospitalisation or prolongation of existing hospitalisation * Results in persistent or significant disability/incapacity * Is a congenital anomaly/birth defect * Is otherwise considered medically significant by the Investigator |

|  |  |
| --- | --- |
| Investigators Assessment |  |
| Seriousness | The Chief/Principal Investigator responsible for the care of the patient, or in his absence an authorised medic within the research team, is responsible for assessing whether the event is serious according to the definitions |
| Causality | The Investigator must assess the causality of all serious adverse events in relation to the trial treatment according to the definition |
| Expectedness | The investigator must assess the expectedness of all SAEs according to the definition given. If the SAE is unexpected and related, then it needs immediate reporting |
| Severity | The Investigator must assess the severity of the event according to the following terms and assessments. The intensity of an event should not be confused with the term “serious” which is a regulatory definition based on patient/event outcome criteria.  **Mild**: Some discomfort noted but without disruption of daily life  **Moderate**: Discomfort enough to affect/reduce normal activity  **Severe**: Complete inability to perform daily activities and lead a normal life |

|  |  |
| --- | --- |
| Notification and reporting |  |
| Adverse Events or Reactions | If the AE is not defined as SERIOUS, the AE is recorded in the study file and the participant is followed up by the research team. The AE is documented in the participants’ medical notes (where appropriate) |
| Serious Adverse Events | Serious Adverse Event (SAEs) that are considered to be ‘related’ and ‘unexpected’ are to be reported to the sponsor within **24 hours of learning of the event** and to the Main REC **within 15 days in line** with the required timeframe. For further guidance on this matter, please refer to Appendix |
| Urgent Safety Measures | The CI has an obligation to inform both the Main Ethics Committee **in writing within 3 days**, in the form of a substantial amendment. The sponsor (Research and Development Office) must be sent a copy of the correspondence with regards to this matter. For further guidance on this matter, please refer to Appendix 2 |
| Annual Safety Reporting | The CI will send the Annual Progress Report to the main REC using the NRES template (the anniversary date is the date on the MREC “favourable opinion” letter from the MREC) and to the sponsor. Please see appendix 2 for further information |

## 

**9. Statistical Considerations**

Primary Endpoint Efficacy Analysis

State when efficacy analysis will conducted with reference to the primary endpoints, including a detailed outline of the methods and timing for assessing recording and analysing efficacy. Please consult with a statistician if assistance is required.

Secondary Endpoint Efficacy Analysis

State when efficacy analysis will conducted with reference to the secondary endpoints, including a detailed outline of the methods and timing for assessing recording and analysing efficacy. Please consult with a statistician if assistance is required.

Sample Size

Statistical explanation with regards to sample size for the study.

Statistical Analysis

Description of statistical methods that will be implemented in the analysis of data, including any interim analyses that are planned and the level of significance that is to be used. Include procedures to account for missing, unused and spurious data, procedures for reporting any deviations from the original statistical analysis plan and the selection of patients to be included in the analyses (e.g. all randomised subjects, dosed subjects, all eligible subjects). Please include any descriptive analysis as well as any statistical tests to be used.

**10. Data Handling**

Confidentiality

The Investigator has a responsibility to ensure that patient anonymity is protected and maintained. They must also ensure that their identities are protected from any unauthorised parties. Information with regards to study patients will be kept confidential and managed in accordance with the Data Protection Act, NHS Caldicott Guardian, The Research Governance Framework for Health and Social Care and Research Ethics Committee Approval.

Further Details to be included in this section:

* What identifiable information will be collected from the subjects?
* Who will have access to the Information and why?
* The Chief Investigator is the ‘Custodian’ of the data.
* Identify if patient identifiable details will be transferred outside the EU as different confidentiality laws apply in this instance.
* The rights of the subject to revoke their authorisation for the use of their PHI.
* The patients will be anonymised with regards to any future publications relating to this study.

**Record Retention and Archiving**

During the course of research, all records are the responsibility of the Chief Investigator and must be kept in secure conditions. When the research trial is complete, it is a requirement of the SU Research Governance is to archive the data for 10 years.

|  |  |
| --- | --- |
| Compliance | The CI will ensure that the trial is conducted in compliance with the principles of the Declaration of Helsinki (1996), and in accordance with all applicable regulatory requirements including but not limited  • UK Policy Framework for Health and Social Care Research (2017)  • Medicines for Human Use (Clinical Trials) Regulations (2004)  • Medical Devices Regulations (EU MDR/IVDR 2017)  and SU policies and procedures and any subsequent amendments |
| Ethical Considerations | This protocol and any subsequent amendments, along with any accompanying material provided to the patient in addition to any advertising material will be submitted by the Investigator to the Su sponsor and then to NHS Research Ethics Committee. Written Approval from the NHS REC Committee must be obtained and subsequently submitted to the SU Sponsor to circulate to participating NHS R&D Departments to obtain Final approval |
| Quality Control and Quality Assurance | A study may be identified for audit by any method listed below:  A project may be identified via the risk assessment process.  An individual investigator or department may request an audit.  A project may be identified via an allegation of research misconduct or fraud or a suspected breach of regulations.  Projects may be selected at random. The Department of Health states that Trusts should be auditing a minimum of 10% of all research projects.  Projects may be randomly selected for audit by an external organisation.  Internal audits will be conducted by a sponsor’s representative |
| Non-Compliance | A noted systematic lack of both the CI and the study staff adhering to SOPs/protocol/ICH-GCP, which leads to prolonged collection of deviations, breaches or suspected fraud  These non-compliances may be captured from a variety of different sources including monitoring visits, communications and updates. The sponsor will maintain a log of the non-compliances to ascertain if there are any trends developing which to be escalated. The sponsor will assess the non-compliances and action a timeframe in which they need to be dealt with. Each action will be given a different timeframe dependant on the severity. If the actions are not dealt with accordingly, the Research Governance Office will agree an appropriate action, including an on-site audit. |

**11. Publication Policy**

Please indicate how the data from the study will be used with regards to publications.

**12. References**

**13. Appendix**

**Appendix 1 – Information with regards to Safety Reporting in Non-CTIMP Research**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Who** | **When** | **How** | **To Whom** |
| **SAE** | Chief Investigator | -Report to Sponsor within 24 hours of learning of the event  -Report to the MREC within 15 days of learning of the event | SAE Report form for Non-CTIMPs, available from NRES website. | Sponsor and MREC |
| **Urgent Safety Measures** | Chief Investigator | Contact the Sponsor and MREC Immediately  Within 3 days | By phone  Substantial amendment form giving notice in writing setting out the reasons for the urgent safety measures and the plan for future action. | Main REC and Sponsor  Main REC with a copy also sent to the sponsor. The MREC will acknowledge this within 30 days of receipt. |
| **Progress Reports** | Chief Investigator | Annually ( starting 12 months after the date of favourable opinion) | Annual Progress Report Form (non-CTIMPs) available from the NRES website | Main REC |
| **Declaration of the conclusion or early termination of the study** | Chief Investigator | Within 90 days (conclusion)  Within 15 days (early termination)  *The end of study should be defined in the protocol* | End of Study Declaration form available from the NRES website | Main REC with a copy to be sent to the sponsor |
| **Summary of final Report** | Chief Investigator | Within one year of conclusion of the Research | No Standard Format  However, the following Information should be included:-  Where the study has met its objectives, the main findings and arrangements for publication or dissemination including feedback to participants | Main REC with a copy to be sent to the sponsor |