Risk Assessment for Clinical Research

Research & Innovation SOP J-5020

University Hospitals of Leicester NHS
NHS Trust

Trust Ref: B15/2026

1. Introduction and Who Policy Applies to

This SOP describes the process for conducting, documenting, and maintaining a proportionate risk-based approach to quality management for clinical research conducted by University Hospitals of Leicester NHS Trust (UHL), to ensure compliance with regulatory requirements and ICH Good Clinical Practice (GCP).

UHL will operate a two-tier risk assessment process comprising a formal centralised risk review and a local feasibility and capacity assessment. A centralised risk review must be completed for all UHL-sponsored trials in the following categories, or where significant or novel risks have been identified:

- Clinical Trials of Investigational Medicinal Products (CTIMPs)
- Clinical investigations of medical devices
- Non-CTIMP trials of novel, complex, or non-standard treatments or interventions
- Trials involving vulnerable populations (as defined in R&I Template T-1090)

This SOP only applies to research requiring a formal centralised risk review. For all other UHL-sponsored or hosted clinical research, an appropriate consideration of local risk must still be undertaken and documented. This should be managed through local Feasibility, Capacity and Capability (C&C) and/or sponsorship review processes, rather than through this SOP.

For full criteria, see R&I Template T-1070: *Risk Assessment Flow Chart*.

2. Definitions

Control	A mechanism, action, system or process implemented to reduce the likelihood of a risk occurring, or minimise the impact if it does occur.
Critical to Quality (CtQ) Factors	Research attributes, processes and data that are essential to ensuring participant safety and generating reliable results that support the scientific objectives of the study. Identified during the research design phase and used to focus risk assessment, oversight and quality management activities on aspects of the research activity that matter most.
Risk	The chance that failures in critical processes, or trial-specific hazards may occur that adversely impact participant safety, or the integrity and reliability of research results.
Risk Assessment	The systematic collection of information to determine the likelihood and severity of harm and identify where additional controls are needed to reduce the risk to as low as reasonably practicable
Risk-Based Monitoring	Research monitoring planned and conducted according to the significance of identified risks, with resources focused on areas most critical to participant safety, data integrity and regulatory compliance (CtQ factors).
Risk management	The culture, processes and structures directed towards the effective management of potential failures, hazards or adverse events.

3. Policy Standards and Procedures

Risk assessment should be used to inform trial design and oversight, whilst ensuring that agreed processes are proportionate to the level of risk. Risk assessment is part of a continuous risk management process, involving:

- Identification of risks
- Evaluation of likelihood and impact
- Implementation of mitigation measures
- Ongoing review of risk throughout the trial lifecycle

In line with ICH-GCP, this process should focus on identifying Critical to Quality (CtQ) factors, defined as the trial aspects that are essential to:

- Participant safety and rights
- Reliability and integrity of trial data

Although the concept of type A, B and C trials has now been retired, it may still be useful for CTIMPs, considering the levels of risk associated with the Investigational Medicinal Product (IMP):

Type A: No higher than standard medical care (trials involving authorised medicinal products used in accordance with the terms of their marketing authorisation or supported by substantial evidence and aligned with standard medical care).

Type B: Somewhat higher than standard medical care (trials involving authorised medicinal products used outside the terms of their marketing authorisation, but where there is sufficient evidence to support safety and efficacy).

Type C: Markedly higher than standard medical care (trials involving non-authorised medicinal products, or authorised products with limited supporting safety data).

This categorisation relates to the IMP only and may not represent the overall risk of the trial. This must be assessed separately, taking into account all protocol elements, including trial procedures, population, data collection, and operational complexity.

2.1 Responsibility for Risk Management

The trial Sponsor retains overall responsibility for ensuring that an appropriate risk management process is in place.

The Chief Investigator (CI) is responsible for:

- Overseeing the risk assessment process
- Ensuring risks are appropriately identified, managed and documented

Responsibilities may be delegated to appropriately trained personnel; however, accountability remains with the CI and Sponsor.

2.2 When to Conduct a Risk Assessment

A risk assessment must be conducted:

- During trial design, prior to finalisation of the protocol
- Before trial initiation
- Throughout the trial lifecycle, with regular review

The risk assessment must be updated:

- Following protocol modifications
- In response to emerging safety data or new evidence
- Following serious breaches, deviations or inspection findings
- Based on outputs from monitoring activities or trial metrics

2.3 Risk Assessment Methodology

Risk assessment must be pragmatic and proportionate. It should prioritise risks that could realistically occur and that would have a meaningful impact on participant safety, protection of rights, data integrity and the reliability of primary and other key trial outcomes. These are referred to as 'CtQ factors' and must form the starting point for the risk assessment process.

If risks are not CtQ, are unlikely to occur, would have minimal impact, or are already adequately controlled through routine clinical care or standard operating procedures, these should not materially influence the overall risk rating (provided clear justification is documented).

Assessment of risk should follow a structured and documented approach, including:

- Identification of CtQ factors
- Identification of risks that could impact CtQ factors, including:
    - Participant safety risks
    - Data integrity risks
- Operational and trial delivery risks
- Evaluation of risk based on:
    - Likelihood of occurrence (considering trial design, population, setting and existing controls)
    - Potential impact on CtQ factors
    - Risk prioritisation, with focus on areas of greatest importance
- Mitigation planning, including:
    - Preventative actions
    - Contingency measures
    - Assessment of residual risk following mitigation

2.4 Link to Monitoring and Oversight (Risk-Based Monitoring)

Risk assessment must directly inform the monitoring and oversight strategy, including:

- The development of a risk-based monitoring (RBM) plan (see *R&I SOP S-1007: Management (Monitoring) of Research Sponsored by UHL*)
- Determination of:
    - Requirement for on-site vs central monitoring
    - Monitoring frequency and intensity
    - Key data and processes requiring oversight

Monitoring activities should focus on CtQ factors and high-risk areas, ensuring efficient and proportionate use of resources.

2.5 Who Should Complete a Risk Assessment?

Risk assessment must be undertaken by a multidisciplinary team, which may include:

- CI, or medically qualified representative
- Pharmacist / Pharmacologist / Toxicologist
- Statistician
- Trial manager
- Data manager

- Research governance or regulatory specialist
- Other relevant personnel (e.g. Research Nurses/Midwives, Allied Health Professionals, Clinical Research Practitioners)

2.6 Documentation and Storage

Risk assessments must be:

- Fully documented using the approved template (T-1067: *Clinical Trial Risk Assessment Tool*)
- Version controlled
- Filed in the Trial Master File (TMF)
- Accessible to relevant trial personnel

Associated documents may include:

- Risk logs/registers
- Monitoring plans
- Mitigation action plans

2.7 On-going Review and Risk Management

Risk assessment must be a continuous process. Risk reviews should be triggered by meaningful changes or emerging signals and should not be repeated unnecessarily where there is no new information or change in risk profile. Review should be informed by:

- Monitoring findings
- Trial metrics, data trends or emerging signals
- Safety reports
- Protocol deviations
- Serious breaches

All reviews must be documented, including justification where no changes are required.

4. Education and Training

None

5. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting Arrangement
Appropriate risk assessment in place for all UHL research	Ongoing audit or monitoring of research activity	R&I Director of Operations	As per R&I monitoring / audit programme	Non-compliance reported to CI and escalated to R&I Governance Meeting
Percentage of clinical research projects with documented ongoing risk review	Ongoing audit or monitoring of research activity	R&I Director of Operations	As per R&I monitoring / audit programme	Non-compliance reported to CI and escalated to R&I Governance Meeting
Alignment between risk assessments and risk-based monitoring plans	Review of monitoring plans against risk assessment outputs	R&I Director of Operations	As per R&I monitoring / audit programme	Non-compliance reported to CI and escalated to R&I Governance Meeting

6. Equality Analysis Assessment

The Trust recognises the diversity of the staff and local community it serves. Our aim therefore is to provide a safe environment free from discrimination, harassment and victimisation and treat all individuals fairly with dignity and respect and, as far as is reasonably possible, according to their needs.

As part of its development, an Equality Analysis on this policy has been undertaken and its impact on equality has been reviewed and no detriment was identified.

7. EDI Statement

We are fully committed to being an inclusive employer and oppose all forms of unlawful or unfair discrimination, bullying, harassment and victimisation.

It is our legal and moral duty to provide equity in employment and service delivery to all and to prevent and act upon any forms of discrimination to all people of protected characteristic: Age, Disability (physical, mental and long-term health conditions), Sex, Gender reassignment, Marriage and Civil Partnership, Sexual orientation, Pregnancy and Maternity, Race (including nationality, ethnicity and colour), Religion or Belief, and beyond.

We are also committed to the principles in respect of social deprivation and health inequalities.

Our aim is to create an environment where all staff are able to contribute, develop and progress based on their ability, competence and performance. We recognise that some staff may require specific initiatives and/or assistance to progress and develop within the organisation.

We are also committed to delivering services that ensure our patients are cared for, comfortable and as far as possible meet their individual needs.

8. Supporting References

- T-1067 - Clinical Trial Risk Assessment Tool
- T-1068 - UHL Risk Matrix Score Table
- T-1069 – UHL Risk Assessment Form EDGE Locations
- T-1070 - Risk Assessment Flow Chart
- T-1071 - UHL Sponsor Review Risk Assessed Checklist EDGE Locations
- T-1072 - UHL Sponsor Review Non Risk Assessed Checklist EDGE Locations
- T-1073 - Multi-Location Checklist
- T-1090 - Vulnerable Populations in Clinical Trials
- SOP S-1007 - Management (Monitoring) of Research Sponsored by UHL
- UHL Risk Management Policy (A12/2002)

9. Key Words

Research, Innovation, Risk, Assessment, Compliance, Review

This line signifies the end of the document

CONTACT AND REVIEW DETAILS	
Guideline Lead: Jen Boston R&I Deputy Director of Operations	**Executive Lead:** Nigel Brunskill R&I Director
Details of Changes made during review: Replaces R&I SOP S-1003. Guidance updated and moved to new template.	