UNIVERSITY OF LINCOLN

CLINICAL GOVERNANCE - STANDARD OPERATING PROCEDURE

CLINICAL RESEARCH RISK ASSESSMENT

CG-QMS SOP CG03

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Version History	**Reason for change**

NOTE: All SOPs are subject to regular review.

Please ensure that the version of this SOP is the most up-to-date.

OUT OF DATE DOCUMENTS MUST NOT BE USED AND HARD COPIES SHOULD BE DESTROYED

1. PURPOSE

This SOP describes the process for the risk assessment of all Clinical Trials in healthcare research sponsored by the University of Lincoln and should be read in conjunction with the University's Risk Assessment Policy

2. SCOPE

This SOP applies to any researcher conducting research falling under the remit of the Secretary of State for Health where a declaration of research sponsor is required. Where the University of Lincoln is sponsor.

3. BACKGROUND

3.1 In line with University of Lincoln Health and Safety policy, a risk assessment must be carried undertaken, and the outcomes taken into consideration when preparing the protocol and supporting documents outlined in SOP CG04 Protocol Development.

3.2 This SOP should be read alongside the University's Risk Assessment policy – available on the H&S portal page.

3.3 It is the responsibility of the Chief Investigator (CI) to ensure that adequate risk assessment is undertaken prior to requesting sponsorship.

3.4 In some instances, it may be appropriate to review and where necessary, revise an existing risk assessment to address any study specific nuances.

3.5 Research Integrity Risk Assessments should also be completed, reviewed or updated to address any study specific nuances.

3.6 Where the study involves a Clinical Trial of an Investigational Medicinal Product the assessment should also take into consideration guidance on the Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products[1]:

3.7 Defining the risks of the IMP using a simple IMP risk categorisation (Type A, B and C) based on marketing status and standard medical care

3.8 Defining the risks associated with trial conduct by examining the trial design, population and procedures to identify specific areas of vulnerability and to determine how any risks can be mitigated.

3.9 Potential risks which may associated with clinical research may be found in appendix A

3.10 The CI may delegate the practical aspects of risk assessment to a trial/data manager or researcher (delegated designee) as appropriate but should take responsibility for providing overall supervision and final sign-off of this task.

4. CROSS REFERENCES

4.1 University of Lincoln Policy:

i. Health & Safety Risk assessment form

4.2 CG-QMS SOP CG04 Protocol Development

4.3 CG-QMS SOP CG07 Trial Master / Site File

5. PROCEDURE

The Chief Investigator (or delegated nominee) shall:

5.1 When preparing the trial protocol, prepare a risk assessment using UoL H&S Risk Assessment Form in line with the University of Lincoln Risk Assessment Policy. The risk assessment must give consideration to:

- Risk to the participant's rights
- Risk to the participants integrity, safety and well being
- Risk to the data quality accuracy of results

[1] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/343677/Risk-adapted_approaches_to_the_management_of_clinical_trials_of_investigational_medicinal_products.pdf

- Risk to organisation, resources and staff
- Risk must be determined prospectively and necessary suitable mitigations should be written into the study protocol and/ or procedures
- It must also:
- Identify all hazards
- Evaluate the likelihood of incident and severity
- Highlight significant and serious risks to patient safety and data integrity
- Establish “tolerance” limits
- Aim to mitigate risk
- Additional points to consider for clinical research when completing the study risk assessment are outlined in appendix A and in the NIHR guidance on the Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products

5.2 Seek expertise of specific disciplines when completing the risk assessment (e.g. Radiology, Pharmacy, Health and Safety, Information Compliance etc)

5.3 Ensure that where vulnerable groups (including pregnant women) are involved, that this should be clearly justified, and any risks mitigated as far as is practicable. Where more than minimal risk remains, these should be clearly justified

5.4 Ensure the study protocol and any relevant study documents (e.g. participant information sheet) outlines the risks and benefits identified in the completed risk assessment including any mitigating factors

5.5 Consider whether a separate research integrity risk assessment is required

5.6 Where the study is a CTIMP classify the risk as either Category A, B, C (see also Appendix B)

- Type A: no higher than that of standard medical care
- Type B: somewhat higher than that of standard medical care
- Type C: markedly higher than that of standard medical care

5.7 Retain a copy of the completed UoL risk assessment in the Study Master File CG07 Trial Master / Site File, reviewing and updating as required.

Note: The Research Governance Team or Health and Safety office may be contacted at any stage for advice related to undertaking a risk assessment for clinical research.

6. FLOW CHART

None required.

7. Appendix A

Justification for the Study and Study Design

Potential Hazard or Harm	Points to consider
Insufficient non-clinical or prior studies	Toxicology and/or experimental data to support use of the treatment in humans. Knowledge of the effects in humans
Plausibility of the treatment regime proposed	Capacity for delivering the treatment; cost; time, inconvenience to the participants; supplies logistics
Unclear objectives / hypothesis or unclear endpoints	Appropriateness of conducting the study; usefulness of the data; would the question be answered; ability to publish
Lack of independent peer review	Expert review of the study design to support the justification
Lack of expert input	Appropriateness of the study design; ability to meet objectives; capacity to deliver the treatment; permissions required e.g. ARSAC license
Randomisation procedure	Robustness: blinding and emergency un-blinding, supplies logistics; withholding effective treatment

Participant Safety, Wellbeing and Rights

Potential Hazard or Harm	Points to consider
Incurring adverse events (AEs)	Likelihood of AEs; expected AEs, including number, and distinguishing between known and unknown adverse events; level of seriousness and severity
Serious adverse event management	Information given to the participant and instructions for notification; system for expedited review, assessment and reporting of SAEs; clinical management of SAEs
Incurring extra treatments or withholding of treatment	Exposure to radiation and chemicals; extra treatments such as surgery or prolonged treatment; treatment may not be as effective as standard
Non-compliance or non-completion of the treatment regimen	Effect on endpoints; safety and efficacy implications; ongoing or follow-on treatment for the patient; possible withdrawal symptoms (CTIMP)
Failure to protect privacy or confidentiality including disclosure of confidential or personal information	Data storage facilities, access and security; participant identification on databases and study notes; disclosure of sensitive or incriminating information.
Failure to exclude pregnancy (if applicable) or failure to follow-up pregnancy outcomes	Effect on the unborn and health of the mother; systems to ensure that eligibility criteria are met; information given to the participant.

Participant Informed Consent

Potential Hazard or Harm	Points to consider

Insufficient or incorrect information given	Legal implications; eligibility criteria should be reflected; possible enrolment of ineligible participants; ethical and moral aspects.
Coercion into participation or exclusions	Incentives used; type and style of information given; language interpretation; eligibility criteria; logistics of the study from the participants' perspective
Entering participants without consent or assent	Legal implications; contravention of human rights; possible misconduct.
Withdrawal	Participant retention strategy; participants ongoing treatment after withdrawal, response to withdrawal requests (such as removal of data and samples); the information given to participants
Withholding new information	Continuing consent and right to withdraw; possible safety implications

Data Integrity

Potential Hazard or Harm	**Points to consider**
Lack of study power	Data could be unusable, objectives not answered;
Incorrect eligibility criteria	Validity of results; study objectives met; potential safety issues
Non-adherence to the protocol	Effect on results; safety issues; compliance to treatment regime and systems to record this; recovery of unused products (CTIMPs)
Incomplete data or incorrect data	Data could be unusable; effect on outcomes and results; implication for future practice
Database back-up and archiving	Loss of the data; inability to reconstruct the study; audit trail to confirm data changes

Study Management

Potential Hazard or Harm	**Points to consider**
Failure to recruit to targets or complete the study	Effect on statistical power and overall results; should the study continue; moral implications if study not completed; needless exposure to risks and adverse events for participants
Non-robust systems for data collection	Accrual of incorrect data and effect on results; safety monitoring (due to late data collection); effect on interim analyses
Study committees fail to meet or failure to act on recommendations of the TSC or DMC	Stopping rules breached; safety monitoring; recruitment targets; effect on interim analyses

Insufficient/lack of monitoring	Stopping rules breached; safety monitoring; incorrect data accrued, effect on results; contravention of legal obligations
Loss of participants to follow-up	Effect on results; effect on safety/efficacy assessment
Fraud	Robustness of computer systems; contracts in place; training

8. Appendix B

MHRA classification	
Type A *No higher than that of standard medical care*	Trials involving IMPs authorised by any EU member state if: • They relate to the authorised range of indications, dosage or form, or; • They involve off label use, if this off label use is established clinical practice and is
Type B *Somewhat higher than that of standard medical care*	Trials involving IMPs authorised by any EU member state if: • Such products are used for a new indication, or; • Substantial dose modifications are made for the licensed indication, or; • They are used in combination for which interactions are suspected Trials involving IMPs not licensed in any EU member state if the drug substance is part of a medicinal product authorised in the EU
Type C *Markedly higher than that of standard medical care*	Trials involving IMPs not authorised in any EU member state