

**NBMLHD HUMAN RESEARCH ETHICS  
COMMITTEE**

**STANDARD OPERATING PROCEDURES**

*Updated September 2022*

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## HREC 001: NSW Health HRECs

### Objectives

- 1.1 The objectives of the NBMLHD HREC are to:
- Protect the mental and physical welfare, rights, dignity and safety of participants of research.
  - Promote ethical principles in human research.
  - Review research in accordance with the [National Statement on Ethical Conduct in Human Research \(2007\) updated 2018](#).
  - Facilitate ethical research through efficient and effective review processes.
  - Protect the privacy and confidentiality of participants and / or their personal health information in compliance with the [Health Records and Information Privacy Act \(2022\)](#).

### Functions

- 1.2 The NBMLHD HREC functions on behalf of the Public Health Organisation are to:
- Provide independent oversight of human research projects in accordance with NSW Health system of single ethical and scientific review and in line with the National Statement requirements to minimise duplication of ethical review.
  - 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.
  - Determine the compliance of a human research project with the *National Statement* and grant, withhold or withdraw ethical approval.
  - Provide advice to the Public Health Organisation on strategies to promote awareness of the ethical conduct in human research.

### Accountability

- 1.3 The NBMLH HREC is directly accountable to the Chief Executive of the Public Health Organisation under which it is constituted. The NBMLHD HREC brings to the attention of the Chief Executive or delegate issues that may be of significant concern.
- 1.4 The minutes of each HREC meeting are confirmed and ratified at the following meeting.
- 1.5 A CE Report is prepared each meeting and ratified at the following HREC meeting. In quarter 3 of each year an Annual Report will be prepared for the CE summarising the previous 4 quarters of HREC activity. The HREC provides the following reports on behalf of the Public Health Organisation:
- Annual National Health and Medical Research Council (NHMRC).
  - Continuous Certification Monitoring requests to the National Health and Medical Research council (NHMRC) and any other reports as required.
  - NSW Privacy Commissioner report in accordance with the requirements of the [Health Records and Information Privacy Act 2002 \(NSW\)](#).
  - Monitoring Measures: The NBMLHD HREC will undertake its review in a timely and efficient manner and have mechanisms to monitor and evaluate its performance.

### Scope of responsibility

- 1.6 The NBMLHD HREC is accredited by the NSW Ministry of Health as a lead HREC. The responsibilities of the HREC are to conduct the scientific and ethical review of human research on behalf of the NSW public health system in the categories of:
- Clinical Trials Phases II, III & IV
  - Clinical Trials drugs, devices and surgery
  - Clinical Trials other
  - Clinical Interventional research other than clinical trials

- Population health and / or public health
  - Qualitative Research
  - Mental Health
  - Paediatric and adolescent medicine research
  - Retrospective / prospective and audit type research
  - Other Health and Medical Research Including – Laboratory research on human specimens, pregnant women and human foetus research, survey research; retrospective / prospective
- 1.7 Review human research applications where the research takes place at:
- Any institutions governed by NSW Public Health Organisations for multi-centre studies; and/or
  - Any institutions governed by Nepean Blue Mountains Local Health District for single-centre studies; and/or
  - External institutions/organisations and investigators seeking research ethics approval from the NBMLHD HREC where there is no other appropriate HREC to provide such review, and it is impractical for the external entity to constitute such a HREC.
  - The HREC may review applications from interstate institutions or organisations within the scope of a scheme of National Mutual Acceptance (NMA) of ethical and scientific review entered into by NSW Ministry of Health on behalf of the NBMLHD HREC.
- 1.8 Monitor Safety as per the NHMRC Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods November 2016, the NSW Ministry of Health Policy Directive – [Safety Monitoring and Reporting for Clinical Trials Conducted in NSW Public Health Organisations \(PD2017\\_039\)](#).
- 1.9 The HREC may provide scientific assessment of new and innovative therapies if required by the Interventional Procedures Assessment Committee (NIPAC) within NBMLHD or the NBMLHD Executive.

### **NBMLHD HREC Subcommittees:**

- 1.10 HREC subcommittees are appointed to advise the NBMLHD HREC on the ethical and scientific aspects of research applications. Members of the subcommittees need not be members of the HREC and are appointed by the Subcommittee Chairperson. The Chairs of the Subcommittees must be a member of the NBMLHD HREC.
- 1.11 NBMLHD HREC Subcommittees may be appointed on an ad hoc basis to carry out a review of specified matter / applications (s). Members of such an ad hoc committee need not be members of the HREC and are appointed by the Subcommittee Chairperson.
- 1.12 The NBMLHD HREC endorses the Terms of Reference of its subcommittees, and which are embedded in the following sections.
- 1.13 The NBMLHD HREC has an Executive Committee comprising of at least the HREC Chairperson, the HREC Deputy Chair or their delegate and a member of the Research Development Governance Unit (RDGU).
- 1.14 The NBMLHD HREC has a Low and Negligible Risk (LNR) Subcommittee comprising of the NBMLHD HREC Chair, HREC Deputy Chair, a member of the RDGU and other members as deemed appropriate by the HREC Chair.

- 1.15 The NBMLHD HREC has a Quality Improvement / Quality Assurance Committee called The Apollo Subcommittee comprising of The Manager of the Clinical Governance Unit (CGU) and other members from the CGU as appointed by the Chair. At least two members and the Chair will review applications.
- 1.16 The minutes and decision of the NBMLHD HREC Subcommittees are noted and ratified at the next HREC meeting.

#### **NBMLHD HREC Executive Committee:**

- 1.17 The HREC Executive Committee is delegated to undertake expedited review and approval of business that does not require full HREC review, including some or all the following:
  - Amendments to current HREC approved research projects.
  - Protocol deviations and violations.
  - Clinical Case Reports / Series.
  - Responses to HREC queries, as approved by the full HREC for HREC Executive Committee review and approval.
  - Annual progress reports and final reports.
  - Requests for extensions of approvals (or annual renewals) without significant change to the project.
  - Significant Safety Issues and Urgent Safety Measures.
  - Noting of correspondence including – Annual Safety Reports, Data Safety Monitoring Board Reports, Safety Update Reports and Data Safety Monitoring Reports.
  - To review and approve applications under the Special Access Scheme (SAS) and Authorised Prescriber Scheme for use of unapproved therapeutic goods via the Therapeutic Goods Administration (TGA) [under sections 19(5) and 41HC of the TGA Act 1989].
  - Any other matters deemed necessary for review by the HREC Executive Subcommittee.
  - The Executive Committee may review urgent HREC business and (as appropriate) grant covering or final approval for the item.

The Executive Committee may seek advice from appropriate sources before reaching a decision.

- The Executive Committee may refer or escalate matters to the full HREC Committee for review.
- The Executive Committee will be considered quorum where the HREC Chair or Deputy Chair and RDGU member are present.

#### **Low and Negligible Risk (LNR) Subcommittee:**

- 1.18 The National Statement permits institutions to establish levels of ethical review that are proportionate to the degree of risk involved. The LNR Subcommittee is delegated to undertake ethical review of Low and Negligible Risk Research as defined in the National Statement.
- 1.19 In addition, it functions as per the NSW Office of Health and Medical Research Guidelines for Low and Negligible (LNR) Research review processes or Exemption form Ethics Review Version 1.1 dated 31 May 2018.
- 1.20 The LNR Subcommittee aims to expedite the review of LNR research applications.

**Apollo Subcommittee: Subcommittee:**

- 1.21 The Apollo Subcommittee (AS) is a subcommittee of the NBMLHD HREC. Its purpose is to review and approve quality assurance and quality improvement initiatives and projects for ratification by the NBMLHD HREC in accordance with the.
  - NSW Health Guideline (GL2007-020) – HRECs – QI & Ethical Review: A Practice Guide for NSW.
  - The NHMRC Ethical Considerations in Quality Assurance, Evaluation Activities (March 2014), and
  - The National Statement on Ethical Conduct in Human Research 2007 (updated 2018).
- 1.22 It is responsible for the review and oversight of the ethical aspects of Quality Improvement Projects in accordance with the National Statement on Ethical Conduct in Human Research (2007 updated in 2018).
- 1.23 Quality Assurance and Quality Improvement includes but is not limited to clinical audits, quality improvement initiatives and projects of various methodologies including redesign, practice development, improvement science and accelerated implementation methodology.
- 1.24 In making recommendations to the HREC regarding the approval of projects submitted to the Committee for review, the following considerations will be taken into account:
  - Privacy and Confidentiality – consent; data collection, usage and storage processes; reporting results.
  - Risks and Burdens - beyond those expected to be experienced as a part of routine care or employment.
  - Appropriateness of qualifications, expertise and/or supervision of personnel proposing to undertake the proposed project.
  - To promote, train, mentor and support the conduct of Practice Improvement in the NBMLHD.
- 1.25 The Apollo Subcommittee shall have delegated authority from the HREC Chair to conduct the review of applications and grant approval for ratification by the HREC.
- 1.26 The Apollo Subcommittee Chair is required to be a member of the NBMLHD HREC. The Chair of a members from the Committee should attend the NBMLHD HREC meeting on a rotating basis.
- 1.27 The Apollo Subcommittee shall provide a quarterly report to the NBMLHD HREC of its activity in the previous months of that quarter, for ratification and reporting to the CE.

## 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. Public Health Organisations are encouraged to establish a pool of inducted members in each membership class who attend meetings as needed to meet the HREC requirements and are available to provide expertise for the research under review.
- 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, Executive Officer 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. The Chief Executive or delegate, in consultation with the Chairperson, may implement a probationary period.
- 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 Public Health Organisation 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 Public Health Organisation.
- 4.2 Orientation involves some or all of 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 4 weeks. 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 Other subcommittees issue similar schedules to their members.

## **HREC 006: Agenda**

- 6.1 The Research Development Governance (RDGO) 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 via the Research Ethics and Governance Information System (REGIS).
- 6.3 Documentation received after the closing date are included on the agenda and/or tabled at the meeting at the discretion of RDGU Officer and/or Chairperson.
- 6.4 New applications received after the closing date are not tabled at the meeting unless decided otherwise.
- 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, LNR and Apollo subcommittees and external expert reviewers for example.
  - f) Amendments to documents or modifications to applications and research projects.
  - g) Annual progress reports and final reports.
  - h) Reports of serious adverse events and suspected unexpected serious adverse reactions;
  - i) New applications for review and, if applicable, the spokesperson or lead reviewer nominated by the HREC to lead the discussion on each application.
  - j) General business.
  - k) 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 has the discretion to appoint one or more members as lead reviewers for the HREC meeting or the subcommittee meeting for each application.
- 7.2 Allocation of applications to lead reviewers is made by the RDGU Officer in consultation with the Chairperson or the Research Manager, 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.

## **HREC 008: Attendance of the Co-ordinating Investigator**

- 8.1 At the request of the HREC Chairperson, the Co-ordinating Investigator is invited to make formal presentation or to respond directly to requests from the HREC for further information, clarification or reassurance.
- 8.2 Where the Co-ordinating Investigator is unable to attend, another key investigator or collaborator is invited to attend, if appropriate. Representatives of the sponsor are not to attend the meeting in place of the Co-ordinating Investigator. Other members of the research team may attend with the Co-ordinating Investigator.
- 8.3 The Co-ordinating Investigator attends 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 RGDU Officer of an HREC is concerned that a forthcoming meeting will not be attended by a quorum of members the RGDU 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 An HREC unable to make a decision on an application or without the necessary expertise is able to seek the advice of an external expert reviewer through the NSW Health Shared Scientific Assessment Committee or through experts identified in the area by the Chairperson and/or the Executive Officer.
- 10.2 The Shared Scientific Assessment Committee provides independent scientific review of clinical drug trials for NSW Health HRECs that are unable to meet 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 Co-ordinating 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 Co-ordinating 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 Co-ordinating Investigator is given the option to identify experts to whom they object.
  - b) A suitable expert reviewer is identified by the Chairperson/ RGDU Officer or by the HREC during the meeting.
  - c) The Chairperson or RGDU 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 RGDU 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 RGDU 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 form 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 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 Co-ordinating Investigator and sent to the Co-ordinating Investigator, or the relevant contact person identified on the application form. Correspondence is not released to the sponsor or any other parties.
- 12.8. Co-ordinating 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 or the HREC Executive Committee or the HREC Chair.

## **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; and
  - h) Reports of serious adverse events and suspected unexpected serious adverse reactions.
  - 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 Coordinating Investigator as an amendment for review by the HREC in the first instance.
- 16.3. 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 in Q 3 of each year (covering the previous 4 quarters of HREC activity), 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 Public Health Organisation to the:
- a) Australian Health Ethics Committee (AHEC) in accordance with the requirements of the NHMRC.
  - b) NSW Privacy Commissioner in accordance with the requirements of the *Health Records and Information Privacy Act 2002 (NSW)*.
  - c) Annual Report to the National Health and Medical Research Council (NHMRC);
  - d) Continuous Certification Monitoring requests to the National Health and Medical Research Council (NHMRC), and any other reports as required.

## 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 Clinical Trials conducted in Australia are subject to various regulatory controls to ensure the safety of participants, The TGA regulate the use of therapeutic goods supplied in clinical trials in Australia under the therapeutic goods legislation <https://www.tga.gov.au/legislation-legislative-instruments>
- 18.3 Clinical Trials sponsors must be aware of the requirements to import, export and manufacture and supply therapeutic goods in Australia.
- 18.4 The following avenues provide for the importation into and / or supply in Australia of unapproved therapeutic goods for use in a clinical trial:
- Clinical Trial Notification (CTN) scheme and,
  - Clinical Trial Exemption (CTA) scheme.
- 18.5 Clinical Trials that do not involve unapproved therapeutic goods are not subject to requirements of the CTN or CTA schemes. It is the responsibility of the Australian clinical trial sponsor to determine whether a product is considered an unapproved therapeutic good.

### CTN/CTA HREC application requirements

- 18.6 The CTN scheme is a **notification** process involving the following:
- The clinical trial sponsor must notify the TGA of the intent to sponsor a clinical trial involving the use of an unapproved therapeutic good. The notification must be submitted online and accompanied by the relevant fee.
  - The TGA may write to the sponsor to provide specified information related to the goods notified in the CTN form.
  - The HREC reviews the scientific validity of the trial design, the balance of risk versus harm of the therapeutic good, the ethical acceptability of the trial process and approves the trial protocol. The HREC is also responsible for monitoring the conduct of the trial.
  - The institution or organisation at which the trial will be conducted, referred to as the 'Approving Authority', gives the final approval for the conduct of the trial at the site, having due regard to advice from the HREC.
  - It is the responsibility of the sponsor to ensure that all the relevant approvals are in place before supplying the unapproved therapeutic goods in the clinical trial.
- 18.7 CTN Form:
- The Online CTN Form can be accessed via the [TGA business services website](#)
  - Further information about CTN can be accessed via the [TGA website](#).
- 18.8 CTA Scheme is an **approval** process involving the following:
- A sponsor submits an application to the TGA seeking approval to supply unapproved therapeutic goods in a clinical trial. The application must be accompanied by the relevant fee.



- The TGA evaluates the summary information about the product including relevant, but limited, scientific data (which may be preclinical and early clinical data) prior to the start of a trial.
  - The HREC is responsible for considering the scientific and ethical issues of the proposed trial protocol.
  - The sponsor must notify the TGA of each trial conducted using the unapproved therapeutic goods approved in the CTA application.
- 18.9 CTA Form: These applications are submitted via a paper-based form. There are two forms that must be completed and submitted by the sponsor and posted to the TGA. The forms can be found at [CTN Forms](#).
- 18.10 Further resources on how to complete CTN and CTA can be found at [Clinical guidance](#) section on the TGA website.
- 18.11 The [Australian Clinical Trial Handbook](#) also provides guidance on conducting clinical trials in Australia using 'unapproved' therapeutic goods.

## HREC 019: Authorised prescriber applications

- 19.1 In accordance with the *Therapeutic Goods Act 1989*, *Therapeutic Goods Regulations 1990* and *Therapeutic Goods (Medical Devices) Regulations 2002*, the Therapeutic Goods Administration (TGA) is able to grant to 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. For further information please refer to Authorised Prescriber Scheme – Guidance for Medical Practitioners, Human Research Ethics Committees, Specialist Colleges and Sponsors. Full details of Authorised Prescribers are available from the TGA at <https://www.tga.gov.au/form/authorised-prescribers> OR frequently asked questions about Authorised Prescribers <https://www.tga.gov.au/frequently-asked-questions-about-authorised-prescribers>
- 19.2 On 1<sup>st</sup> July, 2017, the TGA implemented a change to the application process of the Authorised Prescriber Scheme to streamline access to unapproved therapeutic goods. **This change removed the requirement for a medical practitioner to resubmit their clinical justification to the TGA as this is required to be submitted to and be evaluated by a Human Research Ethics Committee (HREC) or specialist college.** The duration of approval may now also be extended for therapeutic goods which are deemed to have an established history of use – from one year to two years for medical devices and from two years to five years for medicines and biologicals, at the discretion of the Delegate who makes the decision. Please refer to the TGA website for the list of goods that are deemed to have an established history of use <https://www.tga.gov.au/authorised-prescriber-scheme>
- 19.3 Medical practitioners can become Authorised Prescribers under the Therapeutic Goods Act 1989 [http://www.austlii.edu.au/au/legis/cth/consol\\_act/tga1989191/](http://www.austlii.edu.au/au/legis/cth/consol_act/tga1989191/) and its associated regulations. Other health practitioners, including dentists, are not eligible to become Authorised Prescribers. These practitioners may be able to access unapproved therapeutic goods for individual patients under the Special Access Scheme <https://www.tga.gov.au/form/special-access-scheme>
- 19.4 To become an Authorised Prescriber, a medical practitioner must provide the following information which will need to be approved by a Human Research Ethics Committee:
1. **A completed Authorised Prescriber Scheme application Form**  
<https://www.tga.gov.au/sites/default/files/authorised-prescriber-scheme-application-form.pdf>
  2. **A letter to the NBMLHD HREC Chair including the following items;**
    - a. **A clinical justification** for the use of the unapproved goods for evaluation by the HREC including the indication for use, the seriousness of the condition and the expected benefits of the proposed treatment vs its risk. It should also address the circumstance where there are approved treatments for the same indication specifically:
      - i. Have they been attempted
      - ii. Will they be attempted prior to supplying the unapproved good
      - iii. Why are they inappropriate
      - iv. Why is the proposed unapproved good more appropriate than any approved available alternative

- v. How the risk associated with the use of an unapproved good will be managed
  1. The monitoring that will be undertaken
  2. The process of investigation and reporting adverse events
- vi. The following are **NOT** acceptable justifications for the use of an unapproved good;
  1. **That the unapproved good is less expensive**
  2. **Personal preference for an unapproved good**
- b. A determination as to whether any suitable alternative marketed goods are available on the ARTG
- c. **Details of the medical practitioner** including name, contact details, qualifications (speciality training and experience), description of how they propose to use the goods. This should include details that the medical practitioner has the necessary experience to appropriately manage the medical condition and use the product. Details also on access to facilities needed to appropriately administer and monitor treatment. Please include a Curriculum Vitae (CV) with your application for the HREC review.
- d. **Details of the site(s)** at which the goods will be used.
- e. **Details of the unapproved good** whether it is a medicine, biologic or device including name, active ingredient, strength / concentration and dosage form (if applicable), sponsor and whether the good is approved for the indication in another jurisdiction.
- f. **Details on efficacy and expected benefits**, any known / expected adverse effects, risks and safety issues and related toxicology for the unapproved good
- g. **Evidence to support the use of the unapproved good** for example, product information documents (if the good is approved by an overseas regulator), randomised controlled trials, non-randomised controlled trials, individual case studies or consensus opinion of specialist colleges and societies.
- h. **Informed Consent** since the use of unapproved goods is considered experimental, the Authorised Prescriber must obtain the informed consent of each patient for whom they prescribe the unapproved good. The Authorised Prescriber must advise patients':
  - i. That the TGA has not have evaluated the unapproved good's safety, quality and efficacy
  - ii. Of the possible benefits and risks of its use
  - iii. Of the possibility that there may be unknown side effects
  - iv. Of any alternative approved goods

**Note:** An informed consent template is provided if required [here](#)

**Further information can be found** at <https://www.tga.gov.au/book-page/information-medical-practitioners#hrec>

- 19.5 The following things need to be submitted to the HREC to obtain approval:
- Submit the completed Authorised Prescriber Application Form, **PLUS** Letter to the NBMLHD HREC Chair, outlining all the above listed items in section 2 (a-h) above
  - Email your application to the Research Office using the following email.  
[NBMLHD-Ethics@health.nsw.gov.au](mailto:NBMLHD-Ethics@health.nsw.gov.au)
  - Your application will be considered at the next scheduled HREC meeting and you will be notified by email of the outcome. If your application is approved then you will

- receive a HREC approval letter. If your application is not approved or requires further information, then your letter will outline what is required.
- If you have further question you can contact;  
The NBMLHD HREC Executive Office via email or phone  
Phone: 4734 1998  
Email: [NBMLHD-Ethics@health.nsw.gov.au](mailto:NBMLHD-Ethics@health.nsw.gov.au)
- 19.6 Once the HREC has granted approval or endorsement by a specialist college, an application can be made to the TGA to become an Authorised Prescriber. The application must include:
- The HREC letter of approval or specialist college endorsement that must include a declaration that all necessary documentation has been reviewed by the HREC
  - A completed application form
  - Submit to the TGA via post or email;
    - Email  
[EPS@health.gov.au](mailto:EPS@health.gov.au)
    - Post to  
Medicines Shortage Section  
Pharmacovigilance and Special Access Branch  
Therapeutic Goods Administration  
PO BOX 100  
Woden ACT 2606  
Australia
- 19.7 The TGA either authorises or does not authorise applications. Either way the decision will be advised via a letter stating the information relevant to prescribing the unapproved good.
- 19.8 Together with the TGA authorisation, a periodic reporting template will be issued so that as an Authorised Prescriber of an unapproved good, there is a requirement to submit 6 monthly supply reports and report any adverse reactions to the TGA.
- 19.9 Unapproved therapeutic goods generally have not been evaluated for safety, quality and efficacy and could pose unknown risks. As an Authorised Prescriber any adverse event or product defect related to the unapproved good must be reported to the TGA within 15 calendar days of learning of it. These events should also be reported to the NBMLHD HREC.
- 19.10 For the reporting of adverse events to the TGA please see the following link for further information specific to the reporting requirements <https://www.tga.gov.au/reporting-adverse-events>
- 19.11 Once you have been authorised by the TGA as an Authorised Prescriber you may start prescribing that good to patients under your care.
- 19.12 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.

- 19.13 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).
- 19.14 To review access to unapproved therapeutic goods via Authorised Prescribers, the HREC and Public Health Organisation 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 hospital drug and therapeutics committee or delegate; and/or
  - c) Consultation with the scientific subcommittee.
- 19.15 Decisions by the HREC Executive Committee are tabled for ratification at the next HREC meeting.

### **Institutional approval**

- 19.16 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.

## 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:
- 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.
  - 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 should be provided with the following information:
- The product for which approval is sought;
  - Whether that unapproved product is included on the list of products which can be approved by the practitioner;
  - Details about the product to be prescribed, including an assessment of the efficacy and safety of the product;
  - The medical condition for which approval is sought;
  - An assessment of the seriousness of the condition treated;
  - The intended mode of use/treatment and whether this conforms to the treatment protocol; and
  - 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 Public Health Organisation 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 should discuss the use of the product and the approval process with the institution before applying for authorisation.

## HREC 021: Biomedical engineering assessment of equipment / devices

**Purpose:** To describe the procedure to obtain clearance from a Biomedical Engineer for the use of non-TGA approved electromedical equipment / devices in clinical trials.

These guidelines apply to all studies using devices, including clinical trials being undertaken for clinical trial groups, independent research institutes, collaborative groups or investigator-initiated trials.

The types of devices that require a biomedical engineering review are any non-TGA approved equipment/devices (and accessories) that make physical or electrical contact with the patient or transfer energy to or from the patient or detect such energy transfer to or from the patient, or are intended to diagnose, treat or monitor a patient.

Specific exclusions are surgical instruments such as retractors, clamps, forceps, needles, scalpels etc.

- 21.1 When submitting applications to the NBMLHD HREC a copy of their research application will be submitted by the HREC Executive Officer to a Biomedical Engineer at NBMLHD requesting confirmation of compliance with required standards, along with the following:
  - A copy of the HREC application and study protocol
  - The device - for review and return to the researchers
  - Manuals, specifications and known standards of the device
- 21.2 The HREC Executive Officer will submit any specific information on the equipment / device provided by the investigator and requested by the Biomedical Engineer.
- 21.3 The Biomedical Engineer will peruse the material provided and confirm that the equipment / device complies with the required standards. The HREC Executive Officer will receive this information.
- 21.4 Biomedical review and approval should be received prior to the study proceeding for ethical review to the HREC or in parallel as the submission proceeds through the ethical review process.



## HREC 022: Notification of HREC decisions

22.1. The procedures outlined in this section apply to notification of the outcome of full and expedited HREC review.

22.2. Following confirmation of the minutes by the Chairperson, the Co-ordinating Investigator will be notified of the decision in writing within 10 working days of the meeting.

### Requests for modification/further information

22.3. The following information will be included in the letter of notification:

- a) The decision reached by the HREC or HREC Executive Committee;
- b) Requests for modification of or further information for the research project with reference to the *National Statement* or relevant legislation where necessary and the process for approval of the modifications as agreed by the HREC or HREC Executive Committee; and
- c) Notification that a response be provided within 30 days of the request for information being sent out via REGIS. After this time the application is considered withdrawn and the Co-ordinating Investigator will be required to submit a new application.

### Approved research projects

22.4. Final approval for a research project will be given at:

- a) the full HREC meeting where the application was initially considered; or
- b) the full HREC meeting where the response for a request for modification/further information was considered; or
- c) the HREC Executive Committee meeting where the low and negligible risk application was initially considered; or
- d) the HREC Executive Committee meeting where the response to a request for modification/further information was considered.

22.5. The following information will be included in the approval letter:

- a) The decision reached by the HREC or HREC Executive Committee;
- b) A list of all approved documents including version numbers and dates;
- c) A list of all sites for which the ethical and scientific approval applies;
- d) Duration of ethical and scientific approval;
- e) Confirmation that the HREC composition is in accordance with the *National Statement*; and
- f) A statement to the effect that the project cannot commence at a NSW public Health site until site authorisation is granted.

22.6 Additional approval conditions specified by the HREC or HREC Executive Committee for a particular application, for example a requirement for more frequent progress reports, will be included in the approval letter.

- 22.7 The opinion of the HREC or the HREC Executive Committee forms part of the recommendation to the Chief Executive or delegate to authorise the conduct of research at a NSW Public Health Organisation. The research will not commence until this authorisation has been granted.
- 22.8 Approved projects will be expected to commence within 12 months of the date on which a favourable ethical and scientific decision is given by an HREC. A project commences when any study procedure or any part of the protocol is implemented at a site.
- 22.9 Where the project does not commence within 12 months, the Co-ordinating Investigator will provide the HREC with an explanation in the annual progress report.

**Rejected research projects:**

- 22.10 Where the research project is rejected, the following information will be included in the letter of notification:
- a) The decision of the HREC or HREC Executive Committee;
  - b) Full explanation of reasons by reference to the *National Statement* or relevant legislation where necessary; and
  - c) Advice regarding available options for further review.

## HREC 023: Adverse event reporting


### Clinical trials involving therapeutic products

23.1 In November 2016, the National Health and Medical Research Council (NHMRC) overhauled their safety reporting advice, and produced the document [Guidance: Safety monitoring and reporting in clinical trials involving therapeutic goods](#), which replaced the Australian Health Ethics Committee's 2009 Position Statement, Monitoring and reporting of safety for clinical trials involving therapeutic products.

The new Guidance has been endorsed by the [Therapeutic Goods Administration](#).

This updated NHMRC Guidance restructures safety reporting responsibilities of key stakeholders and amends reporting pathways that previously placed an unnecessary burden on Australian investigators and Human Research Ethics Committees (HRECs) while not genuinely contributing to patient safety.

In response, NSW Health has issued a new Policy Directive (PD2017\_039) titled Safety Monitoring and Reporting for Clinical Trials Conducted in NSW Health Organisations (released on 27/10/2017). The new Policy can be found here [http://www1.health.nsw.gov.au/pds/ActivePDSDocuments/PD2017\\_039.pdf](http://www1.health.nsw.gov.au/pds/ActivePDSDocuments/PD2017_039.pdf)

23.2 NSW Public Health organisations implemented the new safety monitoring and reporting policy for all active trials as of 3rd of October 2017.  
For more information regarding safety monitoring and reporting guidelines, please refer  [A letter from Dr Tony Penna, Executive Director of Office for Health and Medical Research, informing sponsors](#).

### 23.3 What changes to reporting requirements have been made?

- Fewer reports will be required
- All safety reporting to the HREC and / or RGO is the responsibility of the sponsor or their delegate (e.g. The Principal Investigator).

#### Key Changes:

- **HRECs will no longer receive:** Single case Adverse Events (AEs), Serious Adverse Events (SAEs) /Serious Adverse Reactions (SARs) and Suspected Unexpected Serious Adverse Reaction (SUSARs)\*, or device/non-therapeutic good trial equivalents or six monthly line listings.
- **HRECs will receive:** All significant safety issues (SSIs), annual safety reports and investigator's brochure updates. These will be submitted to the HREC by the sponsor or their delegate [e.g. The Coordinating Principal Investigator (CPI) or Principal Investigator PI]).

#### Forms to use

- NBMLHD [SSI notification Form](#)
- NBMLHD [Annual Progress Report or Sponsors template](#)

- **Research Governance Office's will no longer receive:** Single case AEs, SAE/SARs, and external SUSARs\* or device/non-therapeutic good equivalents or six-monthly line listings.
- **Research Governance Office's will receive:** all significant safety issues (SSIs), any local SUSARs/USADSs/URSAEs and any research related events that meets the definition of an incident (PD2014\_004).

*\*Note – If an SAE/SAR/SUSAR meets the definition of an SSI, it will be reported to the HREC/RGO through that reporting mechanism.*

**Forms to use**

- NBMLHD [SSI notification Form](#)
- NBMLHD [SUSAR/USADE/URSAE Notification Form](#)

23.4 **Key Definitions:**

- **Therapeutic Goods Trials:** Trials investigating the safety and/or effectiveness of medicines, biologicals or medical devices.
- **Non-Therapeutic Goods Trials:** Trials other than a Therapeutic Goods Trial (e.g. radiotherapy, surgery, psychotherapy trials).
- **Suspected Unexpected Serious Adverse Reaction (SUSAR):** An adverse reaction that is both serious and unexpected.
- **Unanticipated Serious Adverse Device Effects (USADEs):** A serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report (and/or Investigator's Brochure/Instructions for Use).
- **Urgent Safety Measure (USM):** A measure required to be taken in order to eliminate an immediate hazard to a participant's health or safety.
- **Significant Safety Issue (SSI):** A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial.
- **Unexpected & Related SAEs (URSAE):** An adverse event that is:
  - **Serious** – meets the definition of a serious adverse event
  - **Related** – resulted from administration of the trial intervention
  - **Unexpected** – the event is not described in the protocol as an expected occurrence.

**Frequently asked Questions:**

The safety monitoring and reporting FAQs provide information to facilitate the consistent implementation of the OHMR guidance in NSW. Please see <http://www.health.nsw.gov.au/ethics/Pages/safety-faq.aspx> for further detailed information.

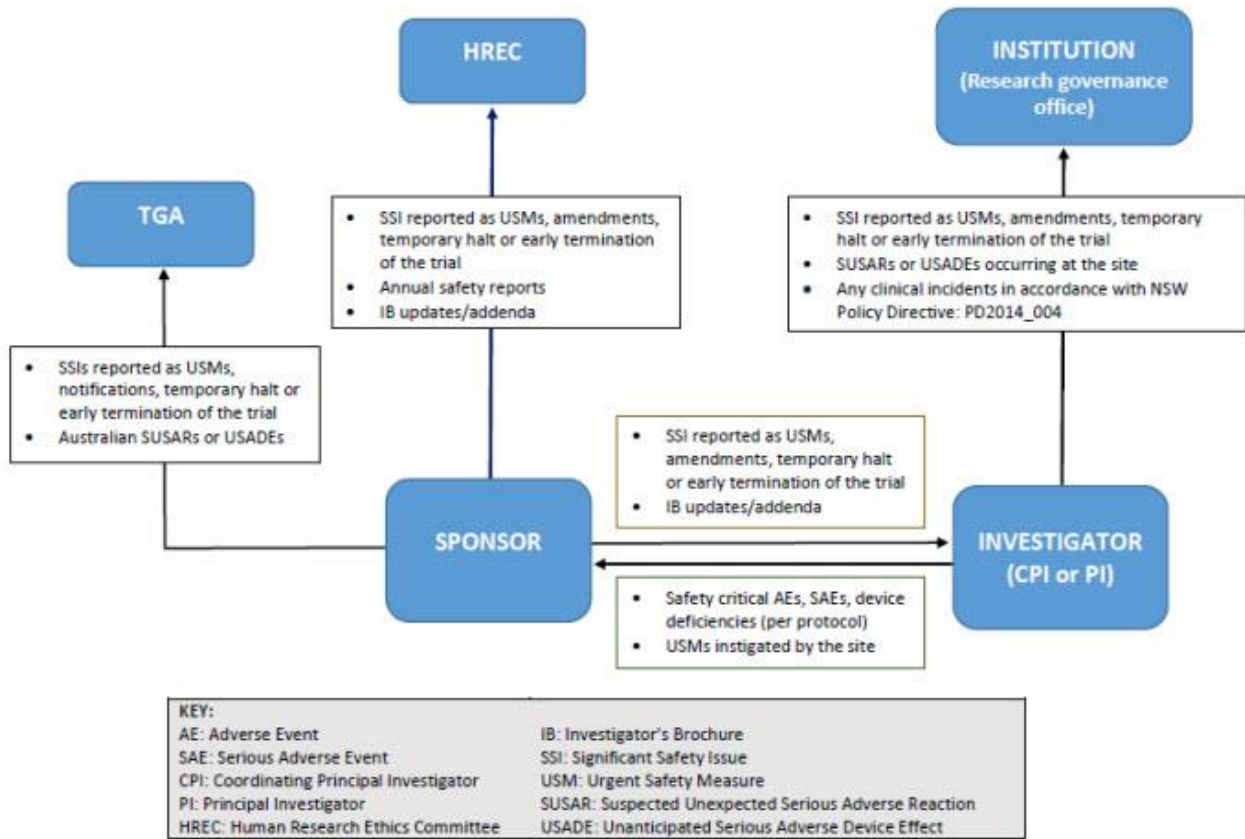
**Safety reporting Pathway for all trials:**

<http://www.health.nsw.gov.au/ethics/Pages/safety-pathways.aspx>

- 23.5 Depending on the complexity, design and risk perceived, the reviewing HREC and/or the Public Health Organisation has the discretion to require that additional information be reported.

**Figure 1: Reporting Pathway for Therapeutic Goods Trials**

As illustrated below, sponsors may report directly to NSW HRECs; however, they must ensure that all communications sent to the HREC adequately identify the trial and provide context in relation to the HREC’s role (e.g. whether there is any impact on patient safety, trial conduct or trial documentation)




**Table 1 – Summary of safety notifications to the HREC and RGO (therapeutic goods trials)**

| <b>Type of Event</b>  | <b>Who Reports</b>                   | <b>To Whom</b>  | <b>When</b>  | <b>How</b>   |
|---|--------------------------------------|---|--|--|
| Significant Safety Issue (SSI) Implemented as an Urgent Safety Measure (USM)  | Sponsor / Delegate                   | The reviewing HREC (and all Investigators participating in the study) | As soon as possible and no later than 72 hours of the sponsor becoming aware of the USM                        | NBMLHD SSI Notification Form or sponsor template                                     |
| Significant Safety Issue (SSI) not implemented as an Urgent Safety Measure (USM)  | Sponsor / delegate                   | The reviewing HREC (and all Investigators participating in the study) | Within 15 days of the sponsor becoming aware of the SSI  | NBMLHD SSI Notification Form or sponsor template                                     |
| All Significant Safety Issues (SSIs)  | Principal Investigator               | The RGO for the site where the event occurred                         | As soon as possible and no later than 72 hours of the PI becoming aware of the SSI                             | NBMLHD SSI Notification Form or sponsor template                                     |
| Suspected Unexpected Serious Adverse Events (SUSARs) and Unanticipated Serious Adverse Device Effects (USAEDEs) occurring at the site | Principal Investigator               | The RGO for the site where the event occurred                         | Within 72 hours of the PI becoming aware of the event  | NBMLHD SUSAR/USADE/URSAE Notification Form   |
| Investigator Brochure Updates /Addenda  | Sponsor / Delegate                   | The reviewing HREC  | As and when updated are generated  | Submitted with a cover sheet or as part of an annual progress / annual safety report |
| Annual Safety Report  | Coordinating Principapl Investigator | The reviewing HREC  | Within annual progress report sent to the HREC or aligned with the safety reporting cycles of global companies | NBMLHD Annual Progress Report or sponsors template                                   |

Text Alternative for above Information Figure 1 and Table 1:

#### Reporting pathway for therapeutic goods trials

The safety reporting flowchart (Figure 1) for therapeutic trials illustrates the safety reporting responsibilities of the Sponsor and the Investigator to the Institution, HREC and TGA. The Investigators responsibilities are to report:

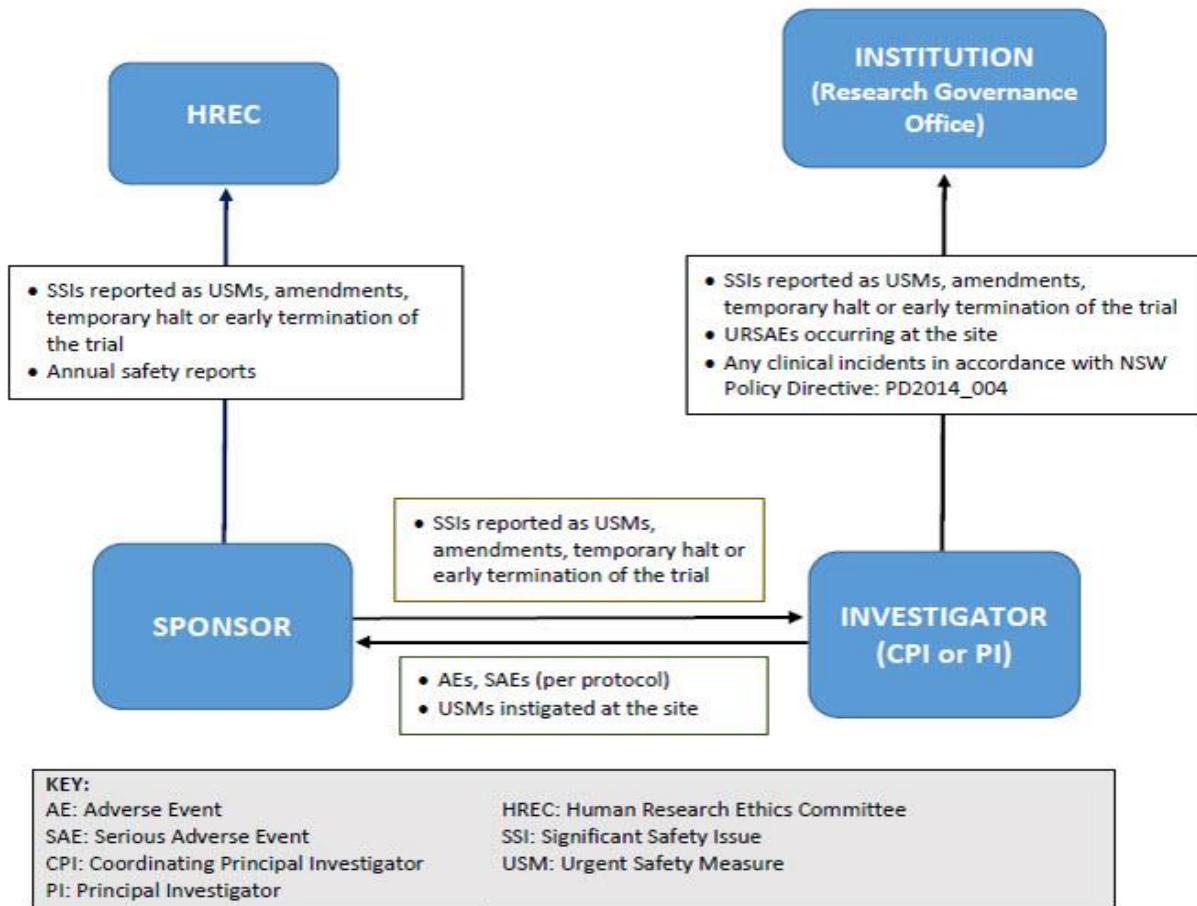
- all safety critical Adverse Events (AE), Significant Adverse Events (SAE), device deficiencies per protocol and Urgent Safety Measures (USM) instigated by the site to the Sponsor and
- all Significant Safety Issues (SSI), Urgent Safety Measures (USM), amendments, temporary halt or early termination of the trial, Suspected Unexpected Serious Adverse Reactions (SUSAR) Unanticipated Serious Adverse Device Effect (USADE) occurring at the site and any clinical incidents in accordance with  [NSW Policy Directive \(PD2014\\_004\)](#) to the Institution (Research Governance Office).

The Sponsor's responsibilities are to report:

- all Significant Safety Issues (SSI), Urgent Safety Measures (USM), amendments, temporary halt or early termination of the trial and Investigator's Brochure (IB) updates to the Investigator
- all Significant Safety Issues (SSI), Urgent Safety Measures (USM), amendments, temporary halt or early termination of the trial, annual safety reports and Investigator's Brochure (IB) updates to the HREC
- all Significant Safety Issues (SSI), Urgent Safety Measures (USM), amendments, temporary halt or early termination of the trial and Suspected Unexpected Serious Adverse Reactions (SUSAR) Unanticipated Serious Adverse Device Effect (USADE) occurred in Australia to TGA.

**Figure 2: Reporting Pathway for Non-Therapeutic Goods Trials**

As illustrated below, sponsors may report directly to NSW HRECs; however, they must ensure that all communications sent to the HREC adequately identify the trial and provide context in relation to the HREC’s role (e.g. whether there is any impact on patient safety, trial conduct or trial documentation).





**Table 3 – Summary of safety notifications to the HREC and RGO (non-therapeutic goods trails)**


| <b>Type of Event</b>   | <b>Who Reports</b>                                      | <b>To Whom</b>  | <b>When</b>   | <b>How</b>                                       |
|--|---|---|---|--|
| Significant Safety Issue (SSI) Implemented as an Urgent Safety Measure (USM)     | Sponsor / Delegate                                      | The reviewing HREC (and all Investigators participating in the study) | As soon as possible and no later than 72 hours of the sponsor becoming aware of the USM | NBMLHD SSI Notification Form or sponsor template |
| Significant Safety Issue (SSI) not implemented as an Urgent Safety Measure (USM) | Sponsor / delegate                                      | The reviewing HREC (and all Investigators participating in the study) | Within 15 days of the sponsor becoming aware of the SSI                                 | NBMLHD SSI Notification Form or sponsor template |
| All Significant Safety Issues (SSIs)   | Principal Investigator                                  | The RGO for the site where the event occurred                         | As soon as possible and no later than 72 hours of the PI becoming aware of the SSI      | NBMLHD SSI Notification Form or sponsor template |
| Unexpected & Related Serious Adverse Event (URSAEs) occurring at the site        | Principal Investigator                                  | The RGO for the site where the event occurred                         | Within 72 hours of the PI becoming aware of the event                                   | NBMLHD SUSAR/USADE/URSAE Notification Form       |
| Annual Safety Report   | Coordinating Principal Investigator or Sponsor Delegate | The reviewing HREC  | Annually (within the Annual Progress Report)  | NBMLHD Annual Progress Report                    |

*Text Alternative to above Information Figure 2 and Table 2*

### Reporting pathway for non-therapeutic goods trials

The safety reporting flowchart for non-therapeutic trials illustrates the safety reporting responsibilities of the Sponsor and the Investigator to the Institution and HREC.

The Investigators responsibilities are to report:

- all safety critical Adverse Events (AE), Significant Adverse Events (SAE) and Urgent Safety Measures (USM) instigated by the site to the Sponsor and
- all Significant Safety Issues (SSI), Urgent Safety Measures (USM), amendments, temporary halt or early termination of the trial, Unexpected & Related SAEs (URSAE) occurring at the site and any clinical incidents in accordance with  [NSW Policy Directive \(PD2014\\_004\)](#) to the Institution (Research Governance Office).

The Sponsor's responsibilities are to report:

All Significant Safety Issues (SSI), Urgent Safety Measures (USM), amendments, temporary halt or early termination of the trial and annual safety reports to the HREC.

### Review of safety reports by the HREC

- 23.6 Safety reports will be reviewed by an HREC subcommittee (such as a scientific review committee) or HREC Executive Committee to determine the appropriate course of action.
- 23.7 If the HREC subcommittee or HREC Executive Committee deems further information is required it will request this from:
- a) an independent expert with expertise in the area; or
  - b) the Co-ordinating Investigator or Principal Investigator who submitted the report with a copy to the other.
- 23.8 For reported deaths the HREC will, at its discretion, request information such as autopsy reports and terminal medical records.
- 23.9 Following review, the HREC will take the appropriate course of action which will include, but not be limited to one or more of the following:
- a) Including a notation on file of the safety-related occurrence;
  - b) Increasing monitoring of the research project;
  - c) Requesting an amendment to the project and/or Participant Information Sheet and Consent Form and any other study documents;
  - c) Suspending ethical approval; and
  - d) Withdrawing ethical approval.

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## **Notification of HREC review outcome**

- 23.10 The HREC will inform the Co-ordinating Investigator of the outcome of the review within 10 working days of the meeting, unless immediate notification is required for urgent safety reasons.
- 23.11 For multi-centre research projects, the Co-ordinating Investigator will provide a copy of the HREC review outcome to the Principal Investigators involved in the study. Each Principal Investigator will provide a copy of this HREC review outcome to the site Research Governance Officer.
- 23.12 The HREC has the discretion to notify the review outcome directly to the Principal Investigators and Research Governance Officers for safety reasons, in which case the Co-ordinating Investigator will be informed of this action.

## **HREC 024: Monitoring approved research projects**

- 24.1 The HREC will monitor approved research projects to ensure compliance with the conditions of approval and to protect the rights, safety and welfare of participants. This includes review of annual progress reports and final reports, safety reports and reports of protocol violations.
- 24.2 The HREC has the discretion to adopt other appropriate mechanisms for monitoring depending on the complexity, design and risk perceived, including:
- a) Discussion of relevant aspects of the project with the investigators, at any time;
  - b) Random inspections of research sites, data, or consent documentation;
  - c) Interviews with research participants or other forms of feedback from them;
  - and
  - d) Request and review reports from independent agencies such as a Data and Safety Monitoring Board.
- 24.3 The HREC will, at its discretion, recommend in the letter of approval that the site co-ordinates on-site monitoring at recommended intervals or randomly throughout the project.

### **Annual progress reports**

- 24.4 Annual progress reports will be submitted to the reviewing HREC by the Coordinating Investigator. The first report will be submitted 12 months from the date of ethical approval.
- 24.5 For a multi-centre research project Principal Investigators, at sites for which the HREC has given ethical and scientific approval, will submit annual progress reports to the Co-ordinating Investigator using REGIS. A copy of the report will be provided to the site Research Governance Officer by the Principal Investigator via REGIS.
- 24.6 The Co-ordinating Investigator will collate site annual progress reports for submission to the reviewing HREC with comments. The Co-ordinating Investigator will notify the relevant site Research Governance Officer if a Principal Investigator does not provide the required report for inclusion into the Collated annual progress report.
- 24.7 The Executive Officer will manage Annual Reporting via REGIS. All reminder notifications are generated and sent via REGIS.

The NBMLHD HREC will suspend or withdraw ethical approval of a research application as information comes to hand regarding each situation.

- Where ethical approval is to be withdrawn:
  - a) The HREC will request the researcher to submit a plan and revised documents for informing participants (if appropriate).
  - b) The institution will see that the investigator promptly suspends the research and makes arrangements to meet the needs of the participants.

- c) An investigator cannot continue with the research if ethical approval has been suspended or withdrawn and must comply with any special conditions imposed by the institution or the HREC. The research may not be resumed unless either:
      - the researcher subsequently establishes that continuance will not compromise participants' welfare; or
      - the research is modified to provide sufficient protection for participants, the modification is ethically reviewed, and the modified research is approved.
  - Where the HREC considers the research should be urgently suspended:
    - a) The instruction to stop will be made by the CE of NBMLHD in association with the HREC Chair. This will be done both verbally and by letter on the day the decision to suspend withdrawal is made.
    - b) The HREC will work with the investigator to explain the reasons for the immediate suspension and the requirements of the HREC to ensure the safety of participants.
    - c) The HREC will meet on an ad hoc basis if necessary to discuss suspension and response/s from the investigator.
- 24.8 Annual progress reports will be added to the agenda and reviewed by the HREC Executive Committee. The HREC will inform the Co-ordinating Investigator of the outcome of the review within 10 working days of the meeting, unless immediate notification is required.
- 24.9 For a multi-centre research project, the Co-ordinating Investigator will provide a copy of the HREC review outcome to the Principal Investigators involved in the project via REGIS.
- 24.10 The HREC will have the discretion to notify the review outcome directly to the Principal Investigators and Research Governance Officers, in which case the Co-ordinating Investigator will be informed of this action.
- 24.11 The HREC will have the discretion to request more frequent progress reports, depending on the complexity, design and risk perceived.

## **Final reports**

- 24.12 Final reports will be submitted to the reviewing HREC by the Co-ordinating Investigator, using REGIS, upon completion of the research project. Final reports will include a copy of the final results and publications if available. If project data and interpretation are fully addressed in a publication, a separate copy of final results will not be required.
- 24.13. For a multi-centre research project Principal Investigators, at sites for which the HREC has given ethical and scientific approval, will submit final site reports to the Co-ordinating Investigator using REGIS. A copy of the report will be provided to the site Research Governance Officer by the Principal Investigator via REGIS.
- 24.14 The Co-ordinating Investigator will collate final site reports for submission to the reviewing HREC, upon completion of the project at all sites with comments. Final reports will include a copy of the final results from all sites for which the HREC has given ethical and scientific approval, and publications if available. If project data and interpretation are fully addressed in a publication, a separate copy of final results will not be required.
- 24.15 Final reports will be added to the agenda and reviewed by the HREC Executive Committee. The HREC file will be archived as an electronic and/or hard copy, according to the Public Health Organisation's archiving policy, once the final report is acknowledged.

## **Protocol deviation/violation reports:**

- 24.16 Protocol deviations are minor or administrative departures from HREC approved protocol procedures whereby data is unusable or not available, but which do not affect the scientific soundness of the research plan or the rights, safety, or welfare of research participants. Examples include: follow up visits that occurred outside the protocol required time frame because of the participant's schedule, or blood samples obtained at times close to but not precisely at the time points specified in the protocol.
- 24.17 At the discretion of the Co-ordinating Investigator (or Principal Investigator in the case of multi-centre research) a list of protocol deviations may be reported with the annual progress report, however, this is not a requirement.
- 24.18 Protocol violations are instances where the protocol requirements and/or regulatory guidelines were not followed, and are generally more serious in nature than protocol deviations. Protocol violations are considered to potentially affect the scientific soundness of the research plan and/or the rights, safety, or welfare of research participants. Examples include: failure to obtain participant consent and participant inclusion/exclusion violations.
- 24.19 Principal Investigators will provide to the HREC written reports of protocol violations in a timely manner. The Principal Investigator will provide a copy of the report and any responses from the HREC to the Research Governance Officer.

## **HREC 025: Payment of fees**

- 25.1 Review of applications and amendments by the HREC will be subject to a fee.
- 25.2 The fees structure is outlined in PD2008\_030 *HREC and Research Governance: Fee Policy for Review of Commercially Sponsored Research*
- 25.3 The Co-ordinating Investigator will provide the HREC with details of the sponsor organisation to which the invoice will be sent.
- 25.4 The HRECs will determine whether the invoices will be paid at the time of application.
- 25.5 The HREC will determine whether to withhold a letter of approval until the fee is received.