Gloucestershire Hospitals
NHS Foundation Trust

SOP 29 – Writing a protocol

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IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the Research & Innovation Webpage for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded version are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive version of all Gloucestershire Hospitals NHS Foundation Trust SOPs appear online. If you are reading this in printed form, check that the version number and date below is the most recent one as shown on the R&I website:

https://www.gloshospitals.nhs.uk/about-us/research-our-hospitals/

The Gloucestershire Hospitals NHS Foundation Trust wishes to acknowledge York Hospitals NHS Foundation Trust and University Hospitals Bristol NHS Foundation Trust who gave permission to use their templates in the development of these SOPs.

Version History Log

This area will be updated with details of all changes made to the SOP whether due for full review or not.

Version	Details of Change	Date Implemented
1.0	Original SOP	01/02/2017
2.0	Rebranding to GHNHSFT, updating of contact details and reference documents	31/03/2018
2.1	Updating of website links, reformatting and addition of appendix 1 detailing protocol content	31/01/2022
3.0	Removal of SOP categories and change of reference codes Insertion of appendix 1 non-CTIMP protocol template Deletion of protocol template for CTIMPS and direction to use the HRA template for CTIMPS only Changed R&D to R&I	03/01/2024

This SOP will be reviewed every two years unless changes to any relevant legislation require otherwise

Related Documents:

Related SOPs can be found in the following location: Research at our hospitals (gloshospitals.nhs.uk)

Glossary

CI	Chief Investigator
CTIMP	Clinical Trial of a Investigational Medicinal Product
GHNHSFT	Gloucestershire Hospitals NHS Foundation Trust
HRA	Health Research Authority
ICH GCP	International Conference for Harmonisation of Good Clinical Practice
IMP	Investigational Medicinal Product
MHRA	Medicines and Healthcare products Regulatory Agency
R&I	Research & Innovation
REC	Research Ethics Committee
TMF	Trial Master File

Contents

1. Introduction, Background and Purpose

The purpose of this SOP is to describe how a study protocol should be written to Good Clinical Practice (GCP) standards so that it is compliant with the Medicines for Human Use (Clinical Trials) Regulations 2004 (and amendments).

A study protocol is a document which describes how a piece of research will be conducted. It is a controlled document which describes a range of activities including, but not limited to the background, rationale, design, population to be researched, oversight, data collection, analysis and archiving of a study.

Details of the stakeholders in the research should be documented, to include the sponsor, chief investigator and the funder.

Documents such as the participant information sheets and consent forms may be appended, along with other documentation which supports robust management of the research.

2. Who should use this SOP

This SOP should be used by investigators and research team members involved in Clinical Trial of a Investigational Medicinal Products (CTIMPs) sponsored by The Trust. However, it is also relevant for researchers preparing protocols for non-CTIMPs and medical device trials.

3. When this SOP should be used

This SOP is applicable when preparing protocols for all CTIMPs that are sponsored by the Trust. It should also be followed for all research proposals that are not CTIMPs, requirements specific to CTIMPs will not apply.

4. Procedure

4.1 Protocol template

4.1.1 All protocols for CTIMPs to be sponsored by the Trust must be based on the following templates and guidance produced by the Health Research Authority (HRA)

(a) CTIMP protocol guidance and a template, available here: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/

and also

(b) Guidance on the design of participant information sheets and consent forms, available here: http://www.hra-decisiontools.org.uk/consent/

4.1.2 Non-CTIMP Research Project:

Studies that fall within the scope of the relevant Medicines and Medical Devices regulations should use the HRA template above.Qualitative research projects will follow the HRA protocol guidance and template; qualitative-protocol-development-tool.docx (live.com).

The template found in appendix 1 can be used for studies that do not fall under the regulation mentioned above.

4.2 Protocol Development

The Protocol should be developed in collaboration with key contributors to the research project. These can include (and are not limited to):

- Chief Investigator (CI)
- Other Key Investigators
- Pharmacy Contact or IMP Specialist or Statistician or Laboratory or sample specialists or collaborators
- Members of any proposed Trial Steering Committee/Data Monitoring Committee or Trial Review Committee
- Members of the funding awarding body
- Commercial supporters of the research Representative of the Sponsor

For all interventional research the protocol should also consider the SPIRIT 2013 Guidelines (Standard Protocol Items: Recommendations for Interventional Trials www.**spirit**-statement.org/).See appendix 2 for standard protocol layout.

For the efficacy of research projects review the COMET Initiative website (http://www.comet-initiative.org/) for the standardised Core Outcome Measures in Effectiveness Trials

The Protocol should be version controlled. The final version of the protocol must be reviewed, amended as necessary and approved by the appropriate clinical trial development team including at the minimum, the CI, the trial statistician and the trial pharmacist (if a CTIMP).

The final version of the protocol to be sent for regulatory approval must be signed and dated by the CI. It is then kept in the Trial Master File (TMF) for Trust Sponsored CTIMPs and Non-CTIMP research projects

4.3 Protocol amendments

Any change of the protocol will constitute an amendment either substantial or non-substantial. The Sponsor will confirm whether the change is substantial or not., please contact R&I on ghn-tr.glos.rdsu@nhs.net to obtain this advice, For managing amendments including urgent safety measures refer to the HRA website.

Changes must be reviewed and approved by the appropriate personnel e.g., CI, pharmacy advisor, statistician, etc. Those studies which fall within the scope of the relevant Medicines and Medical Devices regulations should have a Trial Management Group led by the CI.

5. References

https://www.ct-toolkit.ac.uk/routemap/trial-planning-and-design/

https://www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/

http://www.hra-decisiontools.org.uk/consent/

www.**spirit**-statement.org/

http://www.comet-initiative.org/

Appendix 1 Protocol template for studies not covered by the HRA templates

Please read the accompanying "Guidance for using the Protocol Template for Sponsored Studies (not covered by the HRA templates)" whilst writing your protocol

Guidelines can be found:

https://www.gloshospitals.nhs.uk/about-us/research-our-hospitals/

1 TITLE PAGE

Full/long title of study	
Short title/study acronym	
Protocol version number /date	
IRAS Number	
ISRCTN/Clinicaltrials.gov number	
Sponsor	Gloucestershire Hospitals NHS Foundation Trust
Sponsor reference number	
Funder name and reference number (if applicable)	
Chief Investigator	
Sponsor Representative	Research and Innovation Leadon House Gloucestershire Royal Hospital Great Western Road Gloucester GL1 3NN

2 PROTOCOL VERSION HISTORY

Amendment No. State whether Substantial Amendment (SA) or Non-substantial amendment (NSA)	**Version No.**	**Version Date**	**Brief summary of change(s) and reason for update.**
Initial Application	1.0		Not applicable

3 SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirements.

I agree:

- to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor
- that no activity will commence at participating sites until Sponsor green light is confirmed
- that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

Chief Investigator:

Signature: Date:

…… ……/……/…..

Name (please print):

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Interventional studies only
Research and Innovation representative as Study Sponsor:

Signature: Date:

…… ……/……/…..

Name (please print):

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Position

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4 KEY CONTACTS

Chief Investigator	
Study Co-ordinator/Clinical Trials Unit	
Sponsor	
Joint-sponsor(s)/co-sponsor(s)	
Funder(s)	
Key Protocol Contributors	
Study Management and Oversight Committees	
Statistician	

5 CONTENTS

6 LAY SUMMARY

7 SYNOPSIS

KEY STUDY INFORMATION	
Study Title	
IRAS Number	
Study Design/Type	
Study Participants	
Planned Sample size	
Planned Study Period	
End of study definition	
Single site or multi-site	
Research Aim(s)	
Research objectives	
Intervention(s) (if applicable)	
Archiving period	
SAMPLES (If applicable)	
DATA	

8 LIST OF ABBREVIATIONS

Abbreviation	Full text
CI	Chief Investigator
CRF	Case Report Form
GCP	Good Clinical Practice
GP	General Practitioner
HRA	Health Research Authority
ICF	Informed Consent Form
ISF	Investigator Site File (This forms part of the TMF)
NHS	National Health Service
PI	Principal Investigator
PPI	Patient and Public Involvement
PIS/PIL	Participant Information Sheet/Leaflet
RCT	Randomised Control Trial
REC	Research Ethics Committee
R&I	Research and Innovation
SMG	Study Management Group
SSC	Study Steering Committee
SOP	Standard Operating Procedure
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee

9 FUNDING

Funders	Financial and Non-Financial support given

10 ROLES AND RESPONSIBILITIES

10.1 Role of sponsor and funder

10.2 Study team

10.3 Trial/study management committees/groups and individuals

10.4 Protocol Contributors

11 KEY WORDS

12 BACKGROUND

13 RATIONALE

14 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

14.1 Primary objective

14.2 Secondary objective(s)

14.2.1 Outcome measures/endpoints

14.2.2 Primary outcomes

14.2.3 Secondary outcomes

15 STUDY DESIGN AND SETTING

15.1 Study design

15.2 Study setting

16 PARTICIPANT ELIGIBILITY CRITERIA

16.1 Inclusion criteria

16.2 Exclusion criteria

16.3 Equality, diversity and inclusion considerations

17 STUDY PROCEDURES

17.1 Recruitment

17.1.1 Participant identification

17.1.2 Screening

17.2 Payment

17.3 Informed consent

17.4 Randomisation scheme

17.4.1 Method of implementing the randomisation/allocation sequence

17.4.2 Blinding and Emergency unblinding

17.5 Trial assessments

17.5.1 Baseline data

17.5.2 Follow-up assessments

17.5.3 Qualitative assessments

17.6 Withdrawal criteria

17.7 Clinical samples: collection, storage and analysis

18 ETHICAL AND REGULATORY CONSIDERATIONS

18.1 Research Governance Statement

This study will be conducted in accordance with:

- The principles of Good Clinical Practice, as set out in the International Conference for Harmonisation of Good Clinical Practice (ICH GCP) guidelines
- The UK Policy Framework for Health and Social Care Research.

18.2 Assessment and management of risk

18.3 Research Ethics Committee (REC) and other Regulatory review & reports

18.4 Regulatory Review & Compliance

The study will be performed subject to favourable opinion/ authorisation/permission or equivalent from all necessary regulatory and other bodies. This includes but is not limited to REC, HRA, NHS Trusts.

18.5 Amendments

18.6 End of study

19 PATIENT & PUBLIC INVOLVEMENT

20 PROTOCOL COMPLIANCE

20.1 Protocol Deviations

20.2 Notification of Serious Breaches to GCP and/or the protocol

21 DATA PROTECTION AND PATIENT CONFIDENTIALITY

22 DATA MANAGEMENT

22.1 Data collection tools and source document identification

22.1.1 Source Data

22.1.2 Source Documents

22.1.3 Case report forms

22.1.4 CRFs as Source Documents

22.2 Data handling and record keeping

The database and randomisation system will be designed so as to protect patient information in line with the General Data Protection Regulation. Study staff will ensure that the participants' anonymity is maintained through protective and secure handling and storage of patient information at the study centres (as relevant) in line with the Ethics approval. All documents will be stored securely and only accessible by study staff and authorised personnel. Data will be collected and retained in accordance with the General Data Protection Regulation.

22.3 Access to Data

22.4 Access to the final study dataset

23 STATISTICS AND DATA ANALYSIS

23.1 Sample size calculation

23.2 Planned recruitment rate

23.3 Statistical analysis plan

23.3.1 Summary of baseline data and flow of patients

23.3.2 Primary outcome analysis

23.3.3 Secondary outcome analysis

23.3.4 Subgroup analyses

23.3.5 Adjusted analysis

23.3.6 Interim analysis and criteria for the premature termination of the trial

23.3.7 Participant population

23.3.8 Procedure(s) to account for missing or spurious data

23.4 Other statistical considerations

23.5 Economic evaluation

24 SAFETY REPORTING

Adverse events will be recorded and reported in accordance with GHNHSFT SOP 19 Periodic Safety Reporting to Regulatory Authorities and SOP 20 Adverse events and reaction safety reporting.

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25 QUALITY ASSURANCE, RISK ASSESSMENT AND MONITORING

25.1 Risk Assessment

25.2 Monitoring, audit and inspection

The study will be monitored in accordance with SOP 13 Monitoring. All study related documents will be made available on request for monitoring and audit by the Sponsor, the relevant Research Ethics Committee and for any other regulatory authorities.

25.3 Peer review

26 INSURANCE AND INDEMNITY

This is an NHS-sponsored research study. If there is negligent harm during the clinical trial when the NHS body owes a duty of care to the person harmed, NHS Indemnity covers NHS staff, medical academic staff with honorary contracts, and those conducting the trial. NHS Indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm. Ex-gratia payments may be considered in the case of a claim.

27 FINANCIAL AND OTHER COMPETING INTERESTS

28 FINANCE AND CONTRACTUAL ARRANGEMENTS INCLUDING EQUIPMENT SUPPLY AND INTELLECTUAL PROPERTY

29 PUBLICATION AND DISSEMINATION

29.1 Dissemination policy

29.2 Authorship eligibility guidelines and any intended use of professional writers

30 DOCUMENT STORAGE AND ARCHIVING

Study documents (paper and electronic) will be retained in a secure location during and after the study has finished. All essential documents, including patient records and other source documents will be retained for a period of 5 years following the end of the study. Where study related information is documented in the hard copy medical records – those records will be identified by an alert sticker. Refer to SOP 02 Research Documentation and File Management and SOP 06 Archiving.

31 REFERENCES

32 APPENDICES

32.1 APPENDIX 1 Study Flow Chart

32.2 APPENDIX 2 Schedule of Procedures

32.3 APPENDIX 3 -Data Flow diagram