PoCoG
Psycho-oncology Co-operative Research Group

Applying for ethical approval

SOP ID: SOP-Ethics-130304

SOP development and approval

SOP developed by	Date	Associated document(s)
Michelle Peate Research Program Manager	04/03/13	**SOP_5.3.1-Ethics-130304-NEAF_FAQ**
Michelle Peate Research Program Manager	04/03/13	**SOP_5.3.2-Ethics-130304-HREC_Submission_Checklist**
Michelle Peate Research Program Manager	22/02/13	**SOP_5.3.3-Ethics-130222-Safety_Report_Letter_Template**
Michelle Peate Research Program Manager	22/02/13	**SOP_5.3.4-Ethics-130222-Annual_Report**
Michelle Peate Research Program Manager	20/02/13	**SOP_5.3.5-Ethics-130220-SAE_Report**
Michelle Peate Research Program Manager	22/02/13	**SOP_5.3.6-Ethics-130222-HREC_Cover_Letter_Template**
Michelle Peate Research Program Manager	04/03/13	**SOP_5.3.7-Ethics-130304-Protocol_Amendment_Template**

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Foreword

The Psycho-Oncology Cooperative Research Group (PoGoG) has developed a program of quality assurance for Psycho-Oncology Research. PoCoG's Quality Assurance Process requires documentation of both management and procedural activities. This guidance document provides a standard working tool for applying for ethical approval.

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Table of Contents

Overview

The primary responsibility of Human Research Ethics Committees (HRECs) is to protect the rights and welfare of research participants. National regulations require that the HRECs ensure that criteria for approval of research are met prior to approving a study. The Principal Investigator must provide the HREC with the information necessary to permit an informed decision on whether to approve, reject or require modifications to the protocol prior to approval.

Additionally, the principal investigator must agree to inform the HREC of any changes to the study protocol and any materials used to recruit subjects, as well as any additional risks to subjects associated with the study, adverse events and study progress.

This document describes the procedure for applying to an Australian HREC for ethical approval. The information provided here is a summary, and is based on information available at the time of writing. Due to regular changes in the ethical review process, it is recommended that the researcher contact the HREC research office at the institution they are seeking approval from for the most recent advice and guidance.

Purpose

The purpose of this SOP is to describe the procedure for submitting a psycho-oncology study, to an Australian HREC for review and approval. It is the responsibility of the Principal Investigator to ensure that all required study information is supplied to the HREC. The HREC is ultimately responsible for the rights and welfare of research participants and approval of a study to commence at an investigational site. The HREC review and approval is a demonstration that key criteria as outlined in the NHMRC National Statement on Ethical Conduct in Human Research are met and International Conference on Harmonisation Good Clinical Practice (ICH-GCP) guidelines and adhered to.

Scope

This SOP applies to all interactions by research staff with the HREC in regard to the submission of a study in order to gain full ethical approval to conduct the study and the continued interactions throughout the duration of the study.

Guiding Principles

Local national and state regulations must be adhered to when seeking approval to conduct a study. Individual HREC and institutional guidelines and procedures must be followed when making an application for approval of a study. A study site cannot start recruiting to the study without the written approval of an appropriate HREC and site governance approval. All documents and materials used in recruiting potential research participants, participant information sheet and consent forms, study questionnaires interview questions, recruitment advertisements, letters of invitation and study

correspondence to participants will require approval by the HREC. Further correspondence with the HREC will be required during the course of a study including: protocol amendments, reporting of updated safety information, serious adverse events (SAE), annual reports regarding study progress and final study report. All documentation relating to Ethical approval including submission documents, correspondence, notifications and reports must be retained.

Research studies should be conducted in accordance with applicable legislation and regulatory standards. Thus, this document has been guided by the following resources:

- the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (henceforth referred to as the 'national statement', http://www.nhmrc.gov.au/publications/synopses/e35syn.htm),
- The Australian Code for the Responsible Conduct of Research (http://www.nhmrc.gov.au/publications/synopses/r39syn.htm),
- Therapeutic Goods Administration's Australian Clinical Trial Handbook (http://www.tga.gov.au/industry/clinical-trials-handbook.htm), and
- Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/index.html).
- International Conference on Harmonisation documentation on Good Clinical Practice (ICH-GCP, http://www.ich.org/home.html) and the Therapeutic Goods Administration (TGA) annotated version (http://www.tga.gov.au/industry/clinical-trials-note-ich13595.htm).

Definitions and Abbreviations

Consent Form (CF)	The form which participants sign to indicate their consent to be involved in the study.
Good Clinical Practice (GCP)	An international quality standard that is provided by the International Conference on Harmonisation (ICH). GCP guidelines include protection of human rights as a subject in studies and provide assurances of the safety and efficacy of the newly developed interventions. GCP includes standards on study conduct and the roles and responsibilities of sponsors, investigators, and monitors.
Human Research Ethics Committee (HREC)	HRECs are responsible for the ethical review of research studies involving humans.
Informed Consent	A process by which a person voluntarily confirms their willingness to participate in a particular study, after having been informed of all aspects of the study that are relevant to the person's decision to participate. Informed consent is usually documented by means of a written, signed, and dated participant consent form. However, recorded verbal consent or completion of a questionnaire can be considered acceptable (explicit or implied) if approved by the Human Research Ethics Committee.

International Conference on Harmonisation (ICH)	An international body that defines standards, which governments can transpose into regulations for clinical trials involving human subjects.
Investigator Brochure (IB)	The Investigator's Brochure (IB) is a comprehensive document summarizing the known safety information about an investigational product (i.e. intervention) obtained during a study. The IB is a document of critical importance throughout the intervention development process and is updated with new information as it becomes available. It is intended to provide the investigator with insights necessary for management of study conduct and study subjects throughout a study. It may include details about currently known safety information from in vivo and in vitro preclinical studies and earlier phase research studies, it lists known AEs and current dosage information – so provide site investigators a clear understanding of the possible risks and adverse reactions and of the specific tests, observations, and precautions that may be required.
National Ethics Application Form (NEAF)	A web-based tool developed for submitting research ethics proposals to Human Research Ethics Committees (HRECs). I
National Health & Medicines Research Council (NHMRC)	The NHMRC is Australia's peak body for supporting health and medical research; for developing health advice for the Australian community, health professionals and governments; and for providing advice on ethical behaviour in health care and in the conduct of health and medical research.
Participant Information Sheet (PIS)	An information sheet that outlines the study and the risk, benefits, and obligations of the participant. Also referred to as Plain Language Statement, patient information statement, information for patients, etc.
Principal Investigator (PI)	The investigator responsible for the co-ordination of Chief Investigators and Site Investigators in a multicentre study. Often the Principal Investigator is also Chief Investigator A (CIA) on grant and ethics applications and will lead the Management Committee. Also: Coordinating Investigator.
Protocol	A protocol describes the background, justification, objective(s), design, methodology, statistical considerations, organisation of the study, study duration, and a timeline on which the study is based. This includes the details of eligibility and informed consent, schedule of procedures including adverse event reporting, the calculation of results and reporting standards (including a detailed statistical analysis plan). A protocol provides a common reference document for study investigators, administrators and site staff, detailing individual duties and responsibilities throughout the duration of the study. A protocol enables the research to be undertaken at multiple recruitment sites in a consistent manner which complies with the study methods and requirements. This also provides a document that will enable other researchers to precisely replicate the study.

Protocol Amendment	A written description of a change(s) to or formal clarification of a protocol.
Serious Adverse Event (SAE)	Any event that suggests a significant hazard, contraindication, side effect, or precaution, that may jeopardize the patient, whether or not it is considered to be associated with the intervention, is a SAE.
Sponsor	Government agencies, private organizations, and/or individual researchers who are seeking ways to improve the health of people living with chronic and life-threatening illnesses by sponsoring research studies.
Therapeutic Goods Administration (TGA)	The TGA is Australia's regulatory authority for therapeutic goods. They carry out a range of assessment and monitoring activities to ensure therapeutic goods available in Australia are of an acceptable standard with the aim of ensuring that the Australian community has access, within a reasonable time, to therapeutic advances.

Qualifications and Responsibilities

This SOP applies to those members of the study team involved in communicating with the HREC to ensure appropriate management of all research study activities. This includes the following:

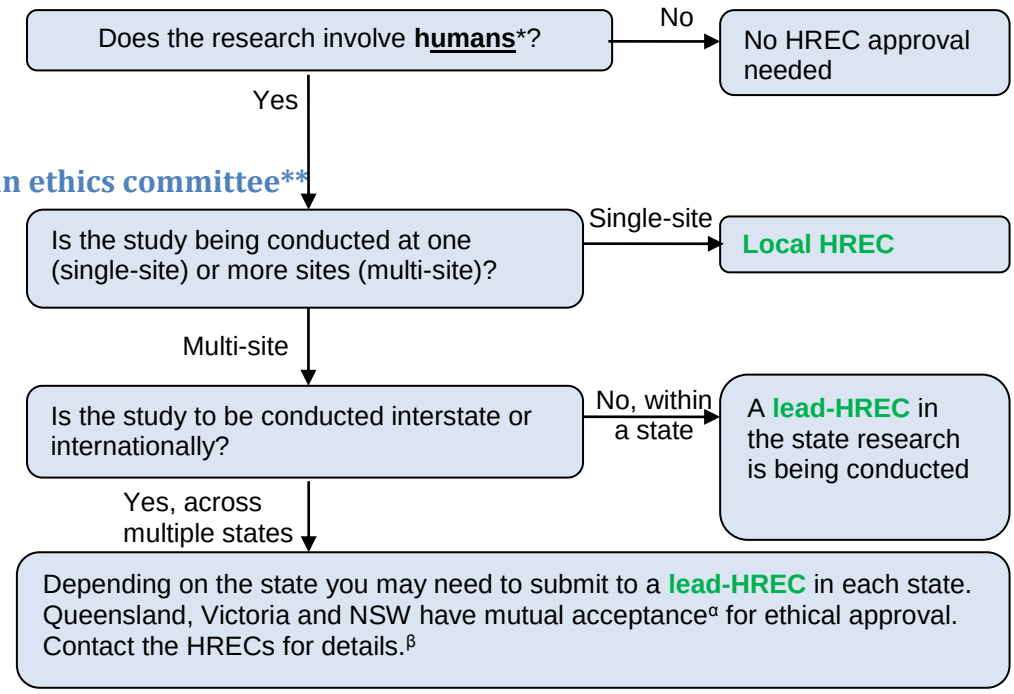
- Principal Investigator
- Co-Investigator
- Research Study/Clinical Trials Manager
- Research Study/Clinical Trials Coordinator
- Research Assistant/Project Officer/Support staff

It is the responsibility of the PI to ensure that approval has been sought prior to the commencement of the study at each site.

1. Procedure(s)

1.1. Before the start of a study

Step 1: Determine if ethical review is required



*Other research that will require submission to an ethics committee includes research on human derived materials, vertebrate animals, genetically modified organisms (GMOs), or biohazardous agents

**In all instances check that the HREC is duly constituted and compliant with the NHMRC Statement.

α Mutual acceptance is the agreement between Departments/ Ministries of Health to accept ethical and scientific review of multicentre studies in public hospitals from a lead ethics committee across the different states.

βA national initiative, the Harmonisation of Multi-Centre Ethical Review (HoMER), is being developed by the NHMRC to enable the recognition of a single ethical and scientific review of multi-centre human research within and/or across Australian jurisdictions.

Step 3: Contact the HREC to obtain appropriate instructions and forms

There are two types of human research ethics applications which require different documentation, one for standard risk and one for low and negligible risk studies. Most studies involving humans (or a patient population) will require the standard risk application, but if in doubt clarify with the HREC before proceeding.

Generally, HRECs will accept submissions on the web-based National Ethics Application Form (NEAF). This form can be obtained from the NHMRC (www.neaf.gov.au) or the NSW, QLD or Victorian state health systems site (www.ethicsform.org/au). The state health systems form allows data to be imported into the Australian Research Ethics Database and is used by HRECs to track and manage the progress of applications. For national submissions create your application in www.neaf.gov.au (this can be imported into the www.ethicsform.org/au directly if needed).

Step 4: Prepare forms and documents

An application needs to be prepared in line with the requirements of the specific HREC. Documentation submitted should include at a minimum the following:

- HREC application form (i.e. the NEAF, single site application or low risk form)
- Study Protocol
- Participant Information Sheet and Consent Form
- Any other documentation to be provided to participants (advertisement, letters of invitation to the study, diary cards, instructions, questionnaires, interview questions)
- Investigator Brochure (if applicable). Please note that any forms that are not completed by participants (such as recruitment forms) do not need to be submitted to the HREC if the details of the data collected are listed in the protocol.
- Regulatory Approval documentation (if applicable). If the study involves the use of an item in a manner that it has not been previously approved, a notification of intent to supply unapproved therapeutic goods under the clinical trial notification (CTN) scheme to the Therapeutic Goods Administration (TGA) is required. For example, a study evaluating the psychosocial impact of an intervention to improve sexual dysfunction in women with breast cancer required CTN approval to use olive oil as a lubricant, as the use of olive oil as a lubricant had not been previously approved.

All documents should be easily identifiable by the ethics application number, version number and/or date. The Principal Investigator should be listed as the applicant. Submit the application for the next scheduled meeting.

Using the NEAF:
Refer to Attachment 5.3.1 for examples of how to address specific questions on the NEAF**.**

If the study will be conducted at more than one site, **Site Specific Assessment (SSA)** forms (also available from the NEAF websites) need to be completed for each site and submitted, once the lead HREC has approved the NEAF, for local governance approval for individual site.

Participant Information Sheet (PIS) and Consent Forms:
Most HRECs will have templates of the Participant Information Sheet and Consent Form containing information that they require. This will generally address the following:

- What is the purpose of this study?
- Why have I been invited to participate in this study?
- What if I don't want to take part in this study, or if I want to withdraw later?
- What does this study involve?
- How is this study being paid for?
- Are there risks to me in taking part in this study?
- What happens if I suffer injury or complications as a result of the study?
- Will I benefit from the study?
- Will taking part in this study cost me anything, and will I be paid?
- How will my confidentiality be protected?
- What happens with the results?
- What happens to my treatment when the study is finished?
- What to do if you want to discuss this study further before deciding?
- Who to contact regarding concerns about the conduct of this study?

In Australia, research involving human subjects is covered by the National Statement on Ethical Conduct in Human Research, which recognises the value of making data available for future research. Although currently not necessary, it is recommended that you consider including in the PIS the possibility of the data collected for this study may have the potential to be used for future research. The PIS should clearly state if further ethical approval will be sought prior to the data being used for future research and include an option for participants to opt-out of this option.

For PoCoG administered studies:
PoCoG's Executive Director and Research Program Manager need to be listed on the application as having access to the study data.

Step 5: Approval process

There are three possible responses from the HRECs:

1. *Approval granted* – In this case SSA applications can be submitted to sites to obtain local governance approval. Once SSA approval is granted, each should be given a copy of the full HREC approval, protocol and approved participant information sheet and consent form prior to commencing.
2. *Conditional approval* - In the event that the HREC approval is granted conditionally, re-submission of the relevant study documentation, with appropriate responses, should comply with the local guidelines and procedures of the HREC.
3. *Approval not granted* – Where HREC approval is not granted, the study cannot be implemented at the site. All documentation relating to the rejection of the study must be retained in the study file.

Hints and tips

It is important to recognise that ethics committees do not review your application with the view to reject your submission. Their role is to review the study for ethical rigour to ensure that any risk to both the participant and the researchers is minimised. This includes reviewing the study for scientific rigour and feasibility, as conducting a poorly designed study that is unlikely to be completed is unethical. Ultimately, the aim is to facilitate research and encourage researchers to consider the implications of the study.

The process of ethical review can be streamlined by:

- ***Having a comprehensive study protocol*** – though there is often an official ethics application form to be completed, such as the NEAF, all the information that the HREC requires should be contained in the protocol as that is where they will go to get the information. It is recommended that a protocol is developed first and the application form populated from the protocol.
- ***Making it very clear what aspect of the research approval is being sought***. It may seem obvious, but it is worthwhile having a clear statement in the cover letter of what you are asking of the HREC.
- ***Clarifying why identifiable information is needed***. One of the main ethical concerns is the identifiable nature of data. Items, such as date of birth, names, and address are risks to participant confidentiality and thus the collection of this information needs to be justified. Where possible participant information should be stored in a de-identified form.
- ***Each application should be personalised***. DO NOT simply copy information from another application. Ensure that the answer used for each question relates to the research being submitted. For instance, it will be very obvious to the HREC

that the ethical implications have not been seriously considered for a state based study if the response to the question refers to national data collection.

1.2. During the course of the study

As a condition of approval, the Principal Investigator is responsible for reporting serious adverse events (SAEs) within the time frame stipulated by the HREC and for providing annual progress reports.

Additional submissions to the HREC may be required during the course of the study (changes must be identifiable by versioning). These may be in the form of:

Study Protocol Amendments

Any protocol amendment must be submitted as per HREC guidelines and procedures. Protocol amendments cannot be implemented until written approval has been received from the HREC, except in the case where participant safety is at risk.

Updates to Participant Information Sheets (PIS) and Consent Forms (CF)

Any amendment required to the PIS/CF for a study must be submitted as per HREC guidelines and procedures. Amended PIS/CF cannot be implemented until written approval has been received from the HREC, except in cases where participant safety is at risk.

Updated Investigator Brochures, advertising material, or any other documents to be provided to study participants

Any updated documents must be submitted to the HREC during the course of the study in line with the HREC guidelines and procedures.

Updated safety information

Updated safety information, including Serious Adverse Event reports (SAE) and safety reports, must be submitted to the HREC in line with HREC guidelines and procedures. A SAE is an event that results in:

- Hospitalisation/prolongation of hospitalisation
- Death/congenital abnormality
- Life threatening/medically important
- Persistent disability

Annual reports on study progress

Annual reports must be submitted to the HREC in line with the HREC guidelines and procedures. These reports represent a summary of the status of the study for the HREC.

Administrative changes

The HREC should be notified of any administrative changes in the conduct of the study or personnel, where applicable.

1.3. At the end of the study

On completion of the study, the HREC is to be notified and a summary of the study and outcomes submitted, as per HREC guidelines and procedures. In cases of premature termination or suspension of the study, the HREC should be notified of the reasons for termination/suspension. A summary of any results should also be submitted to the HREC.

Ensure all documentation relating to ethical review and approval including HREC submission documents, approvals/rejections, correspondence, updates and reports are filed appropriately in the main study file as they are received/ completed.

2. Records management

Documentation of the ethical approval process is important. It is the responsibility of the study coordinating centre and the Principal Investigator to ensure that all the approvals, notifications, and documentation required are obtained and filed.

3. Quality Assurance (QA) - templates, forms and checklists

3.1. Going through the NEAF – FAQs and suggested responses.

This is a comprehensive document that goes through the NEAF and provides guidance on interpretation of questions and gives examples of responses.

3.2. HREC Submission Checklist

A checklist of items needed for submission of the ethics application to the HREC.

3.3. Safety Report Letter Template

In the event of an adverse event, this template can be used to notify the HREC.

3.4. Annual Report Template

This template can be used for HREC reporting, where the HREC does not have an existing template.

3.5. SAE Report Template

A SAE report template to be used where the HREC does not have an existing template.

3.6. HREC Cover Letter Template

This template can be used as a cover letter for HREC ethics submissions.

3.7. Protocol Amendment Template

This template can be used for submitting amendments to HREC, where the HREC does not have an existing template.

4. Useful resources

http://www.health.qld.gov.au/ohmr/documents/regu/rsrch_guide_inves.pdf
https://www.neaf.gov.au