RD&I	NHS University Hospitals Plymouth NHS Trust **STANDARD OPERATING PROCEDURE**

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The definitive versions of all UHPNT RD&I Dept SOPs appear online, not in printed form, to ensure that up to date versions are used. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the Trust's website: https://www.plymouthhospitals.nhs.uk/researchers

Risk Assessment

SOP No: P6

Version No: 6.1

Effective Date: Jan 2019

Supersedes: Version 6.0, Sep 2017

Page: **1** of **11**

Last Review Date: Jan 2019 Next review date: Jan 2022

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1 Purpose and Scope

To document the procedure for assessing the risk rating of a research study so as to make adequate provision to mitigate the risk and to monitor the conduct of the study.

Risk in research studies can be defined as the likelihood of a potential hazard occurring and resulting in harm to the participant and/or an organisation, or to the reliability of the results.

For every trial there is a core set of risks inherent to the protocol that relate to the safety of the participants and the integrity/reliability of the results. All organisations involved need to understand these risks so that the control measures, resources, procedures and processes implemented during the trial ensure the safety of the trial participants, and lead to high-quality results.

Risk Assessment is essentially a process of identifying the potential hazards associated with that trial, and assessing the likelihood of those hazards occurring and resulting in harm. This risk assessment will include:

- the risks to participant safety in relation to the intervention
- all other risks related to the design and methods of the trial (including risks to participant safety and rights, as well as reliability of results)

The design of a study has a major impact on the quality of the results; the more robust the design the less dependence there is on quality control and assurance measures for reliable results. Of critical importance is the identification of areas of potential vulnerability in trial design and planned methodology, which may require mitigation activities to ensure the reliability of the trial results and to protect participants' rights.

Risk assessment should be initiated by the Chief Investigator/protocol author at an early stage in protocol development. It should be reviewed by the sponsor, to agree on the main risks inherent in the trial protocol. A plan to mitigate or manage these risks should be developed, either as part of the trial protocol or outlined in associated documents (such as a monitoring plan).

In scope: research hosted by, and/or sponsored by UHPNT.

Definitions

PI	Principal Investigator
CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
EU	European Union

GCP	Good Clinical Practice
HCA	Health Care Assistants
HRA	Health Research Authority
IMP	Investigational Medicinal Product
MHRA	Medicines and Healthcare products Regulatory Agency
REC	Research Ethics Committee
R&D	Research, Development & Innovation
RO	Research Office
SOP	Standard Operating Procedure
UHPNT	University Hospitals Plymouth NHS Trust

2 Who should read this document?

Staff involved in setting up, reviewing and conducting research, in particular the Chief Investigator (CI) and RD&I Managers. The SOP should also be reviewed by the study Principal Investigator (PI), Trial Co-ordinator/Manager, Research Nurses & Midwives, Health Care Assistants (HCA) and Clinical Trial Administrative staff.

3 Procedure to Follow

3.1. Completing the Risk Assessment Forms: General Guidance

The Risk Assessment process has been split into two parts;

1. Study Risk Assessment translates the risks associated with the trial when reviewing the protocol at which risk mitigation maybe incorporated into the protocol before it is finalised (see appendix 1 for guidance).

2. RD&I approval Risk Assessment translates the risks associated with a Trust sponsored study into an appropriate method and frequency of monitoring as described in SOP QA2 Monitoring; this assessment is filed in the RD&I Study File. The Risk Assessment tool is located at: G:\RandD\Shared\Research Governance Monitoring & Audit (CR)\ Risk Assessment Tool (monitoring)

- The expertise of specific disciplines maybe sought as required when completing the risk assessments as required (e.g. Radiology, Pharmacy etc.).

- Each risk category will have a number of trial specific risks associated with it; these should be recorded in the 'Trial Specific Details' column.

3.1.1. CTIMP Risk Assessment

The Research Governance Manager should be sent a draft protocol prior to submission to any regulatory review body, to ensure that risk mitigation measures have been incorporated into the protocol prior to finalisation for submission.

Considerations in this Risk Assessment Process:

- Risk to the participants rights
- Risk to the participants integrity, safety and well being
- Risk to the data quality accuracy of results
- Risk to organisation, resources and staff

Risk must be determined prospectively and necessary suitable mitigations should be written into the trial protocol and/ or procedures.

For studies run by the Peninsula Clinical Trials Unit (Pen CTU), they will be delegated the task of producing the risk assessment and subsequent monitoring plan.

3.1.2. Non-CTIMP Risk Assessment

For Trust sponsored non-CTIMP studies a risk assessment form may be incorporated into the study protocol appendices, this facilitates a further review if protocol is amended.

3.1.3. Hosted studies

For hosted studies a short risk assessment is attached to the senior managers final check sheet. The studies should be checked to ensure the studies are being monitored by the sponsor or affiliate.

3.2. RD&I Approval Risk Assessment and Monitoring

The risk assessment tool informs together with the Trust monitoring SOP (QA2) on the frequency of monitoring.

The assessment is completed by a member of the RD&I Management team.

3.3. Ongoing Risk Assessment

- Ongoing risk will be commented on in the Monitoring Report Form for a given visit and would also note any changes to monitoring frequency or practice due to findings, amendments or other triggers (which may be identified in the protocol or Monitoring Plan).
- If there is a separate Monitoring Plan this may be updated as a result of this ongoing risk assessment.

- If the protocol is amended the study risk assessment in the protocol appendices will be reviewed and updated if required.

4 Document Ratification Process

The review period for this document is set as ***default of three*** years from the date it was last ratified, or earlier if developments within or external to the Trust indicate the need for a significant revision to the procedures described.

This document will be approved by the ***RD&I Manager or their Deputy***.

Non-significant amendments to this document may be made, under delegated authority from ***a Senior RD&I manager***, by the nominated author. These must be ratified by ***a Senior RD&I manager***.

Significant reviews and revisions to this document will include a consultation with ***appropriately knowledgeable staff***. For non-significant amendments, informal consultation will be restricted to ***staff*** who are directly affected by the proposed changes.

Dissemination and implementation

4.1. Dissemination of this SOP

4.1.1. New SOPs and new versions of existing SOPs: The Research Governance Manager will be responsible for ensuring authorised SOPs are uploaded on the RD&I internet site. Internal Trust Staff are expected to use the RD&I internet site to access latest versions of SOPs and to check the website regularly for updates.

Notice of new or amended procedural documents that have undergone a major amendment will be given *via* the following routes:

- Inclusion in the Trust weekly e-bulletin Vital Signs
- Direct email to Trust Researchers and or teams

4.2. Training in this SOP

4.2.1. All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP.

5 Reference material

ICH GCP (E6-R2) guideline
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf

Transcelerate

http://www.transceleratebiopharmainc.com/wp-content/uploads/2017/09/Site-Level-Risk-Assessment-Considerations.pdf

Appendix: Risk Assessment Guidance for researchers — Appendix 1

Reason for this guidance

To assist researchers in identification and mitigation of risk in research.

This document should be used in conjunction with the current Trust risk assessment SOP and trust protocol templates.

This document identifies:

- the areas that, as a minimum, should be considered when completing the Risk Assessment Form in the CTIMPs protocol appendix;
- Suggested Management Strategies for minimising any identified Hazard

Risk Assessment Criteria and Management Strategies for Identified Risks

HAZARD - RISKS TO PARTICIPANTS' RIGHTS:	Examples	Management Strategies
(i) fully informed consent	• Vulnerability of participant group/capacity to give consent • Consent procedures • Clarity of information provided • Time to consider information • Experience & knowledge of person taking consent • Failure to act on participant's request to withdraw from trial • Consent recorded/filed	• Literature and process approved by REC. • Training and awareness • Supervision of consent process • Communication systems e.g. alerts stickers in patient notes, contact details on consent form • Collect signed consent forms at coordinating centre/on site file • Audit of consent procedures including verification of signed consent forms in clinic records
(ii) Failure to protect participants' privacy	• Breach of Data Protection Act • Breach of confidentiality • Anonymity	• Adherence to normal NHS / University systems • Anonymised or anonymised/linked data • Minimise staff who have access to confidential information • Follow REC approved processes • Training and awareness • Computer security systems

HAZARD - RISKS TO PARTICIPANTS' SAFETY:	Examples	Management Strategies
(i) Hazards of the intervention	• Potential for unexpected adverse events • Clinical management of adverse events • Clinician's experience of intervention • Novel medicinal product / procedure (licensing status, indications, pharmacology, etc) • Unproven effectiveness • Use for new indication • Increased susceptibility of patient population • Novel handling requirements • Equipment safety • Prior clinical study data on intervention	• MHRA approval (CTA) • REC approval • NHS RD&Iapproval • Data Monitoring and Ethics Committee – specify review processes • Adverse event reporting system • Check participant case notes for adverse events • Investigator meeting to review trial and procedures • Local Investigator(s) to sign protocol/declaration
(ii) Hazards of study assessment methods	• Additional invasive tests (e.g. biopsy) • Increased radiological exposure (X-ray)	• Data Monitoring and Ethics Committee • IRMER / ARSAC review • Adverse event reporting systems
(iii) Other *please give details:*	• Systems to monitor and review adverse events • systems to maintain awareness of and to act on new knowledge • ability of participants to report adverse events and study outcomes reliably	• Adverse event reporting systems • Data Monitoring and Ethics Committee

HAZARD - RISKS TO RESEARCHERS:	Examples	Management Strategies
(i) Staff competence / experience to carry out responsibilities	• New clinicians • Clinician's experience of intervention • Clinician's understanding of methodology • Unfamiliar with underlying condition • Unfamiliar with expected adverse events • Inadequate training	• Delegated responsibilities clearly identified and agreed in site file (including supervision requirements) • Assess training needs of research team • systems to maintain awareness of and to act on new knowledge • Investigator meeting to review trial and procedures • Local Investigator(s) to sign protocol/declaration • Project team meetings • CVs for trial staff held in Trial Master File
(iii) Contact with aggressive / violent patients / relatives		
(iii) Contact with harmful chemicals, substances, equipment or organisms	• Provision for containment, shielding, monitoring etc.	• Reference to department SOPs
(iv) Trial proceeding without the necessary regulatory approvals	• Organisation/RD&Iapproval • Research Ethics Committee approval • Clinical Trial Authorisation	• Register all site approvals with trial co-ordinating centre prior to commencement at each site • Site agreements

HAZARD - RISKS TO COMPLETION OF THE TRIAL:	Examples	Management Strategies
(i) Study Power & Recruitment	• Feasibility of study population (restricted access to patients, insufficient patient pool) • Plausibility of treatment effect • Restrictive inclusion/exclusion criteria • staff competence and experience at study sites; • appropriate time scale of study; • length, frequency and means of follow-up • Competing trials • Ineffective communication with patient (before and after trial) • Failure to record consent	• Statistical input to design and power • Recruitment assessment • Pilot studies • External communication and trial promotion • Training in consent process • Trial steering Committee • Trial management group
(ii) Organisational Complexity	• Competence of partner organisations • Multi-centre studies • Multi-disciplinary studies • Non-standardised methods	• Site registration process • Trial coordinator/manager • Site visits • Investigator initiation meetings • Site agreements
(iii) Adequacy of trial management	• Responsibilities/accountability must be defined	• Summary of Trial Management Systems document • Trial Steering Committee • Trial delegation log

HAZARD - RISKS TO RELIABILITY OF THE RESULTS:	Examples	Management Strategies
(i)Study Results	• Violation of Inclusion / exclusion criteria • Financial / non-financial incentives • Robustness of randomisation procedure • Anonymisation arrangements (potential for loss of Blinding) • Source data availability for verification e.g. death certificate, laboratory investigation result. • Results not disseminated / implemented	• Suitability of eligibility criteria • Trial Management Protocol • Independent randomisation • Statistical input to data monitoring and audit • Interim reports • Standardised data collection forms • See section 2.1(i)
(ii) Completeness and accuracy of assessment / data	• Data type and complexity • Familiarity with data collection and entry method • Poor data quality and integrity •	• CRF design • Data Monitoring Committee. staff training • standardisation of assessment • Regular Data quality checks • Source Data verification

HAZARD - RISKS TO THE ORGANISATION:	Examples	Management Strategies
(i) Knock on costs of research projects being inaccurately costed at the outset	The research and treatment costs must be identified correctly and availability of any funding noted; cost of continuation of drugs after research has finished.	
(ii) Impact on clinical services	• Direct impact via tests required • Indirect impact via staff time	• Contact with service early in planning and throughout the trial • Multidisciplinary project teams
(iii) Liability	• Clarity of liability arrangements with collaborators • Legal obligations under UK Regulations for medicinal trials • Clarity of liability information in patient information sheet e.g. arrangements for non-negligent harm	• Clear identification of sponsor • Partnership agreements • Monitoring of collaborating sites • Delegated responsibilities clearly identified and agreed in site file (including supervision requirements) • Systems to ensure reporting obligations for medicinal trials (SUSARs, amendments, termination)

6 Amendment History

Version Number:	6.1
Date Of Amendment:	Jan 2019
Details Of Amendment:	Update of logo and Trust name. SOP edit to reflect current practice.
Version Number:	6.0
Date Of Amendment:	Aug 2017
Details Of Amendment:	Update of SOP template and numbering system. SOP reviewed and re-written.
Version Number:	5.0
Date Of Amendment:	Jan 2015
Details Of Amendment:	Major update to highlight the two phases of risk assessment, the study risk assessment and the monitoring risk assessment.
Version Number:	4.1 (minor amendment)
Date Of Amendment:	Mar 2012
Details Of Amendment:	Cover page - Change of SOP location address.
Version Number:	4.0
Date Of Amendment:	Sept 2011
Details Of Amendment:	Minor amendments