

Human Research Ethics Committees: Ethical Review for External Entities

Summary This policy directive sets out the requirements that must be met for a Human Research Ethics Committee to undertake ethical review of research proposals for individuals or organisations external to the public health system. It contains a pro forma agreement between a public health organisation and an external entity, setting out the terms and conditions upon which such ethical review may be conducted. It also sets out the requirements that must be met for external entities seeking to use the ethical review of a lead HREC.

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Applies to Area Health Services/Chief Executive Governed Statutory Health Corporation, Board Governed Statutory Health Corporations, Affiliated Health Organisations, Affiliated Health Organisations - Declared, Ministry of Health, Public Hospitals

Distributed to Public Health System, NSW Ambulance Service, Ministry of Health, Public Hospitals

Audience Research staff;research governance staff;risk management staff

HUMAN RESEARCH ETHICS COMMITTEES: ETHICAL REVIEW FOR EXTERNAL ENTITIES

1. Human Research Ethics Committees (HRECs) constituted by Public Health Organisations sometimes undertake ethical review of health research that is to be conducted by an external organisation or individual. Examples include:
 - Research undertaken by non-government organisations in their own facilities.
 - Research where the investigators are private GPs and the participants are their private patients.
 - Research where the investigators are doctors who are employees or visiting practitioners at the public health organisation, but the research is not part of their employment or service contract with the public health organisation and involves participants who are not hospital patients.
 - Research undertaken in private hospitals.

In such research, the public health organisation has no role except to provide HREC review.

2. A public health organisation is only to provide HREC review for external entities where there is no other appropriate HREC to provide such review, and it is impractical for the external entity to constitute such an HREC.
3. It is a matter for the Chief Executive of the PHO to determine whether the HREC will undertake this service and for which external entities.
4. Where the HREC does conduct review for external entities:
 - this must be specified in its Terms of Reference (see the Department's Operations Manual for NSW Health HRECs, Departmental Guideline GL2005_059); and
 - the attached "pro forma agreement to undertake ethical review for an external entity" is to be used as the template for a formal agreement with the external entity. This agreement sets out the rights and obligations of each of the parties. It is noted that clause 8.4 of the Agreement (indemnities) may only be varied if the Chief Executive of the Health Service agrees AND the external entity is a not-for-profit or charitable organisation whose aims and objectives are consistent with those of the Health Service. This must also be the case for fees to be waived under Clause 2 of Annexure A. Agreements with "for profit" organisations such as private hospitals, must include clause 8.4 and specify a fee in Annexure A.

External entities and single ethical and scientific review of multi-centre research

A research project is only classified as a multi-centre project if it is to be conducted at more than one site within NSW Health and is within the jurisdiction of more than one NSW Health HREC. External entities cannot automatically take the benefit of the NSW Health single ethical and scientific review system, or review by a lead HREC.

However, there is no barrier to an external organisation using the ethical review of a lead HREC if:

- there is an agreement between the PHO that administers that lead HREC, and the external entity, in accordance with Annexure A; and
- the external entity pays a fee in accordance with the requirements of this policy directive (only certain not for profit organisations are exempt from paying a fee)

This is not an extension of the single ethical and scientific review system to external entities, but a recognition that external entities can request any NSW Health HREC (including lead HRECs) to undertake ethical review on its behalf if it is not practicable for them to constitute their own HREC.

An external entity using the ethical approval of a lead HREC is no different in substance from it using the ethical approval of a non-lead HREC.

External entities do not obtain the benefit of the fee reduction that flows to Public Health Organisations. That is, if an external entity wishes to use the ethical approval of a lead HREC, it must pay a fee in the same way that it does for review by any other NSW Health HREC. Only certain entities are exempt from paying such a fee under this policy.

Examples

A multi-centre trial is being conducted at John Hunter Hospital (HNEAHS), Royal Prince Alfred Hospital (SSWAHS) and Westmead Hospital (SWAHS). The lead HREC for NSW Health is at Westmead Hospital. Private Hospital X is located in Newcastle. Private Hospital X is also a site for this trial. It already has an agreement in the form of Attachment A with HNEAHS that the HNEAHS ethics committee conducts ethics reviews on its behalf. However, HNEAHS would not normally review this trial, as the lead HREC is Westmead.

Private Hospital X has two options in this case:

1. The Principal Investigator at the private hospital can refer the trial for review by HNEAHS HREC in accordance with its existing agreement; or

2. The Principal Investigator at the private hospital can seek to use the ethical approval given by Westmead HREC.

If Private Hospital X takes option 1, the Principal Investigator merely submits the trial for review along with the relevant fee. As there is already an agreement in place between Private Hospital X and HNEAHS, no further agreement is needed. If it is a commercially sponsored trial, the sponsor should provide HNEAHS with the Medicines Australia Form of Indemnity for Clinical Trials (HREC review only) in respect of the private hospital site. The Private Hospital is responsible for its own governance relating to the trial, so no site specific assessment form is required.

In the event that Private Hospital X seeks to rely on the ethical approval of Westmead HREC, it must conclude an agreement in the form of Attachment A with SWAHS, which administers that HREC. This is necessary, in order for that Westmead HREC is aware that it has monitoring responsibilities for the Private Hospital in relation to that trial and for proper indemnities to be in place to protect Westmead HREC. It is completely a matter for SWAHS whether or not it chooses to take responsibility for reviewing the trial on behalf of the private hospital (which it would do as part of its review of the trial for its own and other NSW Health sites). If SWAHS agrees to review the trial on behalf of the private hospital, the private hospital should sign an agreement in the form of attachment A with SWAHS, and pay the relevant fee. If it is a commercially sponsored trial, the sponsor must provide the Medicines Australia Form of Indemnity for Clinical Trials (HREC Review only) in respect of the private site. The private hospital remains responsible for its own governance.

Professor Debora Picone AM
Director-General

ATTACHMENT: PRO FORMA AGREEMENT TO UNDERTAKE ETHICAL REVIEW FOR AN EXTERNAL ENTITY

BETWEEN

[Insert name of Area Health Service or Statutory Health Corporation], an Area Health Service/Statutory Health Corporation incorporated under the Health Services Act 1997 of [Insert Address] (the Health Service).

AND

[Insert name of private organisation/hospital/individual], [insert ACN if applicable] of [Insert Address] (the External Entity).

WHEREAS

- A. The Health Service appoints the members of, and administers, one or more human research ethics committees to provide ethical approval of human research in accordance with the National Statement on Ethical Conduct in Research Involving Humans.
- B. The External Entity conducts or hosts human research which requires approval by a human research ethics committee in accordance with the National Statement on Ethical Conduct in Research Involving Humans, but it is not practicable for the External Entity to appoint and maintain its own ethics committee.
- C. The External Entity wishes to submit applications for research involving humans to one or more of the human research ethics committees appointed and administered by the Health Service for the purposes of obtaining ethical approval in accordance with the National Statement on Ethical Conduct in Research Involving Humans.

IT IS HEREBY AGREED AS FOLLOWS

1. Interpretation

Definitions

“Acceptable Clinical Trial Register” means the Australian Clinical Trials Registry or another clinical trial register that meets the requirements of the International Committee of Journal Editors;

“Application for Ethical Review” means an application submitted to the HREC by the External Entity for review of a human research project that:

- (a) is to be conducted at premises under the direction and control of the External Entity; and/or;
- (b) involves patients or clients of the External Entity as participants in the research; and/or

- (c) uses the resources or staff of the External Entity (including visiting medical officers and independent contractors of the External Entity acting in that capacity);

“Application Form” means any application form for ethical review accepted by the HREC;

“Approved Research Project” means any human research project described in an Application for Ethical Review submitted to the HREC by the External Entity and which has been given ethical approval by the HREC;

“HREC” means each of the human research ethics committees listed in Annexure A, that are appointed and administered by the Health Service;

“Clinical Trial” means any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical interventions include any intervention used to modify a health outcome and include drugs, surgical procedures, devices, behavioural treatments etc;

“CTN Form” means the form “Notification of Intent to Supply Unapproved Therapeutic Goods under the Clinical Trial Notification (CTN) Scheme” published by the Therapeutic Goods Administration;

“CTX Form” means the form “Supply of Unapproved Therapeutic Goods under the Clinical Trial Exemption (CTX) Scheme” published by the Therapeutic Goods Administration;

“Matters of ethical approval” means matters to be reviewed by a human research ethics committee pursuant to the National Statement and which are relevant to whether the conduct of a research project is ethically acceptable;

“Matters of research governance” means matters, excluding Matters of Ethical Approval, which must be considered by the External Entity to determine whether it is a suitable site at which an Approved Research Project should be conducted, including, but not limited to: the proposed cost of the project; the proposed budget; the availability of appropriate equipment, drugs and other resources; and the skills and availability of clinical and non-clinical personnel;

“National Statement” means the National Statement on Ethical Conduct in Research Involving Humans 1999, published by the National Health and Medical Research Council, or any replacement thereof;

“Privacy Legislation” means the Privacy and Personal Information Protection Act 1998 (NSW), the Health Records and Information Privacy Act 2002 (NSW) and the Privacy Act 1988 (Cth) and any statutory instruments made pursuant thereto;

“Sponsor” means a sponsor within the meaning of the TGA legislation;

“Standard Medicines Australia Indemnity” means the current “Medicines Australia Form of Indemnity for Clinical Trials – Standard” as published by Medicines Australia from time to time;

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“**Standard Medicines Australia Indemnity – HREC Review**” means the current “Medicines Australia Form of Indemnity for Clinical Trials – HREC Review only” as published by Medicines Australia from time to time;

“**TGA legislation**” means the Therapeutic Goods Act 1989 (Cth) and any statutory instruments made pursuant thereto;

- 1.2 A reference to this Agreement or another instrument includes any variation or replacement of them.
- 1.3 A reference to all clauses, exhibits, annexures or schedules shall, unless otherwise provided, be a reference to the clauses, exhibits, annexures or schedules of or to this Agreement.
- 1.4 Except where the context otherwise requires:
 - (a) clause headings are for convenient reference only and are not intended to affect the interpretation of this Agreement;
 - (b) where any word or phrase has a defined meaning, any other form of that word or phrase has a corresponding meaning;
 - (c) any reference to a person or body includes a partnership and a body corporate or body politic;
 - (d) words in the singular include the plural and vice versa.

2. Term

- 2.1 This Agreement applies to all Applications for Ethical Review submitted during the Term, which is from *[insert date]* to *[insert date]*
- 2.1 This Agreement applies only to the following trial *[insert name of trial]*

Note: Delete the inappropriate clause.

- 2.2 This Agreement will be reviewed prior to the end of the Term, and may be extended subject to the same terms and conditions for a further term as agreed by the parties in writing.

3. Provision of HREC services

- 3.1 The HREC will accept and review Applications for Ethical Review from the External Entity in accordance with the National Statement.
- 3.2 The Health Service will only accept and review such Applications for Ethical Review where:
 - (a) the External Entity has endorsed the Application for Ethical Review in writing (either by covering letter on the External Entity’s letterhead or on the Application Form); and
 - (b) the Application for Ethical Review is submitted on an Application Form and in compliance with all the HREC’s Standard Operating Procedures.

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3.3 The HREC will review the Application according to its usual procedures including, in the HREC's discretion, referral of the Application for expert scientific or other advice.

3.4 The HREC will monitor the conduct of any Approved Research Project in accordance with the requirements of the National Statement and in accordance with its usual monitoring practices.

4. Fee

4.1 The External Entity will pay the Health Service the fees set out in Annexure A. The fee is non-refundable even if an Application for Ethical Review is unsuccessful or is withdrawn prior to consideration or determination.

5. Records

5.1 The HREC will forward to the External Entity extracts of its HREC Minutes that relate to Applications for Ethical Review and Approved Research Projects on an annual basis.

6. Clinical Trials

6.1 Where the Approved Research Project is a Clinical Trial, the External Entity will ensure that the trial is registered on an Acceptable Clinical Trial Register.

6.2 The Health Service does not become a Sponsor of any Approved Research Project merely by virtue of this Agreement or by virtue of the HREC reviewing or approving an Approved Research Project. The Health Service shall not be named as a Sponsor on a CTN Form or a CTX Form relating to an Approved Research Project, without the prior written approval of the Chief Executive of the Health Service or his or her delegate.

6.3 Where the Approved Research Project is an industry sponsored Clinical Trial, the External Entity shall ensure that the Sponsor provides:

- (a) the Standard Medicines Australia Indemnity in favour of the External Entity; and
- (b) the Standard Medicines Australia Indemnity – HREC Review in favour of the Health Service.

7. Co-operation by the External Entity

7.1 The External Entity shall co-operate fully with the HREC and the Health Service acting in accordance with the National Statement, its standard operating procedures or its authorised policies, in relation to the conduct of any investigation into any complaint arising out of an Approved Research Project, or into any examination of any appeal from any decision of the HREC arising out of an Application for Ethical Review.

7.2 The External Entity shall immediately notify the HREC of any matter which affects the ethical approval of any Approved Research Project or may be relevant to any future decision of the HREC regarding Applications for Ethical Review, including but not limited to: any findings of misconduct or disciplinary action taken against

any investigator; or any breach of any statutory requirement regarding the conduct of research by the External Entity.

8. Responsibilities and Indemnities

- 8.1 The HREC is responsible for reviewing Matters of Ethical Approval in relation to any Application for Ethical Review, and is not responsible for reviewing Matters of Research Governance or for the conduct of an Approved Research Project. It is a matter for the External Entity to authorise the commencement of, and ensure the proper conduct of, an Approved Research Project.
- 8.2 The External Entity, the investigators, the sponsors or any other persons taking part in the conduct of an Approved Research Project (as the case may be) remain responsible for any liabilities which arise from the conduct of an Approved Research Project, including but not limited to any injury to any person (including death), any actions, proceedings, claims, demands, costs, losses, damages and expenses (including any legal costs and expenses) arising directly or indirectly as a result of any unlawful, negligent or criminal act or omission of any person involved in the conduct of the Approved Research Project, and the external entity hereby indemnifies the Health Service against any such liabilities.
- 8.3 The External Entity warrants that it has insurance or other indemnity arrangements sufficient to cover the conduct of all Approved Research Projects. Where the Approved Research Project is a clinical trial, the External Entity warrants that where any investigator or person involved in the conduct of an Approved Research Project is not an employee of the External Entity, that person has sufficient insurance (including professional indemnity insurance) or other indemnity arrangements to cover any liabilities that may arise to them as a result of the conduct of an Approved Research Project.
- 8.4 In the case of any Application for Ethical Review where a Standard Medicines Australia Indemnity – HREC Review is not provided pursuant to clause 6.3, the External Entity hereby indemnifies the Health Service and each member of the HREC against any actions, proceedings, claims, demands, costs, losses, damages and expenses (including any legal costs and expenses) made or prosecuted in any manner, arising directly or indirectly from the HREC's review of any Application for Ethical Review pursuant to this Agreement.

[Note on clause 8.4. This clause may be excluded from the Agreement only if the Chief Executive of the Health Service agrees AND the external entity is a not-for-profit or charitable organisation whose aims and objectives are consistent with those of the Health Service. Agreements with "for profit organisations" such as private hospitals, must include clause 8.4]

- 8.5 This clause survives the termination or expiration of this Agreement.

9. Termination

- 9.1 Either party may terminate this Agreement by giving fourteen (14) days written notice.
- 9.2 Upon termination, the Health Service shall;

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- (a) withdraw from consideration any Applications for Ethical Review for which the HREC has not yet issued a final decision; and
- (b) continue to monitor any Approved Research Projects in accordance with the requirements of the National Statement.

9.3 The parties acknowledge that no damages are payable by either party for termination of this Agreement.

10. Confidentiality

The External Entity notes that the HREC may be required to disclose information included in an Application for Ethical Review, in appropriate circumstances permitted by Privacy Legislation, including the following:

- (a) to deal appropriately, in its discretion, with any complaints made regarding an Approved Research Project;
- (b) to report to any Health Service officer regarding the activities of the HREC;
- (c) to supply any information to the NSW Department of Health in relation to any audit or survey of the HREC's activities;
- (d) to report any incident or adverse event to the Department of Health or any regulatory authority;
- (e) to report to, and as required by, the NSW Privacy Commissioner, the National Health and Medical Research Council, the Australian Health Ethics Committee, or any other statutory body;
- (f) in any circumstance required or permitted by law.

11. Amendment

11.1 This Agreement may be amended, assigned or novated only in writing signed by both parties.

12. Governing Law

12.1 This Agreement is governed by the law in force in New South Wales and the parties submit to the jurisdiction of the Courts of New South Wales.

13. Entire Agreement

13.1 This document contains the entire agreement between the parties about its subject matter. Any previous understanding, agreement, representation or warranty relating to that subject matter is replaced by this Agreement and is of no effect.

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EXECUTED as an Agreement

SIGNED for an on behalf of
[insert name of Area/Statutory Health Corporation]
in the presence of:

Chief Executive

Witness

SIGNED for an on behalf of
[insert name of External Entity]

Witness

Director

Director/Secretary

ANNEXURE A

- 1. Human Research Ethics Committees appointed and administered by the Health Service to which the External Entity may submit Applications for Ethical Review.**

Insert name(s) of relevant ethics committee that will conduct ethical review for the External Entity

- 2. Fees**

*Include details of the fees to be paid by the Entity to the Health service. This may be the HREC's standard schedule of fees (based on Departmental Policy Directive PD2005_628),
OR
a set fee per annum,
OR
a combination of both.*

Note: *Fees should only be waived where the Chief Executive of the Health Service considers there are appropriate reasons for providing the services of the HREC to the External Entity free of charge. This would generally only be the case where the Entity is a charitable or not-for-profit organisation whose aims and objectives are consistent with those of the Health Service.*