Government of South Australia
SA Health

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PROCEDURE: GUIDELINES FOR AN ETHICS APPLICATION – COMMITTEE REVIEW

Studies Requiring Full Ethical Review

Studies involving more than low or negligible risk to a participant must be reviewed by a committee process. The NHMRC National Statement on Ethical Conduct in Human Research [Ref 1] defines low and negligible risk in Section 2.1.6 and 2.1.7 as follows:

- *"Research is 'low risk' where the only foreseeable risk is one of discomfort. Where the risk, even if unlikely, is more serious than discomfort, the research is not low risk.*
- *Research is 'negligible risk' where there is no foreseeable risk of harm or discomfort; and any foreseeable risk is no more than inconvenience. Where the risk, even if unlikely, is more than inconvenience, the research is not negligible risk."*

"Risks include not only physical risks, but also psychological, spiritual and social harm or distress (e.g. stigmatisation or discrimination) and may involve people associated with participants." [Ref 2]

The NHMRC National Statement requires that certain types of research must always be reviewed through a full committee process irrespective of the perceived level of risk. These are:

- Research which involves allocation to one or more experimental treatments (NS3.3).
- Research which includes an evaluation of germline genetic information (NS 3.5).
- Women who are pregnant and the human foetus (NS 4.1).
- Research which requires third party consent. (NS4.4).
- Research in people highly dependent on medical care (NS 4.4).
- Research that is intended to study or expose illegal activity (NS 4.6).
- Research in Aboriginal and Torres Strait Islander people (NS 4.7).

The following sections describe the submission documents[1] which are required for consideration by the committee. If the research is subsequently deemed to be low risk the Chairman may perform the review using an expedited process.

Cover Letter – Investigator Statement

Each submission requires a cover letter from the investigator which provides a rationale for the proposed study. The cover letter should also contain a complete list of all documents which are submitted for approval. The documents should be decribed by exact title, version number and date. The cover letter should include a statement from the investigator which addresses the following issues:

- What is the current standard treatment or process for this patient population at the Royal Adelaide Hospital?
- What are the overall benefits to the study participant or to the field?
- Are there any risks to the study participant?
- Are there any other trials in the unit which recruit a similar participant population? If so, how will it be determined as to which study the participant will be recruited into?

Study Protocol

The protocol is the document used to describe the proposed study. The study protocol provides a narrative by which the ethics committee can understand the purpose and the conduct of the research. It also provides the definitive document of study procedures and principles. It should accurately describe all the procedures and discuss any ethical issues associated with the study. Sample headings for a protocol are provided in Appendix 1. The NEAF form is not suitable for this purpose and is not an alternative to the protocol.

[1] For studies requiring committee review a single hard copy of all documents is required. An electronic copy of all documents must also be submitted by email or through the on-line forms website. All electronic documents should be in MS-Word or searchable PDF format. Scanned PDF documents are undesirable. Each document should be clearly labelled and given a version number and revision date. The version number, revision date, page number and total number of pages of each document should be included in the document footer.

Participant Information Sheet

The HREC requires an Information Sheet to be given to potential research subjects to assist them in their decision about involvement. The RAH HREC encourages the use of the NHMRC endorsed Information Sheet Templates [Ref 3]. A simplified template derived from the NHMRC documents is shown in Appendix 2.

The Information sheet is only one aspect of providing information so that people may come to informed decisions about their involvement in research. It must not replace personal communication between the investigator and the potential subject. The investigator should ensure that the potential subject has the mental capacity and English comprehension necessary and is given sufficient time to consider the verbal and written information provided, and to discuss it with other people, before being asked to give consent to involvement. The Information Sheet should use simple language with minimal technical terminology or jargon. It should be brief but thorough and avoid repetition. The sheet must be translated if non-English speaking subjects are to be recruited. The Information Sheet is to remain the property of the subject and a copy of the signed Consent Form should also be provided on request.

The Information Sheet should have numbered pages and a version number and date in the footer and should be on appropriate departmental letterhead.

Consent Form

The Consent Form is the document to be signed by participants and researchers to record their agreement to participate in the study. The Consent Form must be signed before any study-related procdures are conducted. Where the participant is unable to provide informed consent, an appropriate third party (usually next of kin) may sign the consent. The form should be specifically configured for third party consent. It is not necessary for the Consent Form to repeat information contained in the Participant Information Sheet. Signatures should, where possible, be on the same page as the text. The preferred content for the Consent Form is shown in Appendix 3.

Submission Documents for Drug Studies

Studies of investigational drugs are reviewed by the Investigational Drugs Subcommittee of the Royal Adelaide Hospital Research Ethics Committee. For a drug study the following additional documents are required.

- Investigational Drugs Subcommittee Checklist – PART A (One form for each drug)
- Investigational Drugs Subcommittee Checklist – PART B
- Up-to-date Investigator's Brochure (less than 12 months old) and any other relevant material (e.g. FDA or TGA submission) which gives a full pharmacological description of the investigational drug and its use in the proposed condition. Note that this material must include a full description of pre-clinical and clinical toxicology.
- Completed IDSC Invoicing Details Form.
- Completed TGA CTN document printed on blue paper (if applicable).

Submission Documents for Device Studies

For a study of an investigational device the following additional documents are required.

- Investigational Drugs Subcommittee Checklist – PART A (One form)
- Investigational Drugs Subcommittee Checklist – PART B
- For approved devices.- ARTG Compliance documents
- For non-approved devices - up-to-date Investigator's Brochure or equivalent (less than 12 months old) and any other relevant material.
- Completed IDSC Invoicing Details Form.
- Completed TGA CTN document printed on blue paper (if applicable).

Other documents

Other documents which may be required and must be submitted include:

- Recruitment materials
- Questionnaires
- Patient Diaries and Instructions
- Patient Wallett Card
- Advertisements or radio scripts including web-site advertising
- Radiation Safety Reports (if any exposure to ionizing radiation outside of standard of care)
- Environmental Protection Agency (EPA) Notification Form

Signatures and approvals

Confirmation that the study has been discussed and approved by the department in which you work and the Royal Adelaide Hospital or CALHN is primarily a Research Governance responsibility. However, it would be expected that the ethics submission has been discussed with senior people with delegated authority to approve the conduct of the research. These may be heads of Department, Clinical or Nursing Directors or Allied Health Directors. Ethics approval may require a letter or email to confirm that the research has been discussed and agreed by these people.

Submission Process

The submission of a committee study must be made through the on-line forms website using the NEAF form. The Site Specific Assessment (SSA) process is linked to the on-line ethics submission. If you have not submitted a research study for ethical approval previously it is highly recommended that you consult with the Research Ethics Office prior to submission. This can save much time and effort. The office is attended during working hours. Contact is by phone 8222-4139 or email rah.ethics@health.sa.gov.au

To submit through on-line forms:

- Go to the on-line forms website at www.ethicsform.org/au
- Create your personal account or log in to an existing account
- Create a new project or import a form provided to you by a collaborator
- Select “South Australia”
- Select “NEAF”
- Complete the relevant sections
- Upload any supporting documents
- Complete the “submission” and obtain a submission code which is a code similar to AU/1/A?????
- Email the Ethics Office to advise of the submission code
- Note that the SSA submission may also be completed on-line through the SSA tab.

Submission must be made by the prescribed date which is three weeks before the HREC meeting for a drug study and two weeks before the HREC meeting for a device or non-drug study. A list of submission dates is available on the Ethics Committee website at http://www.rah.sa.gov.au/rec/downloads/REC_Dates_2014.pdf

Scope of Approval

Within SA Health Public Hospitals an ethics review conducted by one ethics committee is accepted by other ethics committees without further review. Before research can commence at any SA Health site Research Governance approval must be obtained.

National Mutual Acceptance Ethical Review Model

SA Health has signed a Memorandum of Understanding to support a national system of streamlined ethical review of clinical trials across participating public health organisations (National Mutual Acceptance).

Under this system, a NHMRC certified HREC provides the single ethical and scientific review of a multi-centre clinical trial application. The RAH HREC was certified to undertake this review on 27 August 2012.

The principles of operation are contained within the Standard Principles for Operation. In brief:

- The NMA applies only to South Australia, Queensland, New South Wales and Victoria.
- The NMA applies only to clinical trials of a drug or device.
- The NMA applies only to research first reviewed on or after 1 November 2013.
- The research is reviewed according to the coordinating HRECs standard policies and procedures.
- Every research project which is to be conducted at one or more sites covered by NMA will be ethically and scientifically reviewed once only by a certified committee.
- The review will be accepted by all other health institutions covered by NMA.
- Public health institutions within South Australia accept reviews only from other public health HRECs – this excludes privately run ethics committees.
- Approval from the Aboriginal Health Research Ethics Committee (AHREC), South Australia, will be required where is required where the research involves ATSIC persons.
- All studies must be submitted on the National Ethics Application Form (NEAF).
- All studies must be recorded on the AU-RED database.
- Before commencement all research must undergo a site specific assessment process at each institution which intends to conduct the research.

Further information about the National Mutual Acceptance scheme is available at the RAH HREC website http://www.rah.sa.gov.au/rec/index.php

Appendix 1 Sample Protocol

1. TITLE (Full title of project)

2. INVESTIGATOR DETAILS AND QUALIFICATIONS

Contact details (location, phone numbers, email) and addresses for correspondence.

3. PURPOSE OF STUDY (general) and AIMS (specific)

4. BACKGROUND AND PRELIMINARY STUDIES (if any)

5. PARTICIPANTS

Selection, Inclusion, Exclusion and Withdrawal Criteria.
How will participants be recruited?
Note: For RAH patients, the initial contact should come from their treating clinician, or someone who was responsible for their care at the RAH.

6. STUDY PLAN AND DESIGN

A clear description of procedures to be performed on patients or volunteers and an indication of whether the procedure is part of normal diagnosis and treatment.

7. OUTCOMES

How will the outcomes of the study be evaluated?
Can the aims be realized?

8. ETHICAL CONSIDERATIONS

Issues which may need special consideration by the committee. This might include possible risks, pain or discomfort and issues of informed consent. Please refer to the NHMRC National Statement on Ethical Conduct in Human Research (available at www.nhmrc.gov.au).

9. SPECIFIC SAFETY CONSIDERATIONS (eg. Radiation, toxicity)

Radiation risks outlined in the **Code of Practice** from the Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) must be followed for all Exposure of Humans to Ionizing Radiation for Research Purposes. (Available at *www.arpansa.gov.au/Publications/codes/rps8.cfm*

The following should be detailed:-

- Why the participants are exposed to ionizing radiation.
- The number of participants to be exposed.
- The precautions to be taken to keep exposure to a minimum

The exposure to radiation needs to be addressed with a formal **Radiation Safety Report** from the RAH Radiation Safety Officer (Peter Collins – contact ext 25478).

You are also required to complete a '**Notification**' form for the REC to submit to the SA Government EPA Radiation Protection Division. An electronic copy is available on RAH Intranet or Internet.

It is the responsibility of the investigator to address the dose constraints for research participants (e.g. no more than 5mSv / year and no more than 10mSv in 5 years).

10. DRUGS/DEVICES

Including the approval status of and detailed information on investigational drugs or devices, if applicable. For studies with investigational drugs or devices or drugs or devices used outside their stated indication complete a CTN drug/device form, and an Invoice Details Form *(Appendix B)*, if applicable.

For all approved clinical trials, it is a HREC condition that it is registered in a publicly accessible trials registry prior to enrolment of the first participant. This is the responsibility of the investigator.

11. ANALYSIS AND REPORTING OF RESULTS

A copy of your datasheet, questionnaire or other relevant material must be provided.
Specify:

- How will data be collected and recorded?
- Who will have access to the research data and results?
- How will the recorded data be stored.
- Who will own the data and results of your research?

12. REFERENCES

13. OTHER RELEVANT INFORMATION

Advertising, Publishing.

14. OTHER ETHICS COMMITTEES TO WHICH THE PROTOCOL HAS BEEN SUBMITTED.

Please give current status, and date of approval.
If using another Institution's format for your protocol, please ensure all of the REC required details are included, and amend to be RAH specific with RAH contact details.

15. DATE OF PROPOSED COMMENCEMENT AND DURATION.

16. SIGNATURES OF INVESTIGATORS

The Principal Investigator to confirm that the protocol has been read and endorsed.
The signatures may be in a covering letter or at the end of the Protocol.

Appendix 2 - Sample Information Sheet

1. The following items will usually be included:-

(i) Purpose of the study.

(ii) If possible benefits from the study, to the subject and/or the Community are outlined, a statement indicating that these benefits are by no means assured.

(iii) All procedures that involve the subject, including the use of drugs or radioisotopes.

(iv) Alternative procedures or treatments for patients, if they elect not to enter the study.

2. The following statements must be included at an appropriate place:

(i) This is a research project and you do not have to be involved. If you do not wish to participate, your medical care will not be affected in any way. Also, you may withdraw from the project at any time after you have commenced.

(include this at or near the beginning of the information sheet).

(ii) Compliance with NHMRC National Statement.

The research will be conducted according to the NHMRC National Statement on Ethical Conduct in Human Research, 2007.

(include this at or near the end of the information sheet).

(iii) Chairperson statement and phone number.

If you wish to speak to someone not directly involved in the study about your rights as a volunteer, or about the conduct of the study, you may also contact the Chairperson, Research Ethics Committee, Royal Adelaide Hospital on 8222 4139.

(include this at or near the end of the information sheet).

3. The following issues must be addressed at an appropriate place:

(i) Foreseeable risks, side effects, discomforts, inconveniences and restrictions, both immediate and late (especially after leaving hospital) that will be involved, eg. travel, absence from work.

(ii) A comparison of the likelihood and probability of adverse effects from other procedures (or drugs) used for the same purpose.

(iii) An explanation that random allocation and/or placebos may be used (where relevant).

(iv) Assurances of confidentiality.

(v) Measures that will be taken in case of an adverse event.

(vi) The name and telephone numbers (work and after hours) of all members of the research group who can be contacted if any problems arise.

4. Radiation risks

In protocols that involve the use of Radiation, there needs to be information about the extra radiation, using the examples of wording contained in the *Code of Practice for Exposure of Humans to Ionizing Radiation for Research Purposes, 2005 – Annex 2*, according to the dose of radiation (*www.arpansa.gov.au/Publications/codes/rps8.cfm*)

5. Drugs

In protocols involving significant drug therapy or devices the following information should be included.

(i) name of medicine(s) / device - generic mandatory, trade name(s) if necessary to study design.

(ii) conditions in which the medicine/device should not be taken - e.g pregnancy.

(iii) whether the drug/device is meant to treat the disease or to relieve symptoms and therefore how important it is to take the medicine.

(iv) how to tell if the medicine/device is working and what to do if it appears not to be working.

(v) when, how and how long to take the medicine/device, before or after meals etc.

(vi) what to do if a dose is missed and the implications of ceasing the medicine/device use for any length of time.

(vii) important side-effects and what to do about them, including effects on driving, work etc.

(viii) interactions with alcohol and other drugs (generic and trade names).

(ix) storage and disposal of medicines/devices.

Appendix 3 Sample Consent Form

On Appropriate Departmental and Health Unit Letterhead

PROTOCOL NAME: _____

INVESTIGATORS: _____

1. The nature and purpose of the research project has been explained to me. I understand it, and agree to take part.

2. I understand that I may/will not benefit from taking part in the trial.*

3. I understand that, while information gained during the study may be published, I will not be identified and my personal results will remain confidential.

4. I understand that I can withdraw from the study at any stage and that this will not affect my medical care, now or in the future.

5. ** I understand that I should not become pregnant during the course of this trial. In the event of a pregnancy occurring, I agree to notify the investigator as soon as is practically possible.

6. *** I understand the statement concerning payment to me for taking part in this study, which is contained in the Information Sheet.

7. **** I have not been a volunteer in any other research projects which have involved radiation exposure in the last twelve months.

8. I have had the opportunity to discuss taking part in this investigation with a family member or friend.

Name of Subject:

Signed: _____

Dated: _____

I certify that I have explained the study to the patient/volunteer and consider that he/she understands what is involved.

Signed: _____

Dated: _____
(Investigator)

* If there is no chance of benefit to a participant, eg mechanistic studies, clause 2 should say "will not benefit".

** The pregnancy clause should be adjusted to the requirements of the study, eg "I should not be pregnant…" or "I should not become pregnant…". If a male should not father a child, please include this statement separately. If not applicable delete.

*** Investigators are responsible for including an appropriate statement regarding payments to subjects on the information sheet. If not applicable delete.

**** For protocols involving radiation exposure to volunteers. If not applicable delete

For third party consent, customise all statements to refer to the participant and include a statement "I undertake to inform my relative/friend that they have been enrolled in this study as soon as they are able to understand".

References

1 National Statement on Ethical Conduct in Human Research. NHMRC 2007 available at https://www.nhmrc.gov.au/guidelines/publications/e72

2 Ethical Considerations in Quality Assurance and Evaluation Activities NHMRC 2014 available at http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/e111_ethical_considerations_in_quality_assurance_140326.pdf

3 Standardised Participant Information and Consent Forms available at http://hrep.nhmrc.gov.au/toolbox/standardised-forms

Revision history

Version 4 M James September 2008
Version 5 A Thornton September 2009
Version 5.1 A Thornton 20 July 2010
Version 6 A Thornton 1 July 2012
Version 7.0 A Thornton 5 October 2014 (rewritten – no tracked changes)