Closing a Trial

<table>
<thead>
<tr>
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<th>Effective date:</th>
<th>Reason for change</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
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</tr>
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<td></td>
</tr>
</tbody>
</table>
Closing a Trial

1. Purpose
The purpose of this Standard Operating Procedure (SOP) is to provide details of how to close a trial. This SOP covers both trials of investigational medicinal products (CTIMPs) and all other trials.

2. Background
Informing the main Research Ethics Committee (REC) who gave approval for the trial about the end of a trial is a legal obligation. In trials of CTIMPs there is also an obligation to inform the Medicines and Healthcare products Regulatory Agency (MHRA).

3. Procedure
3.1 Who?
The Sponsor bears responsibility for informing the REC and MHRA about the end of a trial of an investigational medicinal product (though in practical terms, it is likely to be the Chief Investigator (CI) who actually does this), while the CI is responsible in all other trials.

3.2 When?
Notification of the end of a trial must be reported within specified time limits, as explained below.

3.3 How?

A definition of the end of the trial should be included in the protocol.

Any change to this definition must be notified as a substantial amendment

Notify the main REC (and MHRA if appropriate) within 90 days of the end of the trial, or within 15 days if terminated early.

Send a summary of the final report of the research to the main REC (and MHRA if appropriate) within 12 months of the end of the project.
3.3.1 Definition of the end of the project
The definition of the end of the project should be provided in the protocol and any change to this definition should be notified as a substantial amendment. In most cases, it will be the date of the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol.

Final analysis of the data (following ‘lock’ of the study database) and report writing is normally considered to occur after formal declaration of the end of the project.

3.3.2 Declaration of the end of the project
The main REC which gave a favourable opinion of the research (and MHRA if appropriate) should be notified in writing of the conclusion or early termination of a project using the appropriate form.

There are separate forms for use in CTIMPs and all other trials; both of which are available via the National Research Ethics Service (NRES) website: http://www.nres.npsa.nhs.uk/applications/after-ethical-review/endofstudy/

The appropriate form should be sent to the main REC (and MHRA if appropriate) within 90 days of the end of the project, or within 15 days if the project is terminated early. Where the project is terminated early, or halted temporarily, reasons should be given.

3.3.3 Temporary halt of a study
Where a trial is stopped temporarily for safety reasons, this should be notified to the main REC and MHRA immediately and at least within 15 days from when the trial is temporarily halted. This is done by submitting a notice of substantial amendment (see SOP 5 ‘Regulatory Approvals and Communication’ and SOP 6 ‘Ethics Approval and Communications’ for details). The form should clearly explain the reasons for stopping and the scope, e.g. stopping recruitment and/or interrupting the treatment of participants already included.

To restart the trial, the Sponsor should submit a further notice of substantial amendment and provide evidence that it is safe to restart the trial.

If it is decided not to recommence the trial after a temporary halt, the MHRA and REC should be notified within 15 days of this decision, using the appropriate ‘End of Trial Declaration’ form and including a brief explanation of the reasons for ending the trial.

3.3.4 Final Reports
3.3.4.1 To the Ethics Committee
A summary of the final report on the research should be sent to the main REC within 12 months of the end of the project. See the NRES website for more details: http://www.nres.npsa.nhs.uk/applications/after-ethical-review/endofstudy/#endofstudyFinalreport
The summary of the final report to the REC may be enclosed with the end of study declaration, or sent subsequently.

There is no standard format for final reports. As a minimum, the main REC should receive information on whether the project achieved its objectives, the main findings and arrangements for publication or dissemination of the research, including any feedback to participants.

The REC office will acknowledge receipt of the end of study declaration and final report.

Reports will normally be reviewed by the REC chair and/or another REC member. The full committee will be notified at its next meeting.

3.3.4.2 To the MHRA
A summary of the final report on the research should be sent to the MHRA within 12 months of the end of the project.

For CTIMPs, the MHRA website links to International Conference on Harmonisation Good Clinical Practice (ICH GCP) requirements for the structure and content of clinical trial reports which is acceptable to all regulatory authorities of the ICH regions:

If after the conclusion or early termination of a trial the risk/benefit analysis is considered to have changed, the Sponsor or CI should notify the main REC (and MHRA if appropriate) in case this affects the planned follow-up of trial participants. The plan for further action to inform or protect participants should be described.

3.3.5 Site closure
Each site participating in a trial should be formally closed after the project has come to an end. Site closure may be conducted by a visit or by written communication. In either case, it should be ensured that all trial drugs and/or equipment are accounted for and the documentation in the Trial Site File (TSF) is complete.

A letter (or email) should be sent to the site to confirm closure once all actions are completed. A site closure visit report may also be completed. A template closure visit report form and letter are available.

List of abbreviations
CI         Chief Investigator
CTIMP     Clinical Trial of Investigational Medicinal Product
GCP       Good Clinical Practice
ICH       International Conference on Harmonisation
IMP       Investigational Medicinal Product
MHRA      Medicines and Healthcare products Regulatory Agency
Available Templates
20-1 Closure visit report template
20-2 Site closure confirmation letter template