• Changes to the research team at a particular site (other than the appointment of a new Principal Investigator)
• Changes in funding arrangements
• Changes in the documentation used by the research team for recording study data
• Changes in the logistical arrangements for storing or transporting samples
• Inclusion of new sites in a no local investigator project (SSA exempt)
• Extension of the study beyond the period specified in the application form

How to deal with Amendments

Each sponsor will have their own Standard Operating Procedure to deal with the finder details of both substantial and non-substantial or non-substantial amendments. For research where Institute of Psychiatry, KCL and/or South London and Maudsley Foundation NHS Trust is the sponsor contact:

• SLaM/IoP R&D office for non CTIMPS.
• Joint Clinical Trials Office (JCTO) for CTIMPs

However you must remember that all substantial amendments (excluding urgent safety measures) must be approved by the appropriate ethics committee and/or regulatory body prior to their implementation. Non-substantial amendments do not need to be reported or approved, but it is best practice of the relevant bodies to be notified of these changes. It is the responsibility of the Chief Investigator to ensure that documented records are kept of all amendments and where necessary their approval.

If you are in any doubt about which category of amendment you have then please contact the R&D Office, or for Medicinal Clinical Trials the trial sponsor.

Another good source of information is the ethical committee that has approved your project who may be able to advise you, however the ultimate decision on whether or not the amendment is substantial lies with the sponsor.

Contact details

SLaM/IoP R&D Office
Room W1.08
Institute of Psychiatry, KCL
Tel 020 7848 0251
http://www.iop.kcl.ac.uk/departments/?locator=26

Joint Clinical Trials Office (JCTO)
http://www.jcto.co.uk/

Substantial or Non-Substantial Amendment?

Research & Development Office

South London and Maudsley NHS Foundation Trust

The Institute of Psychiatry

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Amendments are changes made to a study after a favourable ethical or regulatory opinion has been given. There are two main types of amendment. The more important of the two is the substantial amendment. This must be approved by the relevant ethical committee, and if applicable regulatory body, prior to its implementation. There is an exception to this rule. Where an amendment is an urgent safety amendment this can be implemented without receiving approval from ethics or the appropriate regulatory body. The second type of amendment is the non-substantial or minor amendment which does not need to be approved prior to implementation. The process of deciding whether an amendment is substantial or non-substantial can often be difficult. This leaflet outlines both the definitions and examples of both types of amendments to make this process easier.

**Definitions**

**Substantial Amendments**
Amendments to any study specific documentation, the terms of the research ethics committee or clinical trial authorisation application that are likely to affect to a significant degree the:
- Safety or physical or mental integrity of the subjects of the research
- Scientific value of the research
- Conduct or management of the research
- Quality or safety of any investigational medicinal produce used in the trial
- Risk/benefit assessment of the study

Other changes that qualify as a substantial amendment include:
- A change of sponsor(s)
- Appointment of a new Chief Investigator

**Urgent Safety Amendment**
These are usually by nature substantial amendments but is vital to the ongoing safety of subjects:

**Non-substantial Amendments**
Amendments to the details of a study which have no significant implications for the:
- Subjects
- Conduct
- management
- scientific value of the research

**Examples**

**Substantial Amendments**
Substantial Amendments include the following changes
- Purpose of the research
- Design of the research
- Recruitment procedure
- Measures of efficacy
- Schedule of samples
- Addition or deletion of tests or measures
- Number of participants
- Age range of participants
- Inclusion criteria
- Exclusion criteria
- Safety monitoring
- Duration of exposure to the investigational medicinal product(s)
- Dose of the investigational medicinal product(s)
- Comparator
- Participant/patient information sheet
- Consent form
- Questionnaires
- Letters of invitation
- GP/other clinician letters
- Carer/Relatives Information Sheets
- Principal Investigator or addition of new investigators
- trial site or new site
- Chief Investigator
- Sponsor(s)
- CRO assigned significant tasks
- Definition of the end of the trial

**Urgent Safety Amendment**
- Toxicology screening for current trial subjects where problems have been identified with the trial medication.
- Scanning/X-rays of current trial patients where an unexpected adverse reaction, or and unexpected incidence of an adverse reaction has been noted.
- Addition or removal of a questionnaire or therapy which is causing an increased level of stress/anxiety to participants.

**Non-substantial Amendments**
Non-substantial Amendments include the following
- Correction of typographical errors in the protocol or other study documentation
- Non-substantial clarifications of the protocol
- Updates of the investigator’s brochure (unless there is a change to the risk/benefit analysis for the research)