Investigator Responsibilities

Standard Operating Procedure

Office of Health and Medical Research

Queensland Health

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Amendment History

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1  Purpose

To define Investigators’ responsibilities and to provide instruction when performing research projects / clinical study(ies) under applicable regulatory requirements.

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 research project activities by the Principal Investigator.

4  Procedure

4.1  Investigator Responsibilities – Before the Project Commences:

The Investigator

- Should ensure that research projects are carried out according to International Conference on Harmonisation (ICH) GCP guidelines, regulatory authorities requirements and any other local requirements. ICH GCP 4.1.3

- Should have an understanding that when a research project is sponsored by an agency/pharmaceutical company, the investigator may be requested to follow the company’s procedures in order to comply with company obligations, provided that such a request does not result in a requirement for the investigator/s to act beyond their scope of practice, or unreasonably outside the Standard Operating Procedures of the Institution. Agreement between all parties should be discussed before initiating the study.

- Should request a copy of the Sponsors SOPS prior to entering into any signed contract for the conduct of the study.

- Must ensure observation of the Standard Operating Procedures of the Institution and all research staff must operate within their approved Scope of Practice.

- Should ensure that site study staff are appropriately qualified, educated in the project protocol and adequately resourced to conduct the study. ICH GCP 4.2

- Should ensure that all persons assisting with the study are adequately informed about the protocol, the investigational product(s), and their study-related duties and functions. ICH GCP 4.2.4

- Must declare any conflicts of interest, payments etc. from other parties. Notification should be sent to the HREC / site Governance Office, the sponsor and/or CRO. ICH GCP 8.2.4 It should be in the form of a written declaration, and should be noted in the Participant Information Sheet and Consent form.

- Must maintain a list of any delegated duties with respect to the study, and the persons and qualifications of those persons to whom the duties are assigned. A signature / number log must also be maintained for these persons. ICH GCP 8.3.24
• Should be able to demonstrate that adequate participant recruitment is likely to be possible, with necessary time available to conduct the study to GCP requirements, and with adequate facilities and study staff. **ICH GCP 4.2**

• Must present all study related documents to the HREC/RGO as appropriate, for review including the Investigator's Brochure, as well as updates. **ICH GCP 4.4.1 QH RUG**

• Must possess, prior to study commencement, a favourable HREC endorsement and Governance Authorisation of all study related documents, including participant information and consent documents, recruitment procedures, and any other information given to participants. **ICH GCP 4.4.1**

• Should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor. **ICH GCP 4.1.2**

• For investigator initiated research, should ensure a new CTN form is completed, or in the case of CTX a new “notification of intent to conduct clinical study” form, for any new study site subsequently added to a study [http://www.tga.gov.au/docs/pdf/unapproved/ctcompl.pdf](http://www.tga.gov.au/docs/pdf/unapproved/ctcompl.pdf).

• Note: CTN forms sent to the TGA must be *originals*. A copy should be kept in the Study Master File. It is the Sponsors responsibility to submit CTN/CTX forms.

• Should ensure, prior to the commencement of the project, that study records will be made available for any monitoring / auditing process that is due during the conduct of the project. **ICH GCP 4.1.4, ICH GCP 4.9.7, ICH GCP 5.18**

**Investigator Responsibilities – During the Project:**

• Must ensure that the study is conducted according to the approved protocol. **ICH GCP 4.5**

• Must ensure that participants or the legally authorised representative have made fully informed consent, with all study procedures and risks adequately explained and that the principles and essential elements of Informed consent are upheld and included in the information document. **ICH GCP 4.8**

• Must ensure that any payments made to study participants are considered reasonable and appropriate and within the guidelines of the National Statement: [http://www.nhmrc.gov.au/_files_nhmrc/file/health_ethics/hrecs/reference/using_the_national_statement.pdf](http://www.nhmrc.gov.au/_files_nhmrc/file/health_ethics/hrecs/reference/using_the_national_statement.pdf)

• Should inform the participant's primary physician about the participant's involvement in the project - if the participant has a primary physician and if the participant agrees to the primary physician being informed. **ICH GCP 4.3.3**

  *Note: Although a participant is not obliged to give his/her reason(s) for withdrawing prematurely from a study, the investigator should make a reasonable effort to ascertain the reason(s), whilst fully respecting the participant's rights.* **ICH GCP 4.3.4**

• Should comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority(ies) and the HREC. [http://www.nhmrc.gov.au/_files_nhmrc/file/health_ethics/hrecs/reference/090609_nhmrc_position_statement.pdf](http://www.nhmrc.gov.au/_files_nhmrc/file/health_ethics/hrecs/reference/090609_nhmrc_position_statement.pdf)

• Must ensure that necessary medical care is provided to study participants for care required as a result of any adverse events experienced during or following the study that are related to the study. **GCP 4.3**.
Must ensure accountability of the investigational product at the study site(s). **GCP 4.6.1**

Should submit written summaries of the study status to the HREC/RGO annually, or more frequently, if requested by the HREC/RGO. **GCP 4.10.1**

Must ensure that no deviation from the protocol occurs without HREC endorsement, unless it is required to prevent imminent harm to participants. If the protocol deviation results in the creation of a “separate and distinct” therapeutic good as defined in section 16 of the Therapeutic Goods Act 1989, a new notification is required for CTN or CTX studies. **GCP 4.5.2**

Must document any deviation from the protocol for later review. **GCP 4.5.3**

Should provide written reports to the sponsor, the HREC/RGO and, where applicable, the institution promptly on any changes significantly affecting the conduct of the study, and/or increasing the risk to participants. **GCP 4.10.2**

**Investigator Responsibilities – At the Completion of the Project:**

- Should promptly inform the study participants and the institution if the study is prematurely terminated or suspended for any reason. Where required by the applicable regulatory requirement(s), the regulatory authority(ies) should also be informed.

  **Note**: if the investigator terminates or suspends a study without prior agreement of the sponsor, they should inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the HREC, and provide the sponsor and the HREC with a detailed written explanation of the termination or suspension. **GCP 4.12**

- Should, upon completion of the study, where applicable, inform the institution; the investigator/institution should provide the HREC/RGO with a summary of the study’s outcome, and the regulatory authority(ies) with any reports required. **GCP 4.13**

- The investigator should ensure appropriate therapy and follow-up for the participants. **GCP 4.12**

**5 Glossary**

**Adverse event (AE)**

Any untoward medical occurrence in a patient administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product.

**Clinical Trials Notification (CTN)**

A notification scheme whereby all material relating to the proposed trial, including the trial protocol is submitted directly to the HREC by the researcher at the request of the sponsor. The TGA does not review any data relating to the clinical trial.

The HREC is responsible for assessing the scientific validity of the study design, the safety and efficacy of the medicine or device and the ethical acceptability of the study process, and for approval of the study protocol.
The institution or organisation at which the study will be conducted, referred to as the 'Approving Authority', gives the final approval for the conduct of the study at the site, having due regard to advice from the HREC.

CTN trials cannot commence until the study has been notified to the TGA and the appropriate notification fee paid.

**Clinical Trials Exemption (CTX)**

An approval process whereby a sponsor submits an application to conduct clinical trials to the TGA for evaluation and comment.

A TGA Delegate decides whether or not to object to the proposed Usage Guidelines for the product. If an objection is raised, studies may not proceed until the objection has been addressed to the Delegate's satisfaction.

If no objection is raised, the sponsor may conduct any number of clinical trials under the CTX application without further assessment by the TGA, provided use of the product in the trials falls within the original approved Usage Guidelines. Each study conducted must be notified to the TGA.

A sponsor cannot commence a CTX trial until written advice has been received from the TGA regarding the application and approval for the conduct of the study has been obtained from an ethics committee and the institution at which the study will be conducted. There are two forms, each reflecting these separate processes (Parts), that must be submitted to TGA by the sponsor.

Part 1 constitutes the formal CTX application. It must be completed by the sponsor of the study and submitted to TGA with data for evaluation.

Part 2 is used to notify the commencement of each new trial conducted under the CTX as well as new sites in ongoing CTX trials. The Part 2 form must be submitted within 28 days of the commencement of supply of goods under the CTX. There is no fee for notification of trials under the CTX scheme.

**Delegate**

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

**Good Clinical Practice (GCP)**

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical studies that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of study participants are protected.

**Governance Office**

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 study at a study site and ensures that it complies with GCP guidelines. If a study is conducted by a team of individuals at a study 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.

Sub / Associate investigator
Any individual member of the clinical study team designated and supervised by the investigator at a study site to perform study-related procedures and/or to make important study-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
4. Access to Unapproved Therapeutic Goods, Clinical Trials in Australia, Therapeutic Goods Administration, October 2004