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SOP 215 Research Study Amendments

For Use in:	Research
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For:	All staff involved in the conduct of research
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Name of document author:	Ania Spurdens
Job title of document author:	Research Project Manager
Name of document author's Line Manager:	Julie Dawson
Job title of author's Line Manager:	Research Services Manager
Supported by:	Julie Dawson NNUH Sarah Ruthven UEA
Assessed and approved by the:	Julie Dawson: Research Services Manager NNUH Sarah Ruthven: Research Manager UEA
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This Standard Operating Procedure (SOP) is available on the Research & Development pages on the NNUH website

Copies downloaded from the website are only valid on the day of downloading.

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1. Contents

2. Definitions of Terms Used / Glossary

CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
EDGE	Research database used for set up and delivery of research studies
HRA	Health Research Authority
IRAS	Integrated Research Application System
LCRN	Local Clinical Research Networks
MHRA	Medicines and Healthcare Products Regulatory Agency
NNUH	Norfolk and Norwich University Hospitals NHS Foundation Trust
PI	Principal Investigator
R&D	Research and Development Department
REC	Research Ethics Committee
SOP	Standard Operating Procedure
S/TMF	Study/Trial Master File
USM	Urgent Safety Measures

3. Scope

This SOP describes the process for submitting and implementing both substantial and non-substantial amendments for NNUH sponsored studies and when amendments are made to studies hosted by NNUH

Good Clinical Practice (GCP) Guidelines (ICH-E6, SI 2004/1031)

4. Rules

Amendment requirements

An amendment is required if it is necessary to make changes to the research after original approvals from the relevant regulatory bodies (Health Research Authority (HRA), Research Ethics Committee (REC), Medicines and Healthcare products Regulatory Agency (MHRA)) have been received.

Substantial amendments must be reported to all relevant regulatory bodies and the R&D departments of the sponsor and any participating sites.

A substantial amendment is defined as an amendment to the terms of the protocol or any other supporting documentation that is likely to affect to a significant degree:

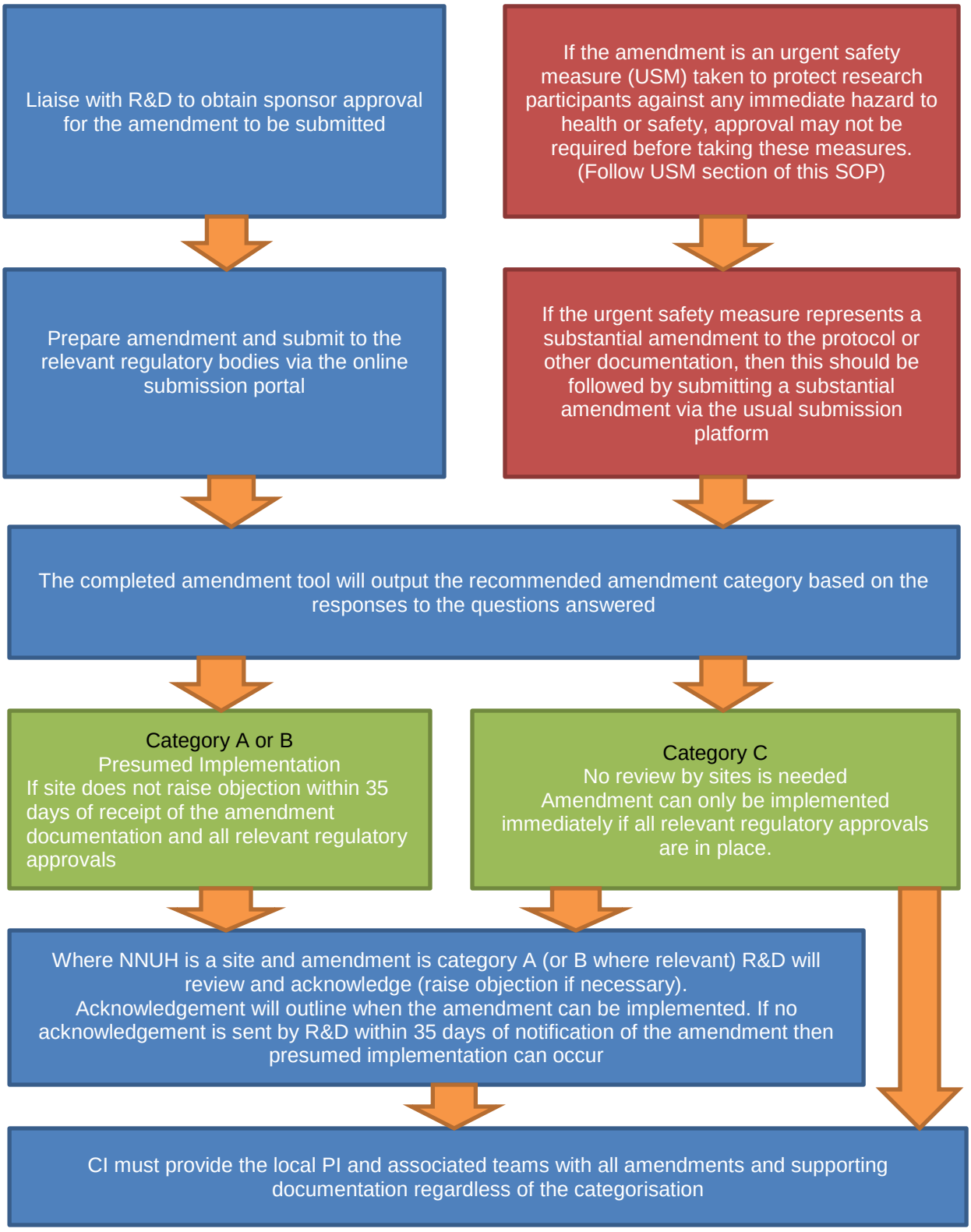
- The safety or physical or mental integrity of the participants of the trial
- The scientific value of the trial
- The conduct or management of the trial
- The quality or safety of any investigational medicinal product used in the trial

Non-substantial amendments need to be notified to the HRA and R&D department, but not to the MHRA or REC. Please note, changes to contact details of the sponsor (sponsor representative), CI or other study staff are classed as a non-substantial amendment but should still be notified to the REC.

The amendment tool categorises the amendment as substantial or non-substantial depending on the information provided. The sponsor should review the amendment tool prior to submission and ensure they agree with the outcome.

5. NNUH Procedure

Flow Chart for Amendments



6. Sponsor Assessment of Amendments

	• It is necessary to identify if an amendment is substantial or non-substantial - see HRA website for details - https://www.hra.nhs.uk/approvals-amendments/amending-approval/examples-of-substantial-and-non-substantial-amendments/
	• The completed amendment tool will categorise the amendment as substantial or non-substantial. The sponsor will review and ensure they agree with the output
	• Email Office.RD@nnuh.nhs.uk with details of the amendment so that the amendment and associated documents can be reviewed
	• R&D will review the amendment and any implications it has for the management and delivery of the study, including any contractual implications
	• R&D will document this review by completing the amendment workflow on the EDGE Database
	• The completed amendment tool will be sent to the Research Services Manager to be locked prior to submission
	• R&D will update sponsorship risk assessment for the study, where necessary
	• Where an amendment relates to the addition of a sub-study on a CTIMP, R&D will require additional actions/approvals within the study management team before approving such amendment.

7. Categorisation of Amendments

When amendments (both substantial and non-substantial) are prepared, the amendment tool will categorise the amendment as either A, B or C.

Category	Definition	Expectation
A	Amendment impacts or affects all participating NHS organisations	NHS organisations are expected to review the amendment and assess continuing capacity and capability
B	Amendment impacts or affects specific participating NHS organisations	Only those participating NHS organisations affected by the amendment are expected to assess continuing capacity and capability following the amendment
C	Amendment has no implications that require management or oversight by NHS organisations hosting the research project. However the amendment should still be provided for information	Participating NHS organisations are NOT expected to consider the amendment

8. Preparation and Submission of Amendments

Follow the guidance on the IRAS website using the link below for all amendment submissions

The amendment tool can be downloaded from the IRAS website - https://www.myresearchproject.org.uk/help/hlpamendments.aspx#Amendment-Tool

The CI or delegate should complete the amendment tool by answering the questions and selecting the appropriate description of changes from the drop downs. The amendment tool contains a Glossary of Amendment Options tab which can be useful when selecting the Area of change and Specific change.

The CI or delegate should also amend any documentation that requires updating as a result of the amendment. A tracked changes and clean copy of any updated documents should be created. Version numbers and dates in the header/footer and document title should be updated to reflect the change.

Once all relevant documentation has been updated and the amendment tool has been completed, the amendment should be submitted to R&D for review. The amendment tool will be locked by the Research Services Manager, and a PDF version of the locked amendment tool returned to the CI or delegate.

The CI or delegate should submit the amended documents to the relevant regulatory bodies via the online submissions portal - https://www.myresearchproject.org.uk/help/hlpamendments.aspx#Online-Submission

Substantial amendments to CTIMP and device trials must be notified to the MHRA. Guidance is available on the IRAS website regarding notifying amendments to the MHRA - https://www.myresearchproject.org.uk/help/hlpamendments.aspx#3

Where the REC gives an unfavourable opinion of a substantial amendment, the CI or delegate may submit a modified amendment taking into account the Committee's concerns. In this case a new amendment tool should be completed, indicating that it relates to a modified amendment at the relevant question. It should then be submitted to the REC directly by email, alongside all supporting documentation.

9. Notifying Participating Sites of Amendments

The CI or delegate should notify participating sites of the amendment once it has been submitted. This can be done immediately after submission (whilst waiting for regulatory approvals to come through) or once all regulatory approvals have been received. There are template emails for notifying sites in England and Wales of amendments available on the IRAS website - https://www.myresearchproject.org.uk/help/hlpamendmentsresearch.aspx#What-happens-after

10. Implementation of Amendments

Unless otherwise stated presumed implementation of an amendment can occur after **35 days** of notifying the site of that amendment (subject to all regulatory approvals being in place), unless the NHS organisation raises an objection within this period or requests additional time to review the amendment.

Details should be outlined in the notification to sites and sites need to be given **35 days** before presumed implementation, thus this email must be read carefully. As a rule of thumb, the case will usually be that:

Category A & B amendments: Where NNUH are a site, R&D will review all amendments once the amendment documents are received, and aim to issue an acknowledgement of the amendment once it has been reviewed (or raise objection where necessary).

Implementation will be confirmed by the Sponsor.

Category C amendments: will be acknowledged by the R&D department.

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11. Urgent Safety Measures (USMs)

	• The Sponsor, CI or PI must take appropriate USMs in order to protect research participants against immediate hazard to their health or safety. Approval is not required *before* taking these measures
	• The MHRA (in the case of CTIMPs), REC and R&D office need to be notified of USM.
	• An immediate, initial notification (ideally **within 24 hours)** should be done by phone to the REC and, in the case of CTIMPs, the MHRA. For MHRA call Clinical Trial Unit on **020 3080 6456** to discuss the issue with a safety scientist. MHRA will provide guidance for USM submission. For REC please call local REC committee that approved the study.
	• Submit USMs to the MHRA and REC in writing within **3 days.** Where NNUH are sponsor, R&D must be involved throughout this process. participating sites should be notified within **3 days** of taking the measures, detailing the measures taken and the justification of the measures.
	• Where USMs are taken and the participant suffers harm, safety reporting procedures should be followed, see SOP 230 Urgent Safety Measures

Records of all discussions, meetings, decision and correspondence regarding the USM must be documented in the Study/Trial Master File (S/TMF).

Where an USM represents a substantial amendment to the protocol or other documentation, a substantial amendment will need to be prepared and submitted following the procedures outlined in this SOP. The amendment must be submitted within 2 weeks of the USM.

12. Procedure for UEA sponsored studies

Where the UEA is the sponsor for the study please contact RIN (researchsponsor@uea.ac.uk).

13. Approval

Author	Ania Spurdens
Role	Research Governance Coordinator
Approved & Authorised NNUH	Julie Dawson
Role	Research Services Manager
Signature	DocuSigned by: Julie Dawson 4CBAB366CF354A2...
Date	15 October 2024 | 9:42 BST
Approved & Authorised UEA	Sarah Ruthven
Role	Research Manager
Signature	DocuSigned by: Sarah Ruthven 50D5F3BEE2F04C1...
Date	03 October 2024 | 11:17 BST

14. Training Implication

Training Implication	**Yes**
Actions required	• Additional training may be required