1. Introduction and who Policy Applies to

This Standard Operating Procedure (SOP) outlines the process for managing research modifications at University Hospitals of Leicester NHS Trust (UHL), where the UHL is a sponsor or research location. It is recognised that research design and subsequently approved documentation used in a research project can require modification. In some cases, additional new documentation may be required.

This SOP applies to modifications of any research being conducted at UHL.

2. Definitions

Modifications to a research project can be;

Substantial - these are modifications to clinical research approvals which are likely to have a substantial impact on the safety or rights of participants or on the reliability or robustness of the data generated by the research. Substantial modifications are further classified as Route A or Route B. The Medicines and Healthcare products Regulatory Agency (MHRA) will process a substantial modification differently depending on whether it is Route A or Route B.

Modification of an Important Detail – these are modifications which do not significantly impact participant safety or rights. The MHRA and Research Ethics Committee (REC) only need to be made aware of these for administrative or oversight purposes. As these types of modifications do not require formal REC or MHRA review, no outcome will be issued. Modifications of an Important Detail may require other approvals (for example, Health Research Authority (HRA) or Health and Care Research Wales (HCRW) approval).

Minor Modifications - are changes that do not fall into the category of 'substantial modification' or 'modification of an important detail'. These can be implemented at any time without informing the MHRA and REC, although other approvals (for example HRA and HCRW Approval) may be required.

A change of investigator at a location in a multi-centre research project, or the addition of a new location which requires investigator oversight, is considered a Modification of an Important Detail under the 2026 regulations.

A change of sponsor will also become a Modification of an Important Detail under the 2026 regulations. This is because it will no longer be a legal requirement for the REC to consider the suitability of the sponsor.

If a change of sponsor requires changes to insurance arrangements and/or study documents (beyond only changing the name of the sponsor within study documents) then this would be a Substantial modification.

3. Policy Standards and Procedures

Determining the categorisation of a modification is the responsibility of the sponsor. For modifications deemed Substantial, the sponsor is responsible for determining whether it is a Route A or Route B substantial modification. If the change meets the definition of a Route B substantial modification, it is eligible for automatic approval by the licensing authority or MHRA. Modification categorisation is based solely on the nature of the modification itself and is independent of whether the clinical research was authorised via automatic authorisation.

For UHL-sponsored research, the documentation (existing approved versions in tracked changes along with new clean versions), and the modification tool must be reviewed via uhl-tr.uhlsponsor@nhs.net prior to submission to the regulatory authorities. Once authorised, the modification tool will be locked by the sponsor, and the study team can submit the modification to the relevant regulatory authorities.

Refer to the Integrated Research Application System (IRAS), HRA and MHRA websites for guidance on submitting modifications.

For all research projects, once the modification and associated documentation has been reviewed and approved by the appropriate regulatory authorities, the following documentation as a minimum must be e-mailed to the designated Research Support Officer (RSO) for processing of continued Confirmation of Capacity and Capability:

i. Completed Modification Tool (IRAS)

ii. Documentation approved by the relevant regulatory authority

iii. Regulatory approvals (REC, HRA, MHRA)

iv. Documents amended in tracked changes.

Some modifications will require Sponsor Green Light following continued Confirmation of Capacity and Capability and this is dependent on the individual research and sponsor requirements.

The relevant workflows in the Edge database must be completed for each modification processed.

3.1. Support Department and Delivery Team Approval

For the continued confirmation of capacity and capability and review of a modification, it is essential that the relevant support departments and research delivery teams are informed of the modification. Where the modification does not affect their specific role within the study, the modification may simply be sent to them for their information only. Where a modification has a direct effect on specific roles, approval from individual support departments or delivery teams will be required prior to UHL confirmation of acceptance of the modification. This will need to be recorded, and where applicable the relevant workflow completed on the Research and Innovation (R&I) central research database (EDGE/Florence).

3.2. Contracts and Finance Approval

For the continued confirmation of capacity and capability, modifications with financial implications must be reviewed by the R&I Finance Team prior to final authorisation. Where a modification requires changes to an

existing contract, or the execution of a new contract, the relevant contractual arrangements must be processed and approved by the R&I Contracts Team or the designated RSO, as applicable.

3.3. Modification Authorisation

For Substantial Modifications: once all necessary documentation has been received, including regulatory approvals, support department approvals, financial approval, and contracting arrangements (as applicable), the designated RSO must forward the modification email template to the R&I Authorisations mailbox for final authorisation (uhl-tr.uhlriauthorisations@nhs.net). Once authorised, all relevant parties must be copied into the authorisation notification email, including any support services and delivery teams involved in the research, and R&I Finance if there are financial implications to the modification. A copy of this final authorisation email must be retained in the Investigator Site File.

***For Minor Modifications, and Modifications of an Important Detail*:** these can be processed and issued directly by the appropriate RSO using the relevant e-mail template for information only. These do not require any MHRA or REC approval but may on occasion require HRA approval. All relevant parties must be copied into the authorisation, including all support services and delivery teams involved in the research, including R&I finance if there are financial implications to the modification.

3.4. Urgent Safety Measures

Where Urgent Safety Measures (USM) are required, it is not appropriate to delay implementation until approval has been granted. In such circumstances, all necessary modifications must be implemented immediately in accordance with the Sponsor's instructions. The modification will be reviewed retrospectively for authorisation by R&I, once approvals have been received from relevant regulatory authorities, following the processes outlined in this SOP.

3.5. Managing Documentation

Any records related to modifications 'under review' should be uploaded to the 'modifications' folder on the Site level of Edge, or to Florence, as appropriate. Once a modification is approved, all relevant records of approval must also be uploaded to the designated project folder on Edge, or its equivalent in Florence. Documents must be uploaded using the 'upload a new version' feature to ensure documents are correctly 'stacked' to clearly indicate the most recently approved version. The RSO will notify relevant staff when the document upload has been completed.

To ensure adequate tracking and oversight, all modifications must be tracked using the R&I Modifications Log (R&I Template T-1056) or an approved equivalent, and maintained on the R&I central research database (Edge or Florence). This will remove the need for document version numbers to be included in authorisation e-mails.

4. Education and Training

None

5. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Modifications correctly categorised (substantial, important detail, minor)	EDGE review of approval documentation and regulatory feedback	R&I Deputy Director of Operations	As per audit and monitoring schedule	Significant findings reported to R&I Governance Meeting
All required regulatory and internal approvals in place prior to implementation	Review of approval documentation against implementation date	R&I Deputy Director of Operations	As per audit and monitoring schedule	Significant non-compliance reported to R&I Governance Meeting
Maintenance and completeness of modification log (tracking and oversight)	Review of log against recorded approvals	R&I Deputy Director of Operations	As per audit and monitoring schedule	Significant non-compliance reported to PI and 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 have been undertaken and its impact on equality have been reviewed and no detriment was identified.

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.

7. Supporting References

T-1056: Modifications Log Template

8. Key Words

Modifications, Amendments, Urgent Safety Measures, Substantial, Important Detail

CONTACT AND REVIEW DETAILS	
Guideline Lead: Jen Boston R&I Deputy Director of Operations	**Executive Lead:** Professor Nigel Brunskill Director of Research & Innovation
Details of changes made during review: Merger of S-1018 and C-2011, which are now obsoleted. Updated guidance and moved to new template	