Standard Operating Procedure

INVESTIGATOR OVERSIGHT OF RESEARCH

SETTING Trust-wide

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: 0117 34 20233 or research@uhbw.nhs.uk

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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.
V3.0	Major update to separate out CI and PI responsibilities more clearly, clarifications and removal of appendix 1 to a new template 121.
V3.1	Departmental name change from Research & Innovation to Research & Development. Updated throughout SOP as a minor amendment.

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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
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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, the CI retains primary responsibility as the health professional with study-wide responsibilities and the PI retains primarily responsibility for the conduct of the trial at their site. They are both responsible for documenting the 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 that they are fully aware of their responsibilities and that 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
SIV	Site Initiation Visit
TMF	Trial Master File
TMG	Trial Management Group
UHBW	University Hospitals Bristol and Weston NHS Foundation Trust
UoB	The University of Bristol

Definitions	
CI	The authorised lead researcher and health professional who takes primary responsibility for the conduct and reporting of that study (regardless of whether or not they are an Investigator at any particular site).
PI	The PI is the person at the site responsible for conducting the research to required standards. The PI may also be the CI when a study is conducted at a single site.

6. Procedure

6.1 Resources

Chief Investigator

- The CI is responsible for working with the sponsor to ensure that adequate resources are in place to conduct the study. This includes funding, staffing and infrastructure. They therefore need to take a lead role in preparation of the grant application and grant costings and fully engage with the sponsor in contracts development and negotiations.
- The CI must understand the budget and support the budget manager where required to ensure the study is delivered within the funding allocated.
- The CI must seek assurance from each PI that appropriate resources are in place, for example, as part of the site feasibility assessment during study set up.
- The CI will take responsibility for ensuring that the terms agreed in funding or collaboration agreements for the study are complied with.

Principal Investigator

The PI is responsible for ensuring that there are adequate resources at their site for conducting the study. Specifically:

- **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 PI may delegate this task to a member of their team but must maintain oversight.
- **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. This should be documented as part of the site's capacity and capability review. Within UHBW this should be done in conjunction with divisional research units, support departments and the R&D department.
- **Infrastructure:** it is the responsibility of the 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 and making sure rooms are available (e.g., at the Clinical Research Facility). Divisional research units can help the PI in securing this resource if required.

6.2 Staff Training/Qualifications and contractual arrangements

Chief Investigator

- The Chief Investigator is responsible for maintaining oversight throughout the project that all members of the central study team have the necessary staff training and qualifications and that appropriate HR arrangements are in place. This may be done, for example, through agreements with registered clinical trials units.
- It will also be achieved by actively contributing to the sponsor's risk assessment and Study Set up and Management Plan which document the requirement for GCP training and training on study specific and organisational SOPs. These documents should all be filed within the Trial Master File.
- The CI is also ultimately responsible for ensuring all research sites have appropriately qualified and trained site staff necessary for conduct of the study. In practical terms, this is achieved through robust site selection processes, contractual arrangements and any

study specific SOPs or other documentation detailing requirements for successful delivery.

Principal Investigator

- 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 PI of an IMP trial is therefore responsible for ensuring that only appropriately qualified personnel with a current license to practice have delegated responsibility to undertake eligibility review and make medical decisions on behalf of participants. Although receiving consent may be delegated to another member of the research team (e.g. a research nurse), eligibility must always be determined by a qualified doctor or dentist unless a specific exception has been made to the MHRA/ethics approved protocol. These processes must be **fully documented**.
- Please note for non CTIMPs eligibility review does not necessarily need to be undertaken by a medically qualified doctor, however that individual would need to be appropriately qualified in that role for the study.
- It is the responsibility of the 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 and that this is filed in the ISF. 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). It is essential that the PI signs the delegation log for specified delegated activities *before* site staff undertake such activities and that a training log has been completed for each staff member.
- It remains the PI's responsibility to confirm that individuals are adequately qualified and trained to undertake delegated tasks. Although certain roles and duties within the trial may be delegated, **the responsibility for the research itself remains with the PI**
- The PI must ensure that all staff have undertaken Good Clinical Practice (GCP) training and study-specific training at a level commensurate with their involvement in the study and have read and understood all UHBW Research & Development 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 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.
- Exceptionally, 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. They must be on the study delegation log and have undertaken study-specific training, where appropriate. 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 for their study role by completing *TMPL_121 Evidence of competencies for medically qualified staff*.
Please note that this process for demonstrating competencies is not available to Foundation 1 and 2 doctors.

- For non UHBW sponsored studies discuss any arrangements relating to the above further with the study sponsor
- The PI must ensure that anyone who has direct involvement with research subjects and/or personal data who is not substantively employed by UHBW has appropriate HR arrangements in place as applicable for the study.

6.3 Communication with Regulatory Authorities and the Sponsor

Chief Investigator

- The CI 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. Communications regarding protocol amendments, urgent safety measures, protocol breaches and pharmacovigilance must be formally documented and saved in the TMF (this list is not exhaustive). See *GD_001 Gaining and Maintaining Authorisations* for more information.
- For UHBW sponsored CTIMPs and complex non CTIMP studies (to be determined by the R&D 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&D allocated to the study will arrange for CI signature and will not proceed with capacity and capability review until it has been fully signed.
- For UHBW sponsored studies, reminders for DSURs and annual progress reports will be generated using the research management system (EDGE) and sent by the R&D team to the clinical trial co-ordinating team. The CI must review and sign off the DSUR.

Principal Investigator

- The PI is responsible for responding to the sponsor within the required timelines for any requests for information made by the regulatory authorities and to assist the CI and the sponsor with requests for information from ethics and the HRA (this list is not exhaustive) in a timely manner.

6.4 Protocol Compliance

Chief Investigator

The CI's responsibilities include:

- Ensuring that the protocol provides Principal Investigators with the information they need to maintain protocol compliance. To that end, they should endeavour to ensure that it provides the necessary information for regulatory and ethics approval and for conduct and management of the study and that it is unambiguous and clearly laid out. The protocol may be supplemented with additional supporting information (e.g., study manual, SIV slides etc). To that end, they must work closely with their trial's unit and the sponsor on protocol development and any amendments to the protocol.

- Reviewing and signing off amendments and putting mechanisms in place to update the participating sites with any amendments
- Ensuring that the TMG, DSMB, steering committees and other oversight bodies referred to in the protocol are established, convened and that relevant discussions and decisions are documented. Also, to attend meetings of such groups
- Notifying regulatory organisations (such as the REC and MHRA) of breaches and SUSARs in accordance with applicable regulations (refer to *GD_001 Gaining & Maintaining Authorisations* for further guidance)
- Ensuring mechanisms are in place for auditable data quality control checks at participating sites (as applicable) and that this is appropriately filed in the TMF.

Principal Investigator

- The /PI is responsible for ensuring that research is conducted in accordance with the protocol and documenting oversight of protocol compliance. This will include (but is not limited to):
    - Ensuring that no patient recruitment begins prior to required regulatory and sponsor authorisations being in place.
    - 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 documented review of laboratory tests and safety data takes place
    - Ensuring clear documentation is made in the patient notes (source data)
    - Documenting notes of meetings where decisions and discussions have taken place, filing in the ISF
    - Documenting review of study data/study queries
    - Ensuring that all team members are notified and trained on protocol amendments and that the amendment is implemented accordingly within the required timelines

6.5 IMP

Chief Investigator

- If the trial is a CTIMP, the CI is responsible for oversight of 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 pharmacy), dispensing, accountability, unblinding (if applicable) and destruction of the study drug. These activities can be assigned to an appropriately qualified pharmacist. A trial specific pharmacy file should be established at all sites, containing any 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.

Principal Investigator

- It is the PI's responsibility to ensure that the IMP is used and managed in accordance with the protocol. This may include, but is not limited to, putting accountability records in place,

ensuring that the drug is stored appropriately and documenting destruction of the IMP. The PI is also responsible for ensuring 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

Chief Investigator

- In order to demonstrate that a system of randomisation is robust and has been followed, the CI 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 location must be documented in the TMF and made available for inspection and should be retained in accordance with the sponsor's archiving guidelines.

Principal Investigator

- The PI is responsible for ensuring that only those members of staff delegated to randomise patients into the study are undertaking randomisation. To that end, the PI must sign off the delegation log for randomising patients before such individuals undertake randomisation. The PI must also ensure that all members of staff who need access to the randomisation system have the necessary training, access rights and permissions and that randomisation does not occur prior to eligibility review sign off.

6.7 Informed consent

Chief Investigator

The CI is responsible for ensuring that:

- the protocol clearly states whether medical staff only or both medical and other health professionals are permitted to obtain consent. For CTIMPs consent should only be received by an appropriately qualified medical, nursing, midwifery or allied health professional who has undertaken appropriate GCP training. Nursing, midwifery or allied health professional staff should also have undertaken appropriate valid informed consent 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 consent form and participant information sheet are age-appropriate and that they clearly explain which organisations have access to the participant's personal data and that consent is obtained for the use of the participant's samples and data for other research purposes, where applicable.

Principal Investigator

- The PI is required to ensure that informed consent is given by and documented for all participants enrolled in a research study and that this is done in accordance with the protocol, approved study documentation and ethical approval.
- The PI must ensure that a copy of the consent form and the associated PIS is filed in the participant's medical notes.

- The 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

Chief Investigator

- The safety of the participants is paramount. It is the CI's 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 documented input in assessing continued safety of participants and benefit/risk considerations in accordance with sponsor requirements.

Principal Investigator

The PI is responsible for ensuring that adverse events (including SAEs and SUSARs) are reported in accordance with the protocol and regulatory timelines.

- The PI should endeavour to ensure that there is a delegated clinician available to undertake safety assessments in the absence of the PI.

6.9 Trial Records

Chief investigator

- It is the responsibility of the CI to ensure that appropriate trial records are established, maintained and made available for monitoring as required.
- Each study must have a TMF which is usually held at the sponsoring organisation (and may be delegated to a clinical trials unit to store/maintain). 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 line with *SOP 014 Essential Research Documents* for UHBW sponsored trials running through a trials unit, prior to study start there may be an agreement to use the trial units own TMF template and processes as long as they meet the required standards. 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 to ensure that there are appropriate quality checks and validation processes for data generated by the study, in accordance with any data management plans. For UHBW sponsored CTIMPs, data management processes should be documented in the sponsor's Data Management Plan which must be completed by the trial unit prior to study-wide greenlighting.
- Arrangements for archiving should be considered before a study has commenced.

Principal Investigator

The PI is responsible for ensuring that:

- there is an ISF in place prior to the site opening to recruitment. The PI should use the ISF template provided by the sponsor. If no template is provided, the UHBW ISF template should be used.
- the ISF is maintained and kept up to date for the duration of the trial
- they accommodate monitoring meeting requests from the sponsor and/or regulatory authorities, including availability to respond to issues which cannot be resolved by other members of the site team
- they comply with the sponsor's close-down and archiving requirements at the end of the study.

6.10 Premature termination or suspension of a trial

Chief investigator

- The CI must promptly inform REC and MHRA (if applicable) and participating sites 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*. The CI will need to work closely with the sponsor with regard to implementing any REC/MHRA requirements, ensuring continuing patient safety and compliance with contractual commitments.

Principal Investigator

- The PI must promptly inform trial subjects if the trial ends prematurely or is suspended and ensure that appropriate arrangements are in place for the continued care of their patients (including access to IMP, as necessary).
- In the event that the local site initiates termination or suspension of the study at site level, the PI is responsible for promptly informing the sponsor and the CI.

7. Dissemination and training in the SOP

- This SOP will be disseminated to applicable research staff (including R&D) and will be available on the R&D website, which is externally accessible.
- 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 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 & Development. Training in Investigator oversight will be recorded and uploaded to the research management database (EDGE) and compliance will be monitored.

8.

RELATED DOCUMENTS AND PAGES	• SOP_001 Authorship, Review, Revision and Approval of Research Procedural Documents produced by Research & Development 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_023 Statement of Chief Investigator Responsibilities • TMPL_043 CTIMP Trial Master File Contents Index • TMPL_044 Investigator Site File Contents • TMPL_121 Evidence of competencies for medically qualified staff
AUTHORISING BODY	Trust Research Group
SAFETY	N/A
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