University Hospitals Bristol NHS
NHS Foundation Trust

Research Guidance sheet No. 12
Amendments to Study Specific Documentation

V3.1_05.10.2010

Substantial Amendments

Defined as amendments to any study specific documentation, the terms of the Research Ethics Committee (REC) application or the terms of the Clinical Trial Authorisation (CTA) application (as applicable) that are likely to affect to a significant degree the:

- Safety or physical or mental integrity of the subjects of the trial;
- Scientific value of the trial;
- Conduct or management of the trial; or
- Quality or safety of any investigational medicinal product used in the trial.

Other changes to the particulars of a study that qualify as substantial amendments include:

- A change of sponsor(s);
- Appointment of a new Chief Investigator (CI);

All substantial amendments must be approved by the Sponsor of the study **prior** to requesting approval from REC, MHRA (Medicines and Healthcare products Regulatory Agency) or NHS host organisations.

Clinical Trials of Investigational Medicinal Products (CTIMPs)
For CTIMPs a request must be made to the MHRA for all substantial amendments made to either the terms of the CTA application or the accompanying documentation, including adding a new research site or a change in Principle Investigator (PI) at an existing site. This form should also be submitted as a signed paper copy to the REC which gave approval for the study and may be submitted by the sponsor, the sponsor's legal representative, the CI or any other person or organisation authorised to do so by the sponsor. Requests for substantial amendments should be made using the application form found on the MHRA website.

All other research
For all other types of research notification of amendments should be made using the 'Notice of Substantial Amendment' form available on the Integrated Research Application System (IRAS) website or on the National Research Ethics Service (NRES) website. This form should be submitted by the CI as a signed paper copy to the REC that gave approval for the study. The relevant forms and more detailed guidance can be found on the IRAS website or at: http://www.nres.npsa.nhs.uk/applications/after-ethical-review/notification-of-amendments/

A substantial amendment may not be implemented without the favourable opinion from the REC that gave a favourable opinion for the study and as applicable, the MHRA. The only exceptions to this rule are urgent safety measures, which may be taken to protect participants from immediate hazard. The main REC must be notified within three days.

Addition of a new research site or a change in PI needs to be notified to the MHRA but not the REC, although a copy of the notification should be submitted to the main REC for information.

Following receipt of approval from the REC and, if applicable the MHRA, the CI/PI must send details of all substantial amendments to host R&D offices either through CSP or direct by copy of the 'Notification of Substantial Amendment' form.

Minor Amendments (Also referred to as administrative amendments)

These can be defined as changes to the details of a study, which have no significant implications for the subjects, the conduct, the management, or the scientific value of the study. Examples may be as follows:

- Correction of typographical errors in the protocol or other study documentation
- Amended contact details for the sponsor or project staff
- Changes in funding arrangements
- Appointment of new support staff
- Changes in the documentation used to record study data
- Changes in the logistical arrangements for the transporting or storing of samples

Amendments deemed to be minor by the sponsor may be made to study specific documentation at any time so long as a record is kept of the amendments. There is no requirement to request approval from the MHRA and/or the main REC or to inform the R&D office. Such changes should be notified in annual reports.