SOP number	**52.003**	Version	**7.0**
Title	**R&I Local Review of Modifications**		

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SOP category	NHS GG&C Hosted Research & Innovation (R&I)

Staff category

Staff Category	**R**	**A**	**C**	**I**
Research & Innovation Systems & Operations Manager		X		
Commercial Research Co-Ordinator	X			
Research Facilitator	X			
Senior Research Administrator	X			
Research Administrator	X			

1. Scope

This SOP applies to R&I office staff during the receipt, processing, review and local approval of modifications to all studies taking place in NHS Greater Glasgow & Clyde (NHSGGC). The process for Sponsor review of modifications is described in SOP 51.021.

2. Purpose

This SOP describes the local procedures which the R&I office undertakes when receiving, processing, reviewing and approving modifications to provide continued management approval of studies that NHSGGC hosts.

3. Procedures

3.1. Background

A modification is any change made to a research project after it receives initial approval. This official definition from the Health Research Authority (HRA) applies to the study protocol and any other documents reviewed by R&I, the Research Ethics Committee (REC), or regulatory authorities.

Changes to documents submitted during the assessment of a request for initial authorisation to the regulatory authority or during the assessment of a request for initial favourable opinion from the REC will not be considered modifications and will be reviewed during the R&I approval process.

Modifications can be classified as substantial modifications, modification of an important detail (MOID) or minor modifications. Examples of each classification can be seen in Appendix 1. Modifications for studies hosted by NHSGGC, require to be submitted to the R&I office for review in order to provide continuing management approval. A modification cannot be implemented without receipt of local R&I continuing management approval, apart from Category C modifications which can be implemented immediately subject to certain conditions, see section 3.2. This is part of the local site R&I management approval process.

3.1.1. UK Process for Study Modifications

From 28 April 2026, the UK introduced major reforms to the regulation of clinical trials. These reforms directly impact how study teams prepare, categorise, submit, and manage changes to approved studies.

The scope of the revised UK process covers commercially and non-commercially sponsored multi-centre and single-site studies.

All changes to approved studies will now be called modifications, replacing the previous amendment terminology.

3.2. Categories and Routes for Modifications

Modifications are formally grouped into clear regulatory categories which then may take different. routes as detailed below. (Categorisation determined by the Sponsor):

- Substantial Modifications (Route A or B)
- Modifications of an important detail
- Minor Modification

3.2.1. Substantial Modifications

These replace 'substantial amendments' and include any change likely to impact:

- Participant safety or rights
- The scientific integrity of the data
- The risk profile of the trial

Two regulatory (MHRA) routes apply:

- Route A: High impact changes requiring full MHRA/REC review (e.g. protocol changes affecting endpoints, dosing, or safety).
- Route B: Lower risk changes.

Timelines and review processes:

For Route A modifications:

- MHRA/REC will validate applications within 7 calendar days.
- Route A modifications will be reviewed within 35 calendar days.
- If a Request for Further Information (RFI) is issued, the process can extend - sponsors may have up to 60 calendar days to respond.
- After the RFI is received the MHRA and/or REC have 10 calendar days to issue a final decision.

For Route B modifications:

- Automatic MHRA approval within 14 calendar days, unless safety issues arise.
- If REC approval is also required then timelines from Route A will apply.

3.2.2. Modifications of an Important Detail (MOIDs)

- Administrative level changes that do not affect participant safety or trial integrity.
- Must still be notified to MHRA/REC for oversight but no opinion will be issued.
- May still need other approvals e.g. HRA, local site

3.2.3. Minor Modifications

- Very small changes that can be implemented immediately.
- No prior MHRA/REC approval or notification required, but may still need other approvals e.g. HRA, local site

Note that Research Tissue Banks and Research Databases continue to use the Notice of Substantial Amendment Form generated in IRAS to notify substantial modifications to the REC.

3.3. Completion of Modification Tool

Modifications will be classified by the Modification Tool into the following categories, this is a separate categorisation to that mentioned in section 3.2:

Category A: A modification that impacts or affects ALL participating NHS organisations, therefore needs to be considered and may need change control actions.
Category B: A modification that impacts or affects SPECIFIC participating NHS organisations. Only at these organisations does it need to be considered and take any change control actions required.
Category C: A modification that has no impact on NHS organisations hence does not require management or oversight. However the modification should still be provided for information.

The Sponsor, or authorised delegate, will complete the Modification Tool in IRAS which will categorise the modification, indicate what reviews are required, and guide Sponsors on submission routes. Once submitted it will be shared with REC and/or for study-wide review as applicable. In Scotland the modification is shared with NRSPCC (National Research Scotland Permissions Coordinating Centre), who then informs R&I for notification and review purposes.

The review applies to both substantial modifications and MOIDs as defined by the Sponsor and runs in parallel to regulatory review. It follows the principle of a 35 calendar day default implementation of modifications for NHS organisations, however this does not apply if the Sponsor/submitting organisation is notified of a query relating to the modification, or a request to allow for additional time to review the modification.

For studies where NHSGGC is the only UK site, the modification will not be received through NRSPCC, but will only come directly from the Sponsor. The Research Administrator will upload modification documentation to SReDA and then process the modification as normal.

For NHSGGC sponsored studies and trials (CTIMP and medical device) review of a modification by R&I will only occur following Sponsor/Co-Sponsor approval and IRAS signoff.

3.4. Category A or B modification review by R&I at NHSGGC

The following process applies to all NHSGGC research studies (Sponsored and/or Hosted), clinical trials and medical device trials. The applicable Portfolio team is responsible for the receipt, review and acknowledgment of all study modifications relating to projects taking place in NHSGGC in their portfolio.

On receipt of a modification, the Research Administrator registers the modification on SReDA's Post Approval tab, under 'Record Licence Wide', within the associated Project by completing the required fields.

- The reference should be 'pending' or 'approved' depending on the state of the modification
- The title should be in the format modification number/date of modification/category (e.g. SM04 10.11.2021 (Cat A)
- The Type and Date of the modification can be found on the Modification Tool, section 1 for the date and section 4 for the type.
- The Research Administrator can add notes to the 'Summary of Modification' field in relation to activity taking place as part of the review (for example the modification has been sent to Pharmacy for review on the following dates).

The RA creates a new modification subfolder within the study email folder. The email subfolder name will be prefixed alphabetically or numerically in order of receipt to R&I. The RA also creates a sub-folder within the e-folder on the common drive and saves all available modification documents. The RA will then send an email to the Sponsor, if appropriate, requesting that the modification is not implemented until confirmation of management approval is granted.

The RA must review the modified documentation along with the Modification Tool to determine whether there will be any impact on NHS resources for NHSGGC.

If no impact then the Research Administrator will:

- Await ethics and any other applicable approvals
- Aim to resolve any queries with the modification
- When ethics approval received, check all documents are present according to the list in the ethics favourable opinion letter

Once any queries have been resolved and any missing documents collated, the Research Administrator will email the standard modification email (Form 52.003B) of continuing management approval to the local PI. The Sponsor's representative and any other required individual will be copied into the email, e.g. Pharmacy, research nurse, study co-ordinators, finance. The email will state that Management Approval is still valid and can contain a snapshot of the approved document list from the REC approval.

If however there are any unresolved issues, queries or questions then the Research Administrator will ask the Commercial Research Co-ordinator or Research Facilitator from the appropriate study portfolio team for guidance.

The entry for the modification in SReDA will now be updated by completing the dates in the appropriate fields, updating any notes and changing the reference to 'Approved'. The approval email will be uploaded to SReDA.

3.4.1. Research Facilitator or Co-ordinator and Support Department Review/ Approval

For all substantial modifications that have financial implications, pharmacy or additional support department implications or contractual changes the Research Administrator will request the Commercial Research Co-Ordinator or Research Facilitators for non-commercial studies review by email. The Research Administrator will also request Pharmacy review if applicable, in accordance with Guideline 52.003A Pharmacy clinical trials – Modification Approvals.

The following must be considered when reviewing the modification:

- Financial implications
- Pharmacy impact or
- Support department implications
- Contractual changes and impact on study budget

The following information requires Commercial Research Co-Ordinator/Research Facilitator review and/ or subsequently support department approval.

- Implementation of modified Protocol
- Change of PI/Sponsor/legal representative/CRO
- Adding additional investigations/tests/scans
- Adding additional nurse/data management time
- Change of dosage
- Change in IMP:
    - Local Stock
    - Formulation
    - Pack Size
    - Dispensing Frequency
    - Fluid Volumes
    - Change in Storage
    - transportation/safety/IMP administration/
- Adding a new study arm/sub-study/new phase
- Early closure of a site/termination
- Study extension
- Change in treatment length
- Changes in supportive medication
- Increase to patient numbers
- Change of local PI

If the Research Facilitator has confirmed that extra resources from pharmacy/pathology/data monitoring/imaging/statistical services etc. are required for implementation of the modification for a **non-commercial** study, the Research Administrator will seek approval from pharmacy/Finance and any other Head(s) of department authorisation approval as required. If the modification provides new funding then the amended contract will be reviewed and negotiated by the Research Facilitator and signed by an authorised signatory of NHSGGC.

When the modification has any impact on NHS resources for a **commercial** study, negotiation between the Commercial Research Co-Ordinator and the Sponsor's representative occurs. An amended contract, or addendum to the contract, will be reviewed and negotiated by the Commercial Research Co-Ordinator and signed by an authorised signatory of NHSGGC. The Commercial Research Co-Ordinator will save the updated budget and contract in the appropriate folders and will make sure the internal redistribution sheet is updated with the new costs and sent to R&I finance.

Once the modification has received favourable opinion from the REC (if applicable), authorisation from the MHRA (if applicable), and review from R&I, the RA will confirm continuing management approval for the modification by email to the local PI (Form 52.003B). The Sponsor's representative and any other required individual will be copied into the email, eg. pharmacy, research nurse, study coordinators, finance. If the study is run through the Clinical Research Facility the email will also be sent to their generic modification email address. The email will state that Management Approval is still valid and can contain a snapshot of the approved document list from the REC approval.

The entry for the modification in SReDA will now be updated by completing the dates in the appropriate fields, updating any notes and changing the reference to 'Approved'. The approval email should be uploaded to SReDA.

3.5. Category C Modification Review by GG&C R&I

Category C modifications will be received in R&I in the same way as Category A and B modifications, but will only require review if local impact is identified. The Research Administrators will log the modification in SReDA, make folders and save the documents as normal.

If it involves any changes to the study end dates, then SReDA will be updated. If there are changes to any of the IMP documentation then it will be sent to pharmacy for information.

The Research Administrator will assess if there are any changes that could affect the financial aspects of the study, or the continued management approval. If there are then the modification will be sent to the Commercial Research Co-Ordinator or Research Facilitator for review in the same way as a Substantial modification.

No acknowledgment of the modification to the Sponsor is required.

4. Referenced documents

- Form 52.003B – Modification Approval Email Category A or B Modification
- Form 52.003E – Modification Acknowledgement Email
- SOP 51.021 – Sponsor Review of Modifications
- Guideline 52.003A Pharmacy clinical trials – Modification Approvals
- Guideline 52.003B Flow Chart for processing Modifications

5. Related documents

- IRAS guidance: https://www.myresearchproject.org.uk/help/hlpments.aspx
- MHRA guidance: https://www.gov.uk/guidance/clinical-trials-for-medicines-modifying-a-clinical-trial-approval

6. Document history

Version	Date	Description	Retrospective Implementation
1.0	06/09/2012	Release of version 1.0 (Process for Sponsor Approval of Amendments and Review by R&D)	No
2.0	10/12/2013	Removal of sponsor process and inclusion of recording of amendments on SReDA.	No
3.0	14/07/2016	Updated to template v1.4 Inclusion of information about categorization of Amendments and UK Process. Supporting documents: • Pharmacy Review Checklist (appendix 4) • Research & Development Q&A (appendix 5) • Pharmacy clinical Trials/ Amendment approval • Flow Chart for processing amendments (saved separately as Supporting Documents)	No
4.0	18/03/2020	Author temporarily changed. Temp. change to "Approved by" "Released by" changed. References to R&D Database staff removed from document. Role of Research Facilitator clarified. Minor typographical changes made to process. Version updated.	No
5.0		Updated due to national changes imposed in March 2021. Changed from PR review to portfolio team review of all amendments. References to R&D changed to R&I throughout. Updated forms associated with this SOP	No
6.0	10/11/2025	General updates	No
7.0	27/07/2026	Updated due to national changes imposed 28Apr2026 'Amendment' changed to 'Modification' throughout Updated forms associated with this SOP	Yes – 28/04/2026

Appendix 1

Examples of Substantial Modifications:

- temporary halt of the trial or temporary halt at a trial location within the UK
- re-start of the trial 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 trial location)
- significant changes to recruitment and consent procedures, including the inclusion of adults lacking capacity in the trial
- significant increase or decrease to the radiation exposures to participants from the protocol
- change of insurance or indemnity arrangements for the trial
- 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 trial at particular trial locations
- any other significant change to the terms of the original REC application
- change of the main objective of the trial
- change of primary or secondary endpoints likely to have a significant impact on the safety or scientific value of the trial
- protocol modification due to new toxicological or pharmacological data or new interpretation of toxicological or pharmacological data which is likely to impact on the risk and benefit assessment
- addition of a trial 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 trial
- change of a diagnostic or medical monitoring procedure likely to have a significant impact on the safety or scientific value of the trial
- 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 an Important Detail (MOIDs):

- changes to the trial identification (for example the trial title)
- submitting the date that the first UK trial participant is recruited
- increase in duration of the trial, provided that the exposure to treatment is not extended, the definition of the end of trial is unchanged and there is no change to monitoring arrangements
- change to contact details for named contacts for the trial, for example the sponsor, sponsor representative or chief investigator
- change of investigator (other than the chief investigator) at a trial location in a multi-centre trial
- addition of new trial locations not listed with the original request for authorisation and REC application where there are no additional documents for submission
- change of the sponsor's legal representative
- change of the sponsor

Examples of Minor Modifications:

- changes in the number of participants per trial site, if any change is insignificant in view of the absolute number of participants
- changes in the processes associated with recording keeping used by the research team for recording trial 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

NHS Greater Glasgow & Clyde Required Documentation for Substantial Modification Review:

Document	All Studies	Where Applicable
All REC reviewed documents	√	
All MHRA reviewed documents, if different from above		√
Modification Tool	√	
REC favourable opinion	√	
MHRA approval		√
Signed amended agreement		√
ARSAC authorisation (for research involving administration of radioactive substances)		√