APPENDIX 4

Monitoring and Audit of Clinical Research Studies

Category:	Policy
Summary:	Implementation of this policy will ensure that the Trust fulfils its statutory obligations which in turn will maintain public confidence in the safety, rights and well-being of participants of research studies undertaken at the OUH Trust and that the reported trial data are accurate, complete, and verifiable from the source documents.
Equality Impact Assessed:	September 2015
Valid From:	July 2024
Date of Next Review:	July 2027
Approval Date/ Via:	TME 01 August 2024 Chief Medical Officer Trust Management Executive
Distribution:	Via Research and Development to: • Researchers within OUH Trust • Research and Development Web Site
Related Documents:	Sponsorship of Clinical Research Studies Policy Capacity and Capability Approval of Clinical Research Policy Integrity in Clinical Research Policy Safety Reporting in Clinical Research Policy Incident Reporting, Investigation and Learning Procedure
Author(s):	Shahista Hussain, Head of R&D Governance
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This Document replaces:	Monitoring & Audit of Research Studies Policy Version 3.0

Lead Director: R&D Director

Issue Date: 01 August 2024

This document is uncontrolled once printed.

It is the responsibility of all users to this document to ensure that the correct and most current version is being used.
This document contains many hyperlinks to other related documents.
All users must check these documents are in date and have been ratified appropriately prior to use.

Document History

Use this table to record the revisions made to the approved policy and record document history.

Date of revision	Version number	Author	Reason for review or update
March 2006	1.2		Reviewed and Updated
May 2007	1.3		Updated to reflect change in processes
July 2010	2.0		Reviewed and Update
September 2015	3.0	Head of R&D Governance	Reviewed and update transferred to new template
July 2024	4.0	Head of R&D Governance	Review and updated to include the compliance an interventional monitoring Updated risk assessment

Consultation Schedule (This is a mandatory heading)

Use this table to evidence your involvement of staff and key stakeholders, where appropriate, in the development and review of documents.

Who? Individuals or Committees	Rationale and/or Method of Involvement
Katie Flight - Deputy Head of R&D Governance	Review of the document and changes
Jo Franklin – Senior Research Support Manager	Review of the document and changes
Lousie Willis – Research Support Manager	Review of the document and changes

Endorsement (This is a mandatory heading)

Use this table to list relevant Divisional and/Directorate leads who have endorsed the policy/procedural document.

Endorsee Job Title

Head Of R&D Operations
Director of R&D

Contents

Who should read this document?

1. This policy applies to anyone conducting research within the Trust, whether such research is sponsored or hosted by the Trust, including Clinical Trials of Investigational Medicinal Products (CTIMPs).

Key Standards/Messages

2. It is the policy of the Oxford University Hospitals NHS Foundation Trust ('the Trust') to:

   2.1. Protect the safety, dignity, rights and well-being of all patients involved in clinical research.
   2.2. Ensure that arrangements are in place for the management and monitoring of research studies, where the Trust has taken on the role of Sponsor or Host Institution, including compliance with the relevant regulations.

3. This document applies to all areas of the Trust, and all employees of the Trust, including individuals employed by a third party, by external contractors, as voluntary workers, as students, as locums or as agency staff.

Background/Scope

4. The UK Policy Framework for Health and Social Care (2017)) requires that, where an organisation is providing care to research participants within studies with external Sponsors, the organisation must ensure that legislation related to research is followed.

5. The framework requires that an organisation taking on the role of 'Sponsor' must confirm that there are proper arrangements in place to initiate, manage, monitor, and finance a study.

6. The Medicines for Human Use (Clinical Trials) Regulations 2004 require that organisations which take on the role of Sponsor of clinical trials must have systems in place for the management of that trial.

7. The objective of monitoring, audit and compliance checks is to verify that:

   7.1. The rights and well-being of the human subjects are protected.
   7.2. The reported trial data are accurate, complete, and verifiable from the source documents.
   7.3. The conduct of the study is in compliance with the currently approved protocol; with Good Clinical Practice (GCP); and in accordance with the applicable local regulatory requirement(s).

Key Updates

8. General review and update to include the compliance check and invertentional monitoring programmes.

9. The Equality Impact Assessment has been updated to the new template version.

Aim

10. This policy sets out a consistent procedure for oversight of the progress of clinical research studies and promoting quality and compliance with the relevant legislation.

Content of the Policy

11. **Trust Sponsored Clinical Trials of Investigational Medicinal Products (CTIMPs)**

12. Prior to trial commencement, a monitoring plan will be written by R&D staff, in conjunction with the trials staff. The monitoring plan will define the approach to be taken in line with the Risk-adapted Approach to the Management of CTIMPs.

13. An initiation visit will be conducted prior to trial start to ensure that everything is in place and that staff are fully aware of their responsibilities for compliance with GCP.

14. During the trial, all trials sponsored by the Trust will be monitored in accordance to the study monitoring plan. These monitoring visits will comprise some or all of the following: examination of the contents of the Trial Master File; examination of a selection of Case Report Forms and the corresponding medical notes, for the purpose of Source Data Verification; and discussion of the trial progress with the investigator team. R&D staff will generate a monitoring report, outlining actions required, and will follow up on these actions.

15. Periodic visits will be made to pharmacy for the purposes of monitoring of IMP handling and examination of the relevant pharmacy files.

16. **Trust Hosted CTIMPs**

17. A selection of hosted trials will be audited. The selection procedure will, in the main, be random, but will include the facility to select specific trials that have previously been identified as high risk.

18. Audits will comprise examination of the contents of the Investigator Site File; examination of a selection of Case Report Forms and the corresponding medical notes; and interviews with the investigator team. R&D staff will generate an audit report, which will be provided to the investigator, along with any recommended actions. The trials team will respond to the findings within the report, outlining any corrective actions to be completed.

19. **Trust Sponsored interventional studies**

20. A selection of interventional studies will be selected for monitoring. The selection procedure will, in the main, be random, but will include the facility to select specific studies that have previously been identified as high risk.

21. The minoring visit will comprise examination of the contents of the Investigator Site File; examination of a selection of Case Report Forms and the corresponding medical notes; , for the purpose of Source Data Verification and a discussion of the trial progress with the investigator team. R&D staff will generate an interventional monitoring report, outlining actions required, and will follow up on these actions.

22. **Compliance Checks – All study types**

23. The R&D team may also perform a compliance check on any study or groups of studies. This may be at the request of a study team; a result of an issue coming to light and being reported to the R&D team; or as a random selection. Particular aspects of study management or participant safety are focused on for example the participant consent process or safety reporting.

24. **Other Research Studies (Non-CTIMPs)**

25. In order to avoid duplication of effort, the R&D team will endeavour to monitor the progress of research studies through copies of correspondence with the relevant ethics committee: via research recruitment reviews; progress reports where applicable substantial amendments; end of study notifications.

26. Investigator teams are required to assist with this process through copying of all such correspondence to R&D.

27. The R&D staff will monitor the submission of such updates and update the R&D project management system (Studyline) accordingly, thus ensuring that indemnity for each study is ongoing.

28. These studies may be audited for compliance in accordance to UK Policy Framework for Health an Social Care (2017) and GCP, where it is deemed to be appropriate.

Review

29. This policy will be reviewed every 3 years, as set out in the Developing and Managing Policies and Procedural Documents Policy.

30. The Trust Management Executive has delegated authority to the Research & Development Lead for the approval of any further supporting or associated documents.

References

31. The Medicines for Human Use (Clinical Trials) Regulations 2004 and Amendments

32. UK Policy Framework for Health and Social Care (2017)

33. ICH Harmonised Tripartite Guideline for Good Clinical Practice.

34. MRC/DH/MHRA Joint Project on the Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products Version 28th March 2011

Appendix 1: Responsibilities

1. The **Chief Executive** has overall responsibility for this policy.
2. The **Chief Medical Officer / Director of R&D / Head of R&D Operations/ Head of R&D Governance/ Deputy Head of R&D Governance/ Senior Research Support Manager** have delegated authority on behalf of the Trust to review and approve monitoring/audit plans and reports.
3. **Chief Investigator (CI) / Principal Investigator (PI)** : Overall responsibility for the conduct of the trial; Facilitate access to trial documents and participant medical records, for the purposes of monitoring, auditing and inspections; Ensure ongoing communication, through copying of relevant correspondence with Research Ethics Committees (REC), Health Research Authority (HRA) and MHRA.
4. **Research and Development Staff** – has the responsibility to provide advice and information to investigators on issues of compliance; to prepare for and conduct the monitoring visit/audit/compliance check; to write the resultant report; and to complete follow-up visits as required; to facilitate communication between the Trust and the investigator / study team; to update electronic study files and database with new information derived from ethics progress reports, annual safety reports, end of study notifications following the Trust R&D Standard Operating Procedures.

Appendix 2: Definitions

1. This section should be used to explain terms and definitions, including abbreviations that may be used throughout the document.

The terms in use in this document are defined as follows:

Sponsor

2. The organisation taking responsibility for initiation, management and financing (or arranging the financing) of a clinical trial or research study.

Host Institution

3. The organisation where the clinical research will take place.

Monitoring

4. The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s). Monitoring is an ongoing activity, throughout the conduct of the trial.

Audit

5. A systematic and independent examination of trial related activities and documents to determine whether the trial related activities were conducted, recorded and reported according to the protocol, the sponsor's SOPs, GCP and the applicable regulatory requirements. Audit is an assessment of compliance with these standards at a given moment in time.

Compliance Check

6. A review of a specific aspect of a research study or a group of studies, for example: Consent or safety reporting.

Clinical Trial of Investigational Medicinal Product (CTIMP)

7. Any investigation in human subjects, other than a non-interventional trial*, intended:

   7.1. To discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more medicinal products,
   7.2. To identify any adverse reactions to one or more medicinal products or
   7.3. To study the absorption, distribution, metabolism and excretion of one or more such products
   7.4. With the object of ascertaining the safety or efficacy of those products
   7.5. Such trials will be governed by the Medicines for Human Use (Clinical Trials) Regulations 2004 and updates.

   * The Medicines and Healthcare products Regulatory Agency (MHRA) view a trial as interventional where a drug is being given as an intervention and assessments are being undertaken to assess the effects. This is not dependant on the prescription of that drug being undertaken as part of the protocol.

Device Trial

8. A clinical investigation designed to establish the performance of a medical device which is intended to reveal adverse events under normal conditions of use, and permit assessment of the acceptable risks having regard to the intended performance of the medical device. Such trials are regulated by the UK Policy Framework and would require the approval of an ethics committee. Trials using non-CE/UKCA marked devices are also regulated by the Medical Devices Regulations (2002)

Interventional Trial / Study

9. Any investigation in human subjects which involves some form of medical intervention: surgical, medical, or psychological, but which is not classified as a CTIMP as defined in 9.6. Such studies are regulated by the UK Policy Framework and would require the approval of an ethics committee.

Non-interventional Study

10. Any investigation in human subjects, who are patients, which is observational and does not involve any intervention in addition to their normal clinical care. Such studies are regulated by the UK Policy Framework would require the approval of an ethics committee.

Investigator Site File

11. A file containing all the information that a site will need to conduct a trial at that site.

Chief Investigator

12. The individual, as identified in the ethics application, who takes overall responsibility for the conduct of a clinical study.

Principal Investigator

13. The individual who takes on responsibility for conduct of the study at a particular site.

Standard Operating Procedure

14. SOPs are documents that describe the procedures that should be followed to ensure consistency in the performance of specific processes or activities.

Appendix 3: Education and Training

1. All staff involved in the conduct of clinical trials will undertake training in Good Clinical Practice (GCP) prior to beginning their involvement in a trial. The process of monitoring and audit is covered within this training.

2. All staff involved in the conduct of monitoring, audit and compliance checks receive training in the use of the trust R&D SOPs. Each individual's training needs will be identified through annual appraisal and supervision.

   Training required to fulfil this policy will be provided in accordance with the Trust's Training Needs Analysis. Management and monitoring of training will be in accordance with the Trust's Core Skills Policy. This information can be accessed via the Practice Development and Education pages on the Trust intranet

Appendix 4: Monitoring Compliance

3. Compliance with the document will be monitored in the following ways.

What is being monitored:	How is it monitored:	By who, and when:	Minimum standard	Reporting to:
Staff of the Trust R&D Department will monitor the implementation of the policy.	Review of database	Head of R&D Governance	At least annually	R&D Team and if required Head of R&D Operations
The Trust R&D Department review this policy to reflect changes in legislation and examples of best practice.	Review of policy	Head of R&D Governance	At least Annually	R&D Team and if required Head of R&D Operations

Appendix 5: Equality Impact Assessment

Equality Impact Assessment Template

1. As part of its development, this policy and its impact on equality, diversity and human rights has been reviewed, an equality analysis undertaken and in order to minimize the potential to discriminate, no adjustments have been identified:

What is being assessed	Existing Policy
Job title of staff member completing assessment	Head of R&D Governance
Name of policy / service / function:	Monitoring, Audit and Compliance Checks of Research Studies
Details about the policy / service / function	To ensure that the Trust has a robust process in place to provide continued assurance that the rights and wellbeing of trial participants are safeguarded, the participants will benefit from the assurance that the trials undertaken at the OUH Trust are appropriately managed and monitored.
Is this document compliant with the Web Content Accessibility Guidelines?	Yes
Review Date	July 2027
Date assessment completed	July 2024
Signature of staff member completing assessment	Shahista Hussain
Signature of staff member approving assessment	Shahista Hussain

2. Screening Stage

Who benefits from this policy, service or function? Who is the target audience?

- Patients
- Staff
- Others (commercial and non-commercial sponsors)

Does the policy, service or function involve direct engagement with the target audience?

Yes - *continue with full equality impact assessment*

3. Research Stage

Impact Assessment

Characteristic	Positive Impact	Negative Impact	Neutral Impact	Not enough information	Reasoning
Sex and Gender Re-assignment – men (including trans men), women (including trans women) and non-binary people.			X		This policy applies to all staff working on research within the trust, regardless of race, religion, disability, age, gender or sexuality
Race - Asian or Asian British; Black or Black British; Mixed Race; White British; White Other; and Other			X		This policy applies to all staff working on research within the trust, regardless of race, religion, disability, age, gender or sexuality
Disability - disabled people and carers			X		This policy applies to all staff working on research within the trust, regardless of race, religion, disability, age, gender or sexuality
Age			X		This policy applies to all staff working on research within the trust, regardless of race, religion, disability, age, gender or sexuality
Sexual Orientation			X		This policy applies to all staff working on research within the trust, regardless of race, religion, disability, age, gender or sexuality
Religion or Belief			X		This policy applies to all staff working on research within the trust, regardless of race, religion, disability, age, gender or sexuality
Pregnancy and Maternity			X		This policy applies to all staff working on research within the trust, regardless of race, religion, disability, age, gender or sexuality
Marriage or Civil Partnership			X		This policy applies to all staff working on research within the trust, regardless of race, religion, disability, age, gender or sexuality
Other Groups / Characteristics - for example, homeless people, sex workers, rural isolation.			X		This policy applies to all staff working on research within the trust, regardless of race, religion, disability, age, gender or sexuality

Sources of information
No protected groups were targeted during the consultation process

Consultation with protected groups

Group	Summary of consultation
N/A	

Consultation with others
Based on the previous version, this update has drawn on feedback from researchers and other staff including members of the R&D team.

4. Summary stage

Outcome Measures
List the key benefits that are intended to be achieved through implementation of this policy, service or function and state whether or not you are assured that these will be equitably and fairly achieved for all protected groups. If not, state actions that will be taken to ensure this.

To ensure that the Trust has a robust process in place to provide continued assurance that the rights and wellbeing of trial participants are safeguarded, the participants will benefit from the assurance that the trials undertaken at the OUH Trust are appropriately managed and monitored.

These outcomes will be equitably and fairly achieved for all protected groups

Positive Impact
List any positive impacts that this policy, service or function may have on protected groups as well as any actions to be taken that would increase positive impact.

No specific positive impacts on protected groups have been identified.

Unjustifiable Adverse Effects
List any identified unjustifiable adverse effects on protected groups along with actions that will be taken to rectify or mitigate them.

No specific adverse effects on protected groups have been identified.

Justifiable Adverse Effects
List any identified unjustifiable adverse effects on protected groups along with justifications and any actions that will be taken to mitigate them.

No specific adverse effects on protected groups have been identified.

Equality Impact Assessment Action Plan

Complete this action plan template with actions identified during the Research and Summary Stages

Identified risk	Recommended actions	Lead	Resource implications	Review date	Completion date
None identified	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable