Amendment guidance – all review bodies

The following document collates all guidance under the IRAS amendment tab on procedures for notifying review bodies of changes to approved applications.

Notifying amendments to the Research Ethics Committee
Notifying amendments to NHS/HSC R&D offices
Notifying amendments to MHRA Medicines
Notifying amendments to MHRA Devices
Notifying amendments to the National Information Governance Board for Health and Social Care
Notifying amendments to ARSAC
Notifying amendments to the Ministry of Justice

Notifying amendments to the Research Ethics Committee

Further ethical review is required for any substantial amendment made once the study has started. A favourable opinion must be obtained prior to implementing the amendment, unless it is an urgent safety measure.

For CTIMPs and clinical investigations of medical devices only, substantial amendments should also be notified prior to the start of the study where, exceptionally, significant changes are requested by the Medicines and Healthcare products Regulatory Agency (MHRA) as part of the regulatory approval process and these changes are relevant to ethical review.

Notification is not required for amendments not meeting the criteria for substantial amendments.

Substantial amendments

A substantial amendment is defined as a change to the terms of the REC application, the protocol or any other document submitted with the application, which significantly affects one of the following:

- The safety or physical or mental integrity of study participants
- The conduct or management of the study
- The scientific value of the study
- The quality or safety of any investigational medicinal product used in the study

Addition of new research sites or changes to the local Principal Investigators listed in Part C of IRAS qualify as substantial amendments if the study requires site-specific assessment (SSA). Please refer to the correspondence from your Research Ethics Committee to check whether your study requires SSA, or seek advice from the REC office.

Notifying substantial amendments – CTIMPs

For all CTIMPs, substantial amendments must be notified to the main REC and the MHRA using the European Commission form, available on the EudraCT website at http://eudract.emea.europa.eu/document.html. The form should be signed by the named applicant.

Please submit a single hard copy of the relevant form to the REC, together with all relevant enclosures.

For guidance on submission of substantial amendments to the MHRA, please see http://www.mhra.gov.uk/.../index.htm.

Amendment guidance – all review bodies
All substantial amendments should be approved in principle by the sponsor(s) before submission.

**Notifying substantial amendments – all other projects**

Please use the NRES Notice of Substantial Amendment form available in IRAS. Access to the form will be enabled in IRAS as soon as your Submission History for the REC form shows there is a completed version of your initial application for ethical review.

The completed Notice of Substantial Amendment form should be either signed in ink by the Chief Investigator or authorised using electronic authorisation in IRAS.

Please submit a single hard copy of the form to the REC, together with all relevant enclosures.

All substantial amendments should be approved in principle by the sponsor(s) before submission.

**Further guidance**

For further guidance about notifying substantial amendments to RECs and review procedures, please see http://www.nres.npsa.nhs.uk/applicants/after-ethical-review/

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**Notifying amendments to NHS/HSC R&D offices**

If any changes to an application are required during the course of review by another body, e.g. the ethics committee, the Principal Investigator must inform the R&D office of the changes to the information and documents originally submitted to the R&D office so that permission of the NHS organisation (R&D approval) is given for the final version of the research.

All amendments made during your study should be notified to the R&D office at each NHS/HSC research site in your study. This applies both to substantial and non-substantial amendments.

All amendments to the protocol or the arrangements for the research must be discussed with the R&D office immediately as they may have an impact on the financial or management arrangements. The notice of amendment should be provided to R&D offices in parallel with ethical and regulatory review so that the implications of the amendment can be assessed and necessary arrangements made. The R&D office should confirm receipt of the amendment. A change control procedure should then be initiated to allow the impact of the amendment to be assessed and relevant arrangements put into place at the site. Once approved by the ethics committee (and MHRA or other regulatory body, where relevant) the amendment should be implemented at the NHS organisation. Finalising revised financial schedules and sending a formal confirmation of the continued permission of the NHS organisation can follow after the implementation, within an agreed timetable, in order to avoid delays to implementation of the amendment.

Where a site is unable to accommodate the requirements of an approved amendment, the research would have to be terminated at that site.

For substantial amendments, R&D offices should be sent a copy of the Notice of Substantial Amendment form submitted to the main REC for ethical review, together with a copy of all enclosures. For CTIMPs, please use the European Commission form available on the EudraCT website at
For all other research, please use the NRES Notice of Substantial Amendment form available in IRAS. Please refer to the guidance on notifying amendments to RECs.

For non−substantial amendments, R&D offices should be notified by letter or email.

If amendments are not submitted to R&D offices as soon as possible, this may delay implementation of the amendment as it may not be possible to make the necessary practical arrangements, e.g. scheduling additional X−rays, to accommodate the requirements of the amendment.

**Notifying amendments to MHRA Medicines**

Any substantial amendment to a clinical trial of an investigational medicinal product (CTIMP) must be notified both to the MHRA and the ethics committee before it is implemented, unless it is an urgent safety measure.

Notification is not required for amendments not meeting the criteria for substantial amendments.

**Substantial amendments**

A substantial amendment is a change to the terms of the request for clinical trial authorisation or the ethics committee application, or to the accompanying particulars or documents, which significantly affects one of the following:

- The safety or physical or mental integrity of study participants
- The conduct or management of the study
- The scientific value of the study
- The quality or safety of any investigational medicinal product used in the study

Addition of new trial sites or changes to investigators listed in the initial applications to MHRA and the ethics committee qualify as substantial amendments.


For further guidance about procedures for notifying substantial amendments to the MHRA, please see: [http://www.mhra.gov.uk/.../index.htm](http://www.mhra.gov.uk/.../index.htm)

**IRAS and EudraCT**

The IRAS Project Team plans to develop functionality to allow information on substantial amendments to be generated in IRAS and exported into the format required for EudraCT. For amendments relating to new sites and investigators, notifications will be integrated with the list of sites in Part C of IRAS and the Site−Specific Information (SSI) Form to minimise form−filling.

Further information about this functionality will be issued in due course.
Notifying amendments to MHRA Devices

The following guidance applies to amendments to clinical investigations of medical devices subject to regulation by the Competent Authority.

You must notify MHRA Devices of all proposed changes to the investigation (not only those classified as substantial amendments for the purposes of ethical review) and await a letter of no objection from MHRA Devices before you implement them. This includes changes made at the request of the REC. Failure to notify proposed changes could result in the manufacturer being liable to prosecution.

When notifying MHRA of changes, please provide the following information in writing:

- the MHRA reference number for the trial;
- details of the proposed change(s) to the clinical investigation plan or the design of the device;
- the reason for the change(s); and
- a signed statement by or on behalf of the manufacturer that the proposed change(s) do not predictably increase the risk to the patient, user or third party.

Notifications should be sent directly to MHRA Devices. Details of where to send notifications can be found on the MHRA website at:
http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=194

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Notifying amendments to the National Information Governance Board for Health and Social Care

NIGB should be notified for information of all amendments to the information provided in your original application.

Please notify NIGB in writing. It is not necessary to submit a Notice of Substantial Amendment form.

Amendments may be implemented immediately. NIGB will contact you if any further information is required or if the amendment could affect the approval given under Section 251 of the NHS Act 2006.

Further guidance may be sought from the NIGB Secretariat (see Contact Us).

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Notifying amendments to ARSAC

ARSAC should be notified for information of any changes to the administration of radioactive materials exposure during a study, e.g. dose changes, new modalities, new classes of study participant.

Such changes will normally meet the criteria for notifying substantial amendments to the Research Ethics Committee (or GTAC). Please provide ARSAC with a copy of the Notice of Substantial Amendment when this is submitted to the REC, together with relevant enclosures (e.g. amendments to protocol and Participant Information Sheet).
In a multi-site study, it is not necessary for each ARSAC certificate holder to notify ARSAC. It is helpful if either the ARSAC certificate holder at the lead site or the trial co-ordinator can provide a single notification. ARSAC will contact certificate holders if any further information is required and/or the changes could affect existing certification.

Further guidance may be sought from the ARSAC Secretariat.

**Notifying amendments to the Ministry of Justice**

The Ministry of Justice should be notified for information of all amendments to the information provided in your original application.

Please notify MoJ in writing. It is not necessary to submit a Notice of Substantial Amendment form.

Amendments may be implemented immediately. MoJ will contact you if any further information is required or if the amendment has any implications for the Research Quality Assurance process.

Further guidance may be sought from Analytical Services (Offender Management and Sentencing) in MoJ (see under Contact Us).

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