RAC draft 25.09.2014

**It is a requirement of Good Clinical Practice (GCP) and the Research Governance Framework for Health & Social Care 2005, that all research projects have a scientifically sound and ethically valid protocol.**

**The protocol is the starting point of any high quality research and all research studies must be conducted according to the protocol. A protocol provides written evidence for the necessity and feasibility of a study, as well as giving a detailed plan of investigation.**

**This document is to be submitted for approval to a Research Ethics Committee. This allows the ethical and peer review processes to validate the scientific and ethical considerations of the study.**

**The guidance detailed below is for basic science research.**

*Note to authors – this template is a guide – all the sections below must be included however this is not exhaustive, other sections may be added. Don’t forget to delete the blue “guides” from each section!*

# PROTOCOL TITLE:

*Descriptive study title*

### Sponsor/s

Name of organisation:

Address:

Telephone:

Fax:

Email:

### Chief Investigator

Name:

Address:

Telephone:

Fax:

Email:

### Name and address of Principal Investigator(s), Co-Investigator(s), Statistician, Laboratories etc

Name:

Address:

Telephone:

Fax:

Email:

Name:

Address:

Telephone:

Fax:

Email:

Name:

Address:

Telephone:

Fax:

Email:

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### Study Synopsis

|  |  |  |
| --- | --- | --- |
| Full Title |  |  |
| Short Title/Acronym |  |  |
| Protocol Version number and Date |  | *The standard protocol version number and date used to identify this study* |
| Study Duration |  | *In months. Estimated duration for the main study protocol (e.g. from when all approvals have been received (REC and R&D) to when the last subject recruited has completed all study processes)* |
| Study Design |  | *Type of study: i.e. basic science* |
| Sponsor/Co-sponsors |  |  |
| Chief Investigator |  |  |
| REC number |  |  |
| Primary objective |  | *Brief statement of key primary objectives* |
| Secondary objective (s) |  |  |
| Number of Subject |  | *Number of subjects 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* |

**IF THE STUDY IS TESTING A DEVICE PLEASE USE THE DEVICE PROTOCOL TEMPLATE.**

IF ANY DEVICE IS TO BE USED WITHIN THE STUDY (WHETHER ROUTINE OR NOT) PLEASE PROVIDE INFORMATION

|  |  |  |
| --- | --- | --- |
| Device Name |  |  |
| Manufacturer Name |  |  |
| Principle intended use |  |  |
| Is the device ce marked and used within its purpose? |  |  |
| Is the device currently used within the department? |  |  |
| Description and Maintenance and storage of device Provide as description of each important component, ingredient or element, property and principle of operation of the investigational device. Describe, if applicable, any anticipated changes in the investigational device during the course of the study. If no changes are anticipated then state this. | | |

# Glossary of Terms and Abbreviations

AE Adverse Event

AR Adverse Reaction

ASR Annual Safety Report

CA Competent Authority

CI Chief Investigator

CRF Case Report Form

CRO Contract Research Organisation

DMC Data Monitoring Committee

EC European Commission

GAfREC Governance Arrangements for NHS Research Ethics Committees

ICF Informed Consent Form  
ISRCTN International Standard Randomised Controlled Trial Number

MA Marketing Authorisation

MS Member State

Main REC Main Research Ethics Committee

NHS R&D National Health Service Research & Development

PI Principal Investigator

QA Quality Assurance

QC Quality Control

Subject An individual who takes part in a clinical trial

RCT Randomised Controlled Trial

REC Research Ethics Committee

SAE Serious Adverse Event

SDV Source Document Verification

SOP Standard Operating Procedure

SSA Site Specific Assessment

TMG Trial Management Group

TSC Trial Steering Committee

### 1. Introduction

### *This should comprise a brief description of the proposed study, a description of the population to be studied, a summary of findings from previous studies that are relevant to the proposed study as well as any other information that provides background for the study should be cited.*

### 2 Study Objectives and Design

### 2.1. Study Objectives

* *Primary Objective*
* *Secondary Objective*
* *Primary End Point*
* *Secondary End point*

### *This should comprise specific statements of the purpose (i.e. aims and objectives) of the study, together with a definition of the primary (and secondary) endpoints of the study*

### 2.2 Study Design & Flowchart

*A description of the main elements of the study design should be given.*

### 2.3 Study Flowchart

*Please include a time/event matrix (flow chart) of study procedures and stages. This desirable as it is particularly useful for determining activities involved during each study visit (e.g. blood tests or scans, treatment, diary completion, adverse event monitoring, physical examination etc).*

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Screen Visit | Pre dose | Day 1 |  |  |  |  |  |  |
| Participant information and informed consent | X |  |  |  |  |  |  |  |  |
| Physical examination |  |  |  |  |  |  |  |  |  |
| Demographics |  |  |  |  |  |  |  |  |  |

### 3. Sample Size, Statistics, Selection and Withdrawal of Subjects

* *Number of subjects and subject selection*
* *Inclusion criteria*
* *Exclusion criteria*

*Include a description that outlines the type of subjects to be studied. Describe how the subjects will be selected for the study e.g. from outpatient clinics, referring physicians or use of advertisements. State how the subjects will be contacted and whether any vulnerable groups be used.*

*Include details of target recruitment numbers for the study with suitable timelines.*

*Please note that the sample size for the study needs to be statistically evaluated. Statistical calculations should be included alongside estimated recruitment numbers. State the number of evaluable subjects required, as the number recruited will be higher, taking into consideration that not all eligible subjects will want to participate in a clinical study when assessing potential recruitment.*

*A description of the statistical methods to be employed, including timing of any planned interim analyses should also be provided. The number of subjects to be enrolled (in multicentre trials, the numbers of subjects for each site) should be stated, together with the rationale for the sample size (the “power calculation”). The level of significance that is to be used in each trial analysis must be stipulated, together with the procedure(s) for accounting for any missing, unused, and spurious data. Procedures for reporting any deviation from the original statistical plan should be described and justified. The data set for any analysis must be clearly stipulated and the population(s) should be clearly defined. Please include any statistical tests to be used*

***Inclusion Criteria***

*A set of criteria that determines that the subject is eligible to participate in the study.*

***Exclusion Criteria***

*A set of criteria that determines that the subject is ineligible to participate in the study.*

***Criteria for Premature Withdrawal***

*Please include detail of what might culminate in a subject’s withdrawal from the study and include suitable text in the Participant Information Sheet. Include a description of any follow-up procedures for these subjects and whether data collection would still be conducted with regards to these subjects.*

### 4. Study procedures

***Informed Consent Procedures***

*It is the responsibility of the Investigator, or appropriately 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.*

*The subject should be given ample time to consider giving their consent for the study. The Investigator (or other qualified person) must explain to the potential subject 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.*

*If there is any further safety information which may result in significant changes in the risk/benefit analysis, the PIS and Informed Consent Form (ICF) must be reviewed and updated accordingly. 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.hra.nhs.uk/research-community/before-you-apply/subject-information-sheets-and-informed-consent/](http://www.hra.nhs.uk/research-community/before-you-apply/participant-information-sheets-and-informed-consent/)

***Risks/burdens***

*Include an outline of the risks/burdens. If applicable include a description of the side effects of the study drug including contraindications.*

***Screening Procedures***

*Detail any study specific screening procedures that the subject will undergo prior to their entry/eligibility into the study. Ensure that all subjects 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.*

***Randomisation Procedures (if applicable)***

*Once screening procedures have confirmed the subject’s eligibility to enter the study, the process of randomisation can commence and needs to be outlined and detailed. Include where applicable:*

* *Allocation ratio and any stratification factors (with levels)*
* *Generation of randomisation codes (manual or automated process)*
* *Individual responsible for randomisation and documentation*
* *Access to code break*
* *Randomisation parameters*

*The randomisation system should be discussed with a statistician, as well as being validated for use. Once the subject has been successfully randomised onto the study, the enrolment of this subject must be documented within an enrolment log.*

***Assigning subjects to treatment arms (non-randomised studies) (if applicable)***

*If subjects are not to be randomised, please state the methodology for assigning subjects onto the treatment arms and that there will be assignment of unique identifiers, including site number and trial reference number, to generate a trial specific subjects identifier. The allocation ratio with regards to this should be discussed with a statistician beforehand.*

***Schedule of Treatment for each visit***

*Outline all treatments/interventions that the subject will undergo at each visit during their participation within the study. Include details of where the interventions will take place (e.g. CRF, hospital clinic etc)*

***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 subject will be followed up and the frequency of the follow up.*

***Study drug/placebo (if applicable)***

*Include detail of the drug/placebo manufacturing, storage and dispensing including details of companies and pharmacies involved*

***Laboratory Assessments (if applicable)***

*Include detailed information as to the parameters for these assessments. If any laboratory assessments, along with the appropriate time points, are required for any point of this study, include detail if specific parameters/normal parameters are required.*

***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 relevant imaging department.*

*Further guidance can be found at:*

<http://www.hra.nhs.uk/?s=radiation>

[*http://www.arsac.org.uk/*](http://www.arsac.org.uk/)

***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.*

### 5. Sample handling and laboratories (if Applicable)

*Outline the laboratories that will be used and which tests/analysis will be conducted.*

***Sample Collection/Labelling/Logging***

*Detail the process of sample collection/labelling and logging from the subject. State how the sample will be logged with regards to the collection, the date sent to the Laboratory and the temperature/conditions at which it was sent to ensure the integrity and viability not compromised.*

***Sample Receipt/Chain of Custody/Accountability***

*Handling of the samples upon arrival at the laboratory needs to be documented. Upon receipt of the samples, the laboratory should ensure that the physical integrity of these samples have not been compromised in transit. If it has, it is important that the study teams, as well as the sponsor, are informed of this. Upon receipt of samples laboratory staff should ensure that all samples are accounted as per the labeling. All samples received should be logged in an accountability log.*

***Sample Analysis Procedures***

*Detail the analysis methodology for the samples, and state if this includes any test that is not considered ‘standard’ for diagnostic purposes.*

***Sample Storage Procedures (if applicable)***

*State how the samples will be stored if not be tested immediately and detail the conditions/vessel of storage.*

***Data Recording/Reporting***

*State how data will be recorded and where and what format the reporting of the results will take.*

### 6. Assessment of Safety

*Define here any serious adverse events that are expected to occur during this study, which will not require formal reporting to the authorities. (Note: Please consider carefully expected adverse occurrences, as listing them here may reduce the administrative burden of the study).*

*Describe the measures that will be used to determine subject safety during the study. These will include physical examination, blood tests and adverse event reporting.*

*Where SAE is related (that is, it resulted from administration of any of the research procedures), to the study procedures or is an unexpected occurrence (that is, the type of event is not listed in the protocol as an expected occurrence) it must be reported to the main REC within 15 days using the NRES template. The form should be completed in typescript and signed by the chief investigator. The Coordinator of the main REC will acknowledge receipt of safety reports within 30 days. A copy of the SAE notification and REC acknowledgement receipt should be copied to the sponsor.*

*All other AEs are reported in the Annual Progress Report to the ethics committee and copied to the sponsor. For multi-site trials Principal Investigators at all sites must report all SAEs to the Chief Investigator first where possible. The Chief Investigator is then responsible for reporting events to the main REC*

*The definition of “serious” may be defined differently within the protocol and it is the responsibility of the research team to adhere to the protocol definition in terms of SAE reporting. Additionally the protocol and other documentation may identify SAEs that do not need immediate reporting and SAEs falling under these categories should be recorded and reported according to the protocol.*

*See Appendix 1 for details of NRES reporting*

### 7. Study oversight arrangements

*Please outline if there will be any data monitoring/steering/safety or other oversight committees set up for this study. Describe the extent of the role of this committee and their involvement within the study.*

### 8. Ethics & Regulatory Approvals

*State the name and address of the REC to which the study protocol and other documentation will be submitted.*

*If any other regulatory approvals are required provide details in this section.*

### 9. Data Handling

***Confidentiality***

*The Investigator has a responsibility to ensure that subject anonymity is protected and maintained. They must also ensure that their identities are protected from any unauthorised parties. Information with regards to study subjects 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 subject 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 identifiable information.*
* *The subjects will be anonymised with regards to any future publications relating to this study.*

***Case Report Form (if applicable)***

*Insert all the parameters that will be recorded in the CRFs (examples already incorporated into the protocol template) and include any further parameters that are study specific. Please state when and who will be responsible for the completion of the CRF throughout the life cycle of the study.*

*Elements to include are: registration/randomisation form, eligibility/exclusion criteria checklist, visit details, date, any study interventional delays, AEs, page for toxicities, withdrawal from study, follow up of outcomes, death, prior/current medication, SAE form,. Please state when and who will be responsible for the completion of the CRF.*

***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, ensure that records are kept for a time period specified by the funder / sponsor.*

***Compliance***

*Include a statement confirming 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 to the Research Governance Framework, Trust and Research Office policies and procedures and any subsequent amendments.*

### 10. Finance and Publication Policy

### *State the amount and source of funding and which organisation will receive and manage the funding.*

### *Include details of anything being provided at no cost (i.e. study drug)*

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

*Please state which public database the study will be registered on (if applicable).*

*(From 30 September 2013, all clinical trial applications which receive a favourable ethical opinion from a Research Ethics Committee (REC) will, as a condition of that favourable opinion, be required to be registered in a publicly accessible trial register.)*

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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Who** | **When** | **How** | **To Whom** |
| **SAE** | Chief Investigator | Within 15 days of CI becoming aware of the event | SAE Report form for Non-CTIMPs, available from NRES website. | Main REC with a copy to the sponsor |
| **Urgent Safety Measures** | Chief Investigator | Immediately  Within 3 days | By phone  Notice in writing setting out reasons for the urgent safety measures and the plan for future action. | Main REC  Main REC with a copy 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 with a copy to the sponsor |
| **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 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 subjects | Main REC with a copy to be sent to the sponsor |