

**Operations Manual:
Human Research Ethics Committee**



Health
South Western Sydney
Local Health District

In accordance with **NSW Health GL2010_013** *Operations Manual: Human Research Ethics Committees*

Issue date: September 2010

AUGUST 2011

CONTENTS

1 BACKGROUND	1
1.1 About this document	1
1.2 Scope.....	1
1.3 Abbreviations	1
1.4 Key definitions.....	1
HREC 001: NSW Health HRECs	6
HREC 002: HREC composition	9
HREC 003: Appointment of members	10
HREC 004: Orientation and training of members	12
HREC 005: Meeting schedules	13
HREC 006: Agenda	14
HREC 007: Lead reviewers	15
HREC 008: Attendance of the Co-ordinating Investigator	16
HREC 009: Quorum requirements	17
HREC 010: External expert reviewers	18
HREC 011: Declaration of interest	19
HREC 012: Confidentiality	20
HREC 013: Decision making	21
HREC 014: Decisions available to the HREC	22
HREC 015: Minutes	23
HREC 016: Duration of HREC approval	24
HREC 017: HREC reporting requirements	25
HREC 018: Clinical Trial Notification and Clinical Trial Exemption schemes	26
HREC 019: Authorised prescriber applications	27
HREC 020: Special Access Schemes	30

1 BACKGROUND

1.1 About this document

This document provides standard operating procedures for SWSLHD Health Human Research Ethics Committee (HREC).

Reference should also be made to the SWSLHD SOPs for the HREC Executive Officer

1.2 Scope

The standard operating procedures apply to human research taking place in SWSLHD, which means research:

- conducted at sites under the control of SWSLHD; and/or
- involving participants, tissue or data accessed through the SWSLHD.

1.3 Abbreviations

CTN	Clinical Trial Notification
CTX	Clinical Trial Exemption
HREC	Human Research Ethics Committee
NEAF	National Ethics Application Form
NHMRC	National Health and Medical Research Council
SAE	Serious adverse event
SUSAR	Suspected unexpected serious adverse reaction
TGA	Therapeutic Goods Administration

1.4 Key definitions

Adverse event

For medicines, also referred to as **adverse experience**, any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event can therefore be any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

For devices, any undesirable clinical occurrence in a subject whether it is considered to be device related or not, that includes a clinical sign, symptom or condition and/or an observation of an unintended technical performance or performance outcome of the device.

[Ref: *Access to unapproved therapeutic goods via the Special Access Scheme (2009)*].

Clinical trial means any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

[Ref: *Notes for Guidance on Good Clinical Practice (CPMP/ICH/135/95): Annotated with TGA comments*].

Co-ordinating Investigator is the individual who takes overall responsibility for the research project and submits the project for ethical and scientific review. They are responsible for ongoing communication with the HREC and passing on any outcomes from this to the Principal Investigators. For single centre research, Co-ordinating Investigator and Principal Investigator are synonymous.

Data & Safety Monitoring Board is an independent data monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy points, and to recommend to the sponsor whether to continue, modify, or stop a clinical trial.

[Ref: *Notes for Guidance on Good Clinical Practice (CPMP/ICH/135/95): Annotated with TGA comments*].

Department of Health is the NSW Department of Health as established under Section 6 of the *Health Administration Act 1982*.

Epidemiological research is the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the control of health problems.

Health services research is research involving the integration of epidemiologic, sociologic, economic and other analytic sciences to study health services.

Human research is research conducted with or about people, or their data or tissue as described in the *National Statement on Ethical Conduct in Human Research (2007)*.

Human Research Ethics Committee (HREC) is a committee constituted in accordance with the *National Statement on Ethical Conduct in Human Research (2007)* to review and where appropriate approve and monitor the ethical and scientific aspects of human research.

Investigator's brochure is a compilation of clinical and non-clinical data on the investigational product(s) relevant to the study of investigational product(s) in human subjects.

[Ref: *Notes for Guidance on Good Clinical Practice (CPMP/ICH/135/95): Annotated with TGA comments*].

Lead HREC is a local HREC accredited by the Director-General of the NSW Department of Health to conduct ethical and scientific review of human research on behalf of the NSW public health system in the categories of: (a) clinical trials/interventional clinical research; and/or (b) general research.

Local HREC is a NSW Health HREC established by a Public Health Organisation to provide ethical and scientific review of human research to be conducted at sites under its control.

Low risk research is research where the only foreseeable risk to the participant is one of discomfort. Discomforts may include minor side-effects of medication, discomforts related to measuring blood pressure or anxiety induced by an interview. Where the risk, even if unlikely, is more serious than discomfort, the research is not low risk.

[Ref: *National Statement on Ethical Conduct in Human Research (2007)*].

Multi-centre research is research that is conducted at more than one site within the NSW public health system, where those sites are within the jurisdiction of more than one NSW Health HREC.

National Statement is the *National Statement on Ethical Conduct in Human Research* (2007).

Negligible risk research is research where there is no foreseeable risk of harm or discomfort and any foreseeable risk is not more than inconvenience to the participants. Inconvenience is the least form of harm that is possible for human participants in research. The most common examples of inconvenience in human research are filling in a form, participating in a survey or giving up time to participate in a research activity. Where the risk, even if unlikely, is more than inconvenience, the research is not negligible risk.

[Ref: *National Statement on Ethical Conduct in Human Research* (2007)].

NSW Health HREC is an HREC established by a Public Health Organisation and registered with the National Health and Medical Research Council.

Online Forms Website is an online system that enables users to electronically complete their applications for ethical and scientific review and site authorisation.

Population health research is research directed towards preventing disease, prolonging life, and promoting health through the organised efforts of society.

Principal Investigator is the individual who takes responsibility for the overall conduct, management, monitoring and reporting of research conducted at a site and submits the research project for site authorisation.

Public Health Organisation under the *Health Services Act 1997 (NSW)* is an Area Health Service, statutory health corporation or affiliated health organisation in respect of their recognised services.

Research is original investigation undertaken to gain knowledge, understanding and insight as described in the *Australian Code for the Responsible Conduct for Research* (2007).

Research Governance Officer is the individual appointed within the Public Health Organisation who is responsible for the management of applications for site authorisation and oversight of authorised research projects.

Research protocol is a document that details the objectives, design, methodology, statistical considerations and organisation of a research project.

Serious adverse event (SAE):

For medicines, also referred to as **serious adverse drug reaction**, is any untoward medical occurrence that at any dose:

- results in death;
- is life-threatening;
- requires in-patient hospitalisation or prolongation of existing hospitalisation;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect; or
- is a medically important event or reaction.

NOTE: The term 'life-threatening' in the definition of 'serious' refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event/reaction which hypothetically might have caused death if it were more severe.

For devices is any adverse medical occurrence that:

- led to a death;
- led to a serious deterioration in health of a patient user or other. This would include:
 - a life threatening illness or injury;
 - a permanent impairment of body function or permanent damage to a body structure;
 - a condition requiring hospitalisation or increased length of existing hospitalisation;
 - a condition requiring unnecessary medical or surgical intervention; or
 - foetal distress, foetal death or a congenital abnormality/birth defect;
- might have led to death or a serious deterioration in health had suitable action or intervention not taken place. This includes:
 - a malfunction of a device such that it has to be modified or temporarily/permanently taken out of service; or
 - a factor (a deterioration in characteristics or performance) found on examination of the device.

[Ref: *Access to unapproved therapeutic goods via the Special Access Scheme* (2009)].

Serious unexpected suspected adverse reaction (SUSAR) is a serious adverse event for which there is some degree of probability that the event is an adverse reaction to the administered drug, and the adverse reaction is unexpected.

Single centre research is research that is conducted at one site only within the NSW public health system (i.e. single-site research) or at two or more sites under the jurisdiction of a single NSW Health HREC.

Site is a facility, location or service where the research is being conducted.

Site authorisation is the authorisation granted by the Chief Executive or delegate of the Public Health Organisation for the commencement of a research project.

Sponsor of a clinical trial is the company, institution or organisation, body or individual that takes overall responsibility for the conduct of the trial and usually initiates, organises and supports the clinical trial.

Therapeutic good is broadly defined as a good which is represented in any way to be, or is likely to be taken to be, for therapeutic use (unless specifically excluded or included under Section 7 of the *Therapeutic Goods Act 1989*). Therapeutic use means use in or in connection with:

- preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury;
- influencing inhibiting or modifying a physiological process;
- testing the susceptibility of persons to a disease or ailment;

- influencing, controlling or preventing conception;
- testing for pregnancy; or
- replacement or modification of parts of the anatomy.

[Ref: <http://tga.gov.au/docs/html/tga/tgaginfo.htm>, last accessed 10/08/2010].

HREC 001: SWSLHD HREC

Objectives

1.1. The objectives of the HREC are to:

- a) Protect the mental and physical welfare, rights, dignity and safety of participants of research;
- b) Promote ethical principles in human research;
- c) Review research in accordance with the *National Statement on Ethical Conduct in Human Research* (2007); and
- d) Facilitate ethical research through efficient and effective review processes.

Functions

1.2. The HREC functions on behalf of the SWSLHD are to:

- a) Provide independent oversight of human research projects;
- b) Provide competent, timely review and monitoring of human research projects in respect of their ethical and scientific acceptability for as long as projects are active;
- c) Determine the compliance of a human research project with the *National Statement* and grant, withhold or withdraw ethical approval; and
- d) Provide advice to the Public Health Organisation on strategies to promote awareness of the ethical conduct of human research.

Accountability

1.3. The HREC is directly accountable to the Chief Executive of the SWSLHD. The minutes of each HREC meeting are forwarded to the Chief Executive or delegate following confirmation.

1.4. The HREC provides an annual report to the Chief Executive or delegate at the end of each financial or calendar year.

1.5. The HREC brings to the attention of the Chief Executive or delegate issues of significant concern.

1.6. The HREC provides the following reports on behalf of the SWSLHD:

- a) Australian Health Ethics Committee (AHEC) report in accordance with the requirements of the National Health and Medical Research Council (NHMRC);
- b) NSW Privacy Commissioner report in accordance with the requirements of the *Health Records and Information Privacy Act 2002* (NSW).

Scope of responsibility

Single-centre research applications

1.7. The HREC provides ethical and scientific review of single-centre research at sites within its jurisdiction.

Ethical and scientific review for external entities

1.8. The HREC reviews human research applications for external institutions/organisations and investigators as approved by the Chief Executive.

- 1.9. Provision of ethical and scientific approval to an external entity is conditional upon the execution of an agreement which specifies the respective legal responsibilities and liabilities for the HREC and the external entity. Refer to Policy Directive 2008_046 *Human Research Ethics Committees: Ethical Review for External Entities*.

Role of the Chairperson

- 1.10. The Chairperson is responsible for the conduct of HREC business and for ensuring that the HREC reaches decisions on all matters. Where the Chairperson is unavailable the meeting will be chaired by the Deputy Chairperson if available, or by the alternate Deputy Chairperson if not.

HREC Executive Committee

- 1.11. The HREC has an Executive Committee comprising at least the HREC Chairperson or their delegate, the Manager of the Ethics and Research Governance Office and one other member of the HREC.
- 1.12. The HREC Executive Committee undertakes expedited review of business that does not require full HREC review, including some or all of the following:
- a) Low and negligible risk research applications;
 - b) Amendments to current HREC approved projects;
 - c) Responses to HREC queries, as approved by the full HREC for HREC Executive Committee review and approval;
 - d) Annual progress reports and final reports; and
 - e) Serious adverse events and suspected unexpected serious adverse reactions reports.
- 1.13. The minutes of the HREC Executive Committee are noted at the next HREC meeting.
- 1.14. The Chairperson has the discretion to delegate to the Executive Officer the authority to undertake review of HREC Executive Committee business that is considered administrative or within the capacity of the Executive Officer such as:
- a) Amendments to Participant Information Sheets and Consent Forms that address changes requested by the HREC and require little interpretation of the ethical impact of the amendments. Changes include standard statements regarding insurance/indemnity, contact details, version control, dates, etc.;
 - b) Amendments to other study documents (e.g. case report forms, patient diaries) that are administrative in nature or of low ethical risk;
 - c) Changes to project personnel; and
 - d) Other issues, on a case-by-case basis, such as responses to HREC queries and annual progress reports and final reports.

HREC subcommittees

- 1.15. HREC subcommittees may be appointed on an ad hoc basis to carry out a review of a specific matter/application(s). Members of such an ad hoc subcommittee need not be members of the HREC, and are appointed by the subcommittee Chairperson.
- 1.16. The minutes of the subcommittee meetings are noted at the next HREC meeting.

Information about the HREC

1.17. SWSLHD will ensure the following information about the HREC is publicly available:

- a) HREC contact details;
- b) Submission closing dates for HREC meetings (and scientific/technical subcommittees if applicable);
- c) HREC meeting dates;
- d) The sites within their jurisdiction for ethical and scientific review.

1.18. The Department of Health ensures that the name and contact details of NSW Health HRECs are publicly available on the Department's website.

1.19. Where the HREC has ceased to function, the Public Health Organisation notifies the Department of Health and the NHMRC and determines the appropriate course of action.

HREC 002: HREC composition

- 2.1. The composition of the HREC is in accordance with the *National Statement*. Minimum membership comprises eight members. As far as possible, men and women are represented in equal numbers and at least one-third of the members are external to the institution for which the HREC is reviewing research. The membership comprises representatives from the following categories:
- a) A Chairperson with suitable experience whose other responsibilities will not impair the HREC capacity to carry out its obligations under the *National Statement*;
 - b) At least two members who are lay people, one man and one woman, with no affiliation with the institution or organisation and not currently involved in medical, scientific, legal or academic work;
 - c) At least one member with knowledge of, and current experience in, the professional care, counselling or treatment of people;
 - d) At least one member who performs a pastoral care role in the community, for example, an Aboriginal elder or a minister of religion;
 - e) At least one member who is a lawyer, where possible one who is not engaged to advise the institution for which the HREC is reviewing research; and
 - f) At least two members with knowledge of and current research experience that is relevant to the applications to be considered at the meetings they attend.
- 2.2. To ensure the HREC is equipped to address all of the relevant considerations arising from the categories of research, some or all of the above membership categories may be represented by more than one person.
- 2.3. No member is appointed in more than one of the membership categories.
- 2.4. The HREC is free to consult person(s) considered by the HREC to be qualified to advise and assist in reviewing applications provided that there is no conflict of interest and an undertaking of confidentiality is given. Such person(s) are not entitled to vote on any matter.

HREC 003: Appointment of members

- 3.1. HREC members are recruited by direct approach, nomination or by advertisement through an open and transparent process.
- 3.2. Prospective members may be invited to observe a meeting of the HREC.
- 3.3. Prospective members are asked to provide a copy of their curriculum vitae to a selection committee comprising the Chairperson, Chief Executive, Manager Ethics and Research Governance Office and at least one other HREC member. The selection committee interviews prospective members, consults with HREC members and makes a recommendation on new appointments to the Chief Executive.
- 3.4. Members are appointed as individuals for their knowledge, qualities and experience and not as representatives of any organisation, group or opinion.
- 3.5. Membership of the HREC is made publicly available.
- 3.6. All members including the Chairperson, Deputy Chairperson and Chairperson of any subcommittee are appointed by the Chief Executive. The letter of appointment includes the date of appointment, length of tenure, indemnity and termination.
- 3.7. Upon appointment, members are provided with an orientation package and asked to sign a statement undertaking:
 - a) that all matters of which he/she becomes aware during the course of his/her work on the HREC will be kept confidential;
 - b) that any conflicts of interest, which exist or may arise during his/her tenure on the HREC will be declared; and
 - c) that he/she has not been subject to any criminal conviction or disciplinary action, which may prejudice his/her standing as an HREC member.
- 3.8. Members are appointed for a period of up to 3 years and may serve only 6 years unless otherwise approved by the Chief Executive or delegate.
- 3.9. The Chairperson, Deputy Chairperson and Chairperson of any subcommittee may serve longer terms with the approval of the Chief Executive or delegate. Members are advised when their term has expired. Reappointment is by application to the Chairperson of the HREC who then makes a recommendation to the Chief Executive or delegate.
- 3.10. New and renewed appointments allow for continuity, development of expertise within the HREC, and regular input of fresh ideas and approaches.
- 3.11. Membership lapses if a member fails to attend:
 - a) Three consecutive meetings without reasonable excuse/apology or exceptional circumstances; and
 - b) At least two thirds of all scheduled HREC meetings in each year, barring exceptional circumstances.
- 3.12. The Chairperson notifies the member of a lapse of membership in writing. Steps are taken to fill the vacancy.

- 3.13. Members seeking to resign or take a leave of absence for an extended period from the HREC are asked to give notice to the Chairperson. Steps are taken to fill the vacancy.
- 3.14. The appointment of any member of the HREC may be terminated if the Chief Executive or their delegate is of the opinion that:
 - a) It is necessary for the proper and effective functioning of the HREC;
 - b) The person is not a fit and proper person to serve on an HREC; or
 - c) The person has failed to carry out their duties as an HREC member.
- 3.15. Members are expected to participate in relevant specialised working groups as required.
- 3.16. The Chairperson is expected to be available between meetings to participate in HREC Executive Committee meetings where required.
- 3.17. The SWSLHD provides indemnity for members of the HREC for liabilities that arise as a result of the member exercising their duties in good faith. Such indemnity is provided through the NSW Treasury Managed Fund.

HREC 004: Orientation and training of members

- 4.1. New HREC members are provided with orientation/training as determined to be appropriate by the SWSLHN.
- 4.2. Orientation involves at least the following:
 - a) Introduction to other HREC members prior to the HREC meeting;
 - b) Provision of an orientation package;
 - c) Informal meeting with the Chairperson and Executive Officer to explain their responsibilities as an HREC member, the HREC processes and procedures;
 - d) 'Partnering' with another HREC member in the same category; and
 - e) Priority given to participate in training sessions.
- 4.3. Each member is:
 - a) expected to become familiar with the *National Statement* and consult other guidelines relevant to the review of specific research applications; and
 - b) encouraged to attend continuing education or professional development activities in research ethics once in each period of appointment.

HREC 005: Meeting schedules

- 5.1. The HREC meets on a regular basis at least every month. The HREC holds at least 11 scheduled meetings in each year for the purposes of reviewing new applications.
- 5.2. Meeting dates and application closing dates are made publicly available.
- 5.3. Additional meetings are held where necessary to ensure that reviews are completed within a timely fashion, to discuss matters relating to the establishment or operating procedures of the HREC or for training purposes.
- 5.4. The schedule of HREC meetings for the calendar year commencing 1 January is ratified by the HREC before or at the last meeting of the previous year. The schedule sets out the dates, times and venues of meetings, and the closing date for submission of applications.
- 5.5. Subcommittee(s) issue similar schedules to their members and are made publicly available.

HREC 006: Agenda

- 6.1. The Executive Officer prepares an agenda for each HREC meeting.
- 6.2. The meeting agenda and associated documents are circulated to HREC members at least 7 days prior to the next meeting electronically and/or as paper copies.
- 6.3. Documentation received after the closing date are included on the agenda and/or tabled at the meeting at the discretion of the Executive Officer and/or Chairperson.
- 6.4. New applications received after the closing dates are not tabled at the meeting.
- 6.5. As a minimum, the agenda includes the following items:
 - a) Attendance and apologies;
 - b) Declarations of conflicts of interest relating to agenda items;
 - c) Confirmation of minutes of the previous HREC meeting;
 - d) Business arising since the previous meeting(s) that the HREC indicated it wished to reconsider;
 - e) Minutes of meetings and any issues for noting and/or approving from the HREC Executive Committee, subcommittees and external expert reviewers for example:
 - Amendments to documents or modifications to applications and research projects;
 - Annual progress reports and final reports;
 - Reports of serious adverse events and suspected unexpected serious adverse reactions;
 - f) New applications for review and, if applicable, the spokesperson or lead reviewer nominated by the HREC to lead the discussion on each application;
 - g) General business; and
 - h) Notification of the date, time and venue of the next scheduled meeting.
- 6.6. The agenda and all documentation are confidential.

HREC 007: Lead reviewers

- 7.1. The HREC will appoint one or more members as lead reviewers for the HREC meeting or subcommittee meeting for each application.
- 7.2. Allocation of applications to lead reviewers is made by the Executive Officer in consultation with the Chairperson, as necessary.
- 7.3. The lead reviewer is provided with a copy of the application and other supporting documentation which they have been allocated to review.
- 7.4. The specific role undertaken by the lead reviewer both at the meeting and following the meeting is at the discretion of the HREC. Local procedures are discussed and agreed by the members.
- 7.5. The Lead reviewer will provide:
 - 7.5.1 A brief overview of the science of the application
 - 7.5.2 An outline of the safety of the study
 - 7.5.3 Issues for ethical consideration
 - 7.5.4 An assessment of whether the study should be ethically approved and if not what issues need to be addressed by the researcher

HREC 008: Attendance of the Investigator

- 8.1. At the request of the HREC Chairperson, the Principal Investigator may be invited to make formal presentation or to respond directly to requests from the HREC for further information, clarification or reassurance.
- 8.2. Where the Principal Investigator is unable to attend, another key investigator or collaborator may be invited to attend, if appropriate. Representatives of the sponsor are not to attend the meeting. Other members of the research team may attend Investigator.
- 8.3. When invited, the Principal Investigator may attend the meeting in person or via telephone or videoconference.

HREC 009: Quorum requirements

- 9.1. A quorum is required at each meeting for the HREC to reach a final decision on any agenda item. The quorum for meetings is at least one member from each of the core categories and the Chairperson/Deputy Chairperson as specified in the *National Statement* attending in person or via telephone or videoconference.
- 9.2. A quorum can be reached where there is less than a full attendance of the minimum membership at a meeting but if the Chairperson is satisfied “that the views of those absent who belong to the minimum membership have been received and considered”, for instance through prior submission of written comments.
- 9.3. Where a quorum is not reached, the HREC will not commence, continue or conclude discussion with the purpose of reviewing an application. The HREC has the discretion to proceed with other business on the agenda as if it were an HREC Executive Committee meeting, provided that the Chairperson (or Deputy Chairperson or alternate Deputy Chairperson) and at least one other member is present.
- 9.4. Where the Executive Officer of the HREC is concerned that a forthcoming meeting will not be attended by a quorum of members the Executive Officer notifies the Chairperson and the following options are considered:
 - a) Postponing and re-arranging the meeting; or
 - b) Cancelling the meeting.

HREC 010: External expert reviewers

Use of external expert reviewers

- 10.1. If the HREC is unable to make a decision on an application or without the necessary expertise, the advice of an external expert reviewer may be sought through experts by the Chairperson and/or the Executive Officer.
- 10.2. Scientific review of clinical drug trials for NSW Health HRECs must be undertaken in accordance with the provisions in Policy Directive 2007_035 *Standards for scientific review of clinical trials*.
- 10.3. Advice from other external expert reviewers is sought through the following procedures
 - a) Notification is sent to the Principal Investigator either before or following the HREC meeting explaining that a final decision will not be made on the application until advice is obtained from an expert reviewer. The letter notifies the Principal Investigator of the issues of concern to the HREC, but does not request further information or clarification. In circumstances where expert scientific opinion is sought, the Principal Investigator is given the option to identify experts to whom they object.
 - b) If possible, a suitable expert reviewer is identified by the Chairperson/Executive Officer or by the HREC during the meeting.
 - c) The Chairperson or Executive Officer initially contacts the prospective expert reviewer(s) by telephone or email to establish whether they are available to provide expert advice within the required time frame and that they have no connection with the research that might give rise to a conflict of interest. The expert reviewer is advised about confidentiality requirements.
 - d) The Executive Officer specifies in writing the issues of concern to the HREC and the expert advice required, and requests written advice and/or attendance (but not voting) at the HREC meeting. The Executive Officer ensures that the expert reviewer declares any conflict of interest and signs a declaration and confidentiality agreement.
- 10.4. A copy of the application is provided together with any supporting documentation required by the expert reviewer. The HREC, or HREC Executive Committee or subcommittee as appropriate, considers the advice of the expert reviewer and makes an independent decision on the ethical and scientific acceptability of the application. The advice is recorded in the minutes.

HREC 011: Declaration of interest

- 11.1. An HREC member declares to the HREC any conflicts of interest they have in relation to an application for ethical and scientific review or any other matter for consideration at that meeting. Conflict of interest includes financial interests, personal, professional or institutional benefits or advantages that depend significantly on the research outcomes.
- 11.2. Declarations are made orally at the meeting prior to the matter being considered or in writing to the Chairperson prior to the meeting. The HREC determines whether the level of interest results in:
 - a) A substantial conflict of interest: a member is excluded from the meeting where there is a substantial conflict of interest until the HREC has concluded consideration of the matter. Being an investigator on a research project is considered to represent a substantial conflict of interest.
 - b) A non-substantial conflict of interest: the member has the discretion to leave during the discussion of the matter.
- 11.3. The minutes record declaration of interest and the decision of the HREC on the procedures to be followed.

HREC 012: Confidentiality

Confidentiality of meetings

12.1. The confidentiality of the HREC proceedings is essential as:

- a) Members do not sit on the HREC in a representative capacity;
- b) Applications need to be discussed freely; and
- c) Applications may have commercial implications.

12.2. HREC meetings are held in private and members are encouraged to raise matters of concern.

12.3. Confidentiality is addressed in two ways:

- a) The HREC Terms of Reference; and
- b) Members signing a statement of undertaking upon appointment.

12.4. Attendance of visitors or observers at a meeting, as appropriate and approved by the Chairperson, is conditional on the attendee signing a confidentiality agreement.

Confidentiality of applications

12.5. Applications, supporting documentation and correspondence are treated confidentially.

12.6. External expert reviewers providing advice to the HREC are asked to sign a confidentiality agreement.

12.7. HREC correspondence is addressed to the Principal Investigator and also sent to the relevant contact person identified on the application form. Correspondence is not released to the sponsor or any other parties.

12.8. Principal Investigators forward information about matters raised in the ethical review to sponsors or other parties where necessary.

HREC 013: Decision making

- 13.1. Members present are allowed reasonable opportunity to express relevant views on matters on the agenda.
- 13.2. The HREC endeavours to reach a decision concerning the ethical and scientific acceptability of a research project by unanimous agreement.
- 13.3. Where a unanimous decision is not reached, the matter is determined by a majority of two-thirds of members present at the meeting, provided that the majority includes at least one layperson.
- 13.4. Any significant minority view (i.e. 2 or more members) is noted in the minutes.
- 13.5. Discussions of significant issues and decisions are recorded in the minutes. Where members wish, a record of their formal dissent from the decision of the HREC is recorded in the minutes.
- 13.6. To encourage free and open discussion and to emphasise the collegiate character of the HREC, particular views are not attributed to particular individuals in the minutes, except in circumstances where a member seeks to have their opinions or objections recorded.
- 13.7. An HREC member unable to attend a meeting may submit comments in writing on agenda items to the Executive Officer or Chairperson prior to the meeting. Submission of written comments is recorded in the minutes.

HREC 014: Decisions available to the HREC

- 14.1. The HREC selects one of the following decisions on any application reviewed at a meeting and the decision is recorded in the minutes:
- a) Approve the application as being ethically and scientifically acceptable;
 - b) Request modification or further information/clarification;
 - c) Seek further advice from external expert reviewer(s); or
 - d) Reject the application.
- 14.2. The Chairperson ensures that one of the above decisions is made on every application considered at an HREC meeting.
- 14.3. Where the HREC decides that further information or clarification is required, the Chairperson ensures that:
- a) Further information or clarification required is specifically identified at the meeting; and
 - b) Delegation of responsibility for considering the further information or clarification and confirming the final HREC opinion is clearly agreed, i.e. the information will need to be re-submitted to the full HREC, a number of HREC members, the HREC Executive Committee, or the HREC Executive Officer.
- 14.4 Members of the HREC that are requested to review further information per above are required to do so within 10 working days of receipt of that information from the investigator/HREC Executive Officer

HREC 015: Minutes

15.1. The Executive Officer prepares the minutes of the HREC meeting in consultation with the Chairperson and other members as necessary. The minutes are subsequently approved by the Chairperson within 10 working days of the meeting.

15.2. The minutes reflect each item listed for discussion on the agenda:

- a) Attendance and apologies;
- b) Declarations of conflicts of interest relating to agenda items;
- c) Confirmation of minutes of the previous HREC meeting;
- d) Business arising since the previous meeting(s) that the HREC indicated it wished to reconsider;
- e) Minutes of meetings and any issues for noting and/or approving from the HREC Executive Committee, subcommittees and external expert reviewers;
- f) Amendments to documents or modifications to applications and research projects;
- g) Annual progress reports and final reports referred to the HREC by the HREC Executive Committee; and
- h) Reports of serious adverse events and suspected unexpected serious adverse reactions referred to the HREC by the HREC Executive
- i) HREC deliberations and decisions on new applications, whether in the main text of the minutes or in attachments:
 - Submission of written comments by members;
 - Summaries of the advice given by expert or lead reviewers;
 - Summaries of the main issues considered;
 - Decisions of the HREC on the application; and
 - Formal dissent from the decision of the HREC by a member and the reason for it and/or any significant minority views (i.e. 2 or more members)
- j) General business; and
- k) Notification of the date, time and venue of the next scheduled meeting.

15.3. The minutes are submitted at the next meeting of the HREC for ratification as a true record. Members are given the opportunity to seek amendments to the minutes prior to their finalisation.

15.4. The minutes are confidential to the HREC and are not disclosed to investigators or sponsors.

15.5. The minutes of HREC meetings are made available to the Chief Executive or their delegate and, upon request, to the Research Governance Officer of the site where the research is to be conducted.

HREC 016: Duration of HREC approval

- 16.1. HREC approval applies for a maximum of five years, except where action is taken to suspend or terminate the decision.
- 16.2. The request to extend the duration of the research project is submitted by the Principal Investigator as an amendment for review by the HREC in the first instance.
- 16.3. The HREC/Executive Committee may agree that the research project should be resubmitted as a new application if it has significantly altered from the original.
- 16.4. HREC approval for an extension applies for a maximum of five years, except where action is taken to suspend or terminate the decision.

HREC 017: HREC reporting requirements

- 17.1. The ratified minutes of each HREC meeting are forwarded to the Chief Executive or delegate.
- 17.2. The HREC provides an annual report to the Chief Executive or delegate by 30th June each year, which includes:
- a) Membership/membership changes;
 - b) Number of meetings;
 - c) Number of research projects reviewed, approved and rejected;
 - d) Monitoring procedures for ethical aspects of research in progress and issues identified by the HREC in undertaking its monitoring role;
 - e) Description of any appeals and complaints received and their outcome;
 - f) Description of any research where HREC approval has been suspended or withdrawn and the reasons for this action;
 - g) General issues including advice on strategies to promote awareness of the ethical conduct of human research in the institution; and
 - h) Resources to assist the HREC in fulfilling its role.
- 17.3. The HREC completes and submits reports on behalf of the SWSLHD to the:
- a) Australian Health Ethics Committee (AHEC) in accordance with the requirements of the NHMRC; and
 - b) NSW Privacy Commissioner in accordance with the requirements of the *Health Records and Information Privacy Act 2002 (NSW)*.

HREC 018: Clinical Trial Notification and Clinical Trial Exemption schemes

- 18.1. Unapproved therapeutic goods have undergone limited or no evaluation of quality, safety or efficacy by the Therapeutic Goods Administration (TGA). Use of these products is considered to be experimental and potentially carries risks that have not been defined in the Australian context.
- 18.2. There are two schemes under which clinical trials involving a new therapeutic good or new uses of a therapeutic good can be conducted in Australia: the Clinical Trial Notification (CTN) scheme and the Clinical Trial Exemption (CTX) scheme.
- 18.3. The investigator's obligations under the *Therapeutic Goods Act 1989* and application forms to conduct clinical trials under the CTN or CTX scheme are detailed at: <http://www.tga.gov.au/ct/index.htm>

CTN/CTX HREC application requirements

- 18.4. The investigator completes all sections of the CTN or CTX form before submission to the HREC, including details of:
- a) Investigational product;
 - b) Comparator product (if applicable);
 - c) All other drugs administered as part of the trial (approved and unapproved);
 - d) Trial site;
 - e) Sponsor; and
 - f) Investigator.
- 18.5. For review of a trial under the CTX scheme, the investigator also provides the HREC with all related correspondence to and from the TGA.
- 18.6. The CTN or CTX form, signed by the Principal Investigator, is provided to the HREC at the time of submission of a new application.
- 18.7. If the application is approved, the HREC signs the CTN or CTX form at section 3 and returns it to the Principal Investigator or the Research Governance Officer.

Adding trial sites following initial notification to the TGA

- 18.8. For additional trial sites which have not been included in the original application to the HREC, a new complete CTN or CTX form is required. This form must indicate that its purpose is to add a trial site at section 1.1 (CTN) or section 1.3 (CTX) of the form.

HREC 019: Authorised prescriber applications

19.1. Under subsections 19(5-9) of the Act and Regulation 12B, the TGA is able to grant a medical practitioner authority to prescribe a specified unapproved therapeutic good or class of unapproved therapeutic goods to specified recipients or classes of recipients (identified by their medical condition). An Authorised prescriber can then prescribe that product for that condition (also known as 'the indication') and no approval from the TGA is required for each individual patient. The legislation requires:

- An Authorised Prescriber to be a medical practitioner;
- A medical practitioner to obtain endorsement from an appropriate HREC; or
- Where a medical practitioner does not have access to an HREC and this can be demonstrated to TGA, the medical practitioner may obtain endorsement from a specialist college having an established expertise relevant to the use of the medicines concerned.

Regulation 12B(4) states that medical devices may only be approved for medical practitioners practising in hospitals. Approval must be obtained from the HREC at the institution at which the practitioner practices. Approval will not be given to medical practitioners to use medical devices outside the hospital setting.

Full details of Authorised Prescribers are available from the TGA at

<http://www.tga.gov.au/hp/ap.htm>

19.2. When reviewing applications to become an Authorised Prescriber, the HREC needs to assess not only the safety of the product in relation to its proposed use, but also the suitability of the medical practitioner. The HREC considers:

- a) The indication for which the product will be prescribed;
- b) Efficacy and safety of the product in relation to its proposed use;
- c) For medicines, the route of administration and dosage form;
- d) Clinical justification for use of the product;
- e) Suitability of the medical practitioner; and
- f) Patient information about the product and the informed consent form.

19.3. The applicant must provide the following documentation to the HREC:

-A cover letter explaining the request and including details of the condition to be treated, its seriousness and why this drug is being used to treat the condition.

-Details of the named prescriber to support the application. This should include information about whether the practitioner is seeking to treat a condition in his/her area of specialty or training and expertise. In general, endorsement will only be given when the practitioner has training and expertise appropriate for the proposed use of the product. A CV will normally demonstrate this training and expertise but the prescriber may submit other information to support his/her request such as past experience in prescribing the drug (attach CV of intended prescriber)

-Information about the drug and its use for the indication for which it will be prescribed, including the route of administration, dosage form, a clinical justification for its use, an assessment of the efficacy and safety of the product in relation to its proposed use, information about its previous use in humans and associated adverse events (attach an investigator brochure or equivalent if available)

-A patient information and consent form

-Any other material to support your request.

19.4. If endorsed, the HREC provides a letter to the applicant in the format suggested by the TGA. The HREC may impose conditions on the endorsement, if required, such as:

- a) Regular reports to the HREC comprising information such as the number of patients prescribed the unapproved product; and
- b) Reporting of adverse events.

19.5. The HREC will review its endorsement of the Authorised Prescriber if it is aware of:

- a) Inappropriate use of the product by the Authorised Prescriber;
- b) Safety concerns about the product;
- c) Failure of the Authorised Prescriber to comply with conditions imposed by the HREC; or
- d) Failure of the Authorised Prescriber to comply with legislation.

19.6. Where the HREC is satisfied that the welfare and/or rights of patients are not or will not be protected, it will:

- a) Advise the medical practitioner and the Chief Executive of its concerns;
- b) Withdraw its approval of the Authorised Prescriber if it is satisfied that the welfare and/or rights of patients are not or will not be protected; and
- c) Report to the TGA (Chief Executive and Chairperson to determine).

19.7. To review access to unapproved therapeutic goods via Authorised Prescribers, the HREC and SWSLHD will determine the best process for considering applications. This process may consist of:

- a) Determination by the HREC Executive Committee; and/or
- b) Consultation with the LHD drug committee or delegate.

19.8. Decisions by the HREC Executive Committee are tabled for ratification at the next HREC meeting.

Institutional approval

19.9. Final responsibility for the use of an unapproved product within an institution always rests with that institution. Medical practitioners working in a NSW Public Health Organisation should discuss the use of the unapproved therapeutic product and identify the approval process with the institution before applying for authorisation.

Letter of endorsement for Authorised Prescriber

[Dr's name]
[Title (if applicable)]
[Dr's address]

Dear Dr [],

Re: Ethics committee endorsement for the purpose of becoming an Authorised Prescriber of an unapproved product under section 19(5) of the Therapeutic Goods Act

The SWSLHN Human Research Ethics Committee hereby endorses you for the purpose of becoming an Authorised Prescriber under section 19(5) of the Therapeutic Goods Act.

This endorsement is restricted to the following circumstances:

Unapproved product: [drug/ device: trade and generic names if available]

Indication for use: [illness/condition/class of patient]

Site(s) covered by the endorsement: [hospital/rooms etc]

Conditions imposed by the HREC: [provision of usage reports to HREC]
[reporting of adverse events to HREC]

Please present a copy of this endorsement letter to the TGA as part of your application to become an Authorised Prescriber.

Yours sincerely
[]
Chair
[] Human Research Ethics Committee
Date //

HREC 020: Special Access Schemes

20.1. The Special Access Scheme (SAS) refers to the arrangements which provide for the import and/or supply of an unapproved therapeutic good on a single patient, case-by-case basis under of the *Therapeutic Goods Act 1989*, *Therapeutic Goods Regulations 1990* and *Therapeutic Goods (Medical Devices) Regulations 2002*. Full details of SAS are available from the Therapeutic Goods Administration (TGA) at <http://www.tga.gov.au/hp/sas.htm>.

20.2. For the purposes of SAS, patients are categorised as follows:

- a) Category A patients: “persons who are seriously ill with a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment”. Medical practitioners can import and/or supply the unapproved therapeutic goods to this category of patient, having obtained the informed consent of the patient or the patient’s legal representative, without the approval of the TGA but the TGA must be notified using the Category A Form Special Access Scheme form.
- b) Category B: “all other patients”. Medical practitioners must obtain approval from a delegated medical officer within the TGA or a delegate outside the TGA (external delegate) to import and/or supply the unapproved therapeutic good.

20.3. The choice of categorisation lies with the prescriber.

‘External Delegates’

20.4. When seeking approval to supply unapproved therapeutic goods to a single patient, if appropriate, medical practitioners may apply to a nominated ‘external delegate’ An ‘external delegate’ is a person external to the TGA, given the delegation to approve the supply of unapproved therapeutic goods.

20.5. HREC responsibilities in relation to SAS are primarily concerned with granting approvals under section 19(1)(a) of the *Therapeutic Goods Act 1989*. In accordance with *Therapeutic Goods Regulation 1990* 47A (6)(b) and *Therapeutic Goods (Medical Devices) Regulations 2002* 10.6(6)(b), all SAS applications approved by an ‘external delegate’ must be approved by an HREC. In practice, external delegations are rare and thus HRECs are not asked to deliberate on such issues as a routine matter.

20.6. Before agreeing to an approval by an ‘external delegate’, the HREC requires the following information:

- a) The product for which approval is sought;
- b) Whether that unapproved product is included on the list of products which can be approved by the practitioner;
- c) Details about the product to be prescribed, including an assessment of the efficacy and safety of the product;
- d) The medical condition for which approval is sought;
- e) An assessment of the seriousness of the condition treated;

- f) The intended mode of use/treatment and whether this conforms to the treatment protocol; and
- g) The clinical justification for use of the unapproved product, including the nature and availability of alternative treatments.

20.7. Further details on the role of HREC in agreeing to an approval by an 'external delegate' are provided in the TGA *Human Research Ethics Committees and the Therapeutic Goods Legislation*, June 2001.

20.8. The HREC and SWSLHD will determine the best process for considering request for approval by an external delegate. This process may consist of:

- a) Determination by the HREC Executive Committee; and/or
- b) Consultation with the hospital drug and therapeutics committee; and/or
- c) Consultation with the scientific subcommittee.

20.9. Decisions by the HREC Executive Committee are tabled for ratification at the next HREC meeting.

Institutional approval

20.10. Final responsibility for the use of an unapproved product within an institution always rests with that institution. Medical practitioners working in a NSW Public Health Organisation within SWSLHD should discuss the use of the product and the approval process with the Executive Officer before applying for authorisation.