



## POLICY: REPORTING ON THE CONDUCT OF A TRIAL

Research Ethics Committee

Tel: (08) 8222 4139

Fax: (08) 8222 3035

Email:

[Health.CALHNResearchEthics](mailto:Health.CALHNResearchEthics@sa.gov.au)

[@sa.gov.au](mailto:Health.CALHNResearchEthics@sa.gov.au)

### Background

This document establishes the policy for information to be provided to the committee in respect of the conduct of Clinical Trials and other Clinical Research which has been approved by the RAH HREC.

The document aligns the requirements of the RAH HREC with the:

- NHRMC National Statement on Ethical Conduct in Human Research issued in March 2007 [Ref 1],
- NHMRC Australian Health Ethics Committee (AHEC) position statement issued in May 2009 [Ref 2],
- Principles of the International Conference on the Harmonisation of Technical Requirements For Registration of Pharmaceuticals For Human Use - Good Clinical Practice [Ref 3] and
- Access to Unapproved Therapeutic Goods – Clinical Trials in Australia (TGA, 2004) [Ref 4]

In the event of a disparity between these guidelines and those required by regulation, the regulatory guidelines take precedence.

### Changes to Trial Documentation

The Research Ethics Committee requires all changes to trial documentation to be communicated to it as soon as possible. Examples of the trial documentation that must be provided include:

- Protocol Amendments
- Changes to the Participant Information Sheet/Consent
- Changes to other trial documentation which impacts on patient safety or the ethical conduct of the trial.
- Patient recruitment documents

Failure to provide this information promptly is in breach of the provisions of ICH-GCP

*“4.10.2 The investigator should promptly provide written reports to the sponsor, the IRB/IEC (see 3.3.8) and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.” [Ref 1]*

Amendments to protocols or Participant/Patient Information Sheets are reviewed by the Chairperson of HREC who may refer them to the Chairperson of the IDSC if they impact on issues relating to drug safety. An amended protocol must not be implemented until it has received HREC approval, subject to clause 3.3.7 of the ICH-GCP Guidelines.

*“3.3.7 Specifying that no deviations from, or changes of, the protocol should be initiated without prior written IRB/IEC approval/favourable opinion of an appropriate amendment, except when necessary to eliminate immediate hazards to the subjects or when the change(s) involves only logistical or administrative aspects of the trial (e.g., change of monitor(s), telephone number(s)).” [Ref 1]*

Examples of the trial documentation that need not be provided include:

- Change to Case Report Forms (CRF)

## **Administrative changes related to the conduct of the trial**

The Committee requires administrative changes that impact on the conduct of a trial to be communicated to it as soon as practical. Examples of the trial documentation that must be provided include:

- Change of Principal Investigator
- Increase of enrolment number at Royal Adelaide Hospital from the originally approved number

## **Adverse events occurring at the local site**

The Research Ethics Committee requires **does not** require notification of an Adverse Event (AE) **unless** it is judged by the researcher to materially impact the continued ethical acceptability of the trial or indicates the need for a change to the trial protocol, including changed safety monitoring. This is in line with the requirements of ICH GCP.

*“4.10.2 The investigator should promptly provide written reports to the sponsor, the IRB/IEC (see 3.3.8) and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to subjects.” [Ref 1]*

## **Serious adverse events and serious adverse device events occurring at the local site**

The Research Ethics Committee requires notification of serious adverse events (SAEs) occurring at the local site within 72 hours. The events must be notified irrespective of whether they are judged to be drug related or not. Initial notification by email satisfies the time line but full details must be provided in due course. The details include:

- Patient or ID details - including Date of Birth, Age, Gender
- Initial or Follow-Up report
- Time of event
- Date of event
- Whether drug related, and name of drug
- Other contributing factor - ie, progressive disease, concurrent medication
- Type of event
- Category of event - ie, life-threatening, requiring prolonged hospitalisation, disability/incapacity, death, infection, etc.
- Description of event
- If SAE is treatment related, whether it is "expected"
- Drug details - names of all, dosings, time and dates of dosings, etc.
- Treatment
- Outcome

There is no prescribed form for reporting a SAE. SAE notifications are not acknowledged by the committee unless specifically requested.

*Note that if the event is drug-related and unexpected the Therapeutic Goods Administration guidelines place obligations on sponsoring organisations to notify TGA.*

The Committee also requires notification of serious adverse device events (SADEs) occurring at the local site within 72 hours. Initial notification by email satisfies the time line but full details must be provided in due course. Information provided should be as described for SAEs (see above).

*Note that if the event is unexpected (an unexpected adverse device events - UADE) the Therapeutic Goods Administration guidelines place obligations on sponsoring organisations to notify TGA.*

SAEs and SADEs are reviewed by the Chairperson of HREC who may refer them to the Chairperson of the IDSC if they impact on issues relating to drug safety. If the SAE or SADE warrants further action the Chairperson will communicate this to the researcher and provide a timeline for any remedial action that may be required. Remedial action may be a change in

procedures or information sheets, a requirement to notify subjects or suspension of recruitment to the trial. Any action will be reviewed following a response from the researcher.

### **Serious adverse events occurring at other sites**

The Research Ethics Committee requires does not require notification of an SAE at a site for which it is not providing monitoring unless it is judged by the local investigator to materially impact the continued ethical acceptability of the trial or indicates the need for a change to the trial protocol, including changed safety monitoring.

### **Other events affecting the conduct of a trial**

The Committee requires notification of any events occurring during the conduct of a trial which could reasonably be expected to reflect on the safety or ethical conduct of the trial at this site. Notification must occur with 72 hours. Examples of events that require notification include:

- Changes to the study status, such as suspension or hold, either in Australia or in an overseas country in which the same or closely related study is being conducted.
- Other communication from sponsors to researchers such as "Dear Investigator" letters.
- Deviations from informed consent process occurring
- Significant deviations from protocol
- Complaints related to study conduct

Events which have no immediate impact on the safety or ethical conduct of the trial may be reported in the annual report to the Committee. Examples of events that should be reported in the annual report include:

- Protocol deviations which do not impact safety or ethical conduct.
- Patient withdrawal of consent except where it is the result of a safety related concern or complaint (see above).
- Study recruitment closure

### **Changes to the Investigator Brochure**

For sponsored trials, the committee requires an updated Investigator's Brochure on an annual basis or more frequently where significant new findings related to the safety of the trial are discovered. The submission of the investigator's brochure from the sponsor should contain a listing of changes and an indication whether the sponsor considers that the new information has impacted on the safety or ethical nature of the trial.

The researcher must review the investigator's brochure and form his/her own view of whether the new information has impacted on the safety or ethical nature of the trial. The researcher must provide this information to the committee in the form of a covering letter.

The submission of the investigator's brochure is reviewed by the Chairperson of HREC who may refer it to the Chairperson of the IDSC if changes impact on issues relating to drug safety. If it is judged that the new information warrants further action the Chairperson will communicate this to the researcher and provide a timeline for any remedial action that may be required. Remedial action may be a change in procedures or information sheets, a requirement to notify subjects or suspension of recruitment to the trial. Any action will be reviewed following a response from the researcher.

### **Line listing of suspected unexpected serious adverse reactions (SUSARs) relating to the study drug(s) or devices.**

It is a requirement of the NHMRC Australian Health Ethics Committee (AHEC) position statement [Ref 2]**Error! Bookmark not defined.** that periodic listings provided by the sponsor are submitted to the HREC. The submission of the line listing from the sponsor should contain an indication of whether the sponsor considers that the new information has impacted on the safety or ethical nature of the trial.

The researcher must review the line listing and form his/her own view of whether the new information has impacted on the safety or ethical nature of the trial. The researcher must provide this information to the committee in the form of a covering letter.

The submission of the line listing is reviewed by the Chairperson of HREC who may refer it to the Chairperson of the IDSC if changes impact on issues relating to drug safety. If it is judged that the new information warrants further action the Chairperson will communicate this to the researcher and provide a timeline for any remedial action that may be required. Remedial action may be a change in procedures or information sheets, a requirement to notify subjects or suspension of recruitment to the trial. Any action will be reviewed following a response from the researcher.

## **Annual safety information (non-sponsored trials)**

For trials involving an intervention or the administration of a non-approved medicine, the researcher must provide to the committee a detailed listing of serious adverse events as for SUSARS provided for sponsored trials (see above). For non-interventional trials this information may be contained within the Annual Report (see below).

## **Annual report**

The researcher shall provide to the committee an Annual Review or Report of the study occurring at this site. The report shall contain the following information:

- Study Identification
- Principal Investigator identification
- Current Status of the Project (Complete/In Progress/Ceased/Not commenced)
- The occurrence of serious adverse events at this site
- The number of subjects entered into the trial
- The number of subjects withdrawn from the trial
- A brief description of the progress of the trial
- Identification of the person completing the form.

Annual reports are reviewed by the Chairperson of HREC and filed with study documentation.

## **Final study closure**

At the conclusion of a trial the researcher must notify the HREC of the site closure using the Annual Review form or similar.

## **Information that does not require submission**

- Publications
- Sponsor newsletters or recruitment updates

## **Revision history**

Version 1.0 M James May 2007

Version 1.1 A Thornton 19 February 2010

## **References**

- [1] NHMRC National Statement on Ethical Conduct in Human Research, 2007 Available at: [http://www.nhmrc.gov.au/health\\_ethics/hrecs/reference/\\_files/090609\\_nhmrc\\_position\\_statement.pdf](http://www.nhmrc.gov.au/health_ethics/hrecs/reference/_files/090609_nhmrc_position_statement.pdf).
- [2] NHMRC Australian Health Ethics Committee position statement: Monitoring and reporting of safety for clinical trials involving therapeutic products, May 2009. Available at: [http://www.nhmrc.gov.au/health\\_ethics/hrecs/reference/\\_files/090609\\_nhmrc\\_position\\_statement.pdf](http://www.nhmrc.gov.au/health_ethics/hrecs/reference/_files/090609_nhmrc_position_statement.pdf)

- [3] International Conference On Harmonisation Of Technical Requirements For Registration Of Pharmaceuticals For Human Use. Available at <http://ichgcp.net/>
- [4] Therapeutic Goods Administration. Access to Unapproved Therapeutic Goods – Clinical Trials in Australia – October 2004 available at <http://www.tga.gov.au/docs/pdf/unapproved/clintrials.pdf>