# Research Governance Standard Operating Procedure 20 – Modifications

| **Document details** | |
|---|---|
| Version | V1.0 27/04/2026 |
| Effective from | 28/04/2026 |
| Review date | 27/10/2026 |
| Owner | Research Governance Team (research-governance@bristol.ac.uk) |
| Originally Prepared by | Emily Avent, Research Quality Officer (emily.avent@bristol.ac.uk) |
| Reviewed by | Helen Young, Associate Director of Research Excellence (helen.young@bristol.ac.uk) |
| Approved by | Helen Young, Associate Director of Research Excellence (helen.young@bristol.ac.uk) Signed by: A Young 2980D9AE1B4941A... |
| Superseded documents | N/A |

| **Document history** | | | | | | |
|---|---|---|---|---|---|---|
| Version | Review date | Reviewer | Section(s) Amended | Updated version | Approver | Effective date |
| | | | | | | |

**Table of Contents**

**1. Glossary** ..... 2

**2. Background** ..... 2

**3. Scope** ..... 3

**4. Responsibilities** ..... 4

**5. Procedure** ..... 4

**6. Related documents** ..... 11

## 1. Glossary

Terminology is explained in the Research Governance Glossary, the most recent version of which can be found on the Research Governance webpages.

## 2. Background

Research Sponsored by the University, in accordance with the **UK Policy Framework for Health and Social Care Research**, can require all kinds of oversight and approval before it begins (see **RG SOP 4 – Approvals** for some examples). However, the intentions for that research, as laid out in the study protocol and IRAS form, can evolve and change. For example, the CI or Sponsor may change; the plan for recruitment may need updating; an issue with the existing, approved protocol may come to light once the study is up and running. In these circumstances, a modification must be made to the approved study documentation.

A modification is a change to a research project after ethical opinion and/or HRA and HCRW Approval has been received. Proposed modifications must always be reviewed by, and agreed with, the Sponsor. Depending on the nature of the modification, this may require notification to, and review by, the bodies who originally approved the study – or even additional bodies who have not been involved in the study to date. Just as the original plan for the study requires oversight to ensure its compliance with ethical and regulatory standards, so does a new, revised plan.

With a handful of exceptions discussed in section 5.8, modifications Sponsored by the University are managed using the HRA's 'Modification Tool', a macro-enabled spreadsheet which solicits information from the user about the nature of the proposed modification, and classifies it based on this.

Modifications are classified along two dimensions. First, the overall modification type; substantial modification, modification of an important detail (MoID) or a minor modification. Secondly, the overall category of the modification for implementation by sites.

### 2.1 Overall modification type – the substantiality of a modification

In practice, substantial modifications are those which the Modification Tool classifies as such, examples of what may be considered a substantial modification can be found in the HRA guidance. While it is useful to bear in mind the guidance and underlying principles behind what governs 'substantiality', a correctly completed Modification Tool provides the primary basis for determining modification classification. This should be considered alongside professional judgement by the RGT, particularly where the outcome appears inconsistent with regulatory guidance or the specifics of the study.

What the tool deems 'substantial' can sometimes be unintuitive, and study teams will occasionally submit to the Sponsor as a MoID or minor modification which is, in fact, substantial. As a general rule, the substantiality of the modification is of primary interest to the NHS REC overseeing the study (if any). For this reason, modifications to Sponsored studies which are in receipt of favourable opinion from a University of Bristol REC will receive a 'non-substantial' classification by the tool, even when they would have received a 'substantial' classification were they under the auspices of an NHS REC (for more information, see Section 3 below).

In the context of CTIMPs, a modification can be considered substantial when, paraphrasing the Clinical Trial Regulations, it "is likely to affect to a significant degree

(a) the safety or physical or mental integrity of the participants of the [study],

(b) the scientific value of the [study],

(c) the conduct or management of the [study], or

(d) the quality or safety of any investigational medicinal product used in the [study];"

Substantial modifications are further classified as Route A or Route B; this is not relevant for the REC opinion but does impact how the MHRA will process the modification. See definitions on the HRA website. Route A substantial modifications are reviewed by the licensing authority and/or ethics committee, whereas Route B substantial modifications are automatically approved by the licensing authority; see the guidance on Automatic approval of Route B substantial modifications by the licensing authority.

2.2 Overall category – the impact on participating organisations
The second dimension of classification is the modification's *category*. This reflects which organisations involved in the study will be affected by the modification. Per the IRAS guidance;

| **Category:** | |
|---|---|
| A | Implications for, or affects, *all* participating organisations. This may involve changes to activity or cost implications. |
| B | Implications for, or affects, *specific* participating organisations. This may involve changes to activity or cost implications for these organisations. |
| C | No implications that require management or oversight by the participating organisations. The modification is still provided 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. |

There are two other possible category outcomes on the Modification Tool; 'new site' when a new site or PIC is added undertaking the same activities as existing sites and 'n/a' for non-notifiable modifications.

As a general rule, the category of the modification is of primary interest to the HRA/HCRW, where HRA/HRCW approval has been sought.

**3. Scope**
This SOP describes the Research Governance Team process for review of modifications to research that is Sponsored by the University, in accordance with the **UK Policy Framework for Health and Social Care Research**. Accordingly, this SOP does not cover modifications to studies Sponsored by other organisations; proposed modifications to these studies are the responsibility of that Sponsor. Modifications to studies registered by the Research Governance Team, in line with **RG SOP 7 – Registering a study** – are not in the scope of this SOP. However, the Study Registration template letters referred to within that SOP do request researchers advise the Research Governance Team of any changes to the registered study which also change or affect the University's role in the research.

This SOP also does not cover (modifications to) Research Tissue Banks or Research Databases. For more information on amending the documentation associated with these, contact the Research Governance Team.

Lastly, the processes for amending research which has been reviewed by a University Research Ethics Review Committee (URERC) are also not in scope *with respect to University Research Ethics Review Committee processes*. Sponsored studies that have, for instance, HRA approval while operating under URERC favourable opinion, must follow both the process in this SOP with respect to those approvals managed through IRAS, and the URERC modifications process with respect to the ethical favourable opinion. Information on the URERC amendment process can be found on the University Research Ethics website.

**4. Responsibilities**

This SOP outlines the roles and responsibilities of **RGOs**, **RHTMs**, **CTO and HoRG** in the assessment, review and authorisation of modifications for University of Bristol Sponsored studies. It provides information on associated administrative processes, including logging the modification on F2 and issuing updated Sponsorship. Lastly, it explains how the **RGC** should pass on correspondence concerning modifications which have been sent to the Research Governance inbox, but not to a member of the team; and how the **RGC and HTC** can assist in ensuring appropriate records of the modification are maintained in F2.

The **RGO, CTO** and **RHTM** responsibilities within this SOP presuppose familiarity with the HRA's Modification Tool.

Research teams are responsible for preparing new or revised study documents (hereafter called 'supporting documents') and a Modification Tool, and submitting these to the Research Governance Team for sponsor review and authorisation.

The **RGOs, CTO** and **RHTMs** are responsible for reviewing the supporting documents and Modification Tool, assisting and facilitating the completion of the modification submission process, logging relevant information in F2 and issuing updated Sponsorship.

**5. Procedure**

There are many ways in which a study might be modified, and consequently, many ways in which the Modification Tool may be configured. The process described in sections 5.1-5.7 captures many of these, though some notable exceptions to or variations upon the core process are covered in section 5.8.

5.1 Notification of intention to modify a study

Researchers wishing to make a modification to their study should contact the Research Governance Team; writing either directly to the member of the team responsible for their study, or to the Research Governance inbox (in the latter case, the **RGC** should determine the member of the team responsible for managing the study in line with the principles of **RG SOP 2 – Triaging new studies**, section 5.2, and pass the record to that team member using the 'chat' function in F2).

Sometimes researchers will have only an approximate understanding of how they wish to modify the study, or what the modifications process for Sponsored studies is. In this case, the responsible **RGT member** should provide links to the IRAS guidance on modifications, **Appendix 1 – Guidance on preparing the modification,** and request that the study team complete a Modification Tool, provide the supporting documentation (with any revisions to existing documents recorded as tracked changes) and return it to that **RGT member** for review.

In other cases, particularly with more experienced study teams, the researcher will contact the RGT with a Modification Tool and the supporting documentation already prepared.

In either case, once the Modification Tool and supporting documentation have been provided to the **RGT member** responsible for the study, the **RGT member** can progress to the next stage of the process, as detailed in section 5.2 below.

5.2 Validating and reviewing a proposed modification

Before completing any other part of the review, the **RGT member** should first check that Section 1 of the Modification Tool has been completed correctly. Incorrectly populating these fields may cause the wrong kinds of information to be solicited in the later parts of the tool, or the tool to provide inaccurate classifications of substantiality and modification category. Only once the **RGT member** has validated that the information in this section is accurate should they proceed to review the rest of the Modification Tool, and the supporting documentation.

The broader review will vary from modification to modification, but should include at least the following:

- Assessment of the proposed modification, as described in both the supporting documentation and the Modification Tool.
    - Are these descriptions consistent with one another?
    - Are the proposed changes in line with the principles of the **UK Policy Framework**, or other regulations?
    - The material can also be usefully reviewed against the considerations in 5.2 of **RG SOP 6 – Sponsoring a study**, and the Study Sponsorship checklist (for instance, if the modification is changing a participant information sheet, does the new PIS meet the conditions laid out in that checklist?).
- Assessment of the Modification Tool.
    - Has the tool been completed correctly, per **Appendix 3 – Validating and reviewing modifications**?
    - Have all fields opened, and been completed, as needed; have the macros failed to enable, suppressing some of the fields?
    - Does the Tool's classification of the modification in Section 4 as substantial, or modification of an important detail, or minor, or category A, B or C, match the **RGT member's** expectations (the HRA provide some examples here) or has the tool been incorrectly populated?
    - Does Section 4 identify the expected bodies for review of the modification?
- Are the Modification Tool and supporting documentation sufficiently comprehensive to capture the intended modification?
    - For instance, if the PIS has been revised to include different cohorts, has the protocol also been updated, and does the Modification Tool also reflect the need for a change to the protocol? Does the submission guidance tab of the Tool advise updating the IRAS form, and if so, has this been completed? Is a new PIS or consent form required for the new cohort?
- Ensure the version control on supporting documentation is updated correctly

For CTIMPs, the **RGT member** will need to determine if the substantial modification is Route A or Route B.

If the **RGT member** is satisfied that the supporting documentation, and Modification Tool, need no changes, they can progress to section 5.4 below; otherwise, where the **RGT member** has identified changes to be made, they should continue to the process as described in section 5.3.

5.3 Returning documents to study team for revision

Where the **RGT member** has identified changes to be made to the Modification Tool or supporting documents, or new documentation is required, they should now return these documents and comments to the study team requesting the revisions are made. Once the study team have made these changes, the **RGT member** should again review the documents following the process described in section 5.2. When the supporting documentation and Modification Tool are ready, the **RGT member** can progress to section 5.4.

5.4 Authorising and submitting the Modification Tool

Once the **RGT member** requires no further changes to the Modification Tool and supporting documentation, the authorised **RGT member** can sign the final version with their name and the research-governance@bristol.ac.uk email address, and 'lock' the tool using the Tool's functionality of the same name. This produces a pdf version of the file. The file name is auto-populated from the IRAS ID and Sponsor modification reference number fields within the tool. The **RGT member** should add the date of authorisation to the end of the file name (N.B. the footer of the Modification Tool is autogenerated upon locking the Tool and includes the date of authorisation and other Tool-specific identifiers – this information is for internal NHS REC and HRA purposes).

The **RGT member** can now return this authorised tool using the appropriate template in **Appendix 4 – Submission guidance**. The Tool should be provided in pdf format, with supplementary submission guidance documents, including a link to **Appendix 2 – Practical steps on how to submit on IRAS portal** if needed. The **RGT member** should return the excel tool to the research team with an appropriate file name to indicate Sponsor review, advising them of any changes (changes to the Sponsor modification reference number and Sponsor modification date can be considered minor changes).

The **RGT member** should also advise the research team that, where applicable and upon submission, they must inform sites (in the case of NHS sites, both the R&D department and the local research team) that the Modification has been submitted, depending on the category of modification and email template outlined in **Appendix 4 – Submission Guidance**. For category A and B modifications, this notification initiates the 35 calendar day site review period. Category C modifications should be shared with sites for their information only.

The study team should submit the Modification Tool using the information in the Submission Guidance tab of the Excel version of the Tool; the **RGT member** should be aware of the following qualifications, and apprise the team of these if needed;

IMPORTANT – IRAS has not been updated (as stated on Modification Tool v2.0) in line with the new classifications and will require study teams to submit using the old classifications. The Modification Tool provides the equivalent old classification to use for IRAS submission in the Submission Guidance tab and at the bottom of the Modification Tool tab once it has been filled out.

*CTIMPs* – For pre-Combined review studies, the **RHTM for CTIMPs or CTO** must submit the modification to the MHRA, while the study team submit to the NHS REC and HRA via the usual

portal. For studies set up using Combined Review, the trial team should upload this through Combined Review and advise the **RHTM for CTIMPs or CTO** that the modification is ready for their authorisation on the same system which submits the modification.

*CIMDs* – All proposed modifications must be notified to the MHRA, even where the Modification Tool has classified these as non-substantial. The study team are responsible, once the **RHTM for CIMDs** has reviewed the modification, for submitting these modifications and they should copy the RHTMs for CIMDs on all correspondence. The Submission Guidance tab of the Tool gives specific instructions on how the modification should be submitted to the MHRA.

*CAG* – Where a study has CAG approval, the CAG must be notified by the study team of all proposed modifications to a study , however minor or seemingly irrelevant to their remit (see **RG SOP 15 – Confidentiality Advisory Group** for more information on the CAG). This is regardless of whether NHS REC or HRA review is required. IRAS guidance further specifies that modifications concerning the following must be submitted to the CAG for review:

- Data flows
- Data items
- Data sources
- Purpose of application
- Data controller
- Data processor
- Duration

*Other review bodies* –The 'Maintaining your approvals' section of the IRAS Help pages contains information on how to modify studies under the coverage of other bodies, such as ARSAC or HMPPS.

**In all cases, Updated Sponsorship must not be issued at this stage; i.e. while confirmation of submission by the Research Team, and/or acceptance of the modification by relevant bodies, is still outstanding.**

5.5 Informing sites

Upon submitting the tool, the submitter will receive an automated acknowledgement email. Following **Appendix 4 – Submission Guidance,** the responsible **RGT member** will advise the study team that, once they have received this acknowledgement email, they must inform sites of the modification. This applies for all modifications regardless of category. For category A and B modifications, informing sites initiates the 35 calendar day site review period. Category C modifications should be shared with sites for their information only. Although non-notifiable modifications do not require submission, the study team still needs to inform sites of the modification where indicated on the Tool.

5.6 Responding to issued REC opinion

There are three possible outcomes that may be received from the initial REC review of a substantial modification; 'favourable opinion', 'favourable opinion subject to conditions', or 'unable to issue a favourable opinion and requests further information'.

Upon receipt of a favourable opinion, the RGT member can proceed to issuing updated Sponsorship, see section 5.7 below.

If 'favourable opinion subject to conditions' is provided, the notice will specify what actions Sponsor must take to meet the specified conditions. The substantial modification is approved only when these conditions are met. The **RGT member** should liaise with the study team to offer support in meeting these conditions and request evidence of how these conditions have been met. Unless specified in the approval letter, it is not necessary to inform the authorities that the conditions have been met. Once the RGT member has evidence of compliance with the conditions they can proceed to issuing updated Sponsorship, see section 5.7 below. In some cases, the authorities may allow a condition of approval to be fulfilled at a specific time point after the modification is implemented. If the condition is not met by the specified time point, the approval is not valid and the implementation must be reversed. The RGT member should add this time limit to the updated Sponsorship template.

If issues are identified that prevent the modification from being approved, the REC will be unable to issue a favourable opinion and will request further information. Sponsor will be informed of these issues and the applicant will have one opportunity to provide further information for the application to be reconsidered. The study team will have 60 days from the date of the decision letter to submit the requested information; either through IRAS for combined review trials, or by email to the relevant authority for non-combined review trials. This can be as a written response or an amended application for approval, and this should be processed by the **RGT member** in line with the instructions in sections 5.2-5.4 above. If the 60-day deadline is missed, the application will be rejected (extensions can be requested by contacting the MHRA or ethics committee directly).

In the event of an unfavourable opinion, the researcher will be required to submit a new modification. The **RGT member** will need to follow the instructions in sections 5.1-5.6 above.

N.B. If the substantial modification is relevant to both the REC and the MHRA, the modification will need to have received a favourable opinion from both prior to proceeding.

5.7 Issue of updated Sponsorship

When a modification has received all necessary approvals, and a record of this has been provided to the **RGT member** (or, confirmation that the Modification Tool has been submitted where applicable has been received), updated Sponsorship can be issued by the RGT member managing the study.

Updated sponsorship is issued by email, except for those modifications concerning a new CI, the University taking over Sponsorship, or the addition of new sites (once confirmation of capacity and capability or equivalent organisational approval for non-NHS organisations, as described in **RG SOP 6 – Sponsoring a study, section 5.5**); these latter three classes of modification require an updated Sponsorship letter, as described in **RG SOP 6 – Sponsoring a study**. On occasion, the timing might be such that updated Sponsorship for modifications can be documented in an updated letter where new sites are being sponsored. The addition of sites should not be held up by (other) outstanding modification approvals.

For issue of updated sponsorship by email, the **RGT member** should refer to **Appendix 5** which explains the various email templates.

Non-notifiable modifications can have updated Sponsorship confirmed at the point of returning the authorised Modification Tool; for all other modifications, confirmation of submission and, where appropriate, approvals, are needed for Sponsorship to be issued.

For studies adopted onto the NIHR portfolio, if the modification updates the recruitment target, or extends the study, the issue of updated Sponsorship is the point at which the **RGT member** should prompt the study team to inform CPMS of these changes.

5.8 Maintaining appropriate records

The **RGT member** managing the study should file all correspondence to the F2 Case, using sub-folders clearly distinguishing the different modifications (for instance, 'Mod 1 - Sub', 'Mod 2 - MoiD', 'Mod 3 - Sub, 'Mod 4 – Minor', etc.)

At point of authorisation, the **RGT member** should:

- Ensure the case guide is populated, including whether the modification is non-notifiable or adds a new site (see table below for categorisations); the approvals required as per the output from the Modification Tool; the **RGT member** may work with the **RGC or HTC** to complete this.
- (**RHTM for CTIMPs, RHTM for CIMDs or CTO** only) Update the modification log spreadsheet within the F2 case for that study to summarise and track the modifications, in addition to updating the case guide.

More generally, as modification approvals are received, the corresponding fields in the F2 Case Guide should be updated and completed; when Sponsorship is updated, this should be logged in the Case Guide.

For those modifications not categorised by the Modification Tool, the following Research Governance process for coding the modifications in the case guide has been agreed for the purposes of internal reporting on this work:

| | |
|---|---|
| Category A | - New site with different activities or same site with changed activities<br>- New PIC, or existing PIC with changed activities<br>- Site closed or withdrawn |
| Category B | - New site, unchanged activities<br>- New PIC, unchanged activities |
| Category C | - All other uncategorised modifications (e.g. non-notifiable modifications).<br>- Submitting the date that the first UK trial participant is recruited (CTIMP only) |

5.9 Bespoke study modification processes

This section covers certain classes of modification that deviate from the pathway described above.

*Change of CI*

First, the study team should update the CI details on the original IRAS Form. The incoming CI must then authorise the amended IRAS Form (this may still show the outgoing CI details, but can be requested from the new CI and signed regardless). The amended IRAS form can then be re-authorised by the Sponsor.

The study team should now prepare a Modification Tool using the process in Sections 5.1-5.7 above, and update the protocol with details of the new CI; this should be prepared with track changes and uploaded along with the CV of the incoming CI.

*Change of Sponsor*
The original Sponsor (whether the University or another organisation) should prepare and submit a Modification Tool, in line with the process in sections 5.1-5.7 of this SOP, with the new organisation providing a letter confirming intention to assume Sponsorship and appropriate insurance confirmation, and signing the original IRAS Form as incoming Sponsor (for studies where the University is assuming Sponsorship, see **RG SOP 12 – Insurance)**.

*Adding NHS organisations when the study previously involved no NHS organisations*
The study team and responsible **RGT member** should work together to complete section 1 of the Modification Tool, indicating that NHS organisations are being added for the first time, and therefore HRA/HRCW approval is being sought, for the first time. The Modification Tool will not display sections 2-4 and the Tool cannot be locked for submission. Instead, following the guidance in the tool, the HRA should now be contacted for advice.

An agreement between the Sponsor and the new NHS sites should be prepared in line with **RG SOP 5 – Agreements**, and the advice of the HRA followed; this will standardly include (at least) preparation of a SoECAT and site documentation.

*Human tissue modifications*
Within the Modification Tool's 'Project Design' area of change there are three items corresponding to human tissue; the below table describes how these relate to different areas of human tissue management.

| | |
|---|---|
| Samples – adding storage or use of human tissue samples under the relevant legislation on Human Tissue for the first time | Adding tissue to the project for the first time (in this case, the relevant section B of the IRAS form must be completed) |
| Samples – non-significant changes (for example, change to the logistical, transporting or storing arrangements) | Where the collection of tissue already has ethical coverage and is to be amended |
| Samples - significant changes (for example to the arrangements for removal, storage or use of samples under the relevant legislation on Human Tissue) | Where the modification needs NHS REC coverage |

*Study extensions*
These must be detailed on a Modification Tool; otherwise, the process in sections 5.1-5.7 above can be followed as usual.

*Adding sites or PICs not previously listed in IRAS form or protocol*
The addition of new sites and PICs can be accomplished using the process described in sections 5.1-5.7. However, it is recommended to add new sites and PICs to the IRAS form/protocol using a standalone modification; this means that these sites and PICs can be set up, in accordance with **RG SOP 5 – Agreements** – while any other modifications are being reviewed. The new organisations can therefore be set up more quickly.

*Modifications to add the involvement of adults lacking capacity for the first time, or extend the involvement of adults lacking capacity to a new nation*
The legislation surrounding the involvement of adults lacking capacity in research is complex, and the specific modification type and level of information needed vary depending on the location of the lead nation and the nations where the modification will be implemented. Consequently, these modifications cannot be processed through the usual Modification Tool route.

Working with the study team, the **RGT member** should contact the REC that originally issued a favourable opinion for the study, identifying in the covering email that the modification relates as above to adults lacking capacity. The REC will advise on how to submit the modification and any additional steps needed. REC email addresses can typically be found in the case on F2, or more generally, on the HRA website.

When extending the involvement of adults lacking capacity to a new nation, the **RGT member** should check that the researchers have considered the different standards and legislation that may apply. The modification may require, for example, the creation of new consent and participant information documents. The **RGT member** can refer the study team to HRA website which provides more information on the requirements that apply in England, Wales, Scotland and Northern Ireland, and also provides helpful templates that can be used when designing consent and information documentation.

*Modifying an OID*
If changes to the study specific content of the OID are required after a sponsorship letter has been issued for that site, the changes should be reviewed and agreed with the site. The OID must be re-signed and re-dated by both parties. An updated sponsorship letter will be prepared which details the changes made for that site. The site does not need to wait for the updated letter to commence the new activity because the changes have been agreed by the parties.

Submission of a Modification Tool for this process is not typically required, though if the OID has been modified, for instance, because the study processes have changed, then a Modification Tool would be needed to cover the change in study processes, and associated documentation.

*Urgent Safety Measures*
Urgent safety measures should be implemented as soon as possible, the modification can be submitted after the change to the study is made within the required time frames. For CIMDs, the MHRA must be notified of this within 3 days.

## 6. Related documents

### Internal documents

Appendix 1 – Guidance on preparing the modification

Appendix 2 – Practical steps on how to submit on IRAS

Appendix 3 – Validating and reviewing the amendment

Appendix 4 – Submission guidance

RG SOP 20 – Modifications – v1.0 27/04/2026

Appendix 5 – Types of updated Sponsorship

Appendix 6 – Updated Sponsorship email templates

RG SOP 2 – Triaging new studies

RG SOP 4 - Approvals

RG SOP 5 - Agreements

RG SOP 6 – Sponsoring a study

RG SOP 7 – Registering a study

RG SOP 12 - Insurance

RG SOP 15 – Confidentiality Advisory Group

**External documents**

**UK Policy Framework for Health and Social Care Research**

**UK Clinical Trials Regulations**