Standard Operating Procedure

UHBW HOSTED RESEARCH MODIFICATIONS

SETTING Trustwide

AUDIENCE Research staff submitting research study modifications for UHBW hosted research and R&D staff processing UHBW hosted research modifications

ISSUE To describe the process of reviewing and implementing research study modification for UHBW hosted research

QUERIES Contact Research & Development department: via research@uhbw.nhs.uk

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Document History

Review date	Version number	Version date	Effective date	Author/ Reviewer	Authorised by
N/A	1.0	19/JAN/2018	14/FEB/2018	Jess Bisset	Diana Benton
SEP/2020	1.1	21/SEP/2020	20/NOV/2020	Sandra Mulligan Karen Morgan	Jess Bisset
OCT/2022	1.2	17/OCT/2022	22/FEB/2022	Jake Harley Karen Morgan	Jess Bisset
FEB/2023	1.3	21/FEB/2023	01/APR/2023	Lucy Riddolls	Nicola Manning
DEC/2024	1.4	27/JAN/2025	27/JAN/2025	Sandra Mulligan Karen Morgan	Jess Bisset
NOV/2025	2.0	15/JAN/2026	28/APR/2026	Sandra Mulligan	Diana Benton (on behalf of TRG)

Version Number	Reason for change
Original V1.0	N/A original
V1.1	Minor clarifications and updates as part of biennial review
V1.2	Minor clarifications and updates as part of biennial review
V1.3	Departmental name change from Research & Innovation to Research & Development. Updated throughout SOP as a minor amendment.
V 1.4	Minor clarifications and updates as part of biennial review
V 2.0	Major update to include updates to the Medicines for Human Use (Clinical Trial) Amendment Regulations (2025), specifically terminology changes from amendments to modifications and process for categorising and receiving approval for modifications.

1. Introduction

During the course of a research study, it may become necessary for the sponsor to modify study specific documents and processes. Modifications can be categorised into substantial modifications, modifications of an important detail, and minor modifications

Where UHBW are a participating location, the sponsor should need to submit the modification to ResearchAmendments@uhbw.nhs.uk for review.

2. Purpose

This SOP is to describe the processes for both UHBW research staff and R&D staff in reviewing, authorizing, and implementing modifications for UHBW hosted research.

3. Scope

In Scope: Modifications submitted for UHBW hosted research.
Out of scope: Modifications submitted for UHBW sponsored research (please see *SOP_019 UHBW sponsored research modifications*)

4. Responsibilities

External sponsors and research staff are responsible for preparing modified study documents and submitting them to ResearchAmendments@uhbw.nhs.uk for review in line with national processes as described on the HRA and MHRA website.

UHBW research staff are responsible for reviewing submitted modifications for capacity and capability in liaison with UHBW R&D staff.

UHBW R&D staff are responsible for reviewing submitted modifications initially for completeness and subsequently for ongoing capacity and capability assessment and for issuing confirmation to sponsor.

5. Abbreviations and Definitions

Abbreviations	
CIMD	Clinical Investigation of a Medical Device
CTIMP	Clinical Trial of an Investigational Medicinal Product
HCRW	Health and Care Research Wales
HRA	Health Research Authority
IRAS	Integrated Research Application System
iCT	Interactive Costing Tool
ISF	Investigator Site File
MHRA	Medicines for Healthcare products Regulatory Agency
REC	Research Ethics Committee
R & D	Research and Development
RMF	Research Management Facilitator
RPA	Research Projects Assistant
RPM	Research Projects Manager (Sponsored Trials)
SMT	Senior Management Team
TMF	Trial Master File

UHBW	University Hospitals Bristol and Weston NHS Foundation Trust

Definitions	
Modification Category A	Implications for, or affects, all participating NHS/HSC organisations hosting the research project.
Modification Category B	Implications for, or affects, specific participating NHS/HSC organisations hosting the research project.
Modification Category C	No implications that require management or oversight by the participating NHS/HSC organisations hosting the research project. However, the modification should still be submitted for information and can be implemented as soon as any regulatory approvals are in place.
Substantial Modification	Substantial modifications are considered to be a modification to a clinical trial approval which is 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 trial. For CTIMPs and CIMD's, substantial modifications are further classified as Route A or Route B, and the MHRA will process a substantial modification differently depending on whether it is Route A or B.
Route A substantial modification	Route A substantial modifications are likely to have a substantial impact on the safety or rights of the participants or on the reliability or robustness of the data generated in the trial
Route B substantial modification	Route B substantial modifications are defined in regulation 11B of the Clinical Trial Regulations
Modifications of an important detail	Modifications of an important detail do not significantly impact the safety or rights of the participants, but the authorities (MHRA and REC) need to be aware of them for administrative or oversight purposes. These types of modification are not reviewed by the REC or MHRA, and no outcome is issued. These may need other approval (e.g. HRA and HCRW approval). Examples of these types of modifications can be found on the HRA website.
Minor modifications	Modifications that do not fall into the substantial modification or modification of an important detail category. Minor modifications may be implemented at any time and without informing the licensing authority or ethics committee at the point of implementation (however, other approvals may be required, which can be determined using the modification tool). The sponsor must keep records of any modifications implemented and, if requested, make them available to the licensing authority or ethics committee.

6. Procedure

6.1 Receipt of modification documents into UHBW

- For any studies which UHBW are hosting, sponsors should submit modification paperwork to **ResearchAmendments@uhbw.nhs.uk**. If modification paperwork is incorrectly submitted through differing routes e.g. into **research@uhbw.nhs.uk** or to the PI/local study team/allocated RMF, personnel receiving the modification should send the paperwork to **ResearchAmendments@uhbw.nhs.uk** to trigger the modification process as described in the flowchart below. (Flowchart A).

- The study type (e.g., CTIMP, regulated investigation of a medical device etc.) and modification type (substantial (Route A or B), modification of an important detail or, minor modification) determines what types of approvals are required for modifications (e.g. MHRA, HRA, REC etc.). It is the responsibility of the sponsor to ensure the appropriate approvals are sought for the modification. HRA assessment should review whether required regulatory approvals are in place and participating sites should only assess whether they have the ongoing capacity and capability to implement the approved modification.

- The RPA is responsible for reviewing received correspondence to identify whether the local PI and study team have been informed of the modification. If not, the RPA should send on necessary paperwork to the local study team (*TMPL_088 Modification notification email*). This e-mail also informs the local study team of the 35-day period from the date of the notification to raise an objection about the modification (if applicable).

6.2 Deciding who in R&D should review the modification

6.2.1 Modification Types

Modification Category A	Implications for, or affects, all participating NHS/HSC organisations hosting the research project.
Modification Category B	Implications for, or affects, specific participating NHS/HSC organisations hosting the research project.
Modification Category C	No implications that require management or oversight by the participating NHS/HSC organisations hosting the research project. However, the modification should still be submitted for information and can be implemented as soon as any regulatory approvals are in place.

6.2.2 Whether an RMF review of the modification is required

- On receipt of an modification the Research Projects Assistant (RPA) should decide whether full review of the modification is required by an RMF. This should be based on the following;
  - If the modification is a Category A or B and is substantial and;
  - If the modification involves an additional arm or;
  - If the modification has implications for funding or;
  - If the modification has implications for support department authorisation or;
  - If the modification has implications for contractual arrangements
  - If the modification has any other major impact on the Trust

- The RMF should then take over review of the modification and completion of the EDGE workflow (*R&D-Host-Modifications workflow*) The RMF should seek input from the Senior Management Team as required for processing of the modification.
- Otherwise, the RPA retains responsibility for the processing of the modification.

6.3 Review of the modification by an RMF

- If a review of the modification is required by an RMF the following should be carried out:
  - RMF reviews whether all support departments have been informed. If not, the modification should be sent immediately with a request for authorisation of the modification from any support departments affected.

  - RMF reviews any amended contracts, liaising initially with the Senior Management Team for advice and with the UHBW legal department as required.
    The RMF should arrange for the signature of the contract amendment document.
  - RMF reviews any changes to funding and where these are negative discuss with the local PI/study team the feasibility of continuing the study on reduced funding. For commercial studies, additional actions relating to the interactive Costing Tool (iCT) may be required.
  - RMF reviews whether the capacity of the current PI/study team will be affected by the proposed modification and discuss feasibility of continuing the study.
  - RMF reviews any other capacity or capability impact by the proposed modification.

6.4 Confirming ongoing capacity and capability

As described in the flowchart below, where all the checks are satisfactory and the required authorisation is in place, the RPA or RMF should email the sponsor with the local PI and study team cc'd to confirm ongoing capacity and capability confirmation.

- There is a template email for this: *TMPL_089 Continuing confirmation of C&C*. The RMF/RPA must ensure the Study title, IRAS ID, R&D reference number and Modification number is clearly referenced in the email.

6.5 Objecting to the modification

Flowchart A – Submission Process of Amendments for UHBW Hosted Studies

Amendment submission received into ResearchAmendments@uhbw.nhs.uk

Category A

RPA reviews received correspondence to identify whether local PI and study team have been informed of the modification. If not, RPA will sends on necessary paperwork to local study team

RPA should also review whether review is required by an RMF. Further details on when a review may be required can be found in section 6.2 above.

RMF/RPA liaises with the local PI and study team to confirm ongoing capacity and capability at this site. Further details of this review can be found in 6.3 above.

When RMF/RPA & local PI & local study team have confirmed ongoing capacity & capability, RPA to review whether all approval paperwork has been received (i.e., HRA approval, REC approval, MHRA approval etc)

Where continued capacity and capability cannot be confirmed RMF/RPA emails sponsor with local PI & study team cc'd confirming the explanation and details for site closure

Category B

RPA reviews whether we are listed as one of the sites affected by the proposed modification. If not RPA to follow process for Category C amendments.

If we are an affected site, the RPA reviews received correspondence to identify whether local PI and study team have been informed of the modification. If not, RPA sends on necessary paperwork to local study team.

RPA should also review whether review is required by an RMF. Further details on when a review may be required can be found in section 6.2 above.

RMF/RPA liaises with local PI and study team to confirm ongoing capacity and capability at this site. Further details of this review can be found in 6.3 above.

Category C

RPA checks that local PI/study team have been sent the modification paperwork (if not RPA to send) and files the paperwork in the electronic study folder.

Once all approval paperwork in place, EDGE workflow (*R&D-Host-Modifications workflow*) is completed and email confirming ongoing capacity and capability is submitted to the sponsor with local PI and study team cc'd in.

- In some instances, it may not be feasible to confirm ongoing capacity and capability for an modification. In this instance, this should be communicated to the sponsor via email with the local PI and study team cc'd in. A discussion and decision should take place about whether the site should be withdrawn from the study or to continue using the unamended protocol.

6.6 Filing and Information Processing within R&D

- **Filing**
  All correspondence relating to modifications in R&D must be saved in the electronic study folder in the 'Modifications' section. Each modification should be assigned its own folder with a label describing modification type and number with a short description e.g. 'Substantial Modification 1 Protocol v2.0'. This will enable easier access to these documents by other members of the R&D department.

- **EDGE records**
  Not all study modifications are required to be recorded on EDGE. However, a modification workflow should be initiated on the study EDGE record (site level) if the changes described in the modification are applicable to the UHBW study site. (See Flowchart A above)

  Category A or B modification (depending on whether the change affects some or all sites). - If the change(s) affect the UHBW site, a Modifications workflow (*R&D-Host-Modifications workflow*) should be added to EDGE and required information completed until confirmation of C&C is issued. This may be the responsibility of the RPA or RMF following the initial RPA assessment (See Section 6.2 above).

  Category A or B modification – Financial changes
  - If the modification changes are financial, the RPA adds the Modifications workflow to EDGE and allocates this to the study RMF to review and update the Modification workflow.

  Category C modifications - No further study wide review required.
  - EDGE workflow not required. These modifications received are passed on to the study team and filed in the Active study folder/Modifications

6.7 Implementing the modification at UHBW site

- After R&D has issued ongoing capacity and capability confirmation for the modification the local PI/study team at UHBW should implement the modification on the advice of the sponsor. The sponsor may have previously confirmed that the modification can be implemented as soon as ongoing capacity and capability is issued by R&D.
- The PI/local study team should ensure correct versions of documents are implemented, and all team members can access the latest versions. The PI/local team should file correspondence in the Investigator Site File (ISF), which may be hard copy or electronic.
- Please note further information on how the REC and HRA process modifications can be found on the HRA website

7. Dissemination and training in the SOP

Plan Elements	Plan Details
The Dissemination Lead is:	Research Operations Manager
Is this document: A – replacing the same titled, expired SOP, B – replacing an	A – replacing the same titled, expired SOP

alternative SOP, C – a new SOP:	
If answer above is B: Alternative documentation this SOP will replace (if applicable):	N/A
This document is to be disseminated to:	All applicable research staff (including R&D)
Method of dissemination:	For major updates to the SOP dissemination will be: 1. To Chief Investigators of UHBW Sponsored CTIMPs 2. Research unit leads across UHBW 3. Head of Research Governance at UoB (where SOP is applicable) All updates (major and minor to the SOP) will be: 1. Updated on the trust MyStaffApp 2. Updated on the R&D website 3. Cascaded in the R&D communications
Is Training required:	All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP. The personal training log of the individual (and the Investigator Site File/Trial Master File if required) should be completed to document that the content of this SOP has been read and understood as described in *SOP_007 Research Training UHBW*

REFERENCES	https://www.hra.nhs.uk/approvals-amendments/amending-approval/examples-of-substantial-and-non-substantial-amendments/ https://www.hra.nhs.uk/approvals-amendments/amending-approval/ IRAS: https://www.myresearchproject.org.uk/help/hlpamendments.aspx
RELATED DOCUMENTS AND PAGES	SOP_007 Research Training SOP_019 UHBW Sponsored research modifications TMPL_088 Modification notification email TMPL_089 Continuing confirmation of C&C Latest versions can be found on the Research & Development Department section of UHBW's website: http://www.uhbristol.nhs.uk/research-innovation/for-researchers/templates-and-sops/
AUTHORISING BODY	Trust Research Group
SAFETY	N/A
QUERIES AND CONTACT	Research & Development department via research@uhbw.nhs.uk

AUDIT REQUIREMENTS	Departmental Quality Management System audits are undertaken annually.