Royal Adelaide Hospital

Investigational Drugs Subcommittee (IDSC) Guidelines

For submission of drug related protocols
Version 9.4 – February 2012

Government of South Australia
SA Health

ROYAL ADELAIDE HOSPITAL
INVESTIGATIONAL DRUGS SUBCOMMITTEE GUIDELINES FOR SUBMISSION OF DRUG RELATED PROTOCOLS

CONTENTS

CONTENTS (Cont.)

PAGE

APPENDICES

1. INTRODUCTION

In order to conduct a research study that involves the use of **any drug** (even if the drug has received marketing approval) on human subjects at the Royal Adelaide Hospital the protocol **must be** submitted to the Investigational Drugs Subcommittee (IDSC) before it can be considered by the Research Ethics Committee (REC).

The IDSC consists of members of the REC and the Drug Committee experienced in clinical pharmacy, clinical pharmacology, drug development and clinical trials. The subcommittee meets monthly, one week before the meeting of the REC, so that its recommendations may be considered as promptly as possible.

In order to streamline the application process for researchers who wish to use investigational drugs, the protocol requirements of the REC have been modified to allow direct submission of multicentre protocols, *without rewriting*, as long as IDSC and REC checklists (Appendix I, II and III) are attached to the protocol. These checklists contain all the items of information which the IDSC and the REC need to consider. It is vital to the timely processing of submissions that these checklists are completed carefully so that members of the IDSC and the REC have all of the basic information they require to make an informed decision.

For any further information or clarification, please contact:

- Executive Officer, Investigational Drugs Subcommittee
  Peter Slobodian, Senior Specialist Pharmacist
  Level 5 Pharmacy, RAH
  Phone: (08) 8222 5793
  Mobile: 0401 123 822 (Speed dial 1640)
  Fax: (08) 8222 4985
  Email: peter.slobodian@health.sa.gov.au

or

- Executive Officer, Research Ethics Committee
  Heather O'Dea
  Level 3, Hanson Institute, RAH
  Phone: (08) 8222 4139
  Fax: (08) 8222 3035
  Email: heather.o'dea@health.sa.gov.au or rah.ethics@health.sa.gov.au

2. NON-APPROVED DRUGS (i.e. CTN or CTX APPLICATIONS)

In Australia there are two ways of initiating a clinical trial of new drugs or new uses of existing drugs - the Clinical Trial Notification (CTN) Scheme and the Clinical Trial Exemption (CTX) Scheme.

The choice of which scheme to follow lies firstly with the sponsor and then with the individual institutional ethics committee.

Notification under the CTN scheme or application under the CTX scheme is required for clinical investigational use involving:

1. Any drug product not entered in the Australian Register of Therapeutic Goods, including any new formulation of an existing drug product or any new route of administration
2. Any use of a marketed drug product beyond the conditions of its marketing approval, including:
    - new indications;
    - extending the use of a drug or drug product to new patient groups, including healthy volunteers;
    - extending the doses or duration of treatments outside the approved range.

2.1 CLINICAL TRIALS EXEMPTION (CTX) SCHEME

The Therapeutic Goods Administration (TGA) of the Commonwealth Department of Health and Ageing is responsible for this scheme. CTX applications are made to the TGA by the sponsoring pharmaceutical company and usually involve drugs which are at an early stage in their development. After approval from the TGA, the protocol must be submitted to the IDSC. Following a recommendation of approval from the Subcommittee, the protocol will be passed on automatically to the REC for consideration at the next meeting.

2.2 CLINICAL TRIALS NOTIFICATION (CTN) SCHEME

Since May 1991, a CTN Scheme has been available as an alternative to the CTX Scheme. Under the CTN Scheme the TGA does not review data relating to a clinical trial before it proceeds. The sponsor notifies the TGA that a clinical trial is to be conducted after approval by the ethics committee of the host institution. CTN applications are the responsibility of the **Principal Investigator** within the hospital. They should be prepared using data provided by the sponsoring pharmaceutical company and submitted to the IDSC. Following a recommendation of approval from the Subcommittee, the protocol will be passed on automatically to the REC for consideration at the next meeting.

Please note, the TGA charges an administration fee of $290 for single site or multiple sites CTN applications

3. APPROVED DRUGS (NON-CTN/CTX APPLICATIONS)

If an investigator plans to use a marketed drug for an approved indication and in an approved dosage regimen, as listed in the TGA approved product information (e.g. product monographs in MIMS), the protocol must still be submitted to the IDSC.

4. SUBMISSION OF DRUG RELATED PROTOCOLS

4.1 NOTES FOR INVESTIGATORS

4.1.1 Before the trial commences:

a.) Any contact between an investigator and a sponsor in relation to the conduct of a clinical trial should clearly delineate the responsibilities of the sponsor, investigator and institution, including responsibilities for compensation and/or treatment in the case of injury or death and for any insurance or indemnity to cover the liability of each of the parties involved.

b.) Investigators and sponsors have a duty to disclose all relevant information requested by the IDSC or the REC including any objections to the protocol which may have been raised by other regulatory bodies.

c.) All communication regarding submitted applications will be between the Investigational Drugs Subcommittee and the Investigator (not between the Subcommittee and the sponsor).

The Principal Investigator must sign all correspondence sent to the Investigational Drugs Subcommittee. Failure to do so will result in delays.

d.) All serious adverse events must be reported to the REC Chairman ***within 72 hours*** of detection and a statement confirming this must appear in the protocol, either as part of the main protocol or as a site specific amendment.

e.) Protocols involving non-marketed drugs must be accompanied by the most recent Investigator's Brochure and/or other relevant material which gives a full pharmacological and toxicological description of the investigational drug and its use in the proposed condition. For such drugs the Investigator's Brochure should not be greater than 12 months old at the time of submission. A list of the information required is included in the IDSC Checklists (Appendix I and II). The checklists must be attached to the protocol application.

f.) For drugs which have never had marketing or clinical trial approval in Australia, the USA or European Union, a Pharmaceutical and Pharmacological Checklist (Appendix V) should also be submitted.

g.) For drugs approved for marketing, a full drug profile is not required but a full justification of the proposed particular use of the drug under investigation must be provided. For these drugs, the IDSC require submission of the drug profile as described in the TGA approved product information (see latest edition of MIMS).

h.) **Investigator Statement**

The subcommittee requires an Investigator Statement to be submitted together with the protocol submission. This statement must be written and signed by the Principal Investigator.

The following questions must be addressed in the statement:

- What is the current standard treatment for this patient population at the Royal Adelaide Hospital?
- What are the overall benefits to the study participant?
- What are the 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?

The Investigator Statement may be included in the covering letter.

i.) **IDSC Meeting Attendance**

The Principal Investigator may attend the IDSC meeting to present their protocol and answer any questions. Protocol presentations will be strictly limited to two (2) minutes. At least 48 hours notice will be given to the Investigator if attendance is required at the IDSC meeting.

j.) **Items Commonly Omitted**

1. Renal Function
The assessment of renal function for inclusion/exclusion of a subject into a clinical trial is more accurately defined by ***estimated creatinine clearance***, rather than serum creatinine. Estimated clearance may be calculated by the Cockcroft and Gault formula. Please note that the eGFR reported as part of a standard laboratory screen is not appropriate for this purpose.

2. RAH Participant Numbers
The IDSC requires that an investigator provides the estimated number of participants to be entered into the clinical trial at the RAH.

3. Justification of Participant Numbers
Statistical justification of overall participant numbers (i.e. power calculation) must be submitted with the protocol.

4. Justification of Doses
Justification of doses of all drugs to be used on the study must be provided.

5. Recruitment
The source of participants must be stipulated. If RAH patients, state the hospital areas from which participants will arise and who will be involved in recruitment. If healthy volunteers, or non-RAH patients, provide details of the procedures for recruitment.

4.1.2 During the clinical trial:

a.) In the case of a death or a serious adverse event, the investigator must report to the Chairman of the REC and to the sponsor within 72 hours (the sponsor then has a responsibility to report to the TGA).

b.) The investigator must report to the REC as soon as possible, any relevant trial which has been stopped or significantly modified due to action taken by regulatory agencies overseas, or any withdrawal from the market or new warnings for safety reasons of any medication involved in the study.

c.) The REC will undertake ongoing monitoring of the progress of the trial. Investigators are responsible for providing an Annual Review to the REC.

4.1.3 After the clinical trial:

a.) In most cases, the trial will have a defined duration and the drug will cease at the completion of the trial. However, in some cases, especially those involving serious disease or illness where the trial is designed to examine clinical efficacy, it may be desirable to continue study drug beyond the pre-specified completion date in trial participants who are benefiting. In these cases, there needs to be a commitment from the sponsor that study medication will be continued after study completion for patients who have been demonstrated to have a benefit. In particular, the subcommittee believes that the sponsor has an obligation to continue the supply of blinded medication or open-label medication (if study treatment is known) at no cost to the patient or hospital, until the drug is marketed and available on a subsidised scheme for the patient's indication. **This issue must be explicitly detailed in the protocol (or covering letter) and in the Patient Information sheet.**

b.) The Principal Investigator is responsible for submitting a report to the REC on the clinical trial, including the major findings and the occurrence of adverse events.

4.2 DOCUMENTS REQUIRED FOR SUBMISSION

4.2.1 FOR PROPOSED NEW USE OF MARKETED DRUG:

Five (5) double-sided collated copies and electronic version[1] (searchable PDF documents only) of the following:

a. Detailed clinical trial protocol
b. Investigational Drugs Subcommittee Checklist – PART A
   (Note: separate checklist must be completed for **each drug** (Appendix I)
c. Investigational Drugs Subcommittee Checklist – PART B (Appendix II)
d. Research Ethics Committee Checklist (Appendix III)
e. Justification of new use of drug
f. Subject information sheet and consent form (written in RAH format - see Appendix VI and VII).
g. Investigator Statement (Refer to Section 4.1.1 (h) on Page 7 for details)
h. Covering letter signed by the Principal Investigator.

One (1) copy and electronic version[1] (searchable PDF documents only) of the following:

i. TGA approved product information (from latest edition of MIMS)
j. Completed Research Ethics Committee Submission (Yellow) Form (Appendix IV)
k. Completed IDSC Invoicing Details Form (Appendix V)
l. Completed TGA CTN document printed on blue paper. (CTN form can be obtained from the TGA website http://www.tga.gov.au/pdf/forms/clinical-trials-forms-ctn-notification.pdf). This will have been completed by the sponsor and forwarded to the Principal Investigator. After approval by the IDSC and the REC, the Chairman of the REC and the General Manager will sign the relevant section of the document before returning it to the Principal Investigator.

[1]Electronic documents must be in searchable PDF format (**maximum document size of 5MB**) on CD, USB (memory stick) or emailed to rah.ethics@health.sa.gov.au. **Password protection must be removed from all documents.**

4.2.2 FOR PROPOSED USE OF A NON-MARKETED DRUG WHICH HAS HAD PREVIOUS CLINICAL TRIAL APPROVAL IN AUSTRALIA, USA OR EU:

Five (5) double-sided collated copies and electronic version[1] (searchable PDF documents only) of the following:

a. Detailed clinical trial protocol
b. Investigational Drugs Subcommittee Checklist – PART A
   (Note: separate checklist must be completed for **each drug** (Appendix I)
c. Investigational Drugs Subcommittee Checklist – PART B (Appendix II)
d. Research Ethics Committee Checklist (Appendix III)
e. Subject information sheet and consent form (written in RAH format - see Appendix VI and VII).
f. Investigator Statement (Refer to Section 4.1.1 (h) on Page 7 for details)
g. Covering letter signed by the Principal Investigator.

One (1) copy and electronic version[1] (searchable PDF documents only) of the following:

h. Up-to-date Investigator's Brochure (less than 12 months old) and any other relevant material (e.g. FDA 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.
i. Agency Comments from TGA (if CTX application).
j. Completed Pharmaceutical and Pharmacological Checklist for each investigational drug (Appendix VI).
k. Completed Research Ethics Committee Submission (Yellow) Form (Appendix IV)
l. Completed IDSC Invoicing Details Form (Appendix V).
m. Completed TGA CTN document printed on blue paper (if applicable). (CTN form can be obtained from the TGA website http://www.tga.gov.au/pdf/forms/clinical-trials-forms-ctn-notification.pdf). This will have been completed by the sponsor and forwarded to the Principal Investigator. After approval by the IDSC and the REC, the Chairman of the REC and the General Manager will sign the relevant section of the document before returning it to the Principal Investigator.

[1]Electronic documents must be in searchable PDF format (**maximum document size of 5MB**) on CD, USB (memory stick) or emailed to rah.ethics@health.sa.gov.au. **Password protection must be removed from all documents.**

4.2.3 FOR PROPOSED USE OF A NON-MARKETED DRUG WHICH HAS NOT HAD PREVIOUS CLINICAL TRIAL APPROVAL IN AUSTRALIA, USA OR EU:

Five (5) double-sided collated copies and electronic version (searchable PDF documents only) of the following:

a. Detailed clinical trial protocol
b. Investigational Drugs Subcommittee Checklist – PART A
   (Note: separate checklist must be completed for **each drug** (Appendix I)
c. Investigational Drugs Subcommittee Checklist – PART B (Appendix II)
d. Research Ethics Committee Checklist (Appendix III)
e. Subject information sheet and consent form (written in RAH format - see Appendix VI and VII).
f. Investigator Statement (Refer to Section 4.1.1 (h) on Page 7 for details)
g. Covering letter signed by the Principal Investigator.

One (1) copy and electronic version[1] (searchable PDF documents only) of the following:

h. Up-to-date Investigator's Brochure (less than 12 months old) and any other relevant material (e.g. FDA 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.
i. Agency Comments from TGA (if CTX application).
j. Completed Pharmaceutical and Pharmacological Checklist for each investigational drug (Appendix VI).
k. Completed Research Ethics Committee Submission (Yellow) Form (Appendix IV)
l. Completed IDSC Invoicing Details Form (Appendix V).
m. Completed TGA CTN document printed on blue paper (if applicable). (CTN form can be obtained from the TGA website http://www.tga.gov.au/pdf/forms/clinical-trials-forms-ctn-notification.pdf). This will have been completed by the sponsor and forwarded to the Principal Investigator. After approval by the IDSC and the REC, the Chairman of the REC and the General Manager will sign the relevant section of the document before returning it to the Principal Investigator.

[1]Electronic documents must be in searchable PDF format (**maximum document size of 5MB**) on CD, USB (memory stick) or emailed to rah.ethics@health.sa.gov.au. **Password protection must be removed from all documents.**

4.2.4 FOR PROPOSED USE OF A MARKETED DRUG WITHIN ITS APPROVED INDICATIONS AND MARKETED FORMULATION.

Five (5) double-sided collated copies and electronic version (searchable PDF documents only) of the following:

a. Detailed clinical trial protocol
b. Investigational Drugs Subcommittee Checklist – PART A
   (Note: separate checklist must be completed for **each drug** (Appendix I)
c. Investigational Drugs Subcommittee Checklist – PART B (Appendix II)
d. Research Ethics Committee Checklist (Appendix III)
e. Subject information sheet and consent form (written in RAH format - see Appendix VI and VII).
f. Investigator Statement (Refer to Section 4.1.1 (h) on Page 7 for details)
g. Covering letter signed by the Principal Investigator.

One (1) copy and electronic version[1] (searchable PDF documents only) of the following:

h. Approved product information (latest edition of MIMS)
i. Completed Research Ethics Committee Submission (Yellow) Form (Appendix IV)
j. Completed IDSC Invoicing Details Form (Appendix V).

[1]Electronic documents must be in searchable PDF format (**maximum document size of 5MB**) on CD, USB (memory stick) or emailed to rah.ethics@health.sa.gov.au. **Password protection must be removed from all documents.**

CHARGES LEVIED FOR SPONSORED TRIALS

Fees are levied for consideration of applications for Research Ethics Committee consideration of all protocols that involve *drugs OR devices.* Funds generated support both the Investigational Drugs Subcommittee and the Research Ethics Committee. The current scale of charges is detailed below. A tax invoice will be forwarded to the Sponsor immediately following receipt of protocol submission.

Please note: for sponsored trials, please complete an IDSC Invoicing Details Form (Appendix IV – IDSC Guidelines; Appendix B – REC Guidelines)

1. MULTI-SITE SPONSORED TRIALS
(Standardised fee structure for all public health HRECs in SA)

PROTOCOL EVALUATION FEES	
	Fee ($) GST excluded
Review of a marketed or unapproved drug/device	3,500
Sub-study add-on review (submitted for review after REC approval is granted to the overarching [full] application)	1,500
Cooperative Trial Group (CTG) application	1,750 (may be reduced or waived depending on level of sponsorship and complexity)

2. SINGLE-SITE SPONSORED TRIALS

PROTOCOL EVALUATION FEES	
Trial Type	**Fee ($) GST excluded**
Using a marketed drug/device	3,000
Using an unapproved drug/device	5,000
Using an unapproved drug/device in a very early phase study	7,500 **PLUS** any cost of independent evaluation

MULTI-SITE / SINGLE-SITE PROTOCOL AMENDMENT EVALUATION FEES	
	Fee ($) GST excluded
Minor / Administrative amendment	200
Other Amendments (e.g. protocol amendments, Investigator Brochure revisions)	600
ARCHIVE RETRIEVAL FEE	
	50 per retrieval

2. NON-SPONSORED TRIALS

PROTOCOL/ AMENDMENT EVALUATION FEES	
Trial Type	**Fee ($) GST excluded**
Investigator-initiated (RAH only)	No charge
ARCHIVE RETRIEVAL FEE	
	10 per retrieval

6. GUIDE TO RESEARCH ETHICS COMMITTEE (REC) CHECKLIST

1. **TITLE** (Full title of project)

2. **INVESTIGATOR DETAILS AND QUALIFICATIONS**
   Include 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)
   This section should include a clear statement of what is the standard of care for patients with this condition at the RAH. Where the research proposal involves alternative care or treatment the rationale for this should be discussed.

5. **PARTICIPANTS**
   SELECTION, INCLUSION AND EXCLUSION CRITERIA (Specific)
   - How will participants be recruited?
   - (For RAH patients, the initial contact should come from their treating clinician, or someone who was responsible for their care at the RAH).
   - Withdrawal criteria.

6. **STUDY PLAN AND DESIGN**

7. **OUTCOMES**
   - How will the outcomes of the study be evaluated?
   - Can the aims be realized?

8. **ETHICAL CONSIDERATIONS**
   A clear description of procedures to be performed on patients or volunteers, with particular emphasis on possible risks, pain or discomfort, and an indication of whether the procedure is part of normal diagnosis and treatment. For guidance, the primary ethical principle is respect for the subjects. It is expected that written consent will be obtained. This must be preceded by provision of information relevant to the subject's participation and presented in a comprehensible form. Where participation in the research involves withdrawal of standard treatment, this poses a potential risk to the patient if the new treatment is ineffective or less effective. This must be declared in the protocol and patient information sheet. The consent form and information sheet should be included with this application. An outline consent form is attached. Guidelines on content and use are attached.

9. SPECIFIC SAFETY CONSIDERATIONS (e.g. Radiation, toxicity)

- 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.
  RAH Intranet → Resource → Safety → Radiation Safety → Code of Practice - pdf file
  or *www.arpansa.gov.au/Publications/codes/rps8.cfm*

- The following should be detailed in Protocol:-
  - 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).

- The **Information Sheet** will need to contain information about the extra radiation, using wording contained in the Code of Practice, according to the dose of radiation.
  RAH Intranet → Resource → Safety → Radiation Safety → Code of Practice - pdf file Annex 2 (p24 of 36) or
  www.arpansa.gov.au/Publications/codes/rps8.cfm

- You are also required to complete a '**New Notification form**' for the REC to submit to the SA Government EPA Radiation Protection Division.
  RAH Intranet → Clinical → Guidelines/Protocols → Research Ethics Committee → New EPA Notification Form.
  Internet: www.rah.sa.gov.au → Research → Research Ethics → Ionizing Radiation, EPA Form.

  - The *'Notification form'* must be completed for each study, completing all sections of the form, except the last section of the HREC certification.
  - The *'Notification form'* may be emailed or a hard copy sent to the REC, to forward to the EPA on behalf of the Investigators. The REC will complete the Certification section at the bottom of the form before forwarding to the EPA.

    Please note, that the 'Notification form' needs to be sent to the EPA by the REC, not direct to the EPA, as the REC needs to record it in the study documentation, and sign it before it is sent.

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.
Please submit 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**

- How will data be collected and recorded?
- Who, apart from yourself (and supervisor if applicable) 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?

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

12. **REFERENCES**

13. **OTHER RELEVANT INFORMATION**

e.g. 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. Before re-writing the protocol it is wise to check if it is acceptable in the current form to the RAH committee.
- NEAF applications are acceptable but should generally be accompanied by a clearly written research protocol and a covering letter addressing RAH specific issues.
- Patient Information Sheets should be amended to be RAH specific with RAH contact details.

15. **DATE OF PROPOSED COMMENCEMENT**.

16. **DATE OF EXPECTED COMPLETION**.

17. **RESOURCE CONSIDERATIONS**

(a) - staffing (own and other Departments)
- facilities (own and other Departments)
- goods and services
- investigations to be undertaken (involvement of other Functional Units)
- any other cost implication of the protocol
- support available (financial and other) or requested to offset costs of project

(b) - Medical Records required

18. FINANCIAL AND INSURANCE ISSUES

- Submissions for commercially sponsored trials of drugs or devices must be accompanied by details of the financial agreement between investigator and sponsor.

- There must be a declaration of any financial interest which the researcher may have in the outcome of the research project – this applies regardless of whether or not investigational drugs or devices are involved.

- Insurance arrangements and indemnity agreements must be included.

19 SIGNATURES OF INVESTIGATORS AND DEPARTMENTAL APPROVAL

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.

Where the research is to be conducted in a Department or Unit of the RAH and the person responsible for that Department (e.g. Clinical Director, Head of Unit, Senior Nurse) is not an investigator, a statement should be provided to indicate that they have consented to this research being conducted in their Department.

7. INSTRUCTIONS TO APPLICANTS FOR RESEARCH ETHICS COMMITTEE APPROVAL

1. Complete the Research Protocol as per the Guidelines.
   - Insert **Page numbers** in the footers.
   - Insert a **Version No.** and **date** also in the footer of Protocols, Patient Information Sheets & Consent Forms.
   - If more than one type of Information Sheet and Consent Form, **identify** the patient group/Information Sheet etc. in the footer.

2. Expedited Approvals. The Chairman of the Research Ethics Committee has the delegated authority to approve protocols between meetings of the Committee in certain cases where the research is simple and / or non-invasive. A list of examples of Chairman's approvals can be found on the RAH Internet or Intranet [Expedited Approvals].

   For this reason, it is strongly advised that applicants submit one copy of a final draft of their protocols for checking (and possible Chairman's Approval) before proceeding to copying to:

   Heather O'Dea,
   Executive Officer,
   Research Ethics Committee,
   Level 3, HANSON INSTITUTE,
   THE ROYAL ADELAIDE HOSPITAL

   Phone: 8222 4139
   Fax: 8222 3035
   Email: rah.ethics@health.sa.gov.au

3. If full Committee approval required, submit **4 hard copies** of the Check list [Appendix A], the final Protocol, Information Sheet, Consent Form, attachments and any supporting information you wish to have considered, to the Executive Officer by the date defined in the separate Form. Please collate the copies.

4. Submissions for full Committee, must include **electronic versions of ALL documents** in a **searchable PDF format**, on CD, USB (memory stick) or emailed to above.
   - Password protection must be removed from all documents.
   - Maximum pdf document size is 5MB. If larger, document needs to be split.

   NOTE: If you are unsure if your study will need to be reviewed by the full Committee, or you are submitting within *2 working days of the final submission date*, please submit the 4 hard copies.

   (A separate list of **Meeting Dates and final dates for submission** is available on the RAH Intranet site, or the Internet).

   RAH Intranet: *Clinical → Guidelines/Protocols → Research Ethics Committee*
   or
   Internet: *www.rah.sa.gov.au → Research → Research Ethics*

8. GUIDELINES FOR PAYMENT OF VOLUNTEERS

In the ordinary course of clinical research no monetary payments (other than for bona fide expenses) should be made to the subjects participating in the programme. However, there are circumstances in which the participants are acting as normal volunteers in a project which is of no possible advantage to themselves and may involve inconvenience, loss of time and possible discomfort. In these circumstances, the payment of an honorarium may be justified subject to the following restrictions:

1. No financial inducements of the kind should be made to individuals who at the relevant time are patients under the care of the Royal Adelaide Hospital.

2. The payment must in no circumstance be offset against the possible risk of the procedure involved. It is only to be regarded as compensation for loss of time, inconvenience and possible discomfort.

3. Great care must be exercised to ensure that the volunteers to whom payment is made are of an age and maturity to be able to make an independent decision.

4. Payment for services of this kind in no way absolves medical staff concerned of their responsibility should the procedure have any untoward consequence.

9. GUIDELINES FOR SELECTION OF VOLUNTEERS

Researchers should be aware of the possibility of exploiting subjects who are in a dependent relationship of any sort. These would include patients, fellow employees, students. Care must be taken to ensure that no subtle coercion is applied to encourage research participation. Junior laboratory personnel could assume that continued employment and/or promotion depend in some way on participation in projects and therefore staff from other areas without an employment relationship should be preferred.

APPENDIX I

INVESTIGATIONAL DRUGS SUBCOMMITTEE CHECKLIST

PART A

Note: For protocols involving multiple investigational drugs, a separate Investigational Drugs Subcommittee Checklist - PART A must be completed for <u>each drug</u>.

Information included	Details
1. Generic name of drug (or code number)	1. Specify the generic name or code number
2. Trade name of drug (if available)	2. Specify the trade name
3. Manufacturer	3. Specify the manufacturer
4. Supply of drug	4.1 Will the Sponsor supply the drug required for the duration of the study at no charge to the RAH? Yes ☐ or No ☐ If **No**, how will the drug be obtained?
	4.2 What arrangements are there for access to the drug after completion of the study (if applicable)?
5. Marketing status in Australia	5.1 Is the drug marketed in Australia? Yes ☐ or No ☐ If **No**, go to Item 6. If **Yes**, please provide a copy of the current TGA approved product information, e.g. from the latest edition of MIMS. Is a copy of TGA approved product information provided? Yes ☐ or No ☐, go to Item 5.2
	5.2 Is the dosage, administration, indications for use or age group of participants proposed for this protocol different from the TGA approved product information? Yes ☐ No ☐ If **No**, go to Item 8 If **Yes**, a.) Please provide details regarding how the dosage, administration, indications for use or age group of participants proposed for this protocol are different to the TGA approved product information b.) Please submit a CTN form.

Note: For protocols involving multiple investigational drugs, a separate Investigational Drugs Subcommittee Checklist - PART A must be completed for <u>each drug</u>.

Information included	Details
6. Marketing/clinical trial status in overseas countries (especially EU and USA)	6. If the drug is not marketed in Australia, has the drug been registered/licensed/approved for marketing by an accepted international regulatory authority? Yes ☐ No ☐ If **Yes**, identify countries and/or regulatory authorities that have registered/licensed/approved the drug.
7. Investigator's Brochure	7.1 If the drug is not marketed in Australia, is an Investigator's Brochure or other relevant material which gives a full pharmacological and toxicological description of the investigational drug and its use in the proposed condition provided? Yes ☐ No ☐ If **No**, please justify and complete Appendix V (i.e. Pharmaceutical & Pharmacological Checklist) If **Yes**, is the Investigator's Brochure or other relevant material greater than 12 months old? Yes ☐ If Yes, please justify. No ☐
	7.2 Does the Investigator's Brochure contain a large number of individual patient safety reports? Yes ☐ No ☐ If **Yes**, is there any new safety information in these reports that would alter the overall assessment of safety, as described in the main body of the Investigator's Brochure, the protocol and the Patient Information sheet? Yes ☐ If **Yes**, please provide details. No ☐
	7.3 If a phase 1 study, does the contents of the Investigator's Brochure comply with the European Medicines Agency (EMEA) guidelines for first-in-human clinical trials? Yes ☐ No ☐ or NA ☐
8. Formulation/description of investigational drug product (include dissolution data for bioequivalence studies)	8.1 Indicate the page number(s) in protocol/ Investigator's Brochure or provide details.
	8.2 Is the drug manufactured under Good Manufacturing Practice (GMP)? Yes ☐ or No ☐
	8.3 If a bioequivalence study, has dissolution data been provided? Yes ☐ or No ☐ or NA ☐

INVESTIGATIONAL DRUGS SUBCOMMITTEE CHECKLIST
PART A

Note: For protocols involving multiple investigational drugs, a separate Investigational Drugs Subcommittee Checklist - PART A must be completed for <u>each drug</u>.

Information included	Details
9. Formulation/description of placebo	9. Indicate the page number(s) in protocol or provide details.
10. Proposed route of administration	10. Indicate the page number(s) in protocol or provide details.
11. Proposed dose(s) and rationale for the dose selected in the protocol	11.1 Provide details regarding the proposed dose.
	11.2 Specify the rationale for the dose to be used in this protocol
12. Investigator's signature	12.1 Investigational Drugs Subcommittee (IDSC) Checklist Part A prepared by: Name (Please Print): Position:
	12.2 Investigational Drugs Subcommittee (IDSC) Checklist Part A checked by: Investigator (Please Print): Signature:

APPENDIX II

INVESTIGATIONAL DRUGS SUBCOMMITTEE CHECKLIST

PART B (Page 1 of 3)

Information included	Details
1. Company sponsoring trial	1.1 Is this protocol sponsored? Yes ☐ or No ☐ If ***Yes***, provide sponsor details.
	1.2 Is a completed IDSC Invoicing Details Form (Appendix IV) attached? Yes ☐ or No ☐
2. CTN/CTX status in Australia	2.1 Is this protocol being conducted as a CTN ☐, CTX ☐ or non-CTN/CTX ☐ application? If a **CTN application**, is a CTN form attached? Yes ☐ or No ☐ If a **CTX application**, is the TGA Agency comments for institutional ethics committees attached? Yes ☐ or No ☐
	2.2 Have any regulatory authorities (e.g. TGA, FDA) or institutional ethics committees raised any objections to this protocol/investigational drug? Yes ☐ or No ☐ If ***Yes***, provide details.
3. Investigators/centres (multi-centre)	3. Is this a single-centre ☐ or multi-centre ☐ trial? If a *multi-centre trial*, provide details of all other investigators/ centres.
4. Trial Registration	4. Where has the trial been registered? ☐ Australian New Zealand Clinical Trial Registry (Australia) ☐ ClinicalTrials.gov (USA) ☐ ISRCTN Register (UK) ☐ Other, please provide details

INVESTIGATIONAL DRUGS SUBCOMMITTEE CHECKLIST

PART B (Page 2 of 3)

Information included	Details
5. Strategic purpose of the trial	5. Specify the strategic purpose of the trial.
6. Proposed location of treatment (e.g. in hospital, at home)	6. Indicate the page number(s) in protocol or provide details.
7. Monitoring of efficacy	7. Indicate the page number(s) in protocol or provide details.
8. Monitoring of safety	8.1 Indicate the page number(s) in protocol or provide details.
	8.2 <u>Renal Function</u> Is the assessment of renal function for inclusion/exclusion criteria defined by estimated creatinine clearance, rather than serum creatinine? Yes ☐ or No ☐ ***Please note: May be a site specific amendment*** If ***No***, please justify.
	8.3 <u>Serious Adverse Events (SAEs)</u> Is there a statement in the protocol that acknowledges that SAEs will be reported to the Chairman of the Research Ethics Committee within 72 hours o them occurring? Yes ☐ or No ☐ ***Please note: May be a site specific amendment***

INVESTIGATIONAL DRUGS SUBCOMMITTEE CHECKLIST

PART B (Page 3 of 3)

Information included	Details
9. No. RAH participants	10. Proposed number of RAH participants to be recruited in this protocol = _____
10. Justification of participant numbers	10. Has a power calculation been performed to justify participant numbers? Yes ☐ or No ☐ If ***Yes***, indicate the page number(s) in protocol or provide details. If ***No***, please justify.
11. Insurance/ indemnity	11. Has the Insurance/indemnity documentation for RAH trials been forwarded to Jenny Latte, Clinical Research Manager Level 3, Hanson Institute? Yes ☐ or No ☐
12. RAH Pharmacy involvement	12. Have arrangements been made for the RAH Pharmacy Department to receive or dispense the drugs involved in this protocol? Yes ☐, No ☐ If ***No***, a) Explain how the drug(s) will be received and dispensed for the purposes of the research protocol. b) Please provide list of all relevant SOPs, evidence of staff training and evidence of quality control/assurance procedures.
13. IDSC Meeting Attendance	13. Would you like to attend the IDSC meeting to present this protocol? Yes ☐, No ☐ Brief oral presentation will only be required. *For student projects, attendance to the IDSC meeting is strongly recommended*. **Please note you may be invited to attend an IDSC meeting. At least 48 hours notice will be given to the Investigator if attendance is required.**
14. Investigator's signature	14.1 Investigational Drugs Subcommittee (IDSC) Checklist Part B prepared by: Name (Please Print): Position:
	14.2 Investigational Drugs Subcommittee (IDSC) Checklist Part B checked by: Investigator (Please Print): Signature:

APPENDIX III

RESEARCH ETHICS COMMITTEE CHECKLIST

Items which are not included in the Protocol should be provided in an attached document.

Information included	Document & Page No
1. Title of project	
2. Investigators and qualifications • Names • location • address for correspondence • phone numbers • email contact details.	
3. Purpose of study (general) and aims (specific)	
4. Background/preliminary studies (if any)	
5. Subjects 5.1 Selection criteria 5.2 Exclusion criteria 5.3 Withdrawal criteria	
6. Study plan and design	
7. Efficacy/method of assessment of outcome	
8. Ethical considerations	
9. Specific safety considerations (e.g. radiation, toxicity) • Radiation Safety Report • Notification Form for EPA, or • Application Form for EPA	
10. Drug/Device information (if applicable) • Submit a CTN Drug/Device Form • Has the trial been registered in a publicly accessible trials registry?	CTN Form Yes ❑ No ❑ Registered Yes ❑ No ❑ State name of Registry and Registration No.:
11. Analysis and reporting of results	
12. References	
13. Other relevant information	
14. Other ethics committees to which submitted	
15. Date of proposed commencement	
16. Date of expected completion	
17. Resource Considerations	
18. Financial Statement	
19. Investigator's signature / covering letter	

APPENDIX IV

RESEARCH ETHICS COMMITTEE SUBMISSION (YELLOW) FORM

Royal Adelaide Hospital Research Ethics Committee

(Name of Ethics Committee)

voted at its meeting on _____ to give FINAL APPROVAL
(Date of Meeting)

for the ## sponsored trial with ## as CRO to be conducted by
(Sponsor)

_____ at **Royal Adelaide Hospital**
(Principal Investigator) *(Site Where Trial Will Be Conducted)*

Protocol Title: [ ]

The following documents have been submitted for review and approval:

Number		*Version*		*Date*	
Patient Information & Consent Form		*Version*		*Date*	
Questionnaire		*Version*		*Date*	
		Version		*Date*	
		Version		*Date*	

Other: (please describe eg. Investigator's Brochure, Advertisement)

Clinical Investigator Brochure	*Version*		*Date*	
Newspaper Advertisement	*Version*		*Date*	
Patient Diary	*Version*		*Date*	

This Ethics Committee is constituted and functions in accordance with the National Statement on Ethical Conduct in Human Research – 2007.

_____ _____ _____

Name Signature Date
REC Chairperson/Executive Officer

Are the above listed documents to be listed on an RAH HREC final approval letter as well as acknowledging on this form?	Yes ❑	No ❑

This form (Yellow Submission Form) may be used to list all submitted documents which require approval and acknowledgement with the Final Approval granted by the Royal Adelaide Hospital Research Ethics Committee (RAH REC). If this form is not used, or documents are not listed on this form, please list all documents in a covering letter of the submission. The RAH REC takes no responsibility for documents omitted to be listed for the submission of the above-named research protocol that you require approval or acknowledgement for. This form can be used as approval and acknowledgement of the listed documents. If you wish to have documents also listed on the final approval letter on the RAH REC letterhead, please indicate above in the tick-box.

APPENDIX V

IDSC INVOICING DETAILS

TRIAL DETAILS

Investigator Name:	
Protocol Title:	
Protocol No.	
Trial Type	Phase 1 ☐ Phase 2 ☐ Phase 3 ☐ Phase 4 ☐ Bioavailability/bioequivalence ☐ Unknown ☐

SPONSOR'S DETAILS

Sponsor Name:	
Sponsor Address:	
Contact person's name and position:	

OR

RAH Cost-Centre (if investigator is paying invoice)				

OFFICE USE ONLY

IDSC Reference No:		**RAH Protocol No:**	

INVOICING RECORD

REC Inv No.	Date Invoiced	Invoice Details	Initial

APPENDIX VI

PHARMACEUTICAL & PHARMACOLOGICAL CHECKLIST

Information included	Document & Page No
1. Structural formula	
2. Physiochemical properties	
3. Preclinical pharmacology (*in-vitro*)	
4. Preclinical pharmacology (*in-vivo*)	
5. Preclinical toxicology (acute studies)	
6. Preclinical toxicology (chronic studies)	
7. Preclinical toxicology (reproduction and teratogenicity)	
8. Preclinical toxicology (mutagenicity and carcinogenicity)	
9. Formulation to be used (including pharmaceutical integrity of drug product, stability, analytical purity, sterility if appropriate, assayed content of active drug)	
10. Pharmacokinetics – animal data	
11. Pharmacokinetics – human data	
12. Clinical data - Phase I - II (pharmacological properties)	
13. Clinical data - phase II - III (desired effects in target disease)	
14. Clinical data – toxicology	
15. Dose-response relationship (estimate of therapeutic index)	
16. Proposed clinical indications	
17. Relevant references	

APPENDIX VII

INFORMATION SHEETS for RESEARCH SUBJECTS

GUIDELINES ON CONTENT AND USE

The Research Ethics Committee requires an Information Sheet to be given to potential research subjects to assist them in their decision about involvement. An Information Sheet must accompany each Consent Form. In order to assist researchers in preparing Information Sheets the following guidelines on content and use have been prepared. The Royal Adelaide Hospital must be identified on the header of the first page of the documents and the above logo is optional.

General

1. The Information sheet is 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.

2. 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.

3. 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.

Style and Content

4. Use simple language with minimal technical terminology or jargon.

5. The sheet must be translated if non-English speaking subjects are to be recruited.

6. Section headings usually aid organisation and readability and should be included.

7. 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.

8. 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) *Chairman 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 Chairman, Research Ethics Committee, Royal Adelaide Hospital on 8222 4139.
   (include this at or near the end of the information sheet).

   (iii) 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.

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

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

   (vi) Assurances of confidentiality.

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

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

9. 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.
   RAH Intranet → Resource → Safety → Radiation Safety → Code of Practice - pdf file Annex 2 (p24 of 36)
   or *www.arpansa.gov.au/Publications/codes/rps8.cfm*

10. In protocols involving drug therapy or devices the following information should be included. (i-xi)

(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) Approximate number of patients treated with the investigational drug to date, at the dose range being studied in the proposed protocol.

(v) If a patient is withdrawing from existing therapy, include a statement that their condition may deteriorate during this time period and what action will be taken to manage this.

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

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

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

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

Consumer Medicine Information (CMI) can be used instead of a list of adverse effects for drug studies.

- Where a marketed drug is used within its stated indication, even though it may be part of a randomised protocol, the CMI is sufficient and no adverse effects need to be included in the Patient Information Sheet, simply a reference to the CMI.
- Where a drug is given in very small dose and is judged by IDSC and the investigator to be unlikely to manifest any of the systemic or long term issues, a CMI may be used and referenced. However, the Patient Information Sheet should indicate that "given over a longer time or in higher doses the drug may exhibit a number of adverse effects. These are included in the attached CMI". Examples of this might be the use of drugs on drug-eluting stents or the use of a single dose of a drug (salbutamol, esmolol) as part of an experimental protocol.
- Where a drug does not fall under one of the above criteria the full list of adverse effects should be given along with a quantitative estimate of the frequency of the event expressed as a percentage. Where the number of people dosed with the drug is too small to obtain a reliable frequency estimate, the number of events and the number of subjects dosed must be given.

(x) Interactions with alcohol and other drugs (generic and trade names).

(xi) Storage and disposal of medicines/devices.

APPENDIX VIII

(ROYAL ADELAIDE HOSPITAL Letterhead)

CONSENT FORM

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 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)

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

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