

**Non-CTIMP Protocol Template**

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 research project, 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 research project. The guidance detailed below is for Clinical Trials of Non Investigational Medicinal Products (Non CTIMPs).

This protocol template is intended for use in clinical research projects and other clinical research studies which **are not** Clinical Trials of Investigational Medicinal Products (CTIMPs).

It is recommended that Section Headings in the protocol template are retained but they may be adapted to suit particular studies or marked as Not Applicable. Other sections may be added as required by the specific research project. It is also recommended that, where appropriate, a Consort flow diagram is completed at the same time as the protocol.

Black text is suggested text and should be amended accordingly.

All coloured guidance text is hidden text and will not print. Follow these instructions to view:

* Word 2003: Open the Tools > Options menu, then go to the View tab. Select the Hidden Text check box, then click OK.
* Word 2007: Click the Office button. Click the Word Options button, and then select Display on the left. Select the Hidden Text check box, then click OK
* Word 2010: Click File then Options. Click Display. Select to show hidden text.

**Research Project Protocol**

|  |  |
| --- | --- |
| Full Title: | *insert the full research project title* |
| Research Project Acronym: | *insert research project acronym* |
| Sponsor: | **insert Sponsor/Co-Sponsor and insert details as appropriate** |
| Sponsor Reference Number: | **insert Sponsor number before finalisation** |
| Funder: | **insert name of Funder** |
| Chief Investigator: | **insert name of CI, including Title** |
| Version Number and Date: | **insert version number and date of each version** |

**If the research project is multi-site, or has a coordinating Trial Centre, add specific details e.g. contact names, addresses etc. on this front page or in an Appendix.**

Contents

[Research Project Summary/Synopsis 5](#_Toc499126366)

[Protocol Approval - <<Insert research project title>> 6](#_Toc499126367)

[Abbreviations 7](#_Toc499126368)

[1. Introduction 8](#_Toc499126369)

[1.1 Background 8](#_Toc499126370)

[1.2 Preclinical Data 8](#_Toc499126371)

[1.3 Clinical Data 8](#_Toc499126372)

[1.4 Rationale and Risks/Benefits 8](#_Toc499126373)

[2. Research Project Objectives and Design 8](#_Toc499126374)

[2.1 Research Project Objectives 8](#_Toc499126375)

[2.1.1 Primary Objective 8](#_Toc499126376)

[2.1.2 Secondary Objective(s) 8](#_Toc499126377)

[2.2 Outcomes 8](#_Toc499126378)

[2.2.1 Primary Outcome 8](#_Toc499126379)

[2.2.2 Secondary Outcome(s) 8](#_Toc499126380)

[3. Research Project Design 8](#_Toc499126381)

[3.1 Research Project Description 8](#_Toc499126382)

[3.2 Research Project Flowchart 8](#_Toc499126383)

[3.3 Research Project Timeline 8](#_Toc499126384)

[4. Research Project Population 9](#_Toc499126385)

[4.1 Number of Participants 9](#_Toc499126386)

[4.2 Inclusion Criteria 9](#_Toc499126387)

[4.3 Exclusion Criteria 9](#_Toc499126388)

[5. Participant Selection and Enrolment 9](#_Toc499126389)

[5.1 Identifying Participants 9](#_Toc499126390)

[5.2 Consenting Participants 9](#_Toc499126391)

[5.3 Screening for Eligibility 9](#_Toc499126392)

[5.4 Ineligible and Non-Recruited Participants 9](#_Toc499126393)

[6. Randomisation and Blinding 9](#_Toc499126394)

[6.1 Randomisation Details 9](#_Toc499126395)

[6.2 Blinding 9](#_Toc499126396)

[6.3 Withdrawal Procedures 9](#_Toc499126397)

[7. Research Project Procedures 9](#_Toc499126398)

[7.1 Schedule of Treatment for each visit 9](#_Toc499126399)

[7.2 Schedule of Assessment (in Diagramatic Format) 10](#_Toc499126400)

[7.3 Follow up Procedures *(if applicable)* 10](#_Toc499126401)

[7.4 Laboratory Assessments *(if applicable)* 10](#_Toc499126402)

[7.5 Radiology Assessments *(if applicable)* 10](#_Toc499126403)

[7.6 Annual Safety Reporting 10](#_Toc499126404)

[7.7 Procedures for reporting blinded ‘ unexpected’ and related’ SAEs 10](#_Toc499126405)

[7.8 Overview of the Safety Reporting Process/Pharmacovigilance responsibilities 10](#_Toc499126406)

[8. Data Collection and Management 10](#_Toc499126407)

[8.1 Data Collection 10](#_Toc499126408)

[8.2 Data Management System 10](#_Toc499126409)

[9. Data Analysis 10](#_Toc499126410)

[9.1 Sample Size Considerations 10](#_Toc499126411)

[9.2 Proposed Analysis 10](#_Toc499126412)

[9.3 Missing Data 11](#_Toc499126413)

[9.4 Transfer of Data 11](#_Toc499126414)

[10. Labs and Samples Analysis 11](#_Toc499126415)

[11. Data Handling & Record Keeping 11](#_Toc499126416)

[11.1 Confidentiality 11](#_Toc499126417)

[11.2 Research Project Documents 11](#_Toc499126418)

[11.3 Case Report Form 12](#_Toc499126419)

[11.4 Record Retention and Archiving 12](#_Toc499126420)

[11.5 Compliance 12](#_Toc499126421)

[11.6 Ethical Considerations 12](#_Toc499126422)

[11.7 Quality Control and Quality Assurance 12](#_Toc499126423)

[11.8 Non-Compliance 12](#_Toc499126424)

[12. Research Project Management and Oversight Arrangements 12](#_Toc499126425)

[12.1 Trial Management Group 13](#_Toc499126426)

[12.2 Trial Steering Committee 13](#_Toc499126427)

[12.3 Data Monitoring Committee 13](#_Toc499126428)

[13. Reporting, Publication and Notification of Results 13](#_Toc499126429)

[13.1 Authorship Policy 13](#_Toc499126430)

[13.2 Publication 13](#_Toc499126431)

[13.3 Peer Review 13](#_Toc499126432)

[14. Research Project Conduct Responsibilities 13](#_Toc499126433)

[14.1 Protocol Amendments, Deviations and Breaches 14](#_Toc499126434)

[14.2 End of Research Project 14](#_Toc499126435)

[15. References 14](#_Toc499126436)

[16. Appendices 14](#_Toc499126437)

# Research Project Summary/Synopsis

|  |  |
| --- | --- |
| **Title** | *Full Title* |
| **Short Title** | *Shortened Title* |
| **Protocol Version Number and Date** | *The Standard Protocol Version Number and Date used to identify this research project* |
| **Methodology** | *Type of research project: single-blind, double-blind, randomised controlled, cross-over, etc.* |
| **Research Project Duration** | *Estimated duration for the main research project protocol (e.g. from when all approvals have been received (REC, MHRA and R&D) to when the last participant recruited has completed all research project processes)* |
| **Research Project Centre** |  |
| **Objectives** | *Brief statement of key primary objectives* |
| **Number of Participants** | *Number of Participants expected to be recruited for the whole research project.* |
| **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 research project* |

# Protocol Approval - <<Insert research project title>>

The clinical research project as detailed within this research protocol (Version XXX, dated XX XXX XX), or any subsequent amendments will be conducted in accordance with the Research Governance Framework for Health & Social Care (2005), the World Medical Association Declaration of Helsinki (1996) and the current applicable regulatory requirements and any subsequent amendments of the appropriate regulations.

By signing this document I am confirming that I have read, understood and approve the protocol for the above research project.

|  |  |
| --- | --- |
| Chief Investigator: |  |
| Signature: |  |
| Date: |  |

|  |  |
| --- | --- |
| Statistician: |  |
| Signature: |  |
| Date: |  |

|  |  |
| --- | --- |
| Sponsor Representative: |  |
| Signature: |  |
| Date: |  |

# 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 |
| ICF | Informed Consent Form |
| ISRCTN | International Standard Randomised Controlled Trial Number |
| MA | Marketing Authorisation |
| MS | Member State |
| NHS R&D | National Health Service Research & Development |
| PI | Principle Investigator |
| QA | Quality Assurance |
| QC | Quality Control |
| 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 |

# 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.***

## 1.1 Background

*This section should include background information, any reviews of previous studies, disease particulars etc.*

## 1.2 Preclinical Data

*Include and relevant preclinical data with reference to up to date literature.*

## 1.3 Clinical Data

*Include all previous clinical data relating to the indication of investigation as documented within the literature.*

## 1.4 Rationale and Risks/Benefits

*A summary of known and potential risks and benefits to human participants 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.*

# 2. Research Project Objectives and Design

## 2.1 Research Project Objectives

### 2.1.1 Primary Objective

*State the main research question you aim to answer with this research project*

### 2.1.2 Secondary Objective(s)

*Detail any secondary objectives if applicable.*

## 2.2 Outcomes

### 2.2.1 Primary Outcome

*Identify a single response variable (primary endpoint/outcome) to answer the primary research question.*

### 2.2.2 Secondary Outcome(s)

*Detail any secondary outcomes.*

# 3. Research Project Design

## 3.1 Research Project Description

*Give details on what exactly you plan to do. Include details on project visits, what interventions/tasks/questionnaires/interviews the participant will undertake etc. and state the endpoints of the project.*

## 3.2 Research Project Flowchart

*A flow chart detailing the research project processes can be included here or attached as an appendix.*

## 3.3 Research Project Timeline

*A schedule detailing the research project process can be included here or attached as an appendix.*

# 4. Research Project Population

## 4.1 Number of Participants

*State the required sample size and the participant population to be recruited e.g. participants with heart disease, healthy volunteers etc.*

## 4.2 Inclusion Criteria

# *State the criterion that deems the participant suitable to take part in the research project.*

## 4.3 Exclusion Criteria

*State the criterion that excludes the participant from taking part in the research project***.**

# 5. Participant Selection and Enrolment

## 5.1 Identifying Participants

*State who will identify the participants for the research project and how this will be done.*

## 5.2 Consenting Participants

*State who will take consent from participants and how this will be recorded e.g. in writing using a consent form.*

## 5.3 Screening for Eligibility

*List any screening requirements such as laboratory or diagnostic testing necessary to meet any noted inclusion or exclusion criteria.*

## 5.4 Ineligible and Non-Recruited Participants

*Detail the procedure for ineligible and non-recruited participants and state how their data will be handled.*

# 6. Randomisation and Blinding

## 6.1 Randomisation Details

*Detail the process of how different arms will be allocated between participants in enough detail to theoretically enable a full reproduction of the process.*

## 6.2 Blinding

*Describe in detail any blinding processes to be used in the research project and describe the procedures for unblinding.*

## 6.3 Withdrawal Procedures

*Give a full description of the withdrawal criteria and the process for withdrawing participants from the research project. Include information on documentation to be completed, if participants will be replaced and if data will be retained (with permission).*

# 7. Research Project Procedures

## 7.1 Schedule of Treatment for each visit

**Outline all treatments/interventions that the participant will undergo at each visit during their participation within the research project.**

## 7.2 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.**

## 7.3 Follow up Procedures *(if applicable)*

**Ensure any follow up procedures required/applicable are documented. If the tests are standard they should be listed, although documented as standard care.**

## 7.4 Laboratory Assessments *(if applicable)*

**Any laboratory assessments, with time points, detailed including if specific parameters/normal parameters are required.**

## 7.5 Radiology Assessments *(if applicable)*

**Any radiological/imaging assessments, give detail with regards to the intervention here.**

## 7.6 Annual Safety Reporting

**CI to 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.**

## 7.7 Procedures for reporting blinded ‘ unexpected’ and related’ SAEs

**In the case of a blinded research project, it is recommended the treatment code for the participant is broken in the reporting of an ‘unexpected and related’ SAE. However, the blind should be maintained for staff that are involved in data analysis and interpretation. The unblinding of single cases by the PI/CI in the course of a clinical research project should only be performed if necessary for the safety of the research project participant.**

## 7.8 Overview of the Safety Reporting Process/Pharmacovigilance responsibilities

## **The CI/PI has the overall pharmacovigilance oversight responsibility. The CI/PI has a duty to ensure that pharmacovigilance monitoring and reporting is conducted in accordance with the sponsor’s requirements.**

**Please outline the process/organisation within the research project team to ensure that all SAE reporting is conducted in accordance with the sponsor’s timelines. Display this information within an organogram to be located in the appendices in section 15 to ensure that there is a clear and distinct reporting process outlined with the research project members detailed within this process.**

# 8. Data Collection and Management

## 8.1 Data Collection

*Detail how data will be collected throughout the course of the research project (e.g. CRFs, questionnaires, interviews etc.) and state how both electronic and manual files will be securely stored (e.g. secured shared drive, locked filing cabinets etc.) and kept confidential.*

## 8.2 Data Management System

**The research project system will be based on the protocol and CRF for the research project and individual requirements of the investigators. Development and validation of the research project database and QC and extraction of data should be described here. If any extracts for analysis are to be made, they should be described here.**

# 9. Data Analysis

*Amend headings for Qualitative Project*

## 9.1 Sample Size Considerations

*Provide justification for the sample size/power calculation or precision taking account of dropout rates and other relevant assumptions, etc. Provide an estimate of the recruitment period in which the required sample size will be achieved and justification for this estimate.*

## 9.2 Proposed Analysis

# *Fully describe the analysis plan including the summary measures to be reported, the methods of analysis and a description of any non-statistical methods that might be used*

## 9.3 Missing Data

# *Describe how missing data will be accounted for and handled. Also describe the strategies in place to minimise the loss of data.*

## 9.4 Transfer of Data

# *If data are to be transferred between sites/collaborators please state how this will be done securely. Please note that all data MUST be anonymised before they are transferred*

# 10. Labs and Samples Analysis

*Detail the laboratory involved and where it is based. Detail if the appropriate accreditations and agreements are in place. Detail what samples will be taken and how they will be analysed. Detail the chain of custody arrangements.*

# 11. Data Handling & Record Keeping

## 11.1 Confidentiality

The Investigator has a responsibility to ensure that participant anonymity is protected and maintained. They must also ensure that their identities are protected from any unauthorised parties. Information with regards to research project participants 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 participants?**
* **Who will have access to the Information and why?**
* **The Chief Investigator is the ‘Custodian’ of the data.**
* **Identify if participant identifiable details will be transferred outside the EU as different confidentiality laws apply in this instance.**
* **The rights of the participant to revoke their authorisation for the use of their PHI.**
* **The participants will be anonymised with regards to any future publications relating to this research project.**

## 11.2 Research Project Documents

**Add or remove as appropriate**

* A signed protocol and any subsequent amendments
* Current Summary of Product Characteristics
* Sponsor Self-Monitoring template for the research project team to complete on a regular basis as detailed by the Monitoring section
* Current/Superseded Participant Information Sheets (as applicable)
* Current/Superseded Consent Forms (as applicable)
* Indemnity documentation from sponsor
* Conditions of Sponsorship from sponsor
* Conditional/Final R&D Approval
* Signed site agreement
* Ethics submissions/approvals/correspondence
* CVs of CI and site staff
* Laboratory accreditation letter, certification and normal ranges for all laboratories to be utilised in the research project
* Delegation log
* Staff training log
* Site signature log
* Participant identification log
* Screening log
* Enrolment log
* Monitoring visit log
* Protocol training log
* Correspondence relating to the research project
* Communication Plan between the CI/PI and members of the research project team
* SAE reporting plan for the research project

## 11.3 Case Report Form

**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 research project specific. Please state when and who will be responsible for the completion of the CRF throughout the life cycle of the research project.**

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

## 11.4 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**.

Archiving of research project documents will be **insert details.**

## 11.5 Compliance

The CI will ensure that the research project 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.

## 11.6 Ethical Considerations

The research project will be conducted in accordance with the principles of good clinical practice (GCP).

In addition to Sponsorship approval, a favorable ethical opinion will be obtained from the appropriate REC and appropriate NHS R&D approval(s) will be obtained prior to commencement of the research project.

## 11.7 Quality Control and Quality Assurance

The CI, PIs and all institutions involved in the research project shall permit research project related monitoring, audits, and REC review. The CI agrees to allow the Sponsor or, representatives of the Sponsor, direct access to all research project records and source documentation.

## 11.8 Non-Compliance

**These non-compliances may be captured from a variety of different sources including monitoring visits, CRFs, 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.**

# 12. Research Project Management and Oversight Arrangements

## 12.1 Trial Management Group

**Each research project, no matter the number of participants or number of collaborating sites, should establish a trial management group (TMG) to set and review the day to day management of the research project. The TMG should include the CI, PI, research project manager or equivalent, research nurse if appropriate. Other grant holders can be included but not all of the co-applicants need to be included.**

The research project will be co-ordinated by a Trial Management Group, consisting of e.g. the grant holder (CI), external PIs, Research Project Manager, Research Nurse, *insert as appropriate*.

## 12.2 Trial Steering Committee

**Suggested text only - amend as appropriate. If no TSC will be established, the reason for not having a TSC should be included in this section instead e.g. remit will be carried out as part of the TMG.**

A Trial Steering Committee (TSC) will be established to oversee the conduct and progress of the research project. The terms of reference of the TSC, the draft template for reporting are detailed in Appendix **insert number here**.

## 12.3 Data Monitoring Committee

**Suggested text only - amend as appropriate. If no DMC will be established, the reason for not having a DMC should be included in this section instead**

An independent Data Monitoring Committee (DMC) will be established to oversee research project progress. The terms of reference of the DMC are detailed in Appendix **insert number here**.

# 13. Reporting, Publication and Notification of Results

## 13.1 Authorship Policy

Ownership of the data arising from this research project resides with the research project team and their respective employers. On completion of the research project, the research project data will be analysed, and a research project report will be prepared

## 13.2 Publication

The research project report will be used for publication and presentation at scientific meetings. Investigators have the right to publish orally or in writing the results of the research project.

Summaries of results may also be made available to Investigators for dissemination within their clinical areas (where appropriate and according to their discretion).

## 13.3 Peer Review

*Document procedures for peer review – these may be funder specific or involve an internal department. Peer review is where an independent “expert” (relevant clinician, allied health professional or a member of any other relevant professional group) examines the proposed project to consider aspects such as design quality, feasibility, acceptability and importance of the topic etc.*

# 14. Research Project Conduct Responsibilities

## 14.1 Protocol Amendments, Deviations and Breaches

The CI will seek approval for any amendments to the Protocol or other research project documents from the Sponsor, REC and NHS R&D Office(s). Amendments to the protocol or other research project docs will not be implemented without these approvals.

In the event that a CI needs to deviate from the protocol, the nature of and reasons for the deviation will be recorded in the CRF, documented and submitted to the Sponsor. If this necessitates a subsequent protocol amendment, this will be submitted to the Sponsor for approval and then to the appropriate REC and lead NHS R&D Office for review and approval.

In the event that a serious breach of GCP is suspected, this will be reported to the Sponsor immediately using the form “Breach Report Form”.

## 14.2 End of Research Project

The end of research project is defined as last participant last visit (LPLV)/database lock/other *insert as appropriate*. The Sponsor, CI and/or the TSC have the right at any time to terminate the research project for clinical or administrative reasons.

The end of the research project will be reported to the Sponsor and REC within 90 days, or 15 days if the research project is terminated prematurely. The CI will ensure that any appropriate follow up is arranged for all participants.

A summary report of the research project will be provided to the Sponsor and REC within 1 year of the end of the research project

# 15. References

# 16. Appendices

**This section should contain the list (**Do not copy and paste the documents (denoted by underlining) as you do not want to make a substantial amendment every time that a substantial amendment is made for these documents**) of all pertinent documents that are associated with the management of the research project.**

**The following is a list of attachments, those with an asterisk\* must be submitted to the Research Ethics Committee with the protocol.**

* Consent Form (versioned and dated appropriately)\*
* Participant Information Sheet (versioned and dated appropriately)\*
* GP letters/ advertisements/any other letters and documents to be given to the participant (versioned and dated appropriately)\*
* An SAE/SUSAR reporting Organogram – who will be the research project members (including BACK UP STAFF for ALL individuals) involved in the identification/reporting of the SAE
* Communication Plan Organogram – how will information be disseminated between the PI/CI and the members of the research project team relating to the protocol and other research project related duties. This plan should ensure that there is always a physician (either PI/Sub-I) trained adequately on the research project to ensure that a research project trained medical physician is available to make any research project related decisions with regards to participant care, mainly with regards to adverse events or intercurrent illnesses.
* Source Data Identification List
* Core Lab Instructions To Investigators (if applicable)
* Specimen Preparation And Handling (if applicable) (e.g. for any specialized procedures that research project team must follow to process a research project specimen, and/or prepare it for postage/courier/shipment)
* Drug Conversion Plan ( if applicable) (e.g. if there is a special regimen for transitioning a participant from their baseline medication over to research project medication)
* Antidote Preparation and Delivery (if applicable) (e.g. special instructions for preparing and delivering any therapy designed to reverse the effects of the research project drug, if applicable)