Standard Operating Procedure

WRITING A RESEARCH PROTOCOL TO GOOD CLINICAL PRACTICE

SETTING Trustwide

AUDIENCE Research staff with the responsibility for writing research protocols to be sponsored by UHBristol.

Standard Operating Procedure (SOP)

Title of Standard Operating Procedure			
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Approved by:	Trust Research Group		
Date for review:	November 2017		

Review date	Version number	Version Date	Effective Date	Reason for change	Author/Responsible person	Authorised by
Original Policy	1.0	28/07/2015	17/08/2015	New SOP	Diana Benton	Diana Benton
19/08/2015	1.1	19/08/2015	14/09/2015	Minor changes to incorporate consultation feedback	Genna Nicodemi	Diana Benton
22/12/15	1.2	22/12/2015	16/03/2016	Minor update to standard wording	Jess Bisset	Diana Benton
28/11/16	1.3	28/11/16	23/12/2016	Updates to standard wording and minor clarifications	Jess Bisset	Diana Benton

1. Purpose

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

The purpose of this document is to describe how a study protocol should be written to Good Clinical Practice (GCP) so that it is compliant with the Medicines for Human Use (Clinical Trials) Regulations 2004 (and amendments). Consequently, this SOP principally focuses on the requirements for a protocol of a clinical trial of an investigational medicinal product (CTIMP). However, many areas covered will also be relevant for protocols of non-CTIMPs.

2. Scope (areas/people in and out of scope should be defined)

In scope: protocols for studies sponsored by UHBristol.

Out of scope: protocols for studies sponsored by organisations other than UHBristol.

3. Definitions/Abbreviations

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
HRA	Health Research Authority
GCP	Good Clinical Practice

4. Procedure

All protocols for CTIMPs to be sponsored by UHBristol must be based on the following templates and guidance produced by the HRA (unless agreed otherwise in advance):

- CTIMP protocol guidance and a template, available here: http://www.hra.nhs.uk/about-the-hra/consultations-calls/closed-consultations/protocol-guidance-template-use-clinical-trial-investigational-medicinal-product-ctimp-consultation-use/#sthash.S6fI8FDk.dpuf
- Guidance on the design of participant information sheets and consent forms, available here: http://www.hra.nhs.uk/resources/before-you-apply/consent-and-participation/consent-and-participant-information/#sthash.m682P3Eu.dpuf

Much of the content of these documents will also be relevant to Non-CTIMP protocols. UHBristol supports their use as a basis for writing protocols for all research to be sponsored by the Trust. Sections only relevant to CTIMPs can be omitted where irrelevant in these cases. Please contact the Research Management Office for further guidance where necessary.

UHBristol provides standard wording for some sections of the protocol. In some cases, the HRA template also contains suggested standard wording. UHBristol standard wording should be used in preference, or in addition to HRA standard wording. It is the responsibility of the CI to ensure that wording used is not in contradiction of any of UHBristol's research SOPs.

UHBristol standard wording for CTIMPs and non-CTIMPs is provided in the appendices to this SOP.

5. References

ICH Harmonised Tripartite Guideline for Good Clinical Practice (1996)
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf

EU COMMISSION DIRECTIVE 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:091:0013:0019:en:PDF

Statutory Instrument 1031: The Medicines for Human Use (Clinical Trials) Regulations 2004
http://www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf

6. Appendices

- **Appendix 1 UHBristol suggested standard wording for IMP protocols**
- **Appendix 2 UHBristol suggested standard wording for Non-IMP protocols**

IMPORTANT NOTE:
This procedure has been screened for equality impact; it was not assessed as having adverse effects on any section of the community.

RELATED DOCUMENTS	Investigational Medicinal Products SOP Research Safety Reporting SOP Monitoring and Oversight of Research Activity SOP
QUERIES	Research Operations Manager or Research Management Facilitators - Research & Innovation Department via 0117 342 0233

Appendix 1 UHBristol suggested standard wording for IMP protocols

Protocol Headings	Standard wording
Details of Sponsor	University Hospitals Bristol NHS Foundation Trust, Research and Innovation, Level 3, UH Bristol Education and Research Centre, Upper Maudlin Street, Bristol BS2 8AE. Tel: 0117 342 0233
CI and Research Team Contact Details	*Enter the Chief Investigator's contact details, including correspondence address and emergency contact details. Include contact details for relevant/key members of the research team.*
Study Medication	*In addition to description of study medication, dose, regimen etc.* Study medication will be stored and dispensed by the trial site's pharmacy department in accordance with Good Clinical Practice, Good Manufacturing Practice and pharmacy department SOPs.
Safety Reporting	Adverse events will be recorded and reported in accordance with University Hospitals Bristol's Research Safety Reporting SOP. *NB identify events that may be excluded from expedited reporting because they are commonly associated with the clinical procedures taking place (e.g. wound infection); these should be agreed with the sponsor prior to submission to REC. Identify reference documents used to justify this decision e.g. Product Information.*
Reference Safety Information (RSI)	The following will be used as the Reference Safety Information (RSI) during the course of this trial: • Summary of Product Characteristics for XX (name of IMP)/Investigator Brochure for XX (name of IMP)/other document (delete and amend as appropriate) If there are any updates made to the document described above, these will be reviewed by the Chief Investigator and Sponsor and a joint decision made whether the updated document will be submitted to the MHRA for use as the RSI in the trial.
Monitoring, Audit and Inspection	The study will be monitored in accordance with University Hospitals Bristol's Monitoring and Oversight of Research Activity SOP. All trial related documents will be made available on request for monitoring and audit by UH Bristol, the relevant Research Ethics Committee and for inspection by the Medicines and Healthcare products Regulatory Authority or other licensing bodies. The monitoring plan will be developed and agreed by the sponsor.
Quality Control	Where applicable, a random sample of x% (at least 10%) of CRFs will be checked, by the trial Research Team or R&I monitor, against entries within the database and with the source data for quality purposes.The percentage checked will be increased if a significant error rate is found. The data from the first patient recruited at a new site will be reviewed. This may include consent records, safety data and primary endpoint data.
Data Handling and Protection	The database and randomisation system will be designed so as to protect patient information in line with the Data Protection Act 1998. Trial staff will ensure that the participants' confidentiality is maintained through protective and secure handling and storage of patient information at the trial centres (as relevant). All documents will be stored securely and only accessible by trial staff and

	authorised personnel. Data will be collected and retained in accordance with the Data Protection Act 1998.
Storage of Records	Study documents (paper and electronic) will be retained in a secure location during and after the trial has finished. All essential documents, including patient records and other source documents will be retained for a period of 15 years following the end of the study. For trials of Advanced Therapy Medicinal Products (ATIMP) documents will be retained for 30 years following the end of the study. Where trial related information is documented in the hard copy medical records – those records will be identified by a 'Do not destroy before dd/mm/yyyy' label where date is 15 years after the last patient last visit. Where electronic records are in use, trust policy will be followed.
Indemnity	This is an NHS-sponsored research study. For NHS sponsored research HSG(96)48 reference no. 2 refers. 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.
Authorisations	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, MHRA, HRA, NHS trusts.
Research Governance Statement	This study will be conducted in accordance with: • The Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments • International Conference for Harmonisation of Good Clinical Practice (ICH GCP) guidelines. • Research Governance Framework for Health and Social Care.

Appendix 2 UHBristol suggested standard wording for Non-IMP protocols

Protocol Headings	Standard wording
Details of Sponsor	University Hospitals Bristol NHS Foundation Trust, Research and Innovation, Level 3, UH Bristol Education and Research Centre, Upper Maudlin Street, Bristol BS2 8AE. Tel: 0117 342 0233.
CI and Research Team Contact Details	*Enter the Chief Investigator's contact details, including correspondence address and emergency contact details. Include contact details for relevant/key members of the research team.*
Safety Reporting	Adverse events will be recorded and reported in accordance with University Hospitals Bristol's Research Safety Reporting SOP. *NB identify events that may be excluded from expedited reporting because they are commonly associated with the clinical procedures taking place (e.g. wound infection); these should be agreed with the sponsor prior to submission to REC. Identify reference documents used to justify this decision.*
Monitoring, Audit and Inspection	The study will be monitored in accordance with University Hospitals Bristol's Monitoring and Oversight of Research Activity SOP. All trial related documents will be made available on request for monitoring, audit and/or inspection by UH Bristol, the relevant Research Ethics Committee and any other licensing bodies as applicable.
Quality Control	Where applicable a random sample of x% (at least 10%) of CRFs will be checked, by the trial Research Team, against entries within the database and with the source data for quality purposes. The percentage checked will be increased if a significant error rate is found.
Data Handling and Protection	The database and randomisation system will be designed so as to protect patient information in line with the Data Protection Act 1998. Trial staff will ensure that the participants' confidentiality is maintained through protective and secure handling and storage of patient information at the trial centres (as relevant). All documents will be stored securely and only accessible by trial staff and authorised personnel. Data will be collected and retained in accordance with the Data Protection Act 1998.
Storage of Records	Study documents (paper and electronic) will be retained in a secure location during and after the trial 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 a 'Do not destroy before dd/mm/yyyy' label where date is 5 years after the last patient last visit. Where electronic records are in use, trust policy will be followed.
Indemnity	This is an NHS-sponsored research study. For NHS sponsored research HSG(96)48 reference no. 2 refers. 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.
Authorisations	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.
Research Governance Statement	This study will be conducted in accordance with: • Good Clinical Practice • Research Governance Framework for Health and Social Care.