Papworth Hospital NHS
NHS Foundation Trust

Document Title: Monitoring Research Studies

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Staff involved in development: *Job titles only*	RM&G Manager, R&D Administration Manager, Research Officers
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Summary of Significant Change(s) (for this version only)

Section(s):	Modification:
	Minor admin changes
Templates	Changes made to the associated templates
4.4	Updates for monitoring CTIMP studies

Key Points of this Document

- This document sets out the roles, responsibilities and procedures to be followed by Papworth Staff who are involved in the monitoring of research studies.
- It provides guidance on the monitoring process including the procedure to be followed prior to, during and after a monitoring visit.

1 Purpose and Contents

a. This document defines the Trust's procedures for the monitoring of Research Studies and Clinical Trials managed by Papworth Trials Unit Collaboration (PTUC) and/or sponsored / hosted by Papworth NHS Foundation Trust. Monitoring includes the inspection of Case Report Forms (CRFs), both electronic and paper, Site specific files and Pharmacy files where applicable.

b. The document describes the purpose of monitoring as described in Good Clinical Practice (GCP: 'a standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected').

c. The document contains guidance on how monitoring visits should be scheduled, performed and documented so as to comply with the Trust-wide policies on Information Governance and Patient confidentiality.

2 Roles & Responsibilities

a. This Policy applies to all personnel that are conducting research at the Trust.

b. Staff involved in the monitoring of studies must comply with the requirements set out in section 4.

c. The Sponsor takes responsibility for the monitoring of their study but may delegate the task to an appropriately trained member of the study team (the monitor).

d. The Principal Investigator (PI) and the research team must be co-operative and assist the monitor in both scheduling the monitoring visits and accessing the required documentation.

e. Copies of all the templates and guidance documents can be found on the Research & Development website: http://www.papworthhospital.nhs.uk/research/index/template-documents/

3 Policy

a. This SOP is mandatory and, as per the Trust's Information Governance and Records Management framework, non-compliance with may result in disciplinary procedures.

4 The Purpose of Monitoring

a. The purpose of study monitoring is defined in GCP and includes:

1. Ensuring the rights and well-being of study participants are protected
2. Checking the reported study data are accurate, complete and verifiable from source documentation.
3. Making sure that the trial is being conducted in compliance with GCP and applicable regulatory requirements
4. Checking that the currently approved protocol and study documents are being used

4.1 Procedure

a. Prior to the start of the study the Sponsor will determine the appropriate extent and nature of monitoring arrangements based on the objective, purpose, design and complexity of the trial. The timing of monitoring visits may vary depending on the duration and complexity of the study and the number of subjects involved. This will be agreed at Research Governance Project Approval System (RGPAS) as part of the local approvals process. (See SOP025: Assessment and Registration of Trust Risk Rating for Research Studies). Based on the risk rating outcome; a monitoring plan will be created before the study starts stating the expected frequency of monitoring visits and the amount of source data verification required. The study will be added to the departments monitoring rota and a monitor assigned. Trial oversight will be conducted in the form of on-site monitoring and central oversight depending on the risk level of the trial. E.g. For low risk studies, this could simply be a review by the Trial Steering Group (TSG). It is recommended that the first two patients recruited to a trial are routinely monitored.

b. If Papworth NHS Foundation Trust is the sponsor of a multi-centre study the extent or nature of monitoring additional sites will be determined during study set-up.

c. Additional monitoring may be undertaken in response to concerns raised re: data quality, patient safety, recruitment etc.

d. The monitoring of a study will be performed by an appropriately trained member of R&D who is independent of the work being reviewed.

4.2 Preparation for the Monitoring Visit

a. The monitor assigned to a trial will schedule the monitoring visit, contacting the PI, study team and other relevant departments in advance to arrange the visit.

b. The monitor will identify the documents that are required and inform the study team.

c. Advance selection of patients will be performed so as to allow the appropriate paperwork (CRFs, medical notes etc.) to be supplied. A letter confirming arrangements for the visit (see TPL013) will be sent. This will contain details of what will be monitored: site file, pharmacy file, electronically stored data, the study ID of the trial subjects (as applicable).

d. The monitor will make themselves familiar with the Protocol, Investigator brochure and case report form (CRF). If the CRF is electronic the monitor should arrange access and any necessary training prior to the monitoring visit.

e. The monitor will request that a room or quiet desk be made available for the monitoring visit.

f. The monitoring report from any previous visits will be reviewed to identify any outstanding actions that need to be revisited.

g. The monitor should request that the clinical research nurse (CRN) or study co-ordinator and the PI are available at the end of the visit to discuss any queries that have been found.

h. If the monitoring visit is triggered due to a specific problem, the monitor will inform the research nurse/co-ordinator of any specific requirements before-hand.

4.3 During the Monitoring Visit

a. The monitor will complete a Case Report Form log (FRM027) for each patient to keep a record of the visits that have been monitored. A record of queries will be compiled using this form.

b. The Site file will be checked using the Site File Report template (TPL010) to ensure that all the required documentation has been filed and that the current approved versions are present. If applicable a summary of action points will be documented to follow up. As a minimum the following will be checked:

1. Delegation Log
2. CVs of any new members of the study team
3. The current approved versions of documents are being used
4. Superseded versions are marked as superseded
5. Patient Consent forms
6. CPA accreditation of laboratories (if applicable)

c. Periodically, specific logs as defined in the study protocol should be checked. For example, screening and enrolment logs.

d. If any Serious Adverse Events (SAEs) have occurred the monitor will check that they have been reported appropriately to the necessary regulatory bodies.

e. Particular attention will be made to checking the Informed Consent Process:

1. The informed consent form will be cross referenced with the GP letter, CRF and medical record to check the patient's identity and that the date of the consent was before any trial related procedure occurred
2. It should be verified that the consent process allowed adequate time for the patient to discuss their participation with their family / GP etc.
3. The informed consent form will be checked to make sure all applicable sections have been completed by the patient and that boxes contain the patient's initials and the patient has printed their own name, date and signed the consent form.
4. The signature of the person taking consent will be checked against the delegation log
5. The version of the consent form will be checked to make sure it was signed when all appropriate approvals were in place.
6. If applicable, subjects have received revised information and signed the revised consent form
7. The original consent form is present in the site file, a copy placed in the medical notes and a copy given to the patient. If this sequence of documentation has not been followed a file note will be placed in the site file.

f. The monitor is responsible for checking that any errors identified in previous monitoring visits have been rectified and that any queries have been signed off.

g. For CTIMPS, the monitor will also be required to visit the pharmacy department at pre-arranged intervals to check the storage of the study medication and drug accountability. Full drug accountability is performed at the end of the trial. In blinded drug studies where Pharmacy knows the treatment allocation there will be the requirement of two clinical trial monitors – A blinded monitor will be designated to perform site monitoring activities except for pharmacy and an unblinded monitor will be designated to perform the site monitoring activities for pharmacy, drug accountability and reconciliation of the blinded investigational products. The unblinded pharmacy monitor will complete the Pharmacy Monitoring Report template FRM044 during the trial to:

1. Verify that IMP storage conditions are adequate
2. Verify that IMP supplies are sufficient – batch numbers, expiration dates and certificates of analyses will be checked
3. Per patient accountability and compliance checks are performed and compared to the corresponding logs
4. Code breaks are checked (if applicable)
5. Drug shipping forms are reviewed
6. IMP destruction protocol (if applicable)
7. Verify that IMP prescriptions are completed correctly
8. IP training has been completed and documented

h. Other applicable supporting departments will also be monitored periodically as detailed in the monitoring plan or protocol.

i. Any deviations from the protocol or amendments will be discussed with the investigator and appropriate actions identified. This should include measures to prevent a recurrence (see SOP 50 Handling of Protocol non-compliance and regulatory compliance Protocol)

j. At the end of the visit the monitor should meet with the CRN/co-ordinator and Principal Investigator to discuss any findings and resolve any queries found during the review of the data.

4.4 Monitoring Report

a. The monitor should complete the Site File Report template (TPL010) and the Case Report Form log (FRM027) within 5 working days of the monitoring visit.

b. The monitoring report should detail the records that have been reviewed, any queries/discrepancies raised and any changes that need to be made along with a recommended date for completion. A summary of the action points should be compiled using the table within the Site File Report template.

c. If any of the discrepancies require the study database to be changed then a Data Amendment form (FRM002) needs to be completed and sent to the database manager.

d. The report will include any general feedback relating to the quality of the data collected and the progress of the study at the site. The report should include timelines for the resolution of any queries and the anticipated date of the next monitoring visit. As a minimum the report should include:

1. The date of the visit
2. Who was present
3. What and who was monitored
4. Details of findings
5. Actions required, by whom and when

e. The report will be sent to the CRN/ Co-ordinator /PI for any queries/discrepancies to be amended within the specified timelines (ideally within 2 weeks, dependant of CRN/co-ordinator/PI workload or available time). Any queries that cannot be completed within the specified timelines will be followed up after the monitoring visit.

f. Once the data queries/actions have been resolved a copy of the final report will be sent to the trial manager of the study to review prior to it being received by the PI.

g. The PI will review and sign off the Data Query form, once all the queries have been resolved.

h. A copy of the signed monitoring report will be filed in the Site file (and the Sponsor file for Papworth Sponsored studies) and a copy sent to R&D for electronic filing. If, for a CTIMP, the visit included Pharmacy then a copy will also be filed in the pharmacy file. (Blinded

studies: If the pharmacy monitoring report contains any information that may un-blind any patients to their study allocation then this MUST NOT be sent to any of blinded team including the PI)

i. If any concerns are raised by the monitor these should be addressed by the study team. If the monitor feels their concerns are not being resolved then they will inform the project manager who, when appropriate, will escalate the issues to the Senior R&D Management group for appropriate action.

j. A CAPA (Corrective Action, Preventative Action) database will be used by the Project managers /audit and monitoring co-ordinator to log the findings of monitoring reports. This will allow the tracking of findings and will allow the oversight of patterns of non-compliance and serious breaches of GCP. (SOP 052 Misconduct and Fraud Good Research Practice and SOP051 serious breach of protocol of GCP in CTIMPS).

5 Central Oversight

a. Remote monitoring may be utilised as a method of maintaining oversight of a site and is considered a part of monitoring, whether site visits are taking place or not. These will include regular communication with the site by email or telephone and regular status updates to the sponsor from the site, regarding recruitment, operational issues such as staff changes, key document amendments, deviations and non-compliances. Remote monitoring should concentrate on those activities which can be reviewed and monitored remotely, such as consistency checking, data completeness, identification of sites with high error rates or protocol violations. Where source data are contained within the CRF these can be accessed and therefore, checked remotely.

5.1 Triggered Monitoring

a. Remote Monitoring or general concerns expressed by a member of the project team may result in an off plan monitoring session. This may require a more in depth assessment of a site, or a review of the risk and revision of monitoring plan. In this case a monitoring visit will be arranged to assess the issues and future monitoring requirements.

6 Risk Management / Liability / Monitoring & Audit

a. The R&D SOP Committee will ensure that this SOP and any future changes to this document are adequately disseminated.

b. The R&D Department will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part

of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).

c. In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the Senior R&D Manager should be gained before any action is taken. SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.

d. The Research and Development Directorate is responsible for the ratification of this procedure.

Further Document Information

Approved by: *Management/Clinical Directorate Group*	Research and Development Directorate
Approval date: *(this version)*	30 March 2015
Ratified by Board of Directors/ Committee of the Board of Directors:	STET
Date:	N/A
This document supports: *Standards and legislation*	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. Research Governance Framework for Health and Social Care (2005)
Key related documents:	Trust Research Policy [Insert list of linked or relevant documents to this SOP]

Equality Impact Assessment: Does this document impact on any of the following groups? If YES, state positive or negative, complete Equality Impact Assessment Form available in Disability Equality Scheme document DN192 and attach.

Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	NO	NO	NO	NO	NO	NO	NO
Positive/Negative							

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Version Control

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5.0	27 April 2015	March 2018	RDD	8 May 2012
5.1	12 May 2015	March 2018	Minor amendment to wording of 4.1c	
5.2	18 May 2015	March 2018	Minor amendment to take out appendices and	

			add as Forms/Templates	

I certify the contents of this SOP has been reviewed and ratified

..... 18 August 2016

Signed by Dr Ian Smith, Clinical Director of R&D — Date

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