Standard Operating Procedure

UHBW SPONSORED RESEARCH MODIFICATIONS

SETTING Trust-wide

AUDIENCE Research staff submitting research study amendments for UHBW sponsored research and Research & Development (R&D) staff processing UHBW sponsored research modifications

ISSUE To describe the process of preparing, submitting, and implementing research study amendments for UHBW sponsored research

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

Document History

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Review date	Version number	Version date	Effective date	Author/ Reviewer	Authorised by
N/A	1.0	08/JAN/2018	14/FEB/2018	Jess Bisset	Diana Benton
SEP/2020	1.1	21/SEP/2020	08/OCT/2020	Sarah Bishop Katharine Wale	Jess Bisset
SEP/2022	2.0	03/OCT/2022	21/NOV/2022	Katharine Wale	Diana Benton on behalf of Trust Research Group
FEB/2023	2.1	20/FEB/2023	01/APR/2023	Lucy Riddolls	Nicola Manning
OCT/2024	2.2	18/OCT/2024	25/OCT/2024	Sandra Mulligan	Jess Bisset
NOV/2025	3.0	28/NOV/2025	28/APR/2026	Jess Bisset	Diana Benton (on behalf of TRG)

Version Number	Reason for change
Original V1.0	N/A – original
V1.1	Minor updates as part of biennial review.
V2.0	Major updates to national requirements and minor clarifications of R&D internal processes.
V2.1	Departmental name change from Research & Innovation to Research & Development. Updated throughout SOP as a minor amendment.
V2.2	Minor updates as part of biennial review.
V3.0	Major update to include updates required by the Medicines for Human Use (Clinical Trial) Amendment Regulations (2025) including new categories of modifications (previously termed amendments).

1. Introduction

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

The type of modification, the type of study and the location in which the study is being delivered all determine which approvals are required and the processes to be followed before the modification can be implemented.

Abbreviations	
ARSAC	Administration of Radioactive Substances Advisory Committee
CIMD	Clinical Investigation of a Medical Device
CWoW	Combined Ways of Working (a new part of IRAS)
CTIMP	Clinical Trial of an Investigational Medicinal Product
HCRW	Health and Care Research Wales
HRA	Health Research Authority
IRAS	Integrated Research Application System
MHRA	Medicines for Healthcare products Regulatory Agency
REC	Research Ethics Committee
R&D	Research and Development
RMF	Research Management Facilitator
RPM	Research Projects Manager (Sponsored Trials)
SMT	Senior Management Team
TMF	Trial Master File

All participating locations must use the latest approved versions of study documents. Any modifications required due to urgent safety measures can be implemented immediately (prior to regulatory review) following the procedure described in *SOP_009 Research Safety Reporting*.

2. Purpose

This SOP describes the processes for both research staff and R&D staff in preparing, reviewing, submitting, and implementing modifications for UHBW sponsored research.

3. Scope

In Scope: Research staff preparing and submitting modifications for UHBW sponsored research. R&D staff reviewing, authorising, and facilitating modification implementation for UHBW sponsored research.

Out of scope: Research staff preparing and submitting modifications for externally sponsored research (please refer to *SOP_020 UHBW hosted research modifications*).

4. Responsibilities

Research staff are responsible for preparing modified study documents and submitting them to R&DSponsorship@uhbw.nhs.uk for sponsor review and authorisation. Research staff are also responsible for submission of authorised modifications to required regulatory authorities and participating sites.

R&D staff are responsible for reviewing modified study documents received into R&DSponsorship@uhbw.nhs.uk and classifying modifications appropriately. R&D staff are responsible for authorising the modification and facilitating the submission process by providing necessary guidance to research staff on required processes.

5. Abbreviations and Definitions

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 amendment should still be submitted for information and can be implemented as soon as any regulatory approvals are in place.
Substantial Modification	A substantial modification can be split further into route A or route B for CTIMPs and CIMDs.
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	Although substantial they do not introduce significant new safety concerns and can be reviewed via proportionate review. These are defined in regulation 11B of the Medicines for Human Use (Clinical Trial) Regulations (Amended) 2025 Tab1._Route_B_substantial_modifications.pdf
Modification of an important detail	This is a modification that does not significantly impact participant safety or rights, which the MHRA and REC only need to be made aware of for administrative or oversight purposes. These types of modification are not reviewed by the REC or MHRA and no outcome will be issued.These may need other approval (e.g. HRA and HCRW approval). Examples of these types of modifications can be found: Update to 'amendment' terminology - Health Research Authority
Minor modifications	Modifications that do not fall into the substantial modification or modification of an important detail category. 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. Examples can be found on the HRA website.
Sponsor representative	The individual within the sponsoring organisation who acts on behalf of the sponsor to ensure that the sponsor's legal, regulatory, governance and oversight responsibilities for a research study are fulfilled

6. Procedure

6.1 Submission of modification to sponsor

- The following flowcharts (A & B) describe the procedure for submission of modifications to UHBW as sponsor, depending on study type (Clinical Trials of Investigational Medicinal Products (CTIMPs) and Clinical Investigation of a Medical Device (CIMD) or other research. Please note sponsor assessment of the modification must take place prior to submission of the modification to regulatory authorities.
- The flowcharts below describe the most common modification processes required. However, depending on study type, it may also be necessary to submit modifications to other regulatory bodies for approval, for example (not an exhaustive list):
    - MHRA Devices
    - Confidentiality Advisory Group
    - ARSAC
- During sponsor assessment of the modification the sponsor representative in R&D will provide further guidance on modification processes not described in this SOP.

Flowchart A – Submission process of Modifications for UHBW sponsored CTIMPs

CI/study team prepares modification paperwork, using tracked changes for changes to study documentation. This includes completing TMPL_060 *CTIMP Modification Assessment Form for Sponsor* and the Modification Tool which is available on the HRA website or on IRAS

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Submits the modification paperwork to R&DSponsorship@uhbw.nhs.uk

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RPM reviews modification paperwork and determines the category of modification, referring to the guidance provided on the HRA website as necessary.

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If RPM has any queries/suggested changes they will liaise with CI/study team until these are resolved.

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Once RPM is satisfied with paperwork and the modification categorisation, they will complete and sign the Sponsor Modification Assessment Form and the Modification Tool and return this via email to the CI/study team. The Sponsor Modification Assessment Form and HRA Modification Tool will indicate which review bodies are required to review the approval.

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The process for submitting the modification depends on the route the study was first submitted through (e.g. CWOW or IRAS). Further information can be found on IRAS and the MHRA website. For details on what happens to the modification after it has been submitted, please refer to the HRA website.

To note for certain modifications payment is due to the MHRA for processing,~~.~~ Latest details of payment process can be found on the MHRA website.

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Simultaneously, the RPM should make any changes to the trial risk assessment as identified on the Sponsor Modification Assessment form in conjunction with the trial manager, CI and any other personnel as necessary. Any mitigations and appropriate sign off of the risk assessment must be in place prior to implementation of the modification (and once all required approvals are in place).

Flowchart B – Submission process of Modifications for UHBW sponsored non-CTIMPs

CI/study team prepares substantial modification paperwork using tracked changes. This includes completing the HRA Modification Tool which is available on the HRA website or on IRAS

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CI/study team submits all modification paperwork to R&DSponsorship@uhbw.nhs.uk where it is picked up by the sponsor representative in R&D. The cover email should provide a brief summary of the reasons for the modification and, where applicable, that staffing and financial resources are available to support the modification.

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Sponsor representative reviews modification paperwork and assesses the category of the modification using the guidance provided on the HRA website.

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If the sponsor representative is unclear on the category of the modification, they will seek advice from a member of the Senior Management Team (SMT) in R&D

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If sponsor representative has any queries/suggested changes they will liaise with CI/study team until these are resolved.

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When sponsor representative is satisfied with the paperwork they will review and lock the HRA Modification tool for submission, will email confirmation to the CI/study team that the sponsor authorises the modification to be submitted and will confirm the category of the modification.

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CI/study team submit locked Modification Tool and the amended documents via online modification submission in IRAS.

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For details on the REC & HRA process once the modification is received, please refer to the HRA website

Submission of modification for HRA/ethics and regulatory approvals

- Submission of modifications is delegated by the sponsor to the trial management team. Further information on how the REC and HRA and regulatory authorities process modifications can be found on the HRA website: https://www.hra.nhs.uk/approvals-amendments/amending-approval/ Please refer to the website for latest guidance.
- For modifications requiring MHRA approval, the submission process depends on the platform used for the initial clinical trial application. Please refer to the latest guidance on the IRAS help pages: https://www.myresearchproject.org.uk/help/hlpamendments.aspx#3.

6.2 Implementing modifications at participating locations

- UHBW as sponsor delegates the responsibility of co-ordinating implementation of modifications at participating locations to the trial management team.
- The HRA Modification Tool automatically categorises each amendment and (depending on the type of modifications selected from the template by the RPM/RMF, will categorise the amendment as follows:

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 regulatory approvals are in place.

- For all participating locations in England modification paperwork should (depending on categorisation) be submitted for either (i) review of ongoing capacity and capability or (ii) notification only.
- This paperwork can be submitted to locations either whilst HRA approval of the modification is pending or once it has been issued. Template emails are provided on the IRAS to use to send to locations.
- For locations outside of England current local R&D approval processes should be followed. As these are constantly being updated it is recommended to contact the R&D office at the participating site for guidance on the submission process.
- When confirmation of ongoing capacity and capability or no objection to the modification is provided by the site(s) or the 35 days calendar time limit in which no objection can be raised has been exceeded the modification can be implemented. All of the correspondence and associated paperwork must be filed in the Trial Master File (TMF).

6.2.1 Implementing modifications at UHBW sites

- Some studies sponsored by UHBW have a trial management team who are separate to the delivery team at UHBW. In these instances, the processes described in 6.2 above should be followed to implement the modification at UHBW (i.e. it will be treated as any other participating location). The trial management team should copy in the R&D Department (ResearchAmendments@uhbw.nhs.uk) into the correspondence for UHBW locations.
- Where no separate trial management team is in place and the study delivery team at UHBW is also co-ordinating and managing the study then the modification may be implemented immediately on receipt of all necessary approvals. This is a pragmatic approach to avoid unnecessary duplicate reviews of modifications which should have already been assessed by

sponsor and the delivery team. Further advice can be provided by the RMF or RPM to the delivery team on modification implementation as required.

7. Dissemination and training in the SOP

This SOP should be disseminated to applicable research staff (including R&D) and will be available on the R&D website.

Plan Elements	Plan Details
The Dissemination Lead is:	Research Operations Manager
Is this document: A – replacing the same titled, expired SOP, B – replacing an alternative SOP, C – a new SOP:	A – replacing the same titled, expired SOP
If answer above is B: Alternative documentation this SOP will replace (if applicable):	
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 MyStaff App 2. Updated on the R&D website 3. Cascaded in 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	N/A
RELATED DOCUMENTS AND PAGES	• SOP_002 Research Sponsorship at UHBW • SOP_007 Research Training UHBW • SOP_009 Research Safety Reporting UHBW • SOP_020 UHBW Hosted Research Modifications • TMPL_060 CTIMP Modification Assessment Form for Sponsor

	Please refer to http://www.uhbristol.nhs.uk/research-innovation for latest versions
AUTHORISING BODY	Trust Research Group
SAFETY	None
QUERIES AND CONTACT	Contact Research & Development department via research@uhbw.nhs.uk
AUDIT REQUIREMENTS	R&D departmental Quality Management System audits are undertaken annually.