Standard Operating Procedure

INVESTIGATOR OVERSIGHT OF RESEARCH

SETTING Trustwide

AUDIENCE Chief and Principal Investigators (CI and PIs) of research sponsored and/or hosted by UHBW

ISSUE To describe oversight of research studies conducted at UHBW

QUERIES Contact Research Operations Manager or Research Management Facilitators: Ext 20233 or research@uhbw.nhs.uk

SOP number	SOP 008	**SOP Version**	2.4
Effective Date	03/SEP/2020	**Review Date**	03/SEP/2022

Document History

Version Number	Reason for change
Original V1.0	N/A
V1.1	Minor – inclusion of 'out of scope', correction of grammatical errors and typos and addition of 'Statement of Chief Investigator Responsibilities' as appendix.
V1.2	Minor – Additional explanation around the role of the CI/PI in consent and who can receive consent. Removal of 'out of scope'
V2.0 (taken to TRG as V1.3)	Amended the 'Statement of Chief Investigator Responsibilities appendix, which is now re-titled 'Statement of Responsibilities for CTIMPs and complex non-CTIMP studies'
V2.1	Updated in line with annual review
V2.2	Section 6.2 updated and new Appendix 1
V2.3	Section 6.2 and Appendix 1 updated
V2.4	Minor updates and clarifications as part of biennial review.

Review date	Version number	Version date	Effective date	Author/ Reviewer	Authorised by
Original SOP	**V1.0**	**27/JUL/2015**	**04/AUG/2015**	**Diana Benton**	**Diana Benton**
19/AUG/2015	**V1.1**	**19/AUG/2015**	**14/SEP/2015**	**Genna Nicodemi**	**Diana Benton**
22/OCT/2015	**V1.2**	**22/OCT/2015**	**29/OCT/2015**	**Paula Tacchi**	**Diana Benton**
07/JUN/2016	**V2.0**	**07/JUN/2016**	**22/AUG/2016**	**Katharine Wale**	**Diana Benton**
23/NOV/2017	**V2.1**	**23/NOV/2017**	**21/FEB/2018**	**Trusha Rajgor**	**Jess Bisset**
25/JUN/2018	**V2.2**	**25/JUN/2018**	**27/JUL/2018**	**Katharine Wale**	**Jess Bisset**
04/DEC/2018	**V2.3**	**04/DEC/2018**	**04/DEC/2018**	**Katharine Wale**	**Valentino Oriolo**
17/AUG/2020	**V2.4**	**17/AUG/2020**	**03/SEP/2020**	**Katharine Wale/Nicola**	**Jess Bisset**

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1. Introduction

Regulation 2 of SI 2004/1031 defines an investigator as:

'The authorised health professional responsible for the conduct of the trial at a trial site, and if the trial is conducted by a team of authorised health professionals at a trial site, the investigator is the leader responsible for that team'.

The Chief Investigator (CI) as defined by SI 2004/1031 is the health professional who takes *primary responsibility* for the conduct of the trial at *all trial sites*. The Principal Investigator (PI) is the health professional who takes responsibility at their own site.

The sponsor may delegate certain duties and responsibilities to both the CI and PI who in turn may delegate those responsibilities to other individuals or teams. However as the CI and PI both remain responsible they must maintain oversight and document evidence of their oversight throughout the duration of the trial.

2. 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 UHBW.

3. Scope

In Scope: Investigators undertaking the role of Chief or Principal Investigator for research sponsored and hosted by UHBW**.**

4. Responsibilities

The Chief Investigator (CI) as defined by SI 2004/1031 is the health professional who takes primary responsibility for the conduct of the trial at all trial sites.
The Principal Investigator (PI) is the health professional who takes responsibility for the conduct of the trial at their own site.

Both the CIs and PIs for UHBW sponsored and hosted research must ensure they are fully aware of their responsibilities and the studies they oversee are conducted in accordance with applicable regulations and this SOP.

5. Abbreviations and Definitions

Abbreviations	
ASR	Annual Safety Report
CI	Chief Investigator
CTIMP	Clinical Trial of Investigational Medicinal Product
CTU	Clinical Trials Unit
DMS	Document Management System
DSMC	Data Safety Monitoring Committee
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
PIS	Participant Information Sheet
REC	Research Ethics Committee
SmPC	Summary of Product Characteristics
TMF	Trial Master File
TMG	Trial Management Group
UHBW	University Hospitals Bristol and Weston NHS Foundation Trust
UoBristol	The University of Bristol
VIC	Valid Informed Consent

Definitions	
CI	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
PI	The PI may be the CI. Where the research involves more than one site, the PI is the person at the site responsible for conducting the research to required standards

6. Procedure

6.1 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 (e.g. support departments) and externally to the Trust 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 UHBW 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 the CI/PI in securing this resource if required.

6.2 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 with a current license to practise, 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 Good Clinical Practice (GCP) training at a level commensurate with their involvement in the study and study-specific training and have read and understood all UHBW 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. Please refer to *SOP_007 Research Training* for further details.

- The Investigator Site File (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 easily located in relation to individual trials and securely archived when applicable. If the ISF is dispersed (e.g. study specific training held separately from rest of ISF), the location of dispersed documentation must be clearly flagged in in the ISF filing.
- CVs are not necessary for UHBW sponsored studies where medically qualified staff at Specialty Trainee, Core Trainee levels or above or nurse practitioners are undertaking specified tasks (e.g. eligibility review and prescribing), *provided that* sufficient evidence is supplied of the individual's competencies (MHRA electronic communication to UHBW R&I Department 18/05/2018). In addition, they must have undertaken study-specific training and be on the study delegation log. For nurse practitioners, please refer to *SOP_022 Extended roles of non-medical clinicians for type A and B Clinical Trial of an Investigational Medicinal Product (CTIMP)* for further information on requirements. If medically qualified staff are not providing CVs, they must demonstrate that they have the necessary competencies by completing the form in Appendix 1 at the end of this SOP.
  Please note that this process for demonstrating competencies is not available to Foundation 1 and 2 doctors.

- 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 UHBW at the time of their involvement.

6.3 Communication with Regulatory Authorities and the Sponsor

- The CI/PI must ensure that appropriate arrangements are in place to maintain communication with regulatory authorities, the sponsor and the host organisation 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 *GD_001 Gaining and Maintaining Authorisations* for more information.
- For UHBW sponsored studies, reminders of required annual reports will be generated using the research management system (EDGE) and sent by the R&I team to the clinical trial co-ordinating team. For hosted studies, the PI should expect to be reminded by the sponsor if/when their input is required.
- If the CI/PI delegates any responsibilities to a member of the research team, this must be documented on the study delegation log and 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 UHBW sponsored CTIMPs and complex non CTIMP studies (to be determined by the R&I department), the Trust requires that CIs sign the 'Statement of Chief Investigator Responsibilities' document (TMPL_023) before the research commences. The Research

Projects Manager in R&I allocated to the study will arrange for CI signature and will not proceed with capacity and capability review until it has been fully signed.

6.4 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 applicable regulations (refer to *GD_001 Gaining & Maintaining Authorisations* for further guidance).

- 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.

6.5 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 completion of a risk assessment if the IMP is 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, containing 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 SOP_006 Investigational Medicinal Products.

- 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.

6.6 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 should be retained in accordance with the sponsor's archiving guidelines.

6.7 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.

6.8 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 *GD_001 Gaining & Maintaining Authorisations* and for UHBW sponsored studies *SOP_009 Research Safety Reporting and SOP_18 Managing Breaches*. 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.

6.9 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.

6.10 Trial Records

- Each study must have a TMF held at the sponsoring organisation. For UHBW 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 UHBW sponsored studies it is a requirement that all participating sites use the UHBW 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 any data management plans.
- Arrangements for archiving should be considered before a study has commenced.

6.11 Premature termination or suspension of a trial

- The CI/PI must 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 *SOP_009 Research Safety Reporting* and *GD_001 Gaining and Maintaining Authorisations*.

7. Dissemination and training in the SOP

- This SOP will be disseminated to applicable research staff (including R&I) and will be available on the R&I website.
- All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP. The personal training log of the individual (and the Investigator Site File/Trial Master File if required) should be completed to document that the content of this SOP has been read and understood as described in *SOP 007 Research Training*.
- In line with SOP_007 Research Training all PIs undertaking CTIMPs at UHBW are required to read and understand the content of this SOP as demonstration of Investigator oversight training. There is no requirement for CIs/PIs to renew Investigator oversight training unless there is a major revision to this SOP which they have not previously been trained on. All major revisions to SOPs are disseminated in accordance with SOP_001 Production and Management of Research Procedural Documents Developed by Research & Innovation. Training in Investigator oversight will be recorded and uploaded to the research management database (EDGE) and compliance will be monitored.

8. Related documents

- Appendix 1 – Statement of Chief Investigator Responsibilities
- SOP_001 Authorship, Review, Revision and Approval of Research Procedural Documents produced by Research & Innovation SOP
- SOP_004 IMP SOP
- SOP_009 Research Safety Reporting SOP
- SOP_010 Monitoring SOP

- SOP_022 Extended roles of non-medical clinicians for type A and B Clinical Trial of an Investigational Medicinal Product (CTIMP)
- TMPL_043 CTIMP Trial Master File Contents Index
- TMPL_044 Investigator Site File Contents

Appendix 1: Evidence of competencies for medically qualified staff

Name of medical doctor	
Grade of doctor *(must be CT1/ST1 or above)*	
Does the medical doctor meet the following criteria? *(please indicate Yes/No and provide evidence where required*	
Good Clinical Practice training (certificate of completion must be within the previous 3 years). Enter 'n/a' if GCP is not required for the study role you will be performing.	Date of completion of GCP:
GMC number Please print off evidence of GMC registration	GMC number:
Current licence to practise. Evidence should be provided along with your evidence of GMC registration.	Yes/No *(please circle)*
Evidence of employment/employment record (a minimum of the previous 3 years) Please print off evidence from ESR (Electronic Staff Record) – see instructions on next page Or, if you are unable to access ESR, please provide information in the next column or on a separate sheet.	Evidence attached Yes/No *(please circle)* Start date at UHB: Current job title: Previous employment if worked at UHB for less than three years with dates and job titles:
Informed Consent training (certificate of completion). Enter 'n/a' if not consenting	Date of completion:
Study-specific training received Please attach evidence of training (eg training log)	Yes/No *(please circle)* If circled 'Yes', please provide: Short title of study: Date of training:

Signature of medical doctor:

Date:

Reviewed and approved by the Principal Investigator:

Name:

Signature:

Date:

How to access ESR (Electronic Staff Record)

Click the ESR shortcut icon on your desktop