Site Initiation and Close Out (Sponsored Clinical Trials)

Standard Operating Procedure

Office of Health and Medical Research
Queensland Health

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Effective date: 01 June 2010
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Author: Katrina Brosnan
Approved by: Dr Jane Jacobs, Director, Research Ethics and Governance Unit

Amendment History

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1 Purpose
To describe the procedures related to site initiation and close-out of a clinical trial.

2 Responsibility / Scope
This standard applies to all Queensland Health employees (including visiting medical officers, visiting health professionals, contractors, consultants and volunteers) who propose to undertake, administrate, review and/or govern human research involving Queensland Health patients and staff.

3 Applicability
Principal Investigator, Sub/Associate-Investigator, Clinical Research Coordinators and other staff delegated trial-related activities by the Principal investigator.

4 Procedure

4.1 Site Initiation
The procedure outlined below refers to a “sponsored” study. Where the investigational study is “investigator initiated” and the “sponsor” is the institution, the investigator should undertake both investigator and monitor roles unless an external monitor has been assigned by the institution.

Prior to initiation the investigator(s) should:
- Arrange with the monitor the scheduled date, time and location of the study initiation visit.
- Review the Investigator’s Brochure and any up-to-date information on the investigational product. The Investigator(s) must be familiar with the product, including pre-clinical toxicology, pharmacology, pharmacokinetics and up-to-date clinical data if applicable. ICH GCP 4.1.2
- Ensure that the procedures stated in the study protocol are applicable in their centre and fully understood.
- Ensure that associate investigator(s), pharmacist(s), research coordinators and any other relevant staff involved with the study have been advised of the meeting and are able to attend.
- Ensure that all approvals and authorisations to conduct the research project have been granted. Approval documentation should be filed in the Site Master File. ICH GCP 8.2.9

During the initiation the investigator(s) or delegate should:
- Establish that the Investigator’s Site Master File contains all the required regulatory documents.
- Provide a list of study personnel and functions in the study to the clinical monitor.
- Provide original and dated curricula vitae of all study personnel / Investigators involved, as per sponsor requirements. ICH GCP 8.2.14
Ensure that the names and contact numbers of the relevant medical and study personnel of the sponsor are available and documented clearly.

Ensure that all relevant study site personnel fill out the Site Personnel/Signature Log. ICH GCP 4.1, QH SOP 1.4.1

Check that the procedures and plans for storage, dispensing and return of investigational product have been agreed and finalised with the Sponsor and Pharmacist (if applicable). ICH GCP 5.14.3

Review the documents used in the shipment of the investigational products to the study site. ICH GCP 4.6.3

Check that the quantity of CRFs that have been requested or shipped to the study site are sufficient for the number of Participants/patients that are likely to be recruited into the study - also allowing for the archiving of one set of intact, unused CRFs. ICH GCP 5.18.4

Check that other related supplies are available, or are to be shipped to the study site at a later date, and that they are available in sufficient quantities.

Check that laboratory facilities and arrangements for the dispatch of samples to the laboratory are organised and that any specialised equipment that may be required will be available throughout the period of the trial, e.g. centrifuge, freezer, etc. Documentation relating to pathology processes and supplies should be stored in the Laboratory Manual.

Establish who will be responsible for CRF completion and clarify the procedure for entering data in the CRF, as well as making changes and corrections. ICH GCP 4.1

Ensure that time will be made available for training in CRF completion. ICH GCP 5.23.4

Ensure an understanding of the requirements that source documents and raw data will need to be available during monitoring visits to enable the monitor to perform source data verification at each monitoring visit. ICH GCP 5.1.2, ICH GCP 6.10

Review the arrangements for organising and maintaining study files.

Ascertain that the procedures relating to the archiving of study records at the end of the study is agreeable to the sponsor, the investigator and the institution. ICH GCP 8.4

Establish the next monitoring visit date and requirements with the Monitor.

4.2 Premature Termination or Suspension of a Trial (ICH GCP 4.12)

If the trial is prematurely terminated or suspended for any reason, the investigator/institution should:

- Promptly inform the trial participants and include, where appropriate, the reason for suspension / early termination of the study.
- Assure appropriate therapy and follow-up for the participants, and, where required by the applicable regulatory requirement(s), should inform the regulatory authority(ies).

In addition:

If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should:

- Promptly inform the sponsor and the institution (HREC / Governance Office).
• Provide the sponsor and the HREC / Governance Office with a detailed written explanation of the termination or suspension.
• Where appropriate, notify the TGA of their discontinuation of involvement.

If the sponsor terminates or suspends a trial, the investigator should:
• Promptly inform the HREC and Governance Office and provide a detailed written explanation of the termination or suspension.

If the HREC terminates or suspends its approval/favourable opinion of a trial the investigator should:
• Promptly inform all participating investigators, site Governance Offices, and notify the sponsor as well as providing all parties with a detailed written explanation of the termination or suspension.

4.3 Site close-out (ICH GCP 4.13)
The investigator(s) should:
• Provide a summary report of the trial’s outcome to the ethics committee / governance office and the regulatory authorities, if required.
• Keep documentation and correspondence in the trial master file in accordance with ICH GCP 8.4.
• Inform the sponsor of the completion of the study.
• Ensure arrangements for archiving of trial documents are clarified (see QH GCP SOP 7 section 4.3).
• Ensure appropriate final disposition of any investigational product. This may include return to the sponsor or destruction of remaining materials. ICH GCP 5.14

5 Glossary
Case Report Form (CRF)
A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial Participant.

Delegate
A person delegated specific but appropriate tasks in relation to the conduct of a clinical trial.

Good Clinical Practice (GCP)
A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial Participants are protected.
Governance Office/r

The Office or coordinated function within a Public Health Organisation which is responsible for assessing the site-specific aspects of research applications, make a recommendation to the District CEO / delegate as to whether a research project should be granted authorisation at that site, and overseeing that authorised research at the site meets appropriate standards (research governance).

Human Research Ethics Committee (HREC)

A body which reviews research proposals involving human participants to ensure that they are ethically acceptable and in accordance with relevant standards and guidelines.

The National Statement requires that all research proposals involving human participants be reviewed and approved by an HREC and sets out the requirements for the composition of an HREC.

International Conference on Harmonisation (ICH)

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator

An individual responsible for the conduct of a clinical trial at a trial site and ensures that it complies with GCP guidelines. If a trial is conducted by a team of individuals at a trial site, one investigator should be designated as the responsible leader of the team and should be called the site Principal Investigator. In this instance they may delegate tasks to other team members.

Investigator initiated trial

A clinical trial that is undertaken by the investigator whereby the investigator and/or their institution takes on the role of the sponsor in addition to their role as investigator.

Monitoring

The act of overseeing the progress of a clinical trial and ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

Sponsor

An individual, company, institution or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Source Documents

Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, Participants’ diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions
certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, Participant files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

Sub / Associate investigator

Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows, clinical research coordinators. The P.I. will designate who will be nominated as Associate Investigators for that site.

6 References

1. Note for guidance on Good Clinical Practice (CPMP/ICH/135/96) annotated with TGA comments DSEB, July 2000, sections 4 and 8.4.

7 Appendices

Appendix 1: Example Initiation check-list
Appendix 2: Example Close out check-list
## APPENDIX 1: INITIATION CHECK-LIST

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<td>Ensure the Site Initiation Meeting is scheduled and all relevant staff are able to attend - (Investigator, Clinical Research Coordinator, Sponsor or CRA, Pharmacist, other relevant people such as laboratory staff). It is usual to confirm the initiation by letter</td>
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<td>Review Investigational Product overview and background</td>
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<td>Review with investigator and relevant staff their understanding of the protocol, study procedures, investigational product, randomization procedures, unblinding procedures and timelines</td>
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<td>Review that site resources are adequate to conduct the trial</td>
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<td>Review with investigator and relevant staff Safety Reporting procedures and principles of Good Clinical Practice (ICH-GCP), including informed consent procedures, investigator responsibilities, record keeping and ethics reporting.</td>
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<td>Review contents of Site Master File to ensure that:</td>
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<td>• the current approved copy of the Protocol, Informed Consent Form &amp; Investigational Brochure are present and align with the ethics committee approval</td>
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<td>• the HREC Approval and Governance Authorisation documentation are present and signed</td>
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<td>• a copy of the CTN/CTX form is present and complete</td>
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<td>• all necessary agreements are present and signed (Clinical Trial Agreement, Indemnities, Insurance)</td>
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<td>• all site staff CVs are present and signed</td>
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<td>• Laboratory normal ranges and relevant accreditation are present</td>
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<td>Complete staff delegations log</td>
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<td>Review investigational product shipment records</td>
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<td>Ensure all protocol required data has been collected</td>
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<td>Finalise accountability and disposition of test drug</td>
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<td>Verify that all study files are complete (see Study Master File checklist)</td>
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<td>Discuss overall study conduct at the site</td>
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<td>Collect final signatures for any data queries, signature logs or reports</td>
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<tr>
<td>Discuss archiving of original data and documents</td>
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<td>Dispose of or return any remaining trial specific supplies</td>
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<td>Formally close the site</td>
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<td>Notify the HREC and /or Governance Office that the study has been closed, and study materials archived.</td>
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