

RESEARCH IN HUMAN SUBJECTS OTHER THAN CLINICAL TRIALS OF INVESTIGATIONAL MEDICINAL PRODUCTS

After ethical review – guidance for sponsors and investigators

This document sets out important guidance for sponsors and investigators on the conduct and management of research with a favourable opinion from a Research Ethics Committee. Please read the guidance carefully. A failure to follow the guidance could lead to the committee reviewing its opinion on the research.

1. Commencement of the research

1.1 It is assumed that the research will commence within 12 months of the date of the favourable ethical opinion.

1.2 The research should not commence at any site until the local Principal Investigator (PI) or research collaborator has obtained management permission from the organisation with responsibility for the research participants at the site.

1.3 If the research does not commence within 12 months of the favourable opinion being issued, the Chief Investigator should send a written explanation for the delay. A further written explanation should be sent after 24 months if the research has still not commenced.

1.4 If the research does not commence within 24 months, the REC may review its opinion.

2. Duration of ethical approval

2.1 The favourable ethical opinion of the REC for a specific research study applies for the duration of the study, except where action is taken to suspend or terminate the opinion, subject to approved substantial amendments. Where the duration of the study is to be extended beyond the period specified in the application form, there is no need to notify or seek approval from the REC.

2.2 Where the research involves the use of “relevant material” for the purposes of the Human Tissue Act 2004, authority to hold the material under the terms of the ethical approval applies until the end of the period declared in the application and approved by the REC. In England, Wales and Northern Ireland, samples may be held after the declaration of the end of the research, for analysis or verification of research data for up to one year (this should be detailed in the application which is approved by the REC. After this period legal authority to hold any human tissue under the ethical approval for this project will expire. To ensure that any continued storage is lawful, either the tissue must be held on premises with a storage licence from the Human Tissue Authority, or an application made for ethical approval of another project before the favourable ethical opinion (including the one year after the declaration of the end of study, if applicable) of the existing project expires. Otherwise the tissue would need to be destroyed in accordance with the HTA Codes of Practice.

3. Progress reports

3.1 Research Ethics Committees can review a favourable opinion in the light of progress reports and any developments relevant to the study. The Chief Investigator is responsible for ensuring the research remains scientifically sound, safe, ethical, legal and feasible throughout its duration. The Chief Investigator should submit a progress report to the REC 13 months after the date on which the favourable opinion was given. Annual progress reports should be submitted thereafter.

3.2 Progress reports should be in the format prescribed by the HRA and published on the website <http://www.hra.nhs.uk/resources/during-and-after-your-study/nhs-rec-annual-progress-report-forms/>

4. Amendments

4.1 If it is proposed to make a substantial amendment to the research, the Chief Investigator should submit a Notice of Substantial Amendment to the REC by accessing the original application form on the Integrated Research Application System (IRAS)

4.2 A substantial amendment is any amendment to the terms of the application for ethical review, or to the protocol or other supporting documentation approved by the REC that is likely to affect to a significant degree:

- (a) the safety or physical or mental integrity of the research participants
- (b) the scientific value of the research
- (c) the conduct or management of the research, including its ongoing legality and feasibility.

4.3 A substantial amendment should not be implemented until a favourable ethical opinion has been given by the Committee, unless the changes to the research are urgent safety measures (see section 8). The Committee is required to give an opinion within 35 days of the date of receiving a valid notice of amendment.

4.4 Amendments that are not substantial amendments (“minor amendments”) may be made at any time and do not need to be notified to the Committee. However, changes to contact details of the CI, sponsor or R&D contact are helpful and can be notified by letter or email.

4.5 Further guidance on amendments is available at. <http://www.hra.nhs.uk/research-community/during-your-research-project/amendments/>

5. Changes to sites

Management permission (all studies)

5.1 For all studies, management permission should be obtained from the participating organisation where it is proposed to:

- include a new site in the research, not included in the list of proposed research sites in the original REC application
- appoint a new PI or Local Collaborator at a research site
- make any other significant change to the conduct or management of a research site.

In the case of any new NHS/HSC site, the Site-Specific Information (SSI) Form should be submitted to the R&D office for review as part of the R&D application.

Site-specific assessment (where required)

5.2 The following guidance applies only to studies requiring site-specific assessment (SSA) as part of ethical review.

5.3 In the case of NHS/HSC sites, SSA responsibilities are undertaken on behalf of the REC by the relevant R&D office as part of the research governance review. The REC's favourable opinion for the study will apply to any new sites and other changes at sites provided that management permission is obtained. There is no need to notify the Research Ethics Committee (or any other REC) about new sites or other changes, or to provide a copy of the SSI Form.

5.4 Changes at non-NHS/HSC sites require review by the REC which reviewed the application for the research. Please submit the SSI Form (or revised SSI Form as appropriate) to the REC together with relevant supporting documentation. The REC will notify the Chief Investigator and sponsor of its opinion within a maximum of 25 days from the date on which a valid SSA application has been received.

Studies not requiring SSA

5.5 For studies designated by the REC as not requiring SSA, there is no requirement to notify the Committee of the inclusion of new sites or other changes at sites, either for NHS/HSC or non-NHS/HSC sites. However, management permission should still be obtained from the responsible participating organisation (see 7.1 above).

6. Urgent safety measures

6.1 The sponsor or the Chief Investigator, or the local Principal Investigator at a research site, may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety.

6.2 The REC should be notified within three days that such measures have been taken, the reasons why and the plan for further action.

7. Serious Adverse Events

7.1 A Serious Adverse Event (SAE) is an untoward occurrence that:

(a) results in death

(b) is life-threatening

(c) requires hospitalisation or prolongation of existing hospitalisation

(d) results in persistent or significant disability or incapacity (e) consists of a congenital anomaly or birth defect (f) is otherwise considered medically significant by the investigator.

7.2 A SAE occurring to a research participant should be reported to the Committee where in the opinion of the Chief Investigator the event was related to administration of any of the research procedures, and was an unexpected occurrence.

7.3 Reports of SAEs should be provided to the REC within 15 days of the Chief Investigator becoming aware of the event, in the format prescribed by the HRA and published on the website:

<http://www.hra.nhs.uk/resources/during-and-after-your-study/progress-and-safety-reporting/>

8. Conclusion or early termination of the research

8.1 The Chief Investigator should notify the REC in writing that the research has ended within 90 days of its conclusion. The conclusion of the research is defined as the final date or event specified in the protocol, not the completion of data analysis or publication of the results.

8.2 If the research is terminated early, the Chief Investigator should notify the REC within 15 days of the date of termination. An explanation of the reasons for the early termination should be given.

8.3 Reports of conclusion or early termination should be submitted in the form prescribed by the HRA and published on the website: <http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/>

9. Final report

9.1 A summary of the final report on the research should be provided to the REC within 12 months of the conclusion of the study. This should include information on whether the study achieved its objectives, the main findings, and arrangements for publication or dissemination of the research including any feedback to participants.

10. Review of ethical opinion

10.1 The REC may review its opinion at any time in the light of any relevant information it receives.

10.2 The Chief Investigator may at any time request that the REC reviews its opinion, or seek advice from the REC on any ethical issue relating to the research.

11. Serious breaches of Good Clinical Practice or the protocol

11.1 To ensure that the REC is able to keep the favourable ethical opinion under review, the sponsor should report to the REC any serious breaches of the protocol or of the principles of Good Clinical Practice. A “serious breach” is defined as a breach of the protocol or, of the principles of Good Clinical Practice which is likely to affect to a significant degree the safety or physical or mental integrity of the research participants, or the scientific value of the research. There is no requirement to notify minor breaches of GCP or the protocol.

11.2 Reports of serious breaches should give details of when the breach occurred, the location, who was involved, the outcome and any information given to participants. An explanation should be given and the REC informed what further action the sponsor plans to take.

12. Long Term Studies

The sponsor and Chief Investigator are responsible for ensuring that the study procedures and documentation are updated in light of legislative or policy changes and also for reasons of good practice (e.g. standards for supporting documentation). This should be documented in the progress report to the REC (see above) and, where necessary, an amendment (see above) should be submitted to the REC. The REC may review its opinion in light of legislative changes or other relevant developments.