DIRECTORATE OF RESEARCH AND INNOVATION

Document Number: GOSH/ICH/SOP/R/010	Version Number: 1
Title: Investigator Site Research Team Responsibilities	
Effective Date:	*Same as implement by date.*

	Name	Position
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1. Scope

This SOP is applicable to

- All Great Ormond Street Hospital for Children (GOSH) or UCL Great Ormond Street Institute of Child Health (ICH) staff working on the delivery of clinical research.

Further to the requirements listed in this SOP, personnel must also comply with:

- Any additional study-specific requirements mandated by the PI, Sponsor or R&I.

2. Purpose

This SOP describes the responsibilities of the research study team, including the Chief Investigator (CI) and Principal Investigator (PI).

3. Definitions/Abbreviations

Chief Investigator (CI) – A health professional who takes primary responsibility for the conduct of the study in the UK, whether or not they are an investigator at any particular study site. The role may be undertaken by a Sponsor's Representative (e.g. the Sponsor's medical director or similar). The CI should be a researcher who is professionally based in the UK.

Clinical Research – As per UK Framework for Health and Social Care Research and HRA/MRC 'Is my study research?' tool.

Digital Research Environment Team (DRE) – As part of the Research and Innovation Strategy, the Trust has procured a data store and digital research platform. The platform and other systems comprise the overall Digital Research Environment (DRE) to work alongside the Electronic Patient Record (EPR) system. Staff working on the DRE will be known as the DRE Team which is a GOSH team providing analytical tools and infrastructure to facilitate research done at GOSH and ICH.

EDGE – A clinical research management system

EPR – Electronic Patient Record

GCP – Good Clinical Practice

Principal Investigator (PI) – A health professional responsible for the conduct of the research at a study site. If the study is conducted by a team at a site, the PI is the leader responsible for that team. There should be one PI for each research site (if there is more than one, each would be a Co-PI). In the case of a single-site study, the CI and PI will normally be the same person.

Sub-Investigator (Sub-I) – A member of the research team designated and supervised by the PI at a site to perform critical study-related procedures and/or to make important study-related decisions. Interventional studies must have at least one Sub-I to ensure appropriate cover if the PI is temporarily unavailable. Although a Sub-I would often be a medical doctor; not all medical doctors are Sub-Is, only those with significant duties.

4. Responsibilities

Duties may be delegated but the responsibility always remains with those listed.

4.1   Chief Investigator (CI) is responsible for:

- The conduct of the study in the UK.
- Completing their duties as per the UK Policy Framework for Health and Social Care Research and the study IRAS declaration.
- Communication with the Research Ethics Committee (REC), including leading the process for applying for REC opinion (initial, amendments and appeals).
- Maintenance and appropriate retention of the Trial Master File (TMF)
- Ensuring compliance with this SOP, the protocol, Good Clinical Practice (GCP) and any applicable legislation, policies, procedures or guidelines.
- Any additional responsibilities delegated by the Sponsor in the Sponsor-CI Agreement.

4.2   Principal Investigator (PI) is responsible for:

- The conduct of the study at the site and all study activity at the study site.
- Adhering to the PI Code of Practice (SD/R/002)

- Satisfying themselves that the research is scientifically sound, safe, ethical, legal and feasible to perform at their site and remains so for the duration of the research, taking account of developments while the research is ongoing.
- Ensuring no study activities are conducted at site until all required approvals are in place.
- Ensuring that they are informed of updates to the study and ensuring these are not implemented at site until all required approvals are in place.
- Ensuring they are aware of any conditions stipulated in the study approvals.
- Satisfying themselves that the information given to potential participants is in a suitable format and is clear and relevant to their participation in the study and aligns with mandatory Trust processes (such as use of EPR).
- The PI is responsible for ensuring key study dates and recruitment are recorded in EDGE in a timely manner and these are updated as required throughout the study.

  The study team must input the key study dates into EDGE as required. The Research Systems and Data Management Team will provide EDGE training.

  Key Study Dates required in EDGE:
    - Site SIV Date - Date of Site Initiation Visit (SIV).
    - Site Open to Recruitment
    - Site Recruitment End Dates (Planned and Actual)
    - Site Closure Dates (Planned and Actual)

  Study recruitment will be recorded in EPR by the study team. These recruitment data will be regularly uploaded to EDGE by the Research Systems and Data Management Team. For this to work, participants must be allocated to the study and their study ID must be included in EPR in the format [R&D number]_[Participant study ID] (e.g. 19CM04_001).
- Communication with local R&D office, CI and Sponsor as appropriate.
- Maintenance and appropriate retention of the site section of the TMF (usually called the Investigator Site File (ISF)) with all appropriate documents until the end of the archive period. The PI must notify the Sponsor, CI and GOSH/ICH Named Archivist in writing if they become unable to do this (e.g. due to relocation and/or retirement), see SOP/R/004 'Archiving'.
- Ensuring each study team member is appropriately trained, qualified and experienced to perform the role they are to undertake before delegating duties to them and that staff have adequate supervision, support and training.
- Maintaining a list of appropriately qualified persons to whom they have delegated significant study-related duties (i.e. a delegation log).
- Ensuring that the R&D office is aware of any changes to PI, Co-PI or Sub-Investigators.
- Ensuring all necessary employment contracts/agreements, including honorary research contracts/letters of access, and other access arrangements are in place before the study starts.
- Ensuring that study staff have access to necessary research/study systems and that this access is withdrawn if no longer required.

- If the study is extracting clinical data from EPR using the digital research environment (DRE), the PI must ensure that they comply with the DRE User Terms and Conditions.
- Ensuring their own and study team compliance with this SOP, the protocol, GCP and any applicable legislation, policies, procedures or guidelines.

4.3   All study staff are responsible for

- Ensuring the safety of study participants and the quality of the data.
- Adhering to the agreed procedures and arrangements for reporting and for monitoring.
- Ensuring they are added to the delegation log for all studies they are working on and performing the duties delegated to them.
- Ensuring their practice meets the requirements of this SOP, the protocol, GCP and any applicable legislation, policies, procedures or guidelines.

5.   Procedure

5.1   Qualifications and Agreements

All research taking place at GOSH/ICH must be registered with and reviewed by the R&D Office to confirm the site has capability and capacity to deliver the study. Part of this assessment (and the general organisational oversight of the study) is ensuring the PI is supported and fully aware of their responsibilities. To assist with this, the PI must sign the PI Code of Practice (SD/R/002). This will be issued by the R&D Office and must be signed and returned to R&D before capability and capacity can be confirmed for each research project.

The PI may be asked to sign agreements by the Sponsor. The PI is authorised to sign agreements on behalf of themselves (e.g. FDA Form 1572) – the PI must ensure that they inform the R&D Office of what they have signed. Copies will go to the Sponsor, R&D and also filed in the site file.

The PI is **not** authorised to sign agreements on behalf of the Trust (such as confidentiality disclosure agreements (CDAs) or Material Transfer Agreements (MTAs)) – these must be signed by a Trust Authorised Signatory (such as the Director of R&I, Deputy Director of R&I, or Chief Finance Officer). The R&D Office can advise on the appropriate signatory if it is unclear.

All staff must ensure they are qualified by education, training, and experience to perform their role throughout the study (see SOP/R/002 'Training Requirements for Staff Participating in Clinical Research').

The PI may delegate activities to members of the research team but must ensure that the members of staff are appropriately qualified, trained and experienced to do the delegated activities and that staff have adequate supervision, support and training. The PI should maintain a list of appropriately qualified persons to whom they have delegated study-related duties, i.e. a delegation log (see SOP 'Training Requirements for Staff Participating in Clinical Research'). The PI must ensure that the study team is adequately informed about the protocol, any intervention(s), and their study-related duties and functions.

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For Clinical Trials of Investigational Medicinal Products (CTIMPs), a PI must be a medically qualified doctor. For other research studies a PI may not have to be a medically qualified doctor; the suitability to be a PI will be assessed by the R&D Office on a case by case basis.

The PI for a study taking place at GOSH/ICH should be either substantively employed or hold an honorary contract with the Trust or UCL. If a PI is a locum at GOSH or holds an honorary contract with GOSH and their substantive employer is another Trust; the R&D Office will assess suitability to be a PI on a case by case basis and with discussion with Deputy Director of R&I and Director of CRF.

The PI must ensure that each member of the research team has an appropriate contract in place (such as an active full or honorary Trust contract or letter of access for research) or appropriate service level agreement (to ensure all HR checks are done) for the full duration of the study. The R&D Office can advise on the appropriate arrangements required.

Staff directly involved in the treatment or evaluation of research participants and/or who make direct and significant contribution to the data may need to complete a financial disclosure if required by the Sponsor. This would usually only be PIs and Sub-Is. All staff must follow the Trust Declaration of Interest Policy.

Students should not normally take the role of CI at any level of study, as this function should be undertaken by supervisors or course leaders. However, the suitability to be a CI at GOSH/ICH will be assessed by the R&D Office on a case by case basis.

If the CI is being delegated substantive responsibilities by the Sponsor, an agreement regarding suitable reimbursement of time may be necessary. This should be discussed with the R&D Office.

5.2 Resources and Feasibility

It must be confirmed that the site has capacity and capability to deliver the research before the study starts (or amendments are implemented). For this, the PI must be able to demonstrate:

- Arrangements are in place for the management of financial and other resources provided for the study.
- They have sufficient time to properly conduct and complete the study within the agreed period.
- They have adequate facilities and staff available for the foreseen duration of the study to conduct the study properly, effectively and safely. This includes non-clinical activities (e.g. data entry and queries, or site file management), as well as participant-focused clinical care and medical cover. This may involve communication with other teams/departments (e.g. pharmacy, radiology, etc).
- For an interventional study, they have someone to delegate as Co-PI or Sub-I to ensure there is appropriate cover if they are temporarily unavailable (e.g. on holiday or other leave).
- The potential for recruiting the required number of suitable participants within the agreed recruitment period.

5.3 Medical Care of Study Participants

As a safety measure, all GOSH patients that take part in research must be linked to the study on EPR.

The PI must ensure that there is adequate medical oversight of participants and that appropriate medical care is provided to a participant for any untoward medical occurrences (including clinically significant laboratory values), related to the study. This oversight and care must be documented in the medical notes.

The PI must also ensure that there are appropriate arrangements in place for the care of the participants after the study (including access to treatment) and that there is appropriate transition to local and/or adolescent or adult services (see Trust Transition to Adolescent or Adult Services Policy).

5.4 Compliance with Protocol

The study team must conduct the study in compliance with the protocol. The study team must not implement any changes from the protocol without agreement by the Sponsor and documented approval from the relevant authorities, except where necessary to eliminate immediate hazards to study participants. Protocol waivers (prospective deviations to the protocol) are not acceptable.

The PI must ensure any deviations to the protocol are documented and explained in accordance with SOP/R/005 'Reporting and Escalation for Research'.

The PI must allow reasonable access to monitors, auditors and inspectors and must ensure queries and/or reports are responded to in a timely manner (see SOP/R/006 'Study Documentation and Monitoring, Audit and Inspection').

5.5 Investigational Medicinal Products (IMP)

In CTIMP and Advanced Therapy (ATIMP) studies, the PI is responsible for the management of IMP at their site. This may be delegated to Pharmacy, or gene and cell therapy laboratories but the accountability remains with the PI.

The PI must ensure that the drug is stored under the correct storage conditions and suitable drug accountability records are maintained.

5.6 Informed Consent

The PI is responsible for ensuring that the ethically approved consent process is followed and appropriately documented (see SOP/R/034 'Informed Consent for Research').

5.7 Records and Reports

All study staff are responsible for ensuring the quality of the study data and that study documentation is appropriately maintained and retained (see SOP/R/006 'Study Documentation and Monitoring, Audit and Inspection' and SOP/R/004 'Archiving').

All staff must adhere to the agreed procedures and arrangements for reporting (see SOP/R/005 'Reporting and Escalation for Research').

5.8 PI Oversight

The PI is responsible for the conduct of the study and for the leadership of the study team at their site. As such, it is essential that there is clear, documented evidence of the PI's oversight and involvement in the study and that the PI is kept appraised of any issues regarding the study (see SOP 'Reporting and Escalation for Research'). The following examples are commonly used to provide suitable evidence of oversight and active study management:

- Acting as the signatory on consent forms (it is not necessary for the PI to take consent for every participant unless required by study Sponsor)
- Documented eligibility assessments
- Documented participation in participant visits
- Sign-off of completed serious adverse event (SAE) forms
- Documented review of safety information (e.g. line listings or safety reports from Sponsor or other sites)
- Regular, minuted meetings with the study team
- Emails/correspondence
- Attendance or availability at monitoring visits
- Documented review of incoming data (e.g. labs, imaging) in a timely manner
- Review of completed CRFs and responses to medical queries
- Providing protocol or specialised training to the team.

5.9 Support and Escalation

If a staff member has questions or queries they can ask for support from a more experienced colleague or their line manager. If the query is related to a specific study, then the study research nurse, PI and/or CRA may also be able to help.

If a staff member becomes aware of an issue or has any concerns then this must be escalated to the appropriate person(s) in a timely manner (see SOP/R/005 Reporting and Escalation for Research).

5.10 Compliance

Compliance with this SOP will be reviewed during routine monitoring/audit.

Systematic or persistent failure to comply with the study procedures and/or this SOP will be seen as non-compliance to GCP and must be bought to the attention of the Head of Governance, Clinical Trials and Contracts who will decide the appropriate action.

6. Related Documents

- SD/R/002: PI Code of Practice

- DRE User Terms & Conditions
- SOP/R/002: Training Requirements for Staff Participating in Clinical Research
- Trust Declaration of Interest and Gifts, Hospitality and Sponsorship Policy
- Trust Transition to Adolescent or Adult Services Policy
- SOP/R/005: Reporting and Escalation for Research
- SOP/R/006: Study Documentation and Monitoring, Audit and Inspection
- SOP/R/034: Informed Consent
- SOP/R/004: Archiving

7. References

- MHRA and HRA Position on who can act as a Chief Investigator
- UK policy framework for health and social care research
- ICH Harmonised Guideline - Guideline For Good Clinical Practice E6(R2)
- MHRA Good Clinical Practice Guide (Grey Guide) – Chapter 11 Investigator Sites
- FDA Guidance on financial disclosures (2013) and FAQs on Form FDA 1572 (2010)
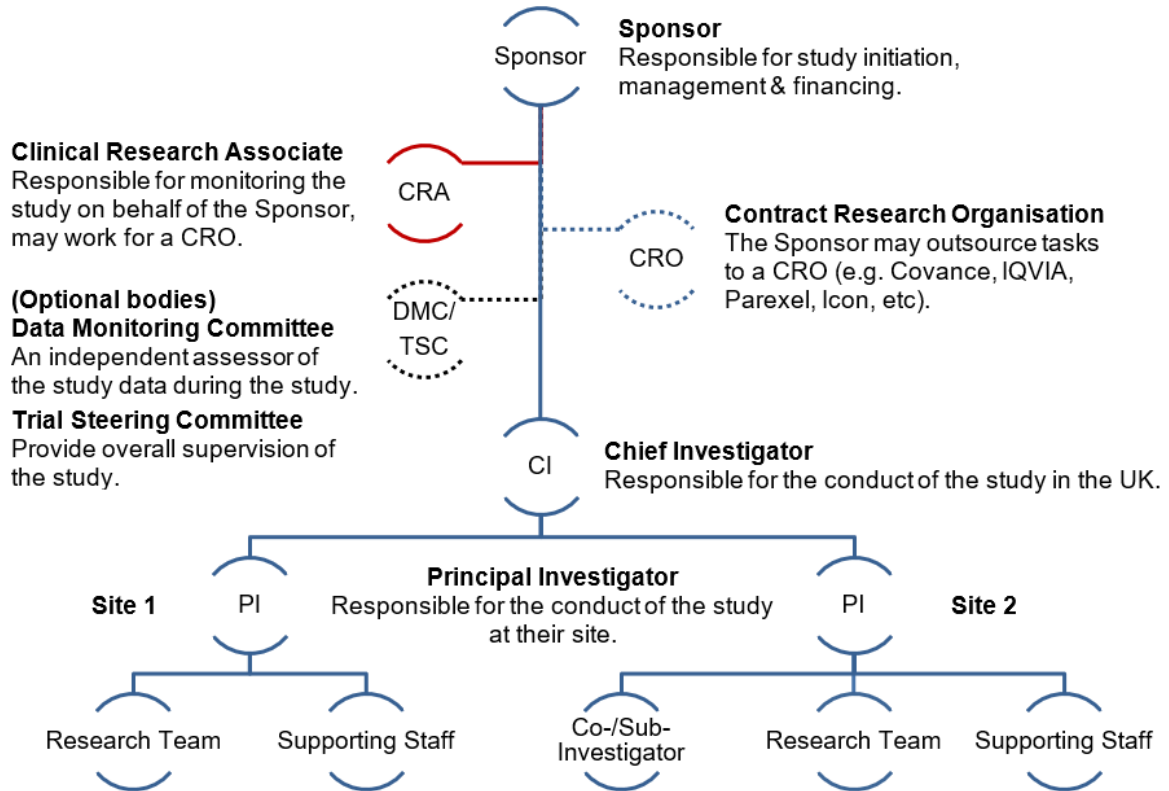- HRA guidance Care After Research: A Framework For NHS RECs

8. Appendices

- Appendix 1: Model of study roles and responsibilities
- Appendix 2: Table of typical roles and activities

Appendix 1: Model of study roles and responsibilities

Sponsor
Responsible for study initiation, management & financing.

Clinical Research Associate
Responsible for monitoring the study on behalf of the Sponsor, may work for a CRO.

Contract Research Organisation
The Sponsor may outsource tasks to a CRO (e.g. Covance, IQVIA, Parexel, Icon, etc.).

(Optional bodies)
Data Monitoring Committee
An independent assessor of the study data during the study.

Trial Steering Committee
Provide overall supervision of the study.

Chief Investigator
Responsible for the conduct of the study in the UK.

Principal Investigator
Responsible for the conduct of the study at their site.

Site 1 — PI

Site 2 — PI

Research Team — Supporting Staff

Co-/Sub-Investigator — Research Team — Supporting Staff

CRA — CRO — DMC/TSC — CI

Appendix 2: Table of typical roles and activities

The PI is supported by a team of professionals that have been delegated to carry out study activities. It is not possible to define set roles and responsibilities for individual job roles (such as a research nurse or trial coordinator) as these can vary considerably from study to study and ultimately depend on what has been delegated to the individual by the PI based on resourcing, experience and the specification of the protocol.

The table below provides a list of job roles that are typically found. However, the list is not exhaustive and the various functions may be undertaken by the same individual.

Role	Typical Activities Undertaken
Sub-investigator or Co-investigator	May undertake part or all of the PI's activities
Doctor, Fellow, Advanced Nurse Practitioner (ANP)* or Nurse	Recruitment, consent, screening, participant assessments, intervention administration, record keeping
Research Coordinator	Study set-up and administrative support (including management of study documents)
Data Administrator or Manager	Case report form data entry, facilitating handling of data queries.
Pharmacists and/or pharmacy technicians	Investigational Medicinal Product management: supply ordering, handling, storage, dispensing, accountability, and destruction
Laboratory staff	Handling and processing of routine samples (biochemistry and haematology). Handling and processing of trial specific samples (e.g. blood biomarkers, throat swab, nasal lavage) Arranging sample storage and shipment.
Technical specialists	Taking X-rays and scans, recording ECGs, performing specialist activities
Specialist assessors	E.g. in oncology trials, the radiologist may take on an important role in interpreting scans (such as RECIST score measurement)

* Advanced nurse practitioner (ANP): As well as providing the care that a nurse practitioner is able to offer, an ANP will have a prescribing qualification and master's level training that allows them to perform additional duties. Evidence of these qualifications must be filed in the site file and the individual's training record. A qualified ANP is also able to:

- take a full patient history
- carry out any physical examinations
- use their knowledge to identify a likely diagnosis
- request appropriate tests to aid diagnosis (blood tests, x-rays, scans)
- refer patients to an appropriate specialist (in the practice or hospital)
- prescribe medicines and non-medical treatments
- arrange follow up and ongoing management