

## Monitoring and Audit of Clinical Research Studies

<b>Category:</b>	Policy
<b>Summary:</b>	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.
<b>Equality Analysis undertaken:</b>	Sep 2015
<b>Valid From:</b>	Jan 2016
<b>Date of Next Review:</b>	Jan 2019
<b>Approval Date/ Via:</b>	TME2016.06 Medical Director Trust Management Executive
<b>Distribution:</b>	Via Research and Development to: <ul style="list-style-type: none"> <li>• Researchers within ORH Trust</li> <li>• Research and Development Web Site</li> </ul>
<b>Related Documents:</b>	Sponsorship of Clinical Research Studies Policy Trust Management Approval of Clinical Research Policy Integrity in Research Policy Research Protocol Amendments Policy Safety Reporting in Clinical Research Policy Incident Reporting Policy
<b>Author(s):</b>	Fiona Parker, Research and Development Manager
<b>Further Information:</b>	Fiona Parker, Fiona.Parker@ouh.nhs.uk
<b>This Document replaces:</b>	Monitoring & Audit of Research Studies Policy Version 2.0

**Lead Director:** Dr Tony Berendt

**Issue Date:** 14<sup>th</sup> January 2016

## Contents

	Page
Introduction.....	3
Policy Statement.....	3
Scope.....	3
Aim.....	3
Definitions.....	3
Responsibilities.....	5
<i>Chief Executive</i> .....	
<i>The Medical Director / Director of R&amp;D / Research &amp; Development Lead /</i> <i>Research and Development Manager</i> .....	
<i>Chief Investigator (CI) / Principal Investigator (PI)</i> .....	
<i>Research and Development Staff</i> .....	
Content of the Policy.....	5
Training.....	6
Monitoring compliance.....	6
Review of this policy.....	7
References.....	7
Equality Analysis.....	7
Document History .....	8
Appendices: 1 Equality Analysis.....	8

## Introduction

1. The Research Governance Framework for Health and Social Care (RGF) 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.
2. The RGF 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.
3. 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.
4. The objective of monitoring, audit and compliance checks is to verify that:
  - 4.1. The rights and well-being of the human subjects are protected.
  - 4.2. The reported trial data are accurate, complete, and verifiable from the source documents.
  - 4.3. 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).

## Policy Statement

5. It is the policy of the Oxford University Hospitals NHS Foundation Trust ('the Trust') to:
  - 5.1. Protect the safety, dignity, rights and well-being of all patients involved in clinical research.
  - 5.2. 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.

## Scope

6. 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).
7. 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.

## Aim

8. 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.

## Definitions

9. The terms in use in this document are defined as follows:
  - 9.1. Sponsor - The organisation taking responsibility for initiation, management and financing (or arranging the financing) of a clinical trial or research study.
  - 9.2. Host Institution – The organisation where the clinical research will take place.

9.3. Monitoring - 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.

9.4. Audit - 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.

9.5. Compliance Check – A review of a specific aspect of a research study or a group of studies, for example: Consent or safety reporting.

9.6. Clinical Trial of Investigational Medicinal Product (CTIMP) - Any investigation in human subjects, other than a non-interventional trial\*, intended:

- To discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more medicinal products,
- To identify any adverse reactions to one or more medicinal products or
- To study the absorption, distribution, metabolism and excretion of one or more such products
- With the object of ascertaining the safety or efficacy of those products
- 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.

9.7. Device Trial - 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 RGF and would require the approval of an ethics committee. Trials using non-CE marked devices are also regulated by the Medical Devices Regulations (2002)

9.8. Interventional Trial / Study - 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 RGF and would require the approval of an ethics committee.

9.9. Non-interventional Study - 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 RGF and would require the approval of an ethics committee.

9.10. Investigator Site File – a file containing all the information that a site will need to conduct a trial at that site.

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

9.12. Principal Investigator - The individual who takes on responsibility for conduct of the study at a particular site.

9.13. Standard Operating Procedure - SOPs are documents that describe the procedures that should be followed to ensure consistency in the performance of specific processes or activities.

## Responsibilities

10. The Chief Executive has overall responsibility for this policy.
11. The Medical Director / Director of R&D / R&D Lead / R&D Manager have delegated authority on behalf of the Trust to review and approve monitoring/audit plans and reports.
12. 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) and MHRA.
13. 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.

## Content of the Policy

### Trust Sponsored Clinical Trials of Investigational Medicinal Products (CTIMPs)

14. 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.
15. 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.
16. During the trial, all trials sponsored by the Trust will be monitored at least twice yearly with follow-up visits if required. 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.
17. Periodic visits will be made to pharmacy for the purposes of monitoring of IMP handling and examination of the relevant pharmacy files.

### Trust Hosted CTIMPs

18. 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.
19. 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.

### Other Research Studies (Non-CTIMPs)

20. 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: progress reports; substantial amendments; end of study notifications.
21. Investigator teams are required to assist with this process through copying of all such correspondence to R&D.
22. The R&D staff will monitor the submission of such updates and update the R&D database accordingly, thus ensuring that indemnity for each study is ongoing.
23. These studies may be audited for compliance with RGF and GCP, where it is deemed to be appropriate.

### Compliance Checks – All study types

24. 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.

### Training

25. 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.
26. 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.

### Monitoring Compliance

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

Aspect of compliance or effectiveness being monitored	Monitoring method	Responsibility for monitoring (job title)	Frequency of monitoring	Group or Committee that will review the findings and monitor completion of any resulting action plan
Staff of the Trust R&D Department will monitor the implementation of the policy.	Review of database	The R&D Manager/Lead	At least annually	R&D Team and if required Director of R&D.
The Trust R&D Department review this policy to reflect changes in legislation and examples of best practice.	Review of policy	R&D Lead and delegated staff	At least Annually	R&D Team and if required Director of R&D.

## Review

28. This policy will be reviewed in 3 years, as set out in the Policy for the Development and Implementation of Procedural Documents.
29. The Trust Management Executive has delegated authority to the Research & Development Lead for the approval of any further supporting or associated documents.

## References

30. The Medicines for Human Use (Clinical Trials) Regulations 2004 and Amendments
31. The Department of Health Research Governance Framework for Health and Social Care 2005
32. ICH Harmonised Tripartite Guideline for Good Clinical Practice.
33. MRC/DH/MHRA Joint Project on the Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products Version 28th March 2011

## Equality Analysis

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

How does this policy affect each characteristic? <b>Protected Characteristic:</b>	Reasonable adjustments required
Disability (all disability including dementia and learning disability)	None required
Sex	None required
Age	None required
Race	None required
Sexual Orientation	None required
Pregnancy and maternity	None required
Religion or belief	None required
Gender re-assignment	None required
Marriage or civil partnerships	None required
Carers	None required
Safeguarding people who are vulnerable	None required

## Document History

Date of revision	Version number	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	Reviewed and update transferred to new template

## Appendix 1: Equality Analysis

Equality Analysis
Policy / Plan / proposal name: Monitoring, Audit and Compliance Checks of Research Studies
Date of Policy: September 2015
Date due for review September 2018
Lead person for policy and equality analysis: R&D Lead
Does the policy /proposal relate to people? If yes please complete the whole form. YES
<p><b>1. Identify the main aim and objectives and intended outcomes of the policy.</b> 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.</p>
<p><b>2. Involvement of stakeholders.</b> Based on the previous version, this update has drawn on feedback from researchers and other staff including members of the R&amp;D team.</p>
<b>Evidence.</b> Population information on <a href="http://www.healthprofiles.info">www.healthprofiles.info</a> search for Oxfordshire.
<b>Disability</b> Not applicable
<b>Disability: learning disability</b> Not applicable
<b>Sex</b> Not applicable
<b>Age:</b> Not applicable
<b>Race:</b> Not applicable
<b>Sexual orientation:</b> Not applicable
<b>Pregnancy and maternity:</b> Not applicable
<b>Religion or belief.</b> Not applicable
<b>Gender re-assignment.</b> Not applicable
<b>Marriage or civil partnerships:</b> Not applicable
<b>Carers</b> Not applicable



<b>Safeguarding people who are vulnerable:</b> Not applicable
<b>Other potential impacts e.g. culture, human rights, socio economic e.g. homeless people</b> Not applicable
<b>Section 4 Summary of Analysis</b> This policy does not show any potential to discriminate. The monitoring, audit or compliance checks (as well as the array of legislation) governing each trial ensures all patients are adequately protected.
How does the policy <b>advance equality of opportunity?</b> Not applicable
How does the policy <b>promote good relations between groups?</b> Not applicable.