Modifications (formerly Substantial Amendments)

Download Print document

Recruitment Phase

The Modifications station follows the Audit station and precedes the Addition of New Trial Locations & Investigators station. This process occurs in parallel with Safety Reporting, Progress Reporting, Ongoing Management & Monitoring, and GCP & Serious Breach Reporting. It also has the potential to occur simultaneously with an MHRA Inspection, Audit, Addition of New Sites & Investigators, Urgent Safety Measures, Temporary Halt, and Early Termination. Modifications are a legal requirement relevant to all trials. This station is part of the 'recruitment phase' group of stations.

Modifications

The amended Clinical Trials Regulations now refer to modifications (in place of the term amendments) of a clinical trial, which are changes made to a research project after approval has been granted.

Health Research Authority (HRA) guidance describes the approval process for modifications under the amended Clinical Trial Regulations. This guidance includes a timeline flowchart and the process for submission for pre-Combined Review trials. The Medicines and Healthcare product Regulatory Agency (MHRA) provides additional guidance on modifications.

Modifications fall into three categories:

- **Substantial Modifications:** Modifications likely to have a substantial impact on participant safety or rights, or on the reliability or robustness of the data generated, requiring review by both the MHRA and the HRA. These modifications are further classified into Route A and Route B substantial modifications.

- **Modifications to an Important Detail:** Modifications communicated only to the REC for administrative or oversight purposes, but which do not require REC approval.
- **Minor Modifications:** Modifications that may be implemented at any time without notifying the MHRA or the REC at the time of implementation.

In their guidance, the HRA provides examples of each category of modification:

- Example of Substantial Modifications
- Examples of Modifications of an Important Detail
- Examples of Minor Modifications

The Modification Tool in IRAS

The Modification Tool, which is an updated version of the Amendment Tool, is accessed from the Integrated Research Application System (IRAS). Further information is available on the HRA website.

Non-CTIMPs

The terminology used when non-CTIMPs are conducted now aligns with CTIMPs and is described on the HRA website. The HRA has guidance on the approvals process for non-CTIMP modifications.

Further Reading

- MHRA: Transitional arrangements for applying for approval for modifications
- IRAS: Modification Guidance
- Addition of New Trial Locations & Investigators station.

Note: The NIHR Clinical Trials Toolkit has been updated to reflect the amended Clinical Trials Regulations, which took effect in the UK on 28 April 2026. Content and terminology has been updated across the CT Toolkit site, however the interactive routemap is still in the process of being updated accordingly.