

## STU-SOP-TM-015 – Standard Operating Procedure on managing modifications to a project

<b>Version No:</b>	4	<b>Effective Date:</b>	17-Apr-2026
<b>Description of changes:</b>	SOP reviewed in light of clinical trial regulations 2025 and GCP updates. Specific references to QPulse as the QMS have been removed. We now only refer to a QMS system.		

List of Abbreviations	
<b>C&amp;C</b>	Capacity and Capability
<b>CI</b>	Chief Investigator
<b>CTIMP</b>	Clinical Trial of an Investigational Medicinal Product
<b>HRA</b>	Health Research Authority
<b>HSC</b>	Health and Social Care
<b>IRAS</b>	Integrated Research Application System
<b>MP</b>	Medicinal Product
<b>MHRA</b>	Medicines and Healthcare products Regulatory Agency
<b>PI</b>	Principal Investigator
<b>R&amp;D</b>	Research and Development
<b>REC</b>	Research Ethics Committee
<b>SOP</b>	Standard Operating Procedure
<b>STU</b>	Swansea Trials Unit
<b>SU</b>	Swansea University
<b>TMF</b>	Trial Master File

### 1. Purpose and Definitions

The purpose of this Standard Operating Procedure (SOP) is to describe the procedures and responsibilities for seeking approvals for and implementing modifications (previously referred to as amendments) for research projects involving Swansea Trials Unit (STU).

As the change from “amendment” to “modification” is implemented there may still be reference to amendments on some websites. There will also be a migration starting in 2026 from IRAS to the Plan and Manage Health are Care Research platform for approvals.

Definitions	
<b>Substantial modification</b>	A modification to 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 research study. Substantial modifications may also need other approvals, for example Health Research Authority (HRA) and Health and Care Research Wales (HCRW) Approval, depending on the modification. See Appendix 1 for examples.
<b>Modification of an important detail (MOID)</b>	A new category of modification will be introduced on 28 <sup>th</sup> April 2026, known as 'modification of an important detail'. This is a modification that does not significantly impact participant safety or rights, which the Research Ethics Committee (REC) only need to be made

	<p>aware of for administrative or oversight purposes. These types of modification are not reviewed by the REC and no outcome will be issued. They are for information only. These modifications may however need other approvals (for example HRA and HCRW approval).</p> <p>See Appendix 1 for examples.</p>
<b>Minor (non-substantial) modification</b>	<p>The term 'minor modification' replaces the term 'non-substantial amendment' and describes changes that do not fall into the category of 'substantial modification' or 'modification of an important detail'.</p> <p>These can be implemented at any time without informing the REC, although other approvals (for example HRA and HCRW Approval) may be required.</p> <p>See Appendix 1 for examples.</p>
<b>Modification Tool</b>	<p>Previously known as the Amendment Tool. The current version located on the IRAS website must be used for all submissions.</p>
<b>Modification category</b>	<p>The completed Modification Tool will output the recommended modification category automatically based on responses to the questions.</p> <p>Sponsor is responsible for ensuring that the Modification Tool is completed correctly and for comparing the outcomes against their own expectations of how the modification should be processed.</p> <p>Modifications are categorised as per Table 1 below:</p>

Examples of substantial and non-substantial modifications are listed in Appendix 1.

**Table 1:**

<b>Category</b>	<b>This category includes any modification to a research project that has:</b>
<b>A</b>	Implications for, or affects, <u>all</u> participating organisations hosting the research project. This may involve changes to activity or cost implications.
<b>B</b>	Implications for, or affects, <u>specific</u> participating organisations hosting the research project. This may involve changes to activity or cost implications for these organisations.
<b>C</b>	<p>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. There are no changes to site activity or cost implications. Participating organisations might need to take some action, such as updating contact details.</p> <p><i><b>Note - Updated Investigator Brochure (IB; CTIMPs only):</b> Where the IB update, annual or otherwise, constitutes a non-substantial modification for REC and MHRA and this is the only modification (e.g. the update to IB does not give rise to updated pharmacy manual or protocol) the updated IB should NOT be submitted for categorisation. These modifications will always be category C and they will not be assessed by NHS/HSC if submitted. The IB should be provided to each participating NHS/HSC organisation</i></p>
<b>New project location</b>	Guidance on adding additional NHS/HSC/PIC sites is provided in the IRAS form.

## 2. Background

For any research project there is a requirement for permissions and approvals to be gained before recruitment can proceed. When the project does not involve the NHS or HSC organisations, local approval procedures should be followed and will likely include sponsor agreement and a local REC opinion to proceed. When the NHS are involved, there are

requirements for an NHS REC favourable opinion, permission by the nation(s) involved and, local R&D confirmation of Capacity and Capability (C&C).

Following the initial project permission, modifications are changes made to any aspect of a research project and are also subject to review. When the NHS are involved, all research project modifications are categorised by the IRAS Modification Tool in line with guidance from the HRA/HCRW for England and Wales and their equivalent bodies in other UK nations where applicable.

This SOP assumes that STU-adopted trials will be led from either Wales or England and refers to the HRA/HCRW as the national approval body. Substantial modifications also require a favourable ethical opinion before implementation.

For projects which involve the NHS, IRAS has a help section for further information on modifications and provides access to the forms required for submitting modifications.

For CTIMPs and medical devices, there are legal requirements for certain types of substantial modifications to be reviewed by the country's competent authority (MHRA in the UK). Further information and guidance can be found on the HRA and MHRA websites (see references).

### 3. Roles and Responsibilities

The **Sponsor** is responsible for deciding whether a modification is substantial or non-substantial and for identifying the approvals required where a modification is substantial. They are also responsible for reviewing and agreeing the proposed modification prior to submission to the relevant review bodies, ensuring that the Modification Tool is completed correctly and for comparing the outcomes against their own expectations of how the modification should be processed.

The **Chief Investigator (CI)** is responsible for submitting all modification documentation for Sponsor oversight and agreement prior to submission for REC review. The CI is also responsible for coordinating the submission of modifications, signing the required documentation, disseminating approved modifications to relevant parties and ensuring that a modification is not implemented until all required approvals and permissions are in place. These responsibilities may be delegated to the Trial Manager or other authorised member of the project team.

The **Trial Manager (TM)** may be delegated responsibility for compiling documentation for modifications, entering information into relevant online systems (e.g. IRAS, CWOW), sourcing applicable notification forms and coordinating signatures with the Sponsor and CI and other required personnel to enable submission for REC review. The TM is also responsible for filing all modification and approval documentation in the Trial Master File (TMF) as essential records and disseminating approved information to research sites.

**External use of SOP:** This SOP and Associated Documents (AD) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

For non-NHS projects with University REC approval, local committee procedures for modifications should be followed.

## 4. Procedure

### 4.1 Creation and management of modification documentation

Each modification should be allocated a modification number which should increase incrementally with every modification. A record of all modifications, where they have been submitted, outcome and implementation date should be kept in a trial specific Modification Log (previously known as amendment log) (STU-AD-TMP-045).

It is usually the CI's delegated responsibility to complete, authorise and submit the appropriate modification forms, together with all relevant documents (in the appropriate format) to the required parties. Completion of the Modification Tool, preparation of any supporting documents and submission of the modification should be reviewed by the Sponsor prior to submission.

The Modification Tool applies to all project-based research (defined as any of the IRAS Project Filter question 2 categories) and replaces the Notice of Substantial Amendment Form and the non-substantial amendment form.

For projects which involve the NHS, HRA, MHRA (CTIMP and device projects only) and IRAS, websites provide information and access to the appropriate modification forms and guidance on the different requirements for each review body (see references).

#### 4.2 Grouping of modifications

If there are several modifications to make to a research project, it is sometimes acceptable to submit them as a group modification. However, if one or more of these modifications are time critical, consideration should be given to submitting these separately to avoid unnecessary delays.

The IRAS website (see references) provides further information and examples of where group modifications are considered appropriate. Modifications which should not be grouped with other modifications are:

- Addition of new NHS/HSC participating organisations or PICs
- Change of the CI or a local Principal Investigator

#### 4.3 Sponsor review and agreement

For all research projects, the CI must notify the Sponsor of their intention to modify the research project by following the processes outlined by the Sponsor. The CI may provide their opinion on whether the modification is substantial or minor; however, the final decision rests with Sponsor, and it is their responsibility to decide categorisation using the Modification Tool.

The CI or their delegate will forward the proposed modification documentation and a part-completed Modification Tool to the Sponsor for review. If approved, Sponsor will lock the Modification Tool and return it as a PDF ready for submission. Copies of this correspondence must be retained in the TMF.

The Sponsor will review the documentation and confirm:

- i) their agreement (or rejection) of the proposed change(s),
- ii) whether the modification categories selected from the dropdown lists within the Modification Tool are appropriate
- iii) whether it requires review by other organisations e.g. the MHRA.

Although it is the Sponsor's responsibility to ensure that no modification involving the NHS is implemented without the required approvals, this is usually delegated to the CI.

#### 4.4 Submission of modifications

The locked Modification Tool and supporting documentation should be submitted for review via online submission via the IRAS website. The detailed process for submitting a modification to the standard and the combined review system can be found on the IRAS help pages,

including the most up to date Modification Tool and at <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/guidance-on-changes-to-non-ctimp-clinical-trials-and-other-research/the-approvals-process-for-non-ctimp-modifications-amendments/>.

Upon submission of all documentation, an automated email will be received which will confirm submission. Validation of the submission will take up to 7 days and the REC review should take no longer than 35 days. The modification will be shared with REC and/or for study-wide review as applicable. For substantial modifications notified to the REC, you should await email communication from the REC with the outcome of their review before implementing the modification.

#### **4.5 Submission of Modifications to the MHRA (CTIMPs or devices only)**

##### **4.5.1 Substantial Modifications**

Some substantial modifications will require approval from the relevant regulatory body (e.g. MHRA) before proceeding. The MHRA website <https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#amending-your-trial-protocol-or-other-documentation> provides guidance on notifying and submitting modifications for both CTIMPs and medical devices. The process for submitting substantial modifications for CTIMPs will change in line with Clinical Trial Regulations 2025 but the online systems are not currently available for use.

For clinical trials authorised via the combined review process you should register to use, prepare and submit the application form using the new part of IRAS.

For clinical trials not approved or yet transitioned over to the combined review process, you should use MHRA submissions. This process should also be used for medical devices.

On receipt of the documentation, the MHRA will acknowledge and validate the submission. If the application is invalid, the person making the submission will be informed of the issue and will need to resubmit. Following receipt of a valid modification, the MHRA will usually review the modification within 35 working days.

After the modification has been assessed, the applicant will be informed of the outcome via email.

For projects involving Northern Ireland the MHRA website will provide up to date information.

##### **4.5.2 Minor modifications**

Minor modifications do not need approval by the regulatory body as they arise. They do however still need to have a completed Modification Tool uploaded to IRAS for the email indicating that the modification does not require study wide review to be sent to the person uploading.

#### **4.5 Following modification approval**

Once the necessary approvals are in place:

- a) REC (and regulatory approvals) for substantial modifications
- b) Email notification of no study wide review needed for minor modifications

the next stage of review is with the HRA/HCRW for studies led by England or Wales. These are national approvals and must be in place before the modifications are submitted to research project locations for local review (STU-SOP-TS-012). Guidance on the email to be sent to research project locations advising them of a modification can be found in Appendix 2.

All correspondence and documents sent (including signed copies of cover letters) to and from the REC, HRA/HCRW, R&D and MHRA must be filed in the TMF.

For multicentre research projects, it is the responsibility of the CI to ensure that all sites involved agree to support the modification. The CI must also distribute the modification documents and approvals to the PI, local departments or other organisations involved (e.g. drug supply company, labs, pharmacy etc.) as required.

The implementation date should be coordinated across all sites and include any database version changes, which requires trial locations to move to a new version.

The CI should discuss with the Sponsor any problems that sites might have in supporting a modification. Such sites may be unable to continue their involvement with the research project.

## 5. References

- HRA modification web pages - <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/guidance-on-changes-to-non-ctimp-clinical-trials-and-other-research/the-approvals-process-for-non-ctimp-modifications-amendments/>
- MHRA modification web pages - <https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#amending-your-trial-protocol-or-other-documentation>
- UK policy framework for health and social care research (2017) - <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/>
- UK Medicine for Human Use (Clinical Trials) Regulations 2025 - <https://www.legislation.gov.uk/ukxi/2025/538/contents>

It is assumed that by referencing the principal regulations that all subsequent amendments are included in this citation.

## 6. Associated Documents

Number	Title	Location
STU-AD-TMP-045	Modification Log	QMS

## 7. Appendices

### Appendix 1: Examples of substantial and minor modifications, and MOIDs

<https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/guidance-on-changes-to-non-ctimp-clinical-trials-and-other-research/update-to-amendment-terminology-for-non-ctimps/#SubstantialModification> Accessed 03 April 2026

#### Examples of substantial modifications:

- Temporary halt of the project or temporary halt at a site within the UK
- Re-start of the project following a temporary halt
- Significant changes to participant information sheets, consent forms, letters to GPs or other clinicians, letters to relatives/carers, and other similar documents (whether generic to the whole study or specific to a particular site)
- Significant changes to recruitment and consent procedures, including the inclusion of adults lacking capacity in the project
- Significant increase or decrease to the radiation exposures to participants from the protocol
- Change of insurance or indemnity arrangements for the project
- Change to the payments, benefits or incentives to be received by participants or researchers in connection with taking part in the study, or any other change giving rise to a possible conflict of interest on the part of any investigator or collaborator
- Change of the chief investigator
- Any other significant change to the conduct or management of the project at particular sites
- Any other significant change to the terms of the original REC application
- Change of the main objective of the project
- Change of primary or secondary endpoints likely to have a significant impact on the safety or scientific value of the project
- Addition of a project arm or placebo group
- Significant change of inclusion or exclusion criteria (for example age range) likely to have a significant impact on the safety or scientific value of the project
- Change of a diagnostic or medical monitoring procedure likely to have a significant impact on the safety or scientific value of the project
- Withdrawal of an independent data monitoring committee
- Any other change of study design likely to have a significant impact on primary or major secondary statistical analysis or on the risk and benefit assessment

#### Examples of Modifications of Important Details (MOIDs)

- Changes to the project identification (for example the project title)
- Increase in duration of the project, provided that the exposure to treatment is not extended, the definition of the end of study is unchanged and there is no change to monitoring arrangements
- Change to contact details for named contacts for the project, for example the sponsor, sponsor representative or chief investigator
- Change of the sponsor's legal representative
- Change of the sponsor

#### Examples of minor modifications

- Addition of a new site and/or investigator
- Changes in the number of participants per site, if any change is insignificant in view of the absolute number of participants
- Changes in the processes associated with record keeping used by the research team for recording project data
- Internal changes to the sponsor's organisation
- Changes in the logistical arrangements for storing or transporting samples
- Changes in technical equipment

- Minor changes to the protocol or other study documentation, for example correcting errors, updating contact points, minor clarifications

## Appendix 2: Suggested wording to research project locations of a modification (based on HRA template email)

**Subject:** [IRAS number; Modification number and date]; Implementation of Modification

### Attachments:

- Confirmation of submission email
- all amended documents
- locked pdf of the Modification
- any applicable regulatory approvals such as REC opinion, if applicable
- HRA and HCRW Approval outcome email for the modification (England and Wales only)

Dear participating organisations, (or name if sending to one organisation),  
I can confirm that all approvals, including HRA and HCRW Approval (organisations in England and Wales only), for the modification to the study insert short study title have been issued. As such, the modification **can now be implemented at your organisation.**

The table below details the final set of documents approved for this modification.

Document	Version Number	Date

**[Option 1 - add if no changes to documents during review by review bodies listed in the Modification Tool.** There **were no** changes to the documents during the reviews by the relevant regulators and review bodies. I outlined the potential impacts of this modification to you in the email detailing the categorisation.]

OR

**[Option 2 - add if documents were changed during regulatory review or during review by the review bodies listed in the Modification Tool.** There **were** changes to the submitted document set during the reviews by the relevant regulators and review bodies. I outlined the potential impacts of this modification to you in the email detailing the categorisation.]

If you need to discuss this amendment further please contact [details].