

CHAPTER 5

MONITORING OF HUMAN RESEARCH

Introduction

5.1 The Australian Defence Human Research Ethics Committee (ADHREC) will monitor over the life of the research protocol the conduct of Defence human research which has received ethical approval,

Protocol register

5.2 ADHREC maintains a register of all research protocols that have been submitted for consideration. This database is actively managed by the ADHREC secretariat and is used to monitor and report protocol status to the Committee at each meeting. A file is raised on each protocol submitted and this is stored securely in the Defence Health Services Division (DHSD). A unique ADHREC Protocol Number is also assigned to each protocol submitted. To facilitate monitoring and management of protocols, researchers must quote their ADHREC protocol number in all correspondence. Failure to do this may result in delays in processing correspondence or reports.

Progress reports

5.3 As a Human Research Ethics Committee (HREC), ADHREC is required to comply with the National Health and Medical Research Committee *National Statement on Ethical Conduct in Human Research* (NHMRC 2007). This involves monitoring the progress of the research protocols that ADHREC has cleared ethically to their completion. To this end, six-monthly progress reports are required from all researchers and are to be sent to the ADHREC secretariat. Reports are to include the following:

- a. a narrative describing the progress to date;
- b. any events of significance occurring in the conduct of the protocol, in particular any adverse outcomes;
- c. the outcomes of completed research;
- d. the maintenance and security of records;
- e. compliance with the approved protocol, including consent procedures and documentation;
- f. any amendments or modifications to the protocol; and
- g. compliance with any other special conditions that ADHREC may have required.

5.4 A reminder letter is sent to each researcher who has a progress report due in any particular month. ADHREC will continue to request progress reports until the researcher confirms that the project has been completed or abandoned, and a final report has been submitted.

5.5 Progress reports are presented to ADHREC at each meeting.

Deviations from an approved protocol

5.6 Any deviations from the approved protocol must be documented in regular progress reports. Any protocol deviations with real or potential ethical implications must be reported to the ADHREC secretariat on occurrence. The report should address the same items required for a report of serious adverse events (paragraph 5.7).

Reporting of serious adverse events

5.7 An adverse event (AE) is defined as any unfavorable or unintended sign, symptom or disease temporarily associated with the use of an investigational product, whether or not related to the investigational product (ICH 1.2 ¹). A serious adverse event (SAE) or reaction is any untoward medical occurrence occurring during a human research study that:

- a. is fatal,
- b. is life-threatening,
- c. requires or prolongs hospitalisation,
- d. is disabling or incapacitating, and/or
- e. is associated with congenital abnormality or a birth defect.

5.8 Other situations that require expedited reporting include pregnancy, important medical events which jeopardise the participants' condition and intervention to prevent one of the previously listed outcomes. Information on AEs and SAEs is available from NHMRC (and from the NHMRC website <www.nhmrc.gov.au>).

5.9 SAE are to be reported to the ADHREC Executive Secretary within 72 hours of occurrence. The report should address the following:

- a. the nature of the SAE, in plain English;
- b. the location at which the SAE occurred (i.e. at the research centre or elsewhere, specify site);
- c. the action taken by the researchers in response to the SAE including whether or not the project was suspended as a result;
- d. the outcome of the SAE;
- e. whether this type of SAE has been reported previously, during this study or during other studies;
- f. what background rate of this event would be expected in normal practice;
- g. state the possible relationship of the SAE to the study, or the study therapy as one of the following:
 - (1) probably related,
 - (2) suspected as related,
 - (3) unlikely to be related, or
 - (4) not related.
- h. if the SAE is likely to be related to the study or study therapy, address what the implications are for the continuation of the study, if any.

¹ International Conference on Harmonisation (ICH) Topic E6 (R1), Guideline for Good Clinical Practice (CPMP/ICH/135/95).

5.10 ADHREC may require that the research be suspended until such time that it is satisfied that it is safe to continue the trial.

5.11 All AEs are to be reported to ADHREC as part of the formal reporting process (i.e. as part of the progress reports) all adverse events are to be reported to ADHREC. Depending on the circumstances, this may take the form of a summary of events.

Final reports

5.12 A final report is required on completion or abandonment of a research project. The first page is to be a summary of the overall project such that it could be used for reporting purposes or to provide an overview to other stakeholders (e.g. clinical or health personnel). The summary should include:

- a. authors and affiliation,
- b. title,
- c. methodologies used,
- d. results, and
- e. outcomes and conclusions.

5.13 The remainder of the report should discuss in detail the points above and include a discussion in terms of any previously published literature with references. This could take the form of a clinical study report. The authors should indicate how the findings will be published and any manuscript prepared for publication should be included. Where an intention to publish has been provided as part of the initial researchers agreement, and that has not been met, the protocol will not be finalised by ADHREC until appropriate justification has been provided for the failure to publish. Copies of the summary and complete report are to be submitted to ADHREC.

5.14 Copies of any manuscripts for publication are to be submitted for review and approval in accordance with Chapter 6—'Manuscript review'. Note that manuscripts intended for publication must be cleared and approved for publication by the relevant Defence sponsor. The ADHREC secretariat will ensure this requirement is understood by researchers. When available, copies of published documents (such as a journal article) are to be forwarded to ADHREC and to the relevant Defence sponsor.

Overdue reports and withdrawal of ethical approval

5.15 If a progress report is not received by the due date, a further two reminder letters will be sent advising of the due date of the report and the consequences of failure to submit the report. There is a six month grace period between the progress report's due date and the withdrawal of ethical approval for the research protocol. Upon withdrawal of approval, the ADHREC secretariat will provide notification of withdrawal to the researcher, to the commanders responsible for Service members participating in the trial and to the Defence sponsor of the research.

Audits

5.16 As detailed in the National Statement, ADHREC may visit researchers at random and audit their study project documentation. It is therefore important that all written ADHREC approvals, information sheets, consent forms and any other study documentation be kept so that researchers can demonstrate adherence to the approved protocol.

Finalisation of files

5.17 ADHREC protocol files will be finalised when a research project is completed, abandoned, or withdrawn or when no correspondence has been received for 12 months. Finalisation means that the protocol is removed from the active protocol list and no further action is taken by the ADHREC secretariat regarding that file, unless contacted by the researcher. Researchers will be notified in writing when a file is finalised. If the researcher wishes to resume the project at a later date, the file can be reactivated. In the case of no correspondence having been received for 12 months, a

finalisation letter will be sent to the researcher at the last known address and a letter will be sent to the commander responsible for the study participants.

Researcher contact details

5.18 To facilitate the management of ADHREC protocols and correspondence, researchers are requested to ensure that they provide contact details to the Executive Secretary. Any change in contact details should be notified promptly. Wherever possible, an email address should be supplied since notices from ADHREC, such as details of upcoming meetings or events, are sent out by e-mail as well as by signal or other means.

5.19 During deliberations of submitted protocol applications, ADHREC may wish to contact researchers to clarify points of fact within a submission. It is therefore advisable that researchers provide a mobile telephone number or after hours telephone details to facilitate this.