Standard Operating Procedure

INVESTIGATOR OVERSIGHT OF RESEARCH

SETTING Trustwide
FOR STAFF Chief and Principal Investigators of research sponsored and/or hosted by UHBristol
ISSUE Oversight of research

Standard Operating Procedure (SOP)

Author:	Diana Benton	Role:	Head of Research & Innovation
Approved by:	Trust Research Group		
Date for review:	27/07/2016		

Review date	Version number	Version Date	Effective Date	Reason for change	Author/Responsible person	Authorised by
Original SOP	1.0	27/07/2015	04/08/2015	n/a	Diana Benton	Diana Benton
19/08/2015	1.1	19/08/2015	14/09/2015	Minor – inclusion of 'out of scope', correction of grammatical errors and typos and addition of 'Statement of Chief Investigator Responsibilities' as appendix.	Genna Nicodemi	Diana Benton
22/10/2015	1.2	22/10/2015	29/10/2015	Minor - Additional explanation around • the role of the CI/PI in consent • who can receive consent Removal of 'out of scope'	Paula Tacchi	Diana Benton
07/06/2016	2.0 (taken to TRG as 1.3)	07/06/2016	22/08/2016	Amended the 'Statement of Chief Investigator Responsibilities appendix, which is now re-titled 'Statement of Responsibilities for CTIMPs and non-CTIMP studies'	Katharine Wale	Trust Research Group

1. Purpose

The purpose of this document is to describe the responsibilities of Chief and Principal Investigators in relation to oversight of research sponsored and hosted by UH Bristol.

2. Scope

In scope: Investigators undertaking the role of Chief or Principal Investigator for research sponsored and hosted by UH Bristol

3. Definitions/Abbreviations

ASR	Annual Safety Report
CI	Chief Investigator: the **Chief Investigator** is the authorised health professional appointed by the sponsor of a research study, whether or not he/she is an Investigator at any particular site, who takes primary

	responsibility for the conduct and reporting of that study.
CTIMP	Clinical Trial of Investigational Medicinal Product
CTU	Clinical Trials Unit
DSMB	Data Safety Monitoring Board
DSUR	Development Safety Update Report
GCP	Good Clinical Practice
IB	Investigator's Brochure
ICF	Informed Consent Form
ISF	Investigator Site File
MHRA	Medicines and Healthcare Products Regulatory Authority
PI	Principal Investigator: the **Principal Investigator** may be the Chief Investigator. Where the research involves more than one site, the Principal Investigator is the person at the site responsible for conducting the research to required standards.
PIS	Participant Information Sheet
REC	Research Ethics Committee
SmPC	Summary of Product Characteristics
TMF	Trial Master File
TMG	Trial Management Group
UoBristol	The University of Bristol
VIC	Valid Informed Consent

4. Resources

The CI/PI is responsible for ensuring adequate resources are in place to conduct the research. This includes funding, staff and infrastructure.

- Funding: a record of trial finances will be kept and maintained in liaison with a member of the Trust finance department. This will specifically document invoicing arrangements with all parties internally and externally to the Trust (e.g. support departments) who will be in receipt of funds as a result of their involvement in the study. The CI will take responsibility for ensuring that the terms agreed in funding or collaboration agreements for the study are complied with.
- Staffing: Before agreeing to start a study, the PI must ensure that adequate resources will be available at their site to deliver the study in accordance with the protocol and agreements in place. Within UHBristol this should be done in conjunction with managers of divisional research teams and the R&I department, if necessary (Research Matron as first point of contact). The CI must seek assurance from each PI that appropriate resources are in place.
- Infrastructure: it is the responsibility of the CI/PI to ensure that there are arrangements in place to enable delivery of the research in accordance with the protocol and agreements prior to the research commencing. This may include identifying and securing imaging, laboratory or pharmacy resource, making sure rooms are available etc. Managers of divisional research teams can help CI/PI in securing this resource if required.

5. Staff Training/Qualifications and contractual arrangements

For IMP trials Part 2(11) of Schedule 1 to SI 2004/1034 states:

'The medical care given to, and medical decisions made on behalf of, subjects shall always be the responsibility of an appropriately qualified doctor or, when appropriate, of a qualified dentist'

The CI/PI therefore is responsible for ensuring that only appropriately qualified personnel assess eligibility and make medical decisions on behalf of participants. For example, whilst receiving consent may be delegated to a member of the research team, eligibility must always be determined by a qualified doctor or dentist. These processes must be **fully documented**.

It is the responsibility of the CI/PI to ensure that all staff involved in the conduct and management of a research study are appropriately qualified and trained to undertake their delegated duties.

This will include, but is not limited to, Clinical Trial Coordinators, Research Nurses, Pharmacy and Radiology staff and Co-Investigators. It may also include clinical staff who are delivering some of the research intervention(s). The CI/PI must ensure that all staff have undertaken GCP training at a level commensurate with their involvement in the study, study-specific training and have read and understood all UH Bristol Research & Innovation SOPs relevant to their role within the study. Staff must document their training in any new or updated documentation (study specific, Trust-wide or relevant legislation) during the course of the study using a study training log.

The ISF should contain an up-to-date, signed copy of research staff CVs as well as certificates and other evidence of relevant training.

If staff are working on multiple studies, it is acceptable to place a file note in the ISF referring readers to a centrally held CV and training log file. The CI/PI must, however, ensure that study specific training is in the ISF and that centrally held files are archived and easily located in relation to individual trials.

The CI/PI must ensure that all team members who have direct involvement with research subjects and /or personal-identifiable data have appropriate HR arrangements in place with UHBristol at the time of their involvement.

6. Communication with Regulatory Authorities and the Sponsor

The CI/PI will make sure that appropriate arrangements are in place to ensure communication with regulatory authorities, the sponsor and the host organisation takes place on an ongoing basis throughout the course of a study. Formal communications must take place around protocol amendments, urgent safety measures, protocol breaches and violations, safety reporting, annual reports and DSURs; this list is not exhaustive. See "Gaining and Maintaining Authorisations" SOP.

For UHBristol sponsored studies and UoBristol sponsored CTIMPs, reminders will be generated using the research management system and sent by the R&I team to the CI.

For hosted studies, the PI should expect to be reminded by the sponsor if/when their input is required.

Further guidance on processes and the requirements of regulatory bodies and the sponsor can be found in the 'Gaining & Maintaining Authorisations' SOP. For UH Bristol sponsored research, please refer to the R&I website.

If the CI/PI delegates any of these responsibilities to a member of the research team, this will be

documented on the study delegation log which will be filed in the ISF.

Please note that it remains the CI/PI's responsibility to confirm that individuals are adequately qualified and trained to undertake delegated tasks. Despite delegating certain roles and duties within the trial, **the responsibility for the research itself remains with the CI/PI**. For UHBristol sponsored research, the Trust requires that CIs sign the 'Statement of Chief Investigator Responsibilities' document before the research commences (see appendix 1).

7. Protocol Compliance

The CI/PI is responsible for ensuring that research is conducted in accordance with the protocol. This will include (but is not limited to):

- Documenting PI involvement in eligibility and dosing decisions (if relevant)
- Ensuring protocol study visit schedules are followed and documented
- Ensuring complete and accurate CRF completion is taking place in a timely manner by appropriately delegated research team personnel
- Ensuring that randomisation and unblinding procedures are in place and followed
- Ensuring that TMG, DSMB, steering committees and other oversight bodies referred to in the protocol are established, convened and documented, attending meetings of such groups and ensuring relevant discussions and decisions are documented.
- Notifying regulatory organisations (such as the REC and MHRA) of breaches and amendments in accordance with the 'Gaining & Maintaining Authorisations' SOP.

The CI/PI must document oversight of protocol compliance. There is a variety of methods that can be used, including reviewing and signing eligibility CRFs, documented review of laboratory tests and safety data, entries in the patient notes, notes of meetings where decisions and discussions have taken place, documented review of study data and/or data queries.

8. IMP

If the trial is a CTIMP, the CI is responsible for IMP accountability at all participating sites. It is the CI's responsibility to ensure that appropriate procedures/arrangements are in place for storage (including risk assessment should the IMP be stored outside of pharmacy), dispensing, accountability, unblinding and destruction of the study drug. These activities can be assigned to an appropriately qualified pharmacist, ensuring that the study delegation log is amended accordingly. A trial specific pharmacy file should be established at all sites, to contain all study specific pharmacy SOPs, the latest version of the study protocol, a current version of the SmPC or IB and all other required documentation required to comply with the legislation. Further information on pharmacy arrangements for IMP trials can be found in the 'IMP' SOP.

It is the CI's responsibility and PI's at their own site to ensure that the latest version of the protocol is provided to all personnel involved in delivering the research, including support departments e.g. pharmacy, labs, radiology etc.

9. Randomisation

In order to demonstrate that a system of randomisation is robust and has been followed, the CI/PI must ensure that the following is documented and stored in an appropriate location:

- The method by which a randomisation list was generated. This can be through the use of a reputable third party; however methods must be described robustly and documented.
- A master randomisation list (where applicable)
- That the master randomisation list was followed (only possible at the end of the trial).

All of the above documentation must be stored in an appropriate location, the whereabouts of

which should be documented within the TMF and made available for inspection and which should be retained in accordance with the sponsor's archiving guidelines.

10. Informed Consent

The CI/PI is required to ensure that informed consent is given by and documented for all participants enrolled in a research study in accordance with the protocol, approved study documentation and ethical approval. For CTIMPs consent should only be received by an appropriately qualified medical, nursing, midwifery or allied health professional who has undertaken appropriate GCP training. For non-CTIMPs consent can also be received by other research staff who have undertaken appropriate valid informed consent training in addition to GCP.

The CI/PI must ensure that where practical, health or social care professionals are notified of the participant's involvement in a research study. This notification can be by means of including a copy of the participant's signed informed consent form and associated PIS in their medical notes and/or by sending a letter to the GP.

11. Safety

The safety of the participants is paramount and it is the CI/PI responsibility to ensure that mechanisms are in place to document and report Adverse Events and other safety concerns in line with the sponsor's requirements. Reporting requirements must be followed, including for serious breaches, annual safety reporting and DSURs, and urgent safety measures (see 'Gaining & Maintaining Authorisations' SOP). Where UHBristol or UoBristol are sponsor please refer to the 'Research Safety Reporting' SOP). CIs should have oversight of all relevant adverse events reported during the research and should provide input in assessing continued safety of participants and benefit/risk considerations in accordance with sponsor requirements. CI involvement (and PI at sites) should be adequately documented.

12. Investigator Sites

CI/PIs must ensure that investigator sites have the capability and capacity to deliver the research as required by the protocol. CI/PIs must ensure that at each site no patient recruitment begins prior to required regulatory and sponsor authorisations being in place. The CI is responsible for putting mechanisms in place to update the participating sites of any amendments and the PIs must ensure all team members are notified and trained and the amendment implemented accordingly. This process will be documented in the TMF and ISF respectively.

13. Trial Records

Each study must have a TMF held at the sponsoring organisation. For UH Bristol sponsored studies the TMF should be organised in line with the appropriate TMF template depending on whether the trial is a CTIMP or non-CTIMP. In addition, at each participating site, an ISF should be established and maintained. For UH Bristol sponsored studies it is a requirement that all participating sites use the UHBristol standard ISF template, unless agreed otherwise prior to study start. It is the responsibility of the CI/PI to ensure that appropriate trial records are established, maintained and made available for monitoring as required.

It is the responsibility of the CI to ensure that there are appropriate quality checks and validation processes for data generated by the study, in accordance with the data management plan.

Arrangements for archiving should be considered before a study has commenced.

14. Premature termination or suspension of trial

The CI/PI will promptly inform trial subjects, the host institution, sponsor, REC and MHRA (if applicable) if the trial ends prematurely or is suspended. For further guidance please refer to the 'Research Safety Reporting' SOP and 'Gaining and Maintaining Authorisations' SOP.

15. List of Appendices

- **Appendix 1 – Statement of Chief Investigator Responsibilities**

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	Authorship, Review, Revision and Approval of Research Procedural Documents produced by Research & Innovation SOP Gaining and Maintaining Authorisations SOP Research Safety Reporting SOP IMP SOP Monitoring SOP
QUERIES	Research Operations Manager or Research Management Facilitators - Research & Innovation Department via 0117 342 0233

Appendix 1 : Statement of Responsibilities for CTIMPs and Complex non-CTIMP Sponsored Studies

Study Title	
R&I Reference Number	

UH Bristol, as the Sponsor, takes responsibility for the quality and conduct of the research study. For CTIMPs, this includes the following areas of legal responsibility, as described in the Clinical Trials regulations:

- Authorisation for clinical trials and research ethics committee opinion
- GCP and the conduct of clinical trials
- Pharmacovigilance
- Manufacture and labelling of investigational medicinal products

Where UH Bristol is Sponsor of a study, it is expected that the Chief Investigator will maintain oversight as described in the UH Bristol Investigator Oversight SOP. Although certain roles and duties within the trial may be delegated (eg to trials units and research nurses), the CI must maintain oversight of the delivery of the trial. More generally, the CI is expected to demonstrate clinical leadership as champion of the study and to work closely with other investigators and staff and with their clinical trials unit (where applicable).

It is the responsibility of the Chief Investigator to comply with regulations (CTIMPs) and to conduct the study in accordance with:

- Medicines for Human Use (Clinical Trials) Regulations 2004 (SI031) and amendments (CTIMPs only)
- Research Governance Framework for Health and Social Care - 2nd edition April 2005
- ICH GCP Guidelines – May 1996
- UH Bristol's Research Policy (current version can be found on both the Trust DMS and R&I website)
- UH Bristol's Research SOPs (current versions can be found on both the Trust DMS and R&I website)

As part of the sponsorship process, the CI and a Sponsor representative will attend an initial Risk Assessment meeting and will document the perceived risks and mitigations. It is the shared responsibility of the Sponsor and the CI to maintain the Risk Assessment throughout the life-cycle of the study.

Further information on CI responsibilities can be found in UH Bristol's Investigator Oversight SOP.

By signing below, I am fully aware and understand my responsibilities as Chief Investigator. I agree to conduct the study in accordance with the applicable legislation, UH Bristol's Research Policy and UH Bristol's Research SOPs.

Signed:	.....
Name:	.....
Date:	.....

Acknowledgement of Sponsor Responsibilities *(as described in UH Bristol's Sponsorship SOP)*

Signed:	.....
Name:	.....
Date:	.....