University Hospitals Birmingham NHS Foundation Trust

CONTROLLED DOCUMENT

Chief Investigators and Principal Investigators in Research Policy

CATEGORY:	Policy
CLASSIFICATION:	Governance
PURPOSE	To set out the responsibilities of Chief Investigators (CI) and Principal Investigators (PI) in research and the conditions for approving an individual as CI or PI
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Contents

1. Policy Statement

1.1 This policy sets out the principles for accepting an individual to act as Chief Investigator[1] (CI) or Principal Investigator (PI) for a clinical research study undertaken at University Hospitals Birmingham NHS Foundation Trust (the 'Trust'), and the responsibilities of CIs and PIs. The purpose is to ensure that there is appropriate leadership and accountability for research studies involving patients and resources of the Trust.

2. Scope

2.1 This policy applies to all clinical research as defined in Appendix B of the Research Governance Policy.

2.2 All clinical research studies must have a CI and most research studies will need a local PI (see paragraphs 3.6 for exceptions).

3. Framework

3.1 This policy may be amended from time to time by authority of the Executive Director of Delivery, provided that such amendments are compliant with the associated Policy for the Development and Management of Controlled Documents.

3.2 Under the Department of Health's Research Governance Framework and the Medicines for Human Use Act (2004), the terms 'Chief Investigator' and 'Principal Investigator' have clearly defined and prescribed roles. NHS Trusts have a primary duty to care for patients and it is essential that this duty is not compromised in clinical research.

3.3 <u>Sponsor</u>

3.3.1 The Department of Health's Research Governance Framework requires that every research study involving patients in the NHS must have a Sponsor.

3.3.2 The Sponsor is defined in the Framework as "the individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study".

3.4 <u>Chief Investigator</u>

3.4.1 The CI is the person designated by the Sponsor to provide overall leadership for the conduct of a study. They would usually

[1] The Chief Investigator is also sometimes referred to as the Coordinating Investigator

be the person who was primarily responsible for designing the research study and writing the protocol.

3.4.2 The CI is accountable to the Sponsor for the overall conduct of the study.

3.4.3 It is for the Sponsor to decide who will act as CI.

3.4.4 Where the Trust is asked to act as Sponsor, the CI would normally be employed by the Trust. If the proposed CI was employed by another organisation, that organisation would be expected to act as Sponsor.

3.5 Principal Investigator

3.5.1 The local PI is the person in the Trust who takes responsibility for implementing the clinical components of a study in the Trust and is accountable through usual clinical management structures for overseeing the conduct of the study in the Trust.

3.5.2 Because most clinical activity in the Trust is consultant-led, and to avoid potential conflicting authorities, the following set of principles generally apply when considering whether someone is appropriate to act as PI for a study:

a) The PI must have direct first-line responsibility for the care of patients. The following would generally be eligible to act as PIs:

- Consultant (including Nurse Consultant and Allied Health Professional Consultants)
- Service lead
- Head of Therapy
- Clinical Nurse Specialists
- Associate Specialist
- Allied Health Professionals

and

b) The PI must be employed by the Trust or hold an honorary clinical contract with the Trust. Locum doctors would not normally be permitted to act as PIs unless they had a sufficiently long-term contract with the Trust so that they would be present in the Trust for the full duration of the study and their appointment was approved by the relevant Divisional Director.

and

c) The PI must be able to provide evidence of appropriate up-to-date training (see below paragraphs 3.7).

3.5.3 There can be only one PI for a study even if the study involves several disciplines.

3.5.4 There will be circumstances where it is appropriate that someone who does not meet para 3.5.2 (a) or 3.5.2 (b) will act as PI; for example where no consultant would normally be expected to be involved in the care of the patient. In such circumstances suitable senior staff such as a head of department, senior manager, senior scientist or equivalent may act as PI. The Divisional Director appropriate for the proposed PI must approve their appointment.

3.5.5 The PI need not necessarily be involved in managing or directing the day to day conduct of the study, but the PI must maintain oversight of the study and will be accountable to the Chief Executive and the Board of Directors for the conduct of the study.

3.5.6 The CI and PI may be the same person if the CI meets the eligibility criteria for PI or is otherwise approved to act as PI for the Trust.

3.6 Changes in PI or CI

3.6.1 If the PI or CI is absent and unable to fulfil their role for a period of up to 4 weeks they must make arrangements for appropriate cover for this period and confirm this with the Sponsor. The PI or CI will retain overall responsibility for the conduct of the study over this period. These arrangements must be documented in the study files.

3.6.2 If the PI or CI is likely to be absent for a period of more than 4 weeks but less than 3 months, the Sponsor is responsible for confirming temporary arrangements for cover. The Sponsor must ensure these arrangements are notified to the Research Ethics Committee and the Research and Development (R and D) Governance Office in the Trust (the Ethics Committee do not need to be notified of absences of less than 4 weeks).

3.6.3 A change in PI or CI is mandatory for absences greater than 3 months.

3.6.4 Paragraphs 3.6.1 to 3.6.3 are consistent with the standard procedures of the National Research Ethics Service, endorsed by the Medicines and Healthcare products Regulatory Agency.

3.6.5 If the existing PI leaves the Trust, or is otherwise unable to continue to act as PI (which may include reasons connected with concerns over the governance of a study) for a period of more than 3 months, a replacement PI must be identified and authorised in accordance with paragraphs 5. Wherever possible, the handover of PI responsibilities must occur before the previous PI leaves. If this is not possible then the research study may be suspended by the R and D Governance Office until a new PI has been approved.

3.6.6 Any proposed change in PI must be notified to the R and D Governance Office and cannot come into effect until approved by the R and D Governance Office.

3.6.7 Paras 3.6.1 to 3.6.6 also apply for CIs for Trust-sponsored studies.

3.6.8 The Sponsor must notify the NHS Research Ethics Committee that reviewed the original application if there is a change in PI. If the study is a clinical trial of a medicine this is regarded as a substantial amendment and cannot be implemented until the amendment has received a favourable opinion from the Research Ethics Committee.

3.6.9 A change in CI is always regarded as a substantial amendment and cannot be implemented until a favourable opinion has been received from the original NHS research ethics committee and, if the study is a clinical trial of a medicine, authorisation from the Medicines and Healthcare Products Regulatory Agency (MHRA).

3.7 Studies without a PI

3.7.1 Where the Trust is providing a routine clinical treatment or procedure for patients recruited into a study from outside the Trust then it may not be necessary to have a local PI. In these cases it is sufficient for the R and D Governance Office to have confirmation from the appropriate service lead that the procedures are consistent with standard care for the patients.

3.7.2 However, if any of the procedures are specific to the study protocol or if the study would result in more patients receiving the treatment or procedure than would otherwise be the case then a local PI is required.

3.8 Experience and Training

3.8.1 A PI must be able to demonstrate sufficient education, experience and training appropriate to the particular study on

which they are leading. The Sponsor is responsible for ensuring that the PI is appropriate.

3.8.2 Researchers wishing to act as PI on a study for the first time in the Trust must have attended the National Institute for Healthcare Research (NIHR) PI Oversight Masterclass run by the Trust's R and D Governance Office.

3.8.3 All active clinical researchers must have a basic level of training in the principles of Good Clinical Practice (GCP[2]) and the UK legislation implementing the EU clinical trials directive.

3.8.4 Online and face-to-face GCP training courses accredited by a pharmaceutical company or the (NIHR) are widely available. If other training has been undertaken, the investigators must seek confirmation from the R and D Governance Office that this is sufficient and meets the criterion.

3.8.5 Refresher training in GCP is required every 2 years, or earlier if recommended by the R and D Governance Office. For example if the R and D Governance Office obtains evidence of poor investigator compliance with research governance standards.

3.8.6 The R and D Governance Office maintains a record of GCP course attendance for researchers and will remind investigators when their GCP training is due.

3.8.7 The R and D Governance Office will suspend all active studies for a PI if their GCP training is not completed within 3 months of the due date.

3.8.8 If there is a significant change in legislation relevant to research governance, then the R and D Governance Office will ensure an appropriate update is provided to all PI's.

3.8.9 Evidence of training in other areas may be required as appropriate (e.g. consent, mental capacity, or study specific procedures).

4. Duties

4.1 Chief Investigators

The outline list of CI responsibilities is set out in Appendix B. This includes some duties of the sponsor that have been delegated to the CI.

[2] The GCP principles are set out by the International Committee on Harmonisation (ICH) and incorporated into EU Directive 2005/28/EC

This may be amended from time to time and an up-to-date list is available from the R and Dt Office.

4.2 Principal Investigators

4.2.1 The outline list of PI duties is set out in Appendix C. This may be amended from time to time and an up-to-date list is available from the R and D Office.

4.2.2 The PI may delegate some or all of their duties. However, this must be documented in the study file with clear evidence that those who have been delegated duties have accepted them.

4.3 Executive Director of Delivery

The Executive Director of Delivery is responsible for the development of the research strategy for the Trust and overseeing its implementation and effective governance.

4.4 Divisional Directors and Clinical Service Leads

Divisional Directors and Clinical Service Leads are required to ensure that they keep abreast of all research within their area of responsibility. They must satisfy themselves that the researchers are sufficiently qualified and trained to undertake the research proposed, that the individual research studies fit with any broadly defined research strategy for the clinical service or division, and that adequate resources are available to enable the research to take place.

4.5 Head of Research and Development Governance

The Head of R and D Governance will:

4.5.1 ensure all research projects are assessed and, when appropriate conditions have been met, duly authorised in accordance with the principles of the NHS Research Governance Framework 2005 and all relevant UK legislation;

4.5.2 check the appropriateness of individuals to act as CI and PI on studies;

4.5.3 put in place procedures to maintain effective oversight of the progress of individual research projects;

4.5.4 require a PI to undergo refresher training if significant governance issues are identified during auditing or monitoring of a study; and

4.5.5 oversee appropriate monitoring and auditing of individual research studies against established principles of good research practice, and to check compliance with Trust policies.

5. Implementation and Monitoring

5.1 Implementation

This policy will be available on the Trust's Intranet Site. The policy will also be disseminated through the management structure within the Trust.

5.2 Monitoring

5.2.1 Appendix A provides full details of how the policy will be monitored by the Trust.

5.2.2 If concerns are raised about the conduct of a study and these cannot be resolved by the PI, then the study may be suspended by the Head of R and D Governance and an investigation will take place. A decision of action will be escalated through the Director of R and D and the Executive Director of Delivery to the Board of Directors.

6. References

Research Governance Framework, second edition (2005, Department of Health

Human Use Act 2004

Medicines and Healthcare Products Regulatory Agency

Standard Operating Procedure for Research Ethics Committees available on: http://www.hra.nhs.uk/documents/2017/01/standard-operating-procedures-version-7-2.pdf

Statutory Instrument 2004/1031 The Medicines for Human Use (Clinical Trials) Regulations 2004

7. Associated Policy and Procedural Documentation

Research Governance Policy

Policy for the Development and Management of Controlled Documents

Reporting Research Incidents and Breaches Policy

Research Passport Policy

Appendix A Monitoring Matrix

MONITORING OF IMPLEMENTATION	MONITORING LEAD	REPORTED TO PERSON/GROUP	MONITORING PROCESS	MONITORING FREQUENCY
Trust R and D Database	R and D Administrator	Head of R and D Governance	Trust R and D Database flags if proposed PI meets standard criteria or not. Record of latest Curriculum Vitae (CV) and evidence of GCP training, and attendance at PI Oversight Masterclasses is maintained on the R and D Governance database. Database will not allow Trust authorisation letter to be generated if a study doesn't have a suitable PI, or the CV is out of date or there is no evidence of GCP training within the past 2 years.	Continuous
Training records and delegated duties logs reviewed as part of governance audits of studies.	R and D Governance Facilitator	R and D Committee	Annual programme of random study audits. 'For-cause' audits where concerns have been raised. Monitoring visits for Trust-sponsored clinical trials	Approximately 5-10% of studies each year for random audits. 1 monitoring visit per year for Trust-sponsored trials.
Annual Research Governance report to the R and D Committee	Head of R and D Governance	R and D Committee	Outcome of research study audits reporting by exception	Annual

Appendix B Chief Investigator Duties

1) Administration

a) The Chief Investigator is responsible for submitting a request for authorisation to undertake the study to the competent authority (MHRA) on behalf of the Trust (as sponsor) – where appropriate.

b) The Chief Investigator is responsible for requesting an opinion from the National Research Ethics Service (NRES) on behalf of the Sponsor.

c) The Chief Investigator is responsible for submitting amendments and reports, including annual reports and the final report, to the MHRA and NRES as required subsequent to authorisation of a study.

d) The Chief Investigator must ensure that all copies of correspondence relating to the study between the Chief Investigator and the ethics committees and regulatory authorities are sent to the Trust's R and D Governance Office.

2) Pharmacovigilence

a) The Chief Investigator is responsible on behalf of the sponsor for reporting, within the statutory timeframes, to the MHRA, NRES and Principal Investigators at participating sites, details of any Suspected Unexpected Serious Adverse Reactions (SUSARs).

b) The Chief Investigator must therefore ensure that all adverse events occurring at any of the approved centres are reported to themselves promptly. The Chief Investigator must also ensure that an assessment has been made, by themselves or a competent expert, and documented, of the seriousness of each event and its relatedness and expectedness to the medicinal product or procedures used in the study in order to determine whether the event is classed as a SUSAR.

c) The Chief Investigator is responsible for generating and submitting an Annual Safety Report (ASR) to the MHRA.

d) The Chief Investigator must ensure that copies of all pharmacovigilence reports sent to the MHRA and ethics committees are also sent to the Trust's R and D Governance Office.

3) Investigational Medicinal Products (IMPs)

a) The Chief Investigator is responsible for ensuring appropriate supply of IMPs to all study sites in accordance with the protocol.

b) The Chief Investigator is responsible for ensuring that the labelling of IMPs conform to Article 15 of EU Directive 2003/94/EC.

4) Protocol Breaches

The Chief Investigator must ensure that any serious breaches in the protocol or principles of good clinical practice at any of the sites (including their own) are reported to the R and D Governance Office within 5 days of becoming aware of the breach. A serious breach is one which is likely to affect to a significant degree the safety or mental or physical health of the participants or the scientific value of the study.

5) Documentation and Archiving

a) The Chief Investigator is responsible for ensuring that a trial master file conforming to the Medicines for Human Use (Clinical Trials) Regulations 2004 is created, maintained and secured throughout the duration of the study and that this file is available for inspection by the sponsor or regulatory authorities with 24 hours notice.

b) The Chief Investigator is responsible for ensuring that site files are created, maintained and secured at each site participating in the study and that these files are available for inspection by the sponsor, regulatory authorities and local NHS management with 24 hours notice.

c) The Chief Investigator is responsible for arranging appropriate archiving of the master file, all site files, raw study data and details of all analyses for a minimum of 5 years after the end of the study.

d) Unless explicitly agreed otherwise with the Trust's Head of R and D Governance, the Chief Investigator shall act as the nominated Archivist for the study in accordance with section 31(A) of Statutory Instrument 2006/1928.

e) The Chief Investigator must ensure each participating site nominates a named archivist who is responsible for provide the Trust R and D Governance Office with details of a single named archivist

Appendix C Principal Investigator Duties

The Principal Investigator takes overall responsibility for the study ensuring that the design of the study is appropriate, that the study is well conducted according to a written protocol, and that reasonable efforts are made to disseminate the results of the research. The PI must be fully conversant with the details of the study protocol and the drugs, devices and procedures used in the study, and be satisfied that the objectives of the study are appropriate and the methods used are valid.

In maintaining an overview of the conduct and progress of the study the Principal Investigator is responsible for ensuring that:

Conduct of the Study

- all those involved in the study are aware of, and abide by, the Trust's policies on Research Governance.
- all those involved in the study are given details of the aims, objectives and plan of the research.
- those involved in the study are clear about their roles and duties in the study and are sufficiently qualified and experienced to undertake these duties.
- all members of the research team have appropriate experience and training.
- a project file is set up and maintained for the study as set out in the Clinical Study Project File document.

Patient Involvement

- all research subjects have freely given consent to their participation in the study, having been given detailed information about the aims and objectives of the study, the risks and benefits and any alternatives.
- a confidential record is maintained of all research subjects invited to take part in the study, whether or not they did agree to take part.
- adverse events and serious adverse events will be reported according to the Trust's policy on reporting research-related adverse events.
- those involved in the study are aware of, and abide by, the Data Protection Act (1998), with particular reference to confidentiality, and any Trust policies on data protection and confidentiality.
- if randomisation and blinding are used to assign patients to different treatment options there is an agreed procedure for breaking the code in an emergency to identify which treatment a particular patient received.

- subjects enrolled in a trial involving medicines are given a card bearing information that identifies that they are involved in a clinical trial.

- patient notes are clearly marked to indicate that the patient has been entered into a trial (patient records that relate to research must be retained for longer than routine patient records).

Data collection, analysis and publication

- data collected is accurate and complete.

- reasonable efforts are made to publish, or disseminate in other ways, the results of the research and that these accurately reflect the findings of the research.

- the Trust's policy on Scientific Misconduct is followed.

Health and Safety

- medicines are stored and dispensed through Pharmacy or by some other mechanism that has been agreed with the Director of Pharmacy.

- any equipment used for the study is compatible with other equipment in the Trust, preferably purchased through the Trust's Supplies Department. Electrical equipment must be checked and approved by Medical Engineering. All equipment must be serviced regularly.

- where appropriate any hazardous material is handled in accordance with COSHH guidelines and that appropriate notifications and risk assessments have been made.