How to guide: Amendments

When a study starts, the protocol and documents are all approved by the Health Research Authority (HRA) and research ethics committee (REC). If there are any changes to documents, processes or dates, these usually have to be notified to the HRA/REC and be reviewed again. A separate approval of this is then issued.

Key information you should be aware of:

- The practice is responsible for ongoing treatment for its patients, and for ensuring that patients and patient data are treated with due care.
- The practice must ensure that it is always using the current approved documents when running a study – this is an essential part of following a protocol.
- The study team is responsible for updating the study and submitting any amendments to the HRA/REC for approval. The practice team cannot make amendments to the study.
- Urgent safety measures can be implemented without amendment approval; in these cases the sponsor will inform you of the change and inform you that it is an urgent safety measure.
- The study team is responsible for letting practices know about all amendments and for sharing documents as appropriate. They must let all sites know of any changes to the study which affect them.
- Practices do not need to send a formal acceptance of an amendment, and the sponsor may implement the amendment if the practice does not object or request more time to consider the amendment, providing the amendment is approved and the appropriate time has elapsed.
- Amendments are named by the sponsor and there is not a defined numerical system, which can lead to confusion; amendments may not seem to run chronologically. You should be informed about all amendments which apply to your practice and it is the sponsor's responsibility to keep you informed.
- If a practice feels unable to implement an amendment, they must communicate with the sponsor as they may not be able to continue with the study without the amendment.

Highlights

- Assessment of feasibility
- Submitting EoIs

See also

- Getting your practice ready to do research guide
- Roles and terminology guide
- Principal Investigator guide
- Data guide

Full guide

Amendments are a necessary part of studies, as they allow the study to respond to emerging requirements and correct any errors.

Amendment processes

- When a change needs to be made to a study (which can be as small as an alteration to the text of one study document), an amendment is required.
- The study team identifies a need for an amendment.
- If practice staff identify a need for an amendment, they must communicate it to the sponsor as the sponsor is responsible for making any changes. They must not make changes without the sponsor's agreement – amendments must go through the process.
- The sponsor submits the amendment, and the automated tool (the amendment tool) determines whether it needs review by the HRA. The amendment may also need to be reviewed by a research ethics committee.
- The amendment tool will produce a decision so the study team can share this with sites.

- The changes may not be made until the amendment has been approved, or the amendment tool has confirmed that approval is not required. You should receive copies of the amendment tool and any approvals.
- The study team needs to share information and updated documents with sites. They may use the following email templates:

Template email for sponsors to share category A or B amendment documents with sites (regulatory approvals outstanding)
Template email for Category A or B amendment documents with sites – where regulatory approvals in place
Template email for sponsors to share category C amendment documents with sites
Template email for sponsors to confirm implementation of an amendment

- The study team also needs to share details of the amendment (plus approval where applicable) with West Yorkshire Research & Development (WY R&D) as your NHS R&D team, and WY R&D will produce an advisory email for the study team, which they are then asked to share with practices.
- The site (practice) must update the site file and documents being used (see section below on updating files).

Amendment categories

Amendments are categorised to determine whether the site (practice) needs to review them before implementing them.

Category:	This category includes any amendment to a research project that has:
A	Implications for, or affects, all participating NHS/HSC organisations hosting the research project.
B	Implications for, or affects, specific participating NHS/HSC organisations hosting the research project.
C	No implications that require management or oversight by the participating NHS/HSC organisations hosting the research project. However the amendment should still be provided for information. *Note - Updated Investigator Brochure (IB; Clinical Trials of Investigational Medicinal Products (CTIMPs) only):* Where the IB update, annual or otherwise, constitutes a non-substantial amendment for REC and MHRA and this is the only amendment (e.g. the update to IB does not give rise to updated pharmacy manual or protocol) the updated IB can be submitted for information only, but would not require categorisation. These amendments 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.
New NHS/HSC site	Guidance on adding additional NHS/HSC sites is provided in the section below. Where the amendment is to add a new NHS/HSC site to the project, the set-up of this new site should proceed according to the process for local study set-up for the nation where the new site is located.

Urgent safety measures

Where patient safety is at risk, urgent changes may be implemented but these must be driven by the sponsor. If you feel the study is creating a risk, you must report it to the sponsor rather than making any changes.

The sponsor must inform all sites of the change. There will often be changes to documents following an urgent safety change – these should be submitted as usual as an amendment.

Practice responsibilities

The practice is responsible for delivering the study in accordance with the study protocol, including all amendments.

The study team is responsible for making any updates to the study documents, and securing all necessary approvals for these. The practice is responsible for replacing all documents with the latest versions in the site file, and only using the current document versions.

The Principal Investigator (PI) must ensure that all staff members are informed of any changes. The delegation log may need to be updated if staff take on new activities.

The sponsor will determine whether participants need to receive updated versions of documents. When the consent form is updated, the sponsor will determine whether participants who have already given consent, need to then sign a new consent form.

Updating files and paperwork

A site file must contain all study documents.

When a document is replaced with an updated version, the following process must be followed:

- Retain all old versions in the study site file.
- If paper versions, the old version should be crossed through and marked 'superseded' (the old versions should be retained in the file clearly marked) and the new version inserted.
- If using electronic site files, it must be made clear which are the current and which the archive versions, for example saving the previous versions of documents in a separate 'archive' folder.

Amendment approvals should also be included in the site file.

Agreeing to or rejecting an amendment

Practices do not need to send a formal acceptance of an amendment, and the sponsor may implement the amendment (when approved) if the practice does not object or request more time to consider the amendment. They may implement category A or B amendments 35 days after they notify the site and may implement category C amendments as soon as they have notified the site. If the practice confirms to the sponsor that they accept the amendment, then it can be implemented sooner than 35 days.

Note that days means calendar days and not working days.

If your practice feels it cannot implement an amendment, it must raise an objection in writing to the sponsor as soon as possible. This must be within 35 days.

If your practice needs more time to consider an amendment, it must notify the sponsor (again, this must be within 35 days). However, it is best practice to progress amendments (or object) as quickly as possible.

Amendment naming and numbering

There is no standard way of naming and numbering amendments. Sometimes the terms 'minor' and 'major' are used, sometimes 'substantial' and 'non-substantial'.

The definitions 'minor', 'major', 'substantial' and 'non-substantial' are simple descriptors – they all still need to be implemented.

Categories of amendment (A, B and C) are more relevant (see above) as they describe whether the amendment needs management or oversight from the site (practice).

Some studies prefer to number amendments starting at 1 and numbering each amendment chronologically; others number substantial amendments separately from non-substantial amendments. Others may use the date or a description rather than a number.

A practice may not always receive every amendment, as category B amendments are not necessarily relevant to all sites (for example if a new site is added to a study, or if a change is made to a different arm of the study). It is the sponsor's responsibility to inform the practice of all amendments applicable to them.

Changes not requiring an amendment

If a study document contains a section designed to include local information or branding (see example below), or information that is not known at the time of the approval (for example a specific URL), then it does not require an amendment, if this is clear at the point of application.

ON UNIVERSITY LETTERHEAD

<Date>

Dear <GP name>

Changes to an Organisation Information Document are a matter between the site and sponsor, so do not require an amendment.

When the study was approved, it will have specified a start and end date. If there are any changes to the study end date, particularly if they are substantial, they will usually be submitted as amendments.

In exceptional circumstances, there may be exemptions to requiring a study amendment. In recent years, the most important to be aware of are:

- For studies affected by the COVID-19 pandemic, for example those which had to pause or implement new methods, restarting or reverting to original methods does not require an amendment, but must be discussed with sites.
- With the introduction of the General Data Protection Regulation (GDPR), the HRA produced template wording to be used in research documentation. If studies used the template wording, they did not require an amendment, but simply needed to notify sites of the update.

If you are not sure, then please contact research@bradford.nhs.uk or discuss with the study sponsor.

Glossary of Acronyms and Terms

RDN	Research Delivery Network
GCP	Good Clinical Practice (training)
OID	Organisation Information Document
PI	Principal Investigator
SIV	Site Initiation Visit
SOPs	Standard Operating Procedures
HRA	Health Research Authority
REC	Research Ethics Committee