Human Research Ethics Committee of
Northern Territory Health and Menzies School of Health Research
(NHMRC Registration Code No: EC00153)

TERMS OF REFERENCE
and
STANDARD OPERATING PROCEDURES

Version 5
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PART A: TERMS OF REFERENCE (TOR)

1. Abbreviations

The following abbreviations are used throughout all parts of this document.

AESC	Aboriginal Ethics Sub-Committee of the HREC
AHEC	Australian Health Ethics Committee
the Code	Australian Code for the Responsible Conduct of Research
CDU	Charles Darwin University
CEO	Chief Executive Officer
CF	Participant Consent Form
CT	Clinical Trial
DSMB	Data Safety Monitoring Board
FT	Fast Track Sub-Committee
HREA	Human Research Ethics Application
HREC	Human Research Ethics Committee of Northern Territory Health and Menzies School of Health Research, unless otherwise specified
IRB	Institutional Review Board
MSHR	Menzies School of Health Research
NHMRC	National Health and Medical Research Council
NMA	National Mutual Acceptance of scientific and ethical review for multi-centre human research projects conducted in public health organisations
NS	National Statement on Ethical Conduct in Human Research 2007 (updated 2018)
NT	Northern Territory
NT Health	Northern Territory Department of Health - NT Regional Health Services
PIS	Participant Information Statement
QESC	Qualitative Ethics Sub-Committee of the HREC
RGO	Research Governance Office
SAE	Serious Adverse Event
SUE	Serious Unexpected Event
TGA	Therapeutic Goods Administration
WWCC	Working With Children Clearance

2. Organisational Structure and Accountability

2.1 Establishment and Structure:
The Human Research Ethics Committee of the Northern Territory Health and Menzies School of Health Research (HREC) is a joint committee established by the Chief Executive Officer (CEO) of Northern Territory Health (NT Health) and the Governing Board of the Menzies School of Health Research (MSHR) to operate as the Human Research Ethics Committee for each institution. The ultimate responsibility for the HREC's maintenance rests with NT Health.

The HREC is registered with the National Health and Medical Research Council (NHMRC) and operates under guidelines established by the Australian Health Ethics Committee (AHEC), a sub-committee of the National Health and Medical Research Council (NHMRC). HREC NHMRC registration number: EC00153

The HREC is advised by three sub-committees: Aboriginal Ethics Sub-Committee (AESC), Qualitative Ethics Sub-Committee (QESC), and Fast Track Sub-Committee (FT). Please refer to Appendix 1 for Sub-committee Terms of Reference. Further sub-committees may be established as required to enable the HREC to discharge its duties.

2.2 Accountability

- The HREC reports annually to the CEO of NT Health and the Board of the Menzies School of Health Research.
- The HREC will report at least annually to, and maintain communication with, the NHMRC's Australian Health Ethics Committee (AHEC) and provide access, upon request, to information in the HREC's records.

2.3 Guiding Principles:

- The *National Statement on Ethical Conduct in Human Research* (NS) is the authoritative Australian document on ethical principles which is subject to rolling review led by the NHMRC. Where it is possible, the HREC ensures that researchers align with the NS, without conflicting with laws or engendering situations where harm is caused.
- The *Australian Code for the Responsible Conduct of Research* (the Code) gives principles for the conduct of research. The HREC interprets the conduct of research by considering the Code.
- As a component of the NT public health system, the HREC considers where appropriate the policies of the sponsoring organisations (NT Health, MSHR), and stakeholder organisations (eg, AMSANT and its members, or retrieval organisations) but is not explicitly bound by these policies in its deliberations.

3. Scope of responsibilities and Jurisdictions

3.1 Vision:
The HREC has a vision to lead Australia in local community engagement and make high quality research available to meet the information needs of the Northern Territory (NT).

3.2 Scope of responsibilities:
The HREC's role is generally to consider the ethical and scientific aspects of human research conducted in the NT or by organisations based in the NT. In doing so, the HREC will take local circumstances and cultural sensitivities into consideration.

The HREC will review the ethical and scientific aspects of human research conducted by the NT DoH, MSHR (domestically and internationally), partner institutions that require specialised review, other organisations from the NT that do not have their own human research ethics committee, and human research projects being conducted in the NT by organisations from outside the NT.

In addition, the HREC will conduct ethical and scientific review of proposals for human research in accordance with review processes accepted or certified for the purpose of eliminating unnecessary duplication of ethical review, such as the Australian National Mutual Acceptance program.

The HREC will consider non-research matters (other than matters of clinical ethics)
that require consideration by a formally constituted Human Research Ethics Committee, e.g. as specified by the Therapeutic Goods Administration, such as special access to a non-approved product.

3.3 Jurisdiction:
There should be no duplication of review between the HREC and individual organisation governance processes, including the data release process. The partner organisations will use best efforts to enable this by delineating clear responsibilities of review and providing appropriate resources to perform those review functions. On being informed of barriers to parallel review, the partner organisations will take timely action to remove those barriers.

The HREC is the designated body in the NT to review all research undertaken in the NT which involves human participants, their data, or biospecimens including genetic material

The HREC may perform the function of an Institution Review Board for research partners in international jurisdictions such as the United States of America.

The HREC will provide institutional support to fulfil the requirements for Therapeutic Goods Administration schemes to access non-approved products such as the therapeutic use exemption.

Partner organisations expect all research to be submitted to the HREC if the study is being undertaken in the NT.

The NT is characterised by diverse geography, populations and Aboriginal culture and languages. The HREC process will incorporate review by Committee members with specific contextual and cultural knowledge relevant to the region(s) where research will be undertaken.

3.4 University Students

University students are generally required to obtain ethical approval from the ethics committees at their respective universities to conduct research. For health research conducted in the NT, with human subjects, students are required to apply to the HREC in the first instance. Once approval from the HREC has been obtained, the student must lodge a request for executive or reciprocal approval from the relevant ethics committee within their university.

3.5 Multi-Site research:

The HREC may accept the review and approval granted by another certified HREC for multi-centre research when the application conforms with NT requirements. For current guidelines relating to National Mutual Acceptance of scientific and ethical review for multi-centre human research projects conducted in public health organisations (NMA) please refer to Appendix 2.

For research that has been reviewed and approved by another ethics committee or by a process that is not part of the NMA, applications will be assessed by the Chair of the HREC on a case by case basis and reciprocal approval may be granted without further HREC review, depending on the risk profile of the research.

It may be necessary to re-review applications which have already received approval and to make conditions specific to the NT environment. The HREC commits to working to minimise such conditions and the associated burden on the researchers, because such burdens may increase the risk of errors in research conduct and thus expose participants to risk. Notwithstanding that commitment there is no limit on the amount of new conditions the HREC may impose if it is necessary for safe and ethical conduct of the research specific to the NT environment.

The HREC, may perform the role of lead HREC for proposals for human research to be conducted at multiple sites in accordance with review processes accepted or certified for the purpose of eliminating unnecessary duplication of ethical review, such as the Australian National Mutual Acceptance program, and subject to any site-specific requirements of participating jurisdictions.

The HREC will continue to meet the targets for timeliness of review set by the NMA working group. Risks to this commitment will be addressed by the ongoing reform process.

4. Membership

4.1 Minimum membership categories

Minimum membership of the HREC is in accordance with the NS and includes the following:

- Chairperson, with suitable experience, whose other responsibilities will not impair the HREC's capacity to carry out its obligations under the NS.
- At least two people who are not affiliated with either NT DoH or MSHR, who do not currently engage in medical, scientific, legal or academic work, and who bring a broader community perspective.
- At least one person with knowledge of, and current experience in, the professional care, counselling or treatment of people; for example, a nurse or allied health professional
- At least one person who performs a pastoral care role in a community
- A lawyer who is not engaged to provide an advisory service to the institutions
- At least two people with current research expertise that is relevant to the research proposals under review. These may be sourced from the list of additional appointments as required.

Additional appointments specific to this HREC include:

- One or more Deputy Chairpersons, with experience equivalent to the Chair, who can fulfil the role of Chair on a short-term basis if required.
- Members with specific expertise (Please refer to Appendix 3).
- An overall balance of members representative of different geographical regions of the NT

4.2 Recruitment for expertise

- It is important that an NT HREC is able to review research affecting NT communities. The HREC is an independent body to review research with transparency and consistency. It is well placed to advocate for the needs of participants and communities while remaining independent and promoting the conduct of good research that benefits the community.
- If no members with the necessary experience or training are available to attend all meetings of the committee, then the HREC will ensure that members with such expertise are available and a structure exists to seek their review of relevant applications (Appendix 3).

4.3 Appointment

- Vacancies may be advertised throughout NT DoH, MSHR, Flinders University, other NT stakeholders, the local press, and other platforms as appropriate. Prospective members may also be considered by direct approach.
- Members of the HREC and AESC are appointed by the CEO, NT DoH and are appointed for a two-year term but have the potential to be re-appointed at the end of each two-year term after review.
- Members receive a formal notice of appointment by the CEO of the NT DoH providing assurance of legal protection for any liability that may arise in the proper and lawful conduct as an appointed member.
- The Director of MSHR is advised of appointments and prepares a letter of welcome to the HREC.
- Appointment of a member may be terminated by the CEO of NT DoH if a member resigns by giving written notice to the Chair or the Ethics Administration Officer; becomes incapable of performing membership duties due to mental or physical ill-health; is absent from three committee meetings in a calendar year without tendering written comments on research proposals and an apology to the Chair; or the Committee has recommended the appointment be terminated

4.4 Confidentiality and Conflicts of Interest

- HREC members and observers are required to adhere to the NT Health Conflict of interest policy and procedure:
- HREC members and observers are required to sign a confidentiality agreement and will maintain the confidentiality of all matters relating to proposals under consideration by the HREC.
- Conflicts of interest are declared throughout each HREC meeting and no member of the HREC adjudicates on proposals in which they may be personally involved (directly or indirectly).

4.4 Induction, Mentoring and Training

- Prospective members attend an initial HREC meeting as an observer.
- New members are provided with mentoring by the HREC Administration Officers, Chair and other members of the HREC.
- Continuing training, education opportunities and resources for specific expertise will be provided (Appendix 3).
- The HREC will maintain a list of resources to explain the procedures and implications of the whole variety of research designs relevant to the NT context. This list will be reviewed yearly by the ethics administrators with suggestions and contributions from members and partner organisations.

4.5 Remuneration

- Membership of the HREC is voluntary and members are not financially compensated for their time.

5. Levels of ethical review and risk assessment

Taking the NS as a guide, the HREC gauges the required level of review and oversight for each project according to its risks, rather than by simplistic rules based on categories of project. Local circumstances may require a higher level of review for some projects than is the case elsewhere. The committee will gauge the level of risk of a project and devote the appropriate resources to its review.

All applications, no matter the level of risk or review, are recorded in the HREC database.
Risk assessment strategies are described in Part B: HREC Standard Operating Procedures and Appendix 4 Risk Assessment Factors

6. Safety Reporting

The HREC adopts in its entirety the reporting requirements of the *NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods* and are described in Part B: HREC Standard Operating Procedures.

7. Community Engagement and Stakeholder Support

The HREC believes that participants and stakeholders (the people) have the capacity to agree to a project that is being conducted with them.

- If the researchers have undertaken meaningful engagement and can show the HREC how they worked with the people to design a project and how they will share the answers with the people, then the HREC will not usually ask for the project to be changed. If the HREC is concerned about whether all the people understand or agree, or if it is not clear what will be done, the HREC will ask for explanations and might ask for changes.
- All research is by nature a collaborative process. While it is not the place of the HREC to demand that specific partners be involved or what role they take, the HREC may request confirmation of feasibility of research that depends on the availability and willingness of partners.

8. Charges

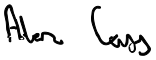
- Charges are levied and negotiated by the hosting institution in cooperation with partner organisations.
- No charge is made for projects where a partner organisation acts as Sponsor and where the PI is an employee of a partner organisation.
- Separate ethics and governance charges apply for projects with commercial Sponsors.
- Charges may be applicable for external expert review.

9. HREC Procedures

In compliance with institutional responsibilities, the HREC will establish, implement, and document working procedures to promote good ethical review as described within the NS. Refer to Part B. HREC Standard Operating Procedures.

10. Review of Terms of Reference

- The Terms of Reference will be read in conjunction with the HREC Standard Operating Procedures and associated appendices.
- The Terms of Reference will be reviewed every three years and will be endorsed by the Chair of the HREC, the CEO of the NT Health or their delegate, and the Director of Menzies School of Health Research.

POSITION	NAME	SIGNATURE	DATE
HREC Chair	Dr Mary Morris		14/06/2022
Chief Executive Officer of NT Health (or delegate)	Dr Frank Daly (or delegate)		
Director of Menzies School of Health Research	Prof Alan Cass		14/06/2022

PART B: HREC STANDARD OPERATING PROCEDURES (SOP)

1. Protocol submissions

- The application submission requirements are documented on the MSHR website.
- Processes are in place to minimise duplication of ethical review.
- The HREC will consider all applications for review. If the submission is in a standard format and the content is reviewable as intended, then the process is as described elsewhere in this document. Otherwise the HREC will respond with advice on the process of review within 5 working days. This may result in the applicants proceeding as intended, withdrawing, resubmitting in a different form or continuing the discussion.
- The most convenient method of submission for review is as a single pdf document; this combines the advantages of electronic communication for timeliness and transparency. Supplementary material may be provided separately (again, a single pdf is requested).

2. Risk assessment and level of review

2.1 Initial risk assessment

The initial assessment of risk is conducted by the ethics administrators. Research projects are then allocated to a certain level of review.
Discussion between administrators and HREC Chair and other members as relevant to the regional context resolves cases where the category of risk is not immediately clear.
Conditions relevant to the NT are considered when determining risk e.g. participant contact, vulnerability and identifiability, data sensitivity, location, and project feasibility. Please refer to Appendix 4 for more detail.

2.2 Increased review

- At any point concerns may arise about a research project which were not initially apparent. The research project may be escalated to a higher intensity of review, such as from administrative process to the Fast Track subcommittee or from Fast Track to the full HREC, without a need to justify the escalation.

2.3 Low risk

- Low risk research is reviewed out of session by the Fast Track committee, a representative group of HREC members. Applications for low risk review are reviewed within ten business days of submission.
- Where the risk to participants is considered, it is important that this refers to the risk consequent to the research, separately considered from the background risk of other activities or conditions of the participant. The relevant question here is often whether the direct risks are greater than those ordinarily encountered during routine clinical practice for that participant?

2.4 Negligible risk

- Where the risk of a research project is negligible and uses existing data, the research may be approved at the administrative level by discussion between the ethics administrators and the HREC chair.
- In the NT a narrower range of research is negligible risk, because of the greater risks to which Aboriginal and Torres Strait Islander people are exposed in every dealing with the healthcare system. While the principle of "no more serious risk than inconvenience" is easily understood there are important exclusions from this risk category which evolve and are included in Appendix 4.
    - Research requiring waiver of consent
    - Research targeting Aboriginal or Torres Strait Islander people
    - Research in which a breach of privacy laws is justified by an appeal to judgment

2.5 Standard care

- The level of risk in research may be connected to the level of risk of standard care in clinical practice, however, it is not simple to protocolise the decision on whether a given intervention, test or process is standard care, and the decision carries legal and financial implications beyond the research.
  The ethical considerations are therefore not simple but have a simple answer: after consideration by experts who are familiar with the condition and its investigations and treatment, and placing heavy weight on actual current practice or evolving practice (such as by surveys, practice audits, analysis of records, purchasing or booking patterns), it will be determined which of any interventions can be considered standard care.

- Further considerations relating to standard care are described in Appendix 4.

3. Meeting Processes

3.1 Frequency of meetings

The HREC meets ten times per year approximately monthly from February to December. The closing date for submission of applications is three weeks prior to the meeting date.
Submission and meeting dates are published on the MSHR websites.
The QESC and AESC meet one week before the HREC. The Fast Track Committee meets electronically as required.
Committee members are informed of meeting dates for each year in November of the preceding calendar year, and additional notice is given three weeks prior to each meeting.

3.2 Attendance at meetings

The quorum of each HREC meeting will be at least eight HREC members representing the minimum membership categories either present in person, or via remote means, or via submission of review comments in advance of the meeting to be considered by those present. The Chair will be satisfied that all those from the minimum membership have had the opportunity to review submissions.
The quorum for sub-committees is described in Appendix 1.

3.3 Preparation of agendas and distribution of papers before meetings

The Ethics Administration Officers will compile the agenda for each meeting and distribute applications, evaluation sheets, previous minutes, and other meeting papers to arrive with committee members at least one week before the meeting date of the QESC and AESC, and at least two weeks before the date of the HREC. Currently meeting papers are delivered electronically.
The Ethics Administration Officers assign each new application to at least two members of the HREC to prepare a brief summary and introduce each application at the HREC meeting, however each member is expected to review each application.

3.4 Preparation of Minutes

The Ethics Administration Officers will prepare Minutes from each relevant meeting and present for review to the Chairs of the HREC, AESC and QESC respectively within one week after the meeting date. Minutes from the AESC and QESC meetings will be presented at the relevant HREC meeting immediately following each AESC and QESC meeting for inclusion in the HREC's deliberations. Minutes from each meeting will be distributed to committee members with other meeting papers before the next meeting.
Hard copies of agenda papers are shredded after the minutes have been confirmed.

3.5 Attendance of Observers and Advisers at Meetings

Observers at HREC meetings may include:

- representatives from the sub-committees: AESC and QESC
- persons who are interested in being appointed as members to an HREC meeting as an observer in order to assist the individual to make an informed decision regarding their potential involvement.
- the Principal Investigator to attend the HREC meeting where it is felt that further explanation of a research project may assist the Committee members, but this is not a common practice.
- expert advisers at HREC meetings. Such advisers are bound by the same confidentiality agreements as HREC members and confidentiality agreements are signed before the expert attends a HREC meeting. Experts invited to elaborate on a specific application being considered by the HREC will attend the HREC meeting for the time that application is being discussed only.
- other persons may be invited to observe meetings from time to time.

In all cases, an observer's attendance will be approved by the Chair in advance of the meeting; their attendance will be recorded in the Minutes of the Meeting; and the observer will be expected to sign a confidentiality agreement with regard to the knowledge obtained during the course of their observations.

3.6 External review

The HREC and/or Chair may request external advice on a complex research project from specialists in the relevant field of research or health practice, either in writing or in person at the HREC meeting.

- Legal review: This will be unusual as the legal implications, separate from the ethical implications of a research project, are rarely the concern solely of the HREC. If the HREC decides that external legal review is necessary, then the applicant will bear the costs of such review which may be considerable.

- Technical review of scientific procedures: The HREC may request the review of a protocol by a disinterested expert, sourced either from resources of members or partner organisations, or where the entire field is unfamiliar, by the recommendation of the researchers. If the external reviewer requires costs, then the HREC will administer those costs but the applicant will bear the costs. The applicant with be consulted if they would like to continue with review including bearing these costs.

- External ethical review because of insufficient resources: If conflicts of interest, illness or other events render the committee unable to review a project, for example one where the pool of reviewers with expertise is small, then several interstate ethics committees have indicated their willingness to assist with review

4. Conduct and structure of meetings and deliberations

4.1 HREC Meeting structure and decision making

After an acknowledgement of the traditional owners of the land upon which the meeting is held and the land upon which the research under review is conducted, the HREC meetings will usually conform to the following format:

- General items will be raised e.g. apologies, observers and new members welcomed, conflicts of interest declared, previous minutes confirmed.
- Business arising will be discussed, and actions noted.
- Expedited reviews will be ratified.
- Resubmissions and new applications will be reviewed: For each application, the allocated spokespeople will summarise the project for the rest of the members and present their comments. Other members are then invited to contribute their opinions. The relevant minutes applicable to each application from the QESC and AESC meetings are considered, and representatives of those sub-committees are invited to clarify aspects of the sub-committee reviews.
- A majority decision is reached regarding an application with one the following outcomes: (a) approved outright, (b) conditional approval with responses to minor issues to be reviewed by the Chair, (c) conditional approval with responses to less minor queries to be reviewed by the Fast Track sub-committee, (d) non-approval with resubmission and responses to major issues to be reviewed by the HREC, (e) non-approval without resubmission. Approval for a research project requires the approval of both the AESC, if applicable, and the HREC. If the Aboriginal Sub-Committee does not approve a project, the HREC will not approve the project. Where there is inconsistency between the recommendations or comments of the HREC and AESC, the Chairs of each Committee meet as soon as possible after the HREC meeting to resolve the inconsistency. The revised recommendation and comment, and reason for the revision, are reported to the next meeting of each committee.

4.2 Expedited and out-of-session and review

The HREC Chair will review the following items out of session, usually within 7 business days:

- Minor amendments.
- SAE's, protocol deviations and violations
- Negligible risk projects e.g. clinical audits
- Requests for reciprocal approval
- Requests for waiver of full HREC review
- Responses to conditional approval
- Annual reports (will usually be delegated to an HREC member)

The Fast Track Sub-committee may review the following items out of session, usually within 10 business days:

- Major amendments
- Low risk projects e.g. some data linkage studies. If the Fast Track Committee decides that the level of risk is not minimal, the applications will be referred to the full HREC.
- Responses to conditional approval

5. Ethical considerations under review

The HREC will ensure that a research study meets the requirements of the NS and considers local circumstances and cultural sensitivities.

The following issues will be considered when reviewing an application:

5.1 Participant information and consent strategies

Requirements for a Participant information sheets (PIS) and consent form (CF) are described on the MSHR websites. The HREC recommends that a PIS and CF should be in the most appropriate medium for the people being consulted as potential participants in each research project.
The HREC will scrupulously review PIS and CF arrangements including but not restricted to:

- the wording of published forms
- the expertise of staff involved in gaining and maintaining consent (by reference to their training, skills and familiarity with the risks to participants characteristic of the NT)
- the cultural context of consent generally and specific to the research procedures
- the conditions of waiver specific to the NT context

5.2 Research procedures

The HREC will review the involvement of participants, their communities and their derived material (such as biological samples and information, whether personal information or analogous information relating to a community). If participant involvement poses risks specific to the NT, or risks are of greater importance in the NT context, then the HREC will advise on minimising such risks and may place conditions on the research project.

5.3 Extended identification

The HREC will consider whether identification of a person or culture or community will cause harm and whether such identification is possible or likely during the research procedures and especially the dissemination of research results. The HREC will clarify the intended procedures and dissemination and may place conditions on the research project.

5.4 Imposed identity

It is generally inappropriate to ascribe causal influence of Indigenous status on healthcare outcomes and such projects are likely to be rejected or to have limiting conditions placed on them.

- Indigenous peoples (whether Aboriginal, Torres Strait Islander or other colonised peoples) have historically been characterised as such only because of colonisation; the act of colonisation defines the people so classified, not other characteristics. It is therefore unlikely that the use of Indigenous as a classifier or stratum is causal or, with due attention to the true causes, independently predictive of outcomes. Where the underlying causes are unable to be examined thoroughly there may be social benefit in using Indigenous status as a proxy predictor but only with the collaboration of Indigenous people.
- It is an often argued but repeatedly demonstrated fact that the diversity in Australian Indigenous peoples is very large, both in terms of the comparable diversity of all humanity and in the diversity seen in similarly sized or dispersed populations elsewhere. This diversity makes it unlikely that a single classifier exposes causal links other than those imposed by colonisation and its impacts. Similar effects apply in many other settings of colonisation.
- Behind the diversity of populations lies the diversity between individuals. Although ethnic identity often carries with it a pattern of genetic inheritance, because culture is most easily transmitted among related individuals, they are not the same. The identity of a person is not determined by their genes, and the genetic predisposition to develop certain conditions or respond to certain medications is due to the genes themselves, not to ethnicity. Any attempt to describe the genetic characteristics of an ethnic identity results in misclassifying individuals. Any attempt to describe an ethnicity using genetic characteristics results in misclassifying individuals. These misclassifications most often increase disadvantage.
- It is important for researchers to consider potential secondary uses of the information from racially or ethnically defined subgroups in research. The risks to people in those subgroups from secondary uses may be greater than the benefits from the primary research use of the information. In cases of doubt the answers are only to be found in engagement with the groups themselves and their members.

5.5 Evidence of community engagement

- If there has been participant involvement in the design and conduct of the project then this HREC's role is merely to be sure that the explanations given to the participants and the protocol are true, valid, fair and match up, with no opportunity for unplanned additions or deviations under the ethical approval.
- The concept of a trial is often legitimately transformed by having the population under study involved in the design. In some case a simple community consultation on a simplified description of a trial, or survey evidence of prevalent attitudes, may be sufficient but trials have been successfully completed with engagement which goes well beyond this and into truly collaborative design.
- If there is participant involvement in the conduct of the study only, as in the use of a Cultural Reference Group, then this HREC will require a statement from the reference group in support of the protocol as reviewed.

5.6 Evidence of stakeholder support

- **Satellite sites**
  The HREC must satisfy itself that the research is feasible within the agreements that are possible between organisations. There are occasions when an individual professional or an organisation are asked to provide services for the researchers, whether purely in the pursuit of research or to supply research material arising from their routine work. None of these are the domain of the HREC except to verify that the participants' interest is not endangered by conflicts arising out of inter-institutional conflict or misplaced loyalties, financial or professional incentives or other conflicts of interest.
- **Consultation**
  Where a group is consulted on proposed research the HREC will satisfy itself that mechanisms for using that consultation in a transparent and principled way have been promised by researchers, and that annual reporting reflects those promises.
- **Collaborative agreements**
  The HREC will satisfy itself that collaborative agreements are not exploitative and enhance the participation of vulnerable groups. Research governance offices and ethics committees must be adequately informed of what constitutes collaboration and how to judge the adequacy of a given engagement process.

5.7 Insurance and indemnity

- The HREC will satisfy itself that participants are informed about foreseeable consequences of the research and protected as far as possible.
- The HREC will also satisfy itself that participants will be able to receive recompense for wilful or negligent actions or omissions of the researchers. This is partly assured by good research governance and the agreements surrounding a research project as articulated in the research protocol.
- In order to ensure that researchers and sponsors have the resources to redress any problems arising due to research practices, an insurance arrangement is often necessary depending on the risk level of the research procedures. The Northern Territory of Australia self-insures for its risks and potential liabilities, an arrangement that satisfies all obligations in respect of "clinical trials insurance".
- Other entities possess their own insurance arrangements, often including contracts or certificates indemnifying the employees of third parties. The specifics of these arrangements are addressed by the RGO and site-specific assessment process rather than the HREC process.

5.8 Other risk factors

Further risk factors taken into consideration during ethical review will be described in Appendix 4.

6. Timely consideration and review of applications

- The start of the ethics review time is from the submission closing date and continues until a decision is sent from the HREC to the applicant.
- Applicants will usually receive an initial response within 10 business days of the HREC meeting.
  On receipt of a complete response from the applicant, the clock then restarts and continues until the further decision is sent from the HREC. The target time is currently 60 days.
- Low risk applications may be submitted at any time, and applicants will receive an initial response within a target time of ten business days of receipt of the application.

7. Managing conflicts of interest

7.1 Conflicts of interest involving HREC members and advisers

- A conflict of interest will include any:

  - Personal involvement or participation in research under review
  - Personal relationship with a researcher or researchers under review
  - Financial interests in research under review
  - Involvement in competing research.
- Existing conflicts of interest will be declared on appointment of members to the HREC.
- Any conflicts of interest that arise during the term of appointment to this HREC will be communicated to the Chair of the HREC either in writing before each meeting or verbally at each meeting where it will be recorded in the Minutes. Where a conflict of interest exists, the significance of conflict will be determined by the remaining members of the HREC. Members or advisors with that conflict may be requested to withdraw from any discussion or decision-making regarding applications with which they have the conflict of interest. The absence of the member concerned will be noted in the Minutes.
- On occasions when the Chair is absent or excluded because of a conflict of interest, the Deputy Chair will assume the position of Chairperson. If both the Chairperson and the Deputy Chairperson are absent or excluded, the meeting will appoint a Chair who will then take the lead in responding to the researchers.

7.2 Conflicts of interest involving researchers

- Researchers must declare during the application process any conflicts of interest – real or perceived – the applicants may have in carrying out the research (examples include access to participant records during the course of normal professional duties; personal involvement with participants; payments to participants; or other potential conflict or ethical issue).
- Applications must include details of how these conflicts will be managed by the researcher and the responsible institution.
- Where a conflict of interest exists, the significance of conflict will be determined by the HREC.

8. Communication

8.1 Methods of communication

The primary means of communication with the HREC is electronic, whether by email or such electronic ethics management system as the HREC decides to adopt. This enables verification of the timing, content and source of the communications more accurately than by hardcopy communication. The HREC therefore requires a nominated point of contact that will be monitored and from which responses will be sent. Initial inquiries are welcomed by telephone or email.

Approval letters will be sent by email.

Where a hardcopy document is required by this HREC for legal or institutional reasons, an email confirming receipt will be sent by the HREC to the nominated email address of the research team; that email will mark the moment of official receipt.

Communications sent to the nominated email address will be considered to have been received, as it is a condition of ethics review that the address is monitored and available for responses.

8.2 Notification of decision

- The principal researcher will be notified by email of the HREC decision within 10 working days from the HREC meeting date. Letters of approval to researchers will state the terms under which approval has been given including the reporting requirements. In cases where the application has not been approved outright, the reasons for non-approval are linked to the NS.
- The Ethics Administration Officers will advise University HRECs of the outcomes of application for ethics approval that have been submitted by their respective students.
- The Ethics Administration Officers will advise the NT RGO of the outcomes affecting all NT Health sites.

9. Record keeping

- The HREC Administration Officer will maintain a record of all human research projects considered by the HREC.
- The applications for human research projects will be preserved in the form in which they are submitted and approved, including any associated documents and amendments subsequent to approval.
- The HREC Administration Officers will maintain an electronic database recording all actions relating to an application and its review.
- Where more than one review body has reviewed a proposal, details of other review bodies will be recorded.
- Records are stored in accordance with the MSHR Data Management Policy

10. Monitoring of approved research

10.1 Monitoring requirements

- Researchers are responsible for notifying the HREC that appropriate mechanisms for monitoring research are in place.
- The HREC will assess the level of risk, size and complexity of research when assessing the appropriateness of monitoring arrangements and determining the reporting requirements of specific projects.
- Reporting requirements and other conditions of continued ethical approval are stated in the letter of approval sent to the Principal Investigator and it is the Principal Investigator's responsibility to adhere to these requirements.
- Ethics approval should remain current until all relevant approved components of a project that have been subject to ethical review have been completed, including data analysis, dissemination of results and feedback to stakeholders and participants.

10.2 Progress Reports

- Progress reports will be submitted at least annually by the researchers to the HREC. Report templates may be downloaded from the MSHR website.
- HREC members will review progress reports and major concerns will be escalated to the Chair or Fast Track.
- A final progress report is due at the completion of the project.
- Should a progress report not be received by the due date, the Ethics Administration Officers have the capacity to remind researchers of their reporting obligations.
- Failure to submit a progress report three months from the due date will result in termination of ethics clearance and all named investigators will be advised in writing that approval for the project has expired and notified of the reasons for the decision.
- Should an investigator named on a new application be an investigator on a project which has failed to provide an annual progress report, the new application will not receive notification of HREC approval until such time as the progress report for the existing project is received and has been approved.

10.3 Variations (Amendments)

Researchers must report to the HREC as soon as possible:

- any proposed variation to the protocol of the original approved project,
- any information, either published or unpublished sources, that the researcher becomes aware of since the original application was approved that may affect continued ethical approval,
- if the project is discontinued prior to its original completion date,
- any serious adverse events
- any conflicts of interest which may arise during the course of the research,
- any other unforeseen events that may affect the continued ethical approval of a project.

10.4 Safety Reporting (All studies including clinical trials)

- The HREC adopts in its entirety the reporting requirements of the *NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods.*
- The HREC may require researchers to establish an independent data safety monitoring board (DSMB) with the frequency of monitoring determined by the HREC.
- The opinion of the DSMB (or equivalent) will be considered in regard to the likelihood that an event was related to the study, the likelihood of further incidences, and an opinion with regard to any increased risks associated with continuation of the research and the necessity of any proposed amendments to the research protocol and/or conduct to reduce the likelihood of reoccurrence.
- In considering the report, the HREC Chair must consider all the facts provided and may seek additional information as necessary, from the DSMB, the research team and/or the research site in order to make a decision as to whether the trial should be discontinued; be suspended pending amendments to protocol; continue with amendments to protocol including the PIS; or continue under the current protocol.
- If the Chair decides that the project should be discontinued, or suspended pending amendments to protocol, the decision will be communicated to both the Principal Investigator and the Head of the Responsible Institution. All such reports and decisions regarding the continuation of the research must be lodged with, and recorded by, the Ethics Administration Officer. The HREC should include details regarding the number and outcomes of such reports in its annual report to the AHEC and the establishing Institutions.

- The HREC Chair will respond to the Principal Investigator in writing, within two weeks of receiving the written report. Reasons for the HREC's decision must be incorporated in the response. The Principal Investigator has the right to appeal the Chair's decision under "Appeals Process".
- TGA therapeutic use exemption: The risk assessment is performed by the clinical experts requesting its use. The HREC will verify that the product will be used in a way that is thought to be safe and beneficial, that the governance is sufficient to ensure such performance and that sufficient thought has been given to audit and review of the product's use. This relies on the clinical expert who requests the approval. The clinical expert must provide information on the population to be treated, the indications and contraindications, the governance process by which it is assured that the product is used appropriately and any plans for audit or case review of the results of using the product.

10.5 Auditing Approved Projects

The HREC may decide to undertake an audit on any of the projects being conducted with its approval to ensure that approved protocols are being adhered to.

Should the HREC choose to undertake an audit, the Principal Investigator/s of the project/s to be audited will be notified at least 3 working days in advance of the proposed audit.

Procedures for undertaking such audits may include:

- site visits,
- inspection of documentation and/or data storage, and
- interviews with research staff, participants and/or resource providers

Should the HREC choose to undertake an audit, this will be done at the HREC's expense unless otherwise agreed between the Principal Investigator and the HREC in advance (e.g. costs of accompanying researchers on a field trip).

The audit committee will include as a minimum:

- One member of the HREC who has relevant research experience;
- One member of the HREC who is not an institutional member
- One member of the AESC;
- An invited non-HREC person with relevant expertise in the type of research being audited.

The nominated members of the audit committee must have no involvement in, or conflict of interest with regard to, the research project to be audited.

The findings of the audit committee will be reported in writing to the Principal Investigator and the HREC.

In the event of a finding that may require suspension of the research, the Responsible Institution will also be notified of the requirement, the reasons, and any steps required in order to re-commence the research project.

The HREC should include details regarding the number and outcomes of such reports in its annual report to the AHEC and the establishing institutions.

11. Withdrawal or suspension of HREC approval

- If the HREC finds reason to believe that the continuation of a research project might compromise the welfare of its participants, it will immediately seek to establish whether ethical approval should continue or be withdrawn.
- If the HREC has reason to withdraw or suspend ethical approval at any time during the course of a research project, the Principal Investigator and the head of the responsible institution will be informed in writing as soon as possible of the withdrawal.
- If ethical approval is withdrawn or suspended during the course of a research project, the researcher must immediately cease all research and make arrangements to meet the needs of the participants.
- Research may not be resumed until the concerns of the HREC have been addressed and the researcher establishes that participants' welfare is not compromised.
- Modified research protocols must be reviewed and approved by the HREC before research can recommence.

12. Complaints and Appeals

Complaints are received by the Ethics Administration Officers who ensures that the next steps are transparent and fair, and that conflicts of interest are handled. If there are no conflicts of interest, the Chair and Ethics Administrators will take the lead and involve others as required. There are two classes of complaint:

Complaints about a project.

Complaints about the HREC.

12.1 Complaints about a project.

- The HREC participates in the investigation of potential breaches of the Code, using the model process in the Guide to Managing and Investigating Potential Breaches of the Code (the Investigation Guide).
- Any complaints about a project may be made in person, by mail, by telephone or by email to the ethics administrators.
- According to the Investigation Guide we will make enquiries and if we find a need to investigate further, we may approach the researchers for clarification. There may be problems with doing so, for example if the complainant may suffer harm from the researcher becoming aware of their complaint, or the researcher's career may suffer even in the absence of serious wrongdoing. We may seek help from the researcher's institution, the research sponsor or jurisdictional authorities such as the NT government or the NHMRC if we think there may be serious consequences.

12.2 Complaints about the HREC.

- Where there is serious concern that the HREC has not been diligent or fair in its assessment of a matter (normally of a research project but potentially of reports or of other complaints), a complaint may again be lodged with the Ethics Administration Officer. Initial contact and discussion with the Chair and Ethics Administrators may result in satisfaction for all parties.
- If not, then the hosting institution may be asked to provide guidance.
- If this does not result in agreement, then the eventual indemnification is by the NT Health and the CEO may therefore be asked to review the case. The response may require outside assistance in confidence from content experts or respected peers such as other HREC chairs and administrators, or jurisdictional leads on ethics and governance.

Example strategies to resolve these complaints are:

- The HREC may be asked to review the matter again, taking into explicit consideration the advice of the an outside expert.
- The HREC may be asked to consider whether it believes that it can retain jurisdiction or refer to another committee for review.
- These options will be considered without threatening the essential independence of the HREC.

12.3. Appeals Process

- Where a Principal Investigator of a research proposal disagrees with a decision of the HREC, the Principal Investigator may request in writing to the Chair of the HREC that the decision be reconsidered, giving reasons why the researcher feels that the HREC decision is incorrect. The reasons why the decision is incorrect must be based on the NS.
- Face to face meetings may occur between researchers and the HREC Chair and the HREC when written and telephone communication does not resolve issues about research proposals.
- The HREC must reconsider the application, including further information supplied by the Principal Investigator, at the next available meeting (subject to the normal closing dates for applications).
- If after a reconsideration of a research proposal the Principal Investigator remains dissatisfied with the decision, or reasons for a decision of the HREC, the Principal Investigator may request in writing to the MSHR Director or the NT DoH CEO that an independent review of the HREC decision be undertaken. This review will be conducted by a review committee consisting of people who have previous or current experience as members of a research ethics committee but are not current members of the HREC or Aboriginal Sub-Committee, and with minimum membership as defined in the NS. This review should be completed within three months of the receipt of the request for review.
- The review committee will make an independent decision on the research proposal and, where requested by the Principal Investigator or the relevant institutional head, will consider whether the reasons for the original HREC were reasonable and whether there were any errors in the process undertaken by the HREC, and make recommendations in regard to these considerations.

APPENDIX 1: SUB-COMMITTEE TERMS of REFERENCE and PROCEDURES

A 1.1. Aboriginal Ethics Sub-Committee (AESC)

AESC Scope
Approval from the AESC is required where the research project involves research in, or concerning:

- The experience of Aboriginal and Torres Strait Islander people as an explicit focus of all or part of the research;
- Data collection explicitly directed at Aboriginal and Torres Strait Islander people;
- Aboriginal and Torres Strait Islander people, as a group, are to be examined in the results;
- A significant number of the population are likely to be of Aboriginal and Torres Strait Islander origin;
- The information has an impact on one or more Aboriginal and Torres Strait Islander communities; or
- Aboriginal and Torres Strait Islander health funds are a source of funding.

In deference to the diversity of individual communities across the NT the AESC will engage and make assessments as to the most appropriate group to assist and provide approval.

Applications for research being conducted with people from the Tiwi Islands from researchers affiliated with Menzies School of Health Research are considered by the HREC but not considered by the Aboriginal Ethics Sub-Committee unless other communities are to be involved in the research.

AESC Guiding principles
In considering health research proposals, members are guided by the NS, the NHMRC *Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders*, and principles and priorities specific to Aboriginal people in the NT including promoting education of Aboriginal people in the conduct of research and promoting employment opportunities for Aboriginal people in health research.

AESC Roles and responsibilities

- To protect the interests of Aboriginal people involved in health research, and of the wider Aboriginal community affected by health research.
- To ensure research is conducted in a culturally appropriate manner.
- To consider the ethical issues involved in research proposals from the perspective of Aboriginal people, with particular attention to the specific interests of Aboriginal participants in research projects and the interests of Aboriginal communities affected by research projects.
- To advise the HREC of ethical issues in relation to each research proposal involving Aboriginal people, to advise of recommendations to improve each proposal, and to advise of decisions of the AESC on whether or not to approve each proposal.
- To ensure research projects involving Aboriginal people will benefit Aboriginal people.

AESC Meeting procedures, decisions and reporting

- General committee procedures are as described for the HREC in SOP section 3.
- A majority decision is reached regarding an application with one the following outcomes: (a) approved outright, (b) conditional approval with responses to minor issues to be reviewed by the Chair, (c) conditional approval with responses to less minor queries to be reviewed by the Fast Track sub-committee, (d) non-approval with resubmission and responses to major issues to be reviewed by the HREC, (e) non-approval without resubmission.
- The AESC reports to the HREC through the AESC Chair (or their delegate) by attending the subsequent HREC meeting, at which the minutes of the AESC are included in deliberations.
- Where the HREC disagrees with an AESC decision, the Chair of the HREC will discuss the issues of concern with the AESC and request that the AESC and HREC work towards a consensus.
- If the AESC does not approve a project, the HREC will not approve a project.

AESC Membership

- All vacancies on the AESC are advertised through the same processes as the HREC membership recruitment. Members are appointed by the CEO, NT DoH for a two-year term and may be re-appointed at the end of each two-year term.
- Members receive a formal notice of appointment by the CEO of the NT DoH providing assurance of legal protection for any liability that may arise in the proper and lawful conduct as an appointed member.

The members of the AESC are a minimum of three Aboriginal people, who can be from the following categories:

- a person with experience in health service delivery including allied health
- a person with experience in health research
- a person with experience in community engagement
- a community member or Aboriginal elder not engaged in research or service delivery

The Sub-Committee also has one non-voting member, who is scientific adviser and is not necessarily an Aboriginal person.

AESC Meeting attendance
A minimum of three members must be present at each Sub-Committee meeting, either present in person, or via remote means, or via submission of review comments in advance of the meeting to be considered by those present. The Chair of the AESC will be satisfied that all those from the minimum membership have had the opportunity to review submissions.
If less than three members are present and another meeting cannot be scheduled before the next meeting of the HREC, the AESC meets informally out of session to provide advice to the HREC. An informal AESC meeting does not have the right of veto described above.

A1.2. Fast Track Committee (FT)

FT Roles and responsibilities
The Fast Track Sub-committee may review the following items out of session:

- New applications for research projects with relatively minor ethical implications.
- Responses to conditional approval (applications that have been considered by the HREC and require revisions prior to approval and that have been delegated to the FT for consideration and final approval)
- Major amendments

FT Decisions and reporting

- The Ethics Administration Officer will send items for review out of session to the FT via email.
- The FT will return their deliberations via email to the Ethics Administration Officer within ten days.
- If the Fast Track Committee decides that the level of risk is not minimal, the applications will be referred to the full HREC.
- Any research applications approved by the FT will be subject to the same monitoring and reporting procedures as those projects approved by the full HREC.

FT Membership
The Fast Track Committee membership will consist of a minimum of three members of the HREC and one member of the AESC. One of these members will be appointed by the main committee as Chair of the Fast Track Committee for a period of 6 months Other members will be appointed for the period between each meeting of the HREC.

FT Meeting attendance
The FT does not meet in person. Deliberations are conducted out of session by email.

A1.3. Qualitative Research Ethics Sub-Committee (QESC)

QESC Roles and responsibilities
The QESC will provide advice to the HREC in specialised areas of investigation such as:

- Social science research
- Qualitative research
- Policy and program evaluation
- Linguistic research
- Evaluation of programmes of work
- Economic evaluation
- Policy analysis
- Education research

QESC membership and meeting attendance

- The minimum membership will be three people with experience in the areas of expertise listed above.
- Members will not receive formal notice of appointment by the CEO of the NT DoH but will be welcomed to the committee in an advisory role by the Director of MSHR.
- There is no minimum attendance at QESC meetings, however members may review applications either present in person, or via remote means, or via submission of review comments in advance of the meeting to be considered by those present.

QESC Meeting procedures, decisions and reporting

- General committee procedures are as described for the HREC in SOP section 3.
- The QESC reports to the HREC through a QESC member attending the subsequent HREC meeting, at which the minutes of the QESC are included in deliberations.
- The QESC does not have the same power of veto as the AESC.

APPENDIX 2: NMA and NT SPECIFIC REQUIREMENTS

The National Mutual Acceptance (NMA) is a national system for mutual acceptance of scientific and ethical review of multi-centre human research projects conducted in publicly funded health services or other signatories of the NMA Memorandum of Understanding across Australian jurisdictions. Under NMA, multi-site research receives ethical review by a single lead committee, with that committee accepting the responsibilities of the HREC for reporting and further review, including of amendments. This HREC requires all such communication to be notified to the NT HREC. By participating in the NMA, the NT is generally agreeing to accept this ethical review from an accredited NMA reviewing HREC without further ethical review for research in the NT's public health services. However, similar to other jurisdictions, specific requirements and exceptions will be in place.

NT HREC review
Approval from the appropriate NT HREC is required where the research project involves research in, or concerning:

- The experience of Aboriginal and Torres Strait Islander people as an explicit focus of all or part of the research;
- Data collection explicitly directed at Aboriginal and Torres Strait Islander people;
- Aboriginal and Torres Strait Islander people, as a group, are to be examined in the results;
- A significant number of the population are likely to be of Aboriginal and Torres Strait Islander origin;
- The information has an impact on one or more Aboriginal and Torres Strait Islander communities; or
- Aboriginal and Torres Strait Islander health funds are a source of funding.

Single ethical review exceptions
Phase 0 (first time in human) and Phase 1 clinical trials will not be accepted under the single ethical review for clinical trials for Northern Territory public health system institutions. Where a Certified HREC from another jurisdiction has provided prior approval for a Phase 0 or Phase 1 clinical trial application, these applications will be re-reviewed scientifically and ethically by the appropriate HREC in the Northern Territory in addition to any research governance/specific assessment/institutional authorisation requirements.

Projects with approval by another HREC
The Chair of the HREC and the ethics administrator will undertake a risk-based assessment of applications received with prior ethical approval and determine if further review is warranted.
This HREC reserves the right to review the elements of a project which affect vulnerable people or communities including but not limited to ethical elements described in SOP 5 and Appendix 4.
Specific elements to be assessed include Participant Information and Consent Form and associated consenting strategies.

This may entail ethical and scientific re-review of the project or amendment. If the AESC and HREC have serious concerns with an application that has prior approval from another HREC, this HREC may express their concerns in writing to the original HREC and request a comment. If the HREC becomes aware of any modifications to a project, including conflicts of interest, which may have arisen since initial approval by another HREC, the Chair will request from the researcher a report on the management of these changes and require that the researcher informs the original approving HREC of these changes. The HREC may require a resubmission of the application for consideration by the full HREC.

Research Partners and Site-Specific Assessment

- Acceptance of a HRECs ethics review is not mandatory under the scheme; it is up to individual institutions participating in the research project to decide whether they will accept the review outcome from a certified institution's HREC or conduct their own review.
- The Chief Investigators will be required to undertake a site-specific assessment (SSA) within each health service and be authorised in compliance with the RGO standard operating procedures prior to any research activities.

APPENDIX 3: HREC MEMBERSHIP EXPERTISE

A3.1 Membership

Minimum membership

Currently the minimum membership of a Human Research Ethics Committee is eight members comprising:

- a chairperson;
- a lay woman and a lay man representing the community and not affiliated with either NT DoH or MSHR and who does not currently engage in medical, scientific, legal or academic work
- a person with knowledge of, and current experience in, the professional care, counselling or treatment of people,
- a person who performs a pastoral care role in a community,
- a lawyer, and
- two persons with current research experience that is relevant to research proposals to be considered at the meetings they attend. For a full ethics review, all these roles must have been available to review applications.

The Chair will have a professional connection to the sponsoring institutions. If not an employee or academic affiliate of one of the institutions, an honorary contract will be negotiated.

At least half of the members must have a professional connection to the partner institutions.
At least one third of the members must be independent of the sponsoring institution.

General criteria for membership

- experience of a broad range of community activities
- able to learn, understand and apply research ethics principles
- interest in health and heath research issues
- able to read and understand HREC application documents
- able to appreciate the interests of potential research participants and the potential risks and benefits of research proposals, and to assess the balance between the two
- able to actively participate in and contribute to Committee discussions on research proposals and other research ethics issues
- availability to attend meetings and to participate in out-of-session activities as required, including participating in the Fast Track Committee which considers and responds to applications eligible for fast-tracking within short timeframes

A3.2 Expertise

Members with specific expertise are required. Expertise may be drawn from the following areas:

- Pragmatic clinical trials
- Early Phase clinical trials
- Data linkage
- Statistical analysis of high dimensional data
- Analysis of genomic data
- Linguistic research
- Evaluation of programmes of work
- Economic evaluation
- Policy analysis
- Clinical service delivery in a hospital setting
- Clinical service delivery in an Aboriginal community setting
- Pathology, pharmacy and pharmacology
- Epidemiological research and statistics
- Laboratory research
- Social science research
- Qualitative research

A3.3 Training

Administrative Support
The Ethics administration staff participate in on-the-job training, monitor NHMRC updates and current literature, attend seminars and undertake other training opportunities when available and accessible.
Admin staff will keep a register of current members and training provided.
The HREC will maintain a list of resources to explain the procedures and implications of the variety of research designs relevant to the NT context. This list will be reviewed yearly by the ethics administrators with suggestions and contributions from members and partner organisations.

Education opportunities
HREC members will undertake an induction and be provided with other opportunities for continued training during their appointment at least every two years.
The HREC will publicise the resources of partner organisations to maintain and increase the expertise of members. Where members do not have such access and there is a need, the HREC will use best efforts to locate the necessary education from within the partner organisations' resources.
Where partner organisations are unable to provide necessary resources the HREC will arrange education sessions to ensure sufficient expertise.

Data linkage
Training in the procedures of Data Linkage itself and the legal and regulatory requirements will be made available to new members who should familiarise themselves with their role in review.
Contact and regular updates with the NMA Data linkage Working Group will be maintained as mandated by their procedures.

Clinical trials
At least half of a quorum of members of the HREC must have a current GCP certificate.
The HREC will ensure that information is made available to explain trial designs and their ethical importance, including novel trial designs.

Early phase trials
These often pose a greater risk to participants than in other research; a risk which by definition is largely unknown or incalculable.
The HREC will ensure that members with training and experience in basic biomedical sciences have reviewed these applications and given a judgment on whether the information presented is sufficient to allow robust review by an educated lay person or requires further information and advice.
If further advice is required, the HREC will take steps to obtain external expert review.
The final review will take into account not only the internal scientific validity of the protocol but the context of delivering the protocol in the NT, or recruiting potential NT participants from groups who would otherwise not have had their needs considered in the design of the research.

Qualitative research expertise
The review of qualitative projects is complex and nuanced and requires both specific expertise and broad representation. This HREC will maintain this broad expertise within the membership and ensure that authoritative review is carried out and communicated thoroughly to the applicants.
The structure for this review will take account of the advice of experienced qualitative researchers and will normally include a dedicated sub-committee for the review of qualitative applications, reporting their important findings to the main committee.

Policy Evaluation
Norms of policy evaluation differ from those of most human research. In order to balance these norms against the requirements for clarity, quality and ethics, the HREC will ensure that advice is available from experienced policy researchers

External technical review
Contact is made through the jurisdictional representatives to the NMA Jurisdictional Working Group which may be made through the Chief Health Officer in the NT. These currently include National technical review committee for early phase trials (organised by NSW, hosted and administered by Bellberry), W&C Adelaide, Royal Perth *etc.*

Appendix 4: RISK FACTORS CONSIDERED IN ETHICAL REVIEW

A4.1 Research requiring specific risk assessment

- Research requiring waiver of consent
- Research targeting Aboriginal or Torres Strait Islander people
- Research in which a breach of privacy laws is justified by an appeal to judgment

A4.2 Risk level examples

Low Risk

An example where the risks may be identical or lower during research is a clinical trial comparing two interventions already in standard practice: while there may be a high probability of poor outcomes, these may be inherent in the standard treatment and the use of these interventions in a research project imposes no quantifiable risk. These are delicate judgments requiring expert review from clinicians with experience in research methodology.

Even then, the direct risk to participants during the research is not the only criterion by which the level of review is determined:

- where the research is complex (such as the clinical trial example above),
- where the analytic outcomes may pose risks to the participants (such as "bad news stories" about vulnerable groups or reports which may increase stigma),
- where future use of processed data or biological specimens is not clearly limited.

Non-Negligible Risk

- Where waiver of consent is required for a procedure which may be standard practice or a close extension of research, the research may be low risk but is not negligible risk. For example, drawing further blood samples from a venepuncture which is itself a routine component of care.
- Where the research procedure is a clinical trial that allocates an entire unit (for example a ward, service, or site) to some intervention, even if that intervention is standard care. If all allocations can be considered standard care then this may be low risk research, but not negligible risk.
- Where data already gathered for a similar purpose is to be analysed in a way that relates to the express purpose for which it was gathered (for example the records of a diabetes clinic are used to determine the proportion of time the average service user spent within target blood glucose control range) this may be negligible risk research.
- Where the research purpose departs strongly from the original purpose (the diabetes clinic's records are used to investigate Did Not Attend rates) the research is not negligible risk.
- Where the research poses other risks such as identification of communities it is not negligible risk.

A4.3 Standard Care in Research

A decision on whether an intervention or a process is standard care depends on the participants who are expected to receive that care, and how ready the providers are to deliver a certain model of care. It is very difficult to write rules on how to decide what is standard care. The main aim is to minimise harm to participants. With this in mind, an intervention which is new at the site may well be a component of standard care in the context of the wider health system (for example, practitioners may be familiar with its use, systems may be in place for its use, evidence may be in favour elsewhere).

- Where an intervention is standard care but is not currently available in a location because of simple resource constraint, then its deprivation is not standard care.
- Where an intervention is available but not taken up because of client or patient fear, distrust or preference, then its avoidance is not standard care.
- Where an intervention is genuinely considered to be at least equivalent in effectiveness to another intervention, and is clearly standard care in other locations despite being uncommon or even absent in current practice at the location in question, then it may be considered standard care.

A4.4 Risk of Identification

Owing to the systematic division of people by external characteristics, many people are disadvantaged in health access and the behaviour of the health system in relation to them. Even without any intention to do so, a system which applies such disadvantage is institutionally racist. Aboriginal and Torres Strait Islander people bear the heaviest such burdens but other groups, determined by externally imposed racial qualifiers or socioeconomic indicators, have analogous disadvantages. Research should have the effect of removing those disadvantages but, by its design or context, some research may not do so.

Identification
It is possible that reporting outcomes by race may worsen the conditions of life for members of certain races, where the outcomes are due not to race itself but to the constellation of other predictors associated with race. These potential outcomes must be considered by the researchers and explicitly addressed, and research projects that do not justify the risks to the satisfaction of the committee will not be approved.
Identification as a member of an externally attributed race may be useful to participants in certain types of research.

For example, social and healthcare intensity are due to institutional racism rather than the ethnic characteristics of a group. A person may have lower intensity of treatment for sepsis or cardiac disease because of perceptions about their race. In research about sepsis or cardiac disease seeking to explain this phenomenon, after accounting for other characteristics, then it is appropriate to identify people by race.
In the same setting, however, it is inappropriate to ascribe biological causality to race because that is likely to worsen the racialised delivery of healthcare.

Community identity
Communities of the NT, as elsewhere, are sources of pride and strength, and it is a clear and consistent message that identification of a community as the unit of reporting may only be done with support from that community. Indirect identification of groups of communities may be more acceptable and less risky, and any such risk must be identified by the researchers and justified to the satisfaction of the HREC.

A4.5 Determination of research access or process by race

In general, research must not pose a risk of increasing racialised delivery or outcomes of healthcare without a compelling reason.

An example is where access to healthcare might be impaired without such racial division, for example where it is not acceptable or possible for a certain group to access the healthcare that is provided for a certain condition that is detected in the research project. These justifications may require background or preliminary data before starting the research project proper.

Analysis by race
In a similar way to the foregoing examples, it may be appropriate to use "Indigenous status" from national databases as a covariate in analyses, because further work to identify and remove barriers to access, of the design of acceptable and appropriate healthcare itself, may depend on the prevalence and severity of the current disadvantage. Where this is clearly known, the risks of worsening the situation because of false determinism, resulting in despair or nihilism, must be addressed. Research projects which seek only to affirm poor outcomes for a certain race will not be approved without such justification.

Ethnicity or race?

- Because of racism, its pervasive presence, and its public unacceptability, the terms race and ethnicity have become almost useless. Ethnicity originally referred to a self-ascribed identity as a member of a group defined by culture and customs, while race originally referred to a clearly distinct group of people with a common ancestor. It can clearly be stated that in human society race is biologically meaningless with the knowledge that more than one clearly distinct group may share many common ancestors. The median or reference individual from a "race" is not more different from the reference individual of another race than each individual within a race differs from others within that race. Race does not determine the appropriate choice of treatment for a person of that race.
- Race is unfortunately not meaningless in the current world, however. Opportunities and outcomes are largely determined by what one's race seems to be to those who provide those opportunities and determine those outcomes. When it is clear that race is almost the only feature necessary to decode whether a young woman with a murmur has a harmless congenital defect or life-threatening rheumatic heart disease, then race is unfortunately a valid data point. Where it loses validity in this example is when reporting is by race, rather than disease or predisposing risk factor.
- Race is related to biological ancestry; and biological ancestry is related to the inheritance of certain individual genetic elements; and some genetic elements may be used as predictors of the best choice of treatment for people who possess them but not for other members of the race who do not possess them. Racially divided drug cupboards are ethically unsound in an era when it is possible to test whether a person has such a genetic element or not and treat entirely separately from the issue of race.

- Ethnicity is important as a source of pride or self-worth, as a reservoir of strength in hard times or a source of teaching. It is not a substitute for the word race and there are many racially mixed ethnicities in the world. Where ethnicity is a target for discrimination, it adopts the characteristics of race described above. Where ethnicity is shorthand for certain beliefs or actions that are more common in certain ethnicities, then it is a valid classifier to describe such actions or behaviours.
- The use of ethnicity or race is not proscribed by the HREC, but the research must justify any identification, division or analysis by race by causal arguments, not only reference to existing disparities.

A4.6 Health Literacy

60% of Australians do not have sufficient health literacy to navigate the healthcare system. Where healthcare or research providers do not have sufficient language proficiency in the preferred language of the participants then interpreters must be provided, or research will not be approved. In all cases the HREC will advocate for explanations in the simplest possible language, which is most straightforward to interpret either for those of low health literacy and only one language, or into a second language.

A4.7 Waiver of consent

- Research may be done using a person's data, in which case the HREC may provide a waiver of consent using the provisions of the NS and privacy legislation:
  - NS 2018 esp s4
  - NT Information Act
  - Australian Privacy Principles
  - Australian Information Act

- For a clinical trial, waiver of all consent is not generally considered appropriate. There are several novel designs of trial such as cluster randomisation between variants of standard care, where individual consent is not only excessive but is of greater risk than the trial itself.
- For a clinical trial which requires for its scientific validity and therefore its future use to society that persons without consent are enrolled, the benefit:harm ratio must be made clear to the HREC and must favour participation.

A4.8 Cluster allocation

- Individual consent may not be required for research in which entire clusters of individuals are allocated to an intervention. In this case the options for the HREC to consider are waiver of all consent (low risk interventions, standard care), consent by institutional authority (low risk interventions, not locally standard care) or "presumed" or "deemed" consent with extensive public education programmes and opportunity at several points to withdraw, but stopping short of individual prospective informed consent. In each case participants must be given reasonable opportunity to learn about the research project and assured that they are permitted to receive treatment outside of the research project if they decline to participate.
- Members of a group may be allocated to a certain intervention, for example an entire hospital may amend its usual practice on a certain date, and compare the process and outcomes with and without the new intervention (or compare between hospitals with and hospitals without the intervention). This is known as cluster methodology and there are guidelines for its valid use. It is necessary where interventions may not be delivered to individuals alone, or where the presence of people who are exposed to the intervention changes outcomes for others who may or may not be exposed directly.
- It may be appropriate to waive individual consent, if the HREC is satisfied that the risk is low and there is no reason to believe that a group might have objections to a particular intervention. If the proper assessment of the intervention requires such a design, or if other designs cannot feasibly answer the question, and the interventions are standard care, then Institutional consent may be provided for allocation by protocol, including randomised allocation.

A4.9 CONSENT

A4.9.1 Unable to consent

A person may be enrolled in a research project despite being unable to give informed consent, under the standard conditions for waiver of consent. In particular, if the risk of participation is not greater than standard care, the standard provisions of the National Statement regarding waiver of participation are relevant.

In the enrolment of participants who are likely to be unable to consent, the following provisions are used (given here rather than the schedule because of the importance of this HREC in NT protections):

A 4.9.2 Initial waiver
Consent to participate in a clinical trial may be obtained, and information on the clinical trial may be given, after the decision to include the participant in the clinical trial, provided that this decision is taken at the time of the first intervention on the participant, in accordance with the protocol for that clinical trial, and that all of the following conditions are fulfilled:
(a) due to the urgency of the situation, caused by a sudden life-threatening or other sudden serious medical condition, the participant or, in the case of an infant his or her parent or guardian is unable to provide prior consent and to receive prior information on the clinical trial;
(i) the assessment of this incapacity must not include any conclusions based on language or cultural compatibility;
(b) the research protocol has been approved by the reviewing HREC;
(c) the participant does not indicate unwillingness to participate in the clinical trial;
(d) the clinical trial relates directly to the medical condition because of which it is not possible within the therapeutic window to obtain prior consent from the participant;
(e) it is essential to include in the clinical trial participants who are unable to consent, without whom data of comparable validity cannot be obtained;
(f) the clinical trial poses a minimal risk to, and imposes a minimal burden on, the participant in comparison with the standard treatment of the participant's condition;

A 4.9.3 Consent to Continue
Following an intervention pursuant to the initial waiver, consent will be sought to continue participation in the clinical trial, and information on the clinical trial will be given, in accordance with the following requirements:

(a) regarding infants and persons with a legally designated representative, the consent will be sought by the investigator from his or her legally designated representative without undue delay and information regarding the aims and conduct of the trial will be given as soon as possible to the participant and to his or her legally designated representative;
(b) regarding other participants, the consent will be sought by the investigator without undue delay from the participant or a culturally and legally appropriate representative, whichever is sooner; and information regarding the aims and conduct of the trial will be given without undue delay to the participant or a culturally and legally appropriate representative, whichever is sooner.

For the purposes of 5.9.3(b), where consent has been obtained from the legally designated representative, consent to continue participation in the clinical trial will be obtained from the participant as soon as he or she is capable of giving informed consent.

A 4.9.4 Withdrawal of data
If the participant or, where applicable, his or her legally designated representative does not give consent, he or she will be informed of their right to object to the use of data obtained from the clinical trial.

A 4.9.5 Consent never obtained
a) Where the provisions of 5.9.3 (consent to continue) are not able to be fulfilled the researchers will provide an explanation to the HREC in writing for each participant. A non-exhaustive list of reasonable grounds for failing to fulfil these provisions is given in the Schedule.
b) The HREC will provide the Chair or delegate to review the explanation and determine whether the grounds were reasonable, and whether any further information is required from the researchers.
c) If the grounds are found to be reasonable then the HREC permits use of data and permits the research to continue.
d) If the grounds are found not to be reasonable the HREC may take action as follows or otherwise:

- Require specific further actions to fulfil the provisions of 5.9.3, and report on their result
- Require the withdrawal of data pertaining to the participant for whom 5.9.3 was not fulfilled (there is an assumption that this will not usually be employed owing to the risk of informative censoring of data, which may threaten scientific validity, rebuttable if the data is sensitive or its retention would pose risks to the specific participant or their family or community)
- Suspend the research project pending a review of consent procedures, in cases where there is suspicion that this provision is being used frivolously, systematically or to avoid good clinical practice
- Institute procedures for a breach of Good Clinical Practice

Example of reasonable grounds for failing to hold consent conversation (non-exhaustive)

- Participant died before an opportunity for consent conversation AND the research intervention was not responsible AND the research intervention was non-novel
- Participant is not contactable despite extensive efforts, including by conversations with the next of kin which did not lead to a consent conversation
- Participant and appropriate substitute decision maker are not contactable despite extensive efforts
- Participant died AND the research intervention was not responsible AND the researchers and an independent clinician agree that contact for the purposes of a consent conversation would distress the next of kin unduly

APPENDIX 5: KEY DOCUMENTS and WEBSITES

Organisational links to access submission documentation:
Link to DoH website https://health.nt.gov.au/professionals/nt-health-research/research-ethics

Link to Menzies website https://www.menzies.edu.au/page/Research/Ethics_approval/

The HREC is guided by the following documents:

1. *National Statement on Ethical Conduct in Human Research 2007* https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018
2. *Australian Code for the Responsible Conduct of Research* https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018
3. *Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders* https://www.nhmrc.gov.au/about-us/resources/ethical-conduct-research-aboriginal-and-torres-strait-islander-peoples-and-communities
4. *Keeping research on track II* https://www.nhmrc.gov.au/about-us/resources/keeping-research-track-ii
5. *Declaration of Helsinki* https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
6. *Belmont Report* https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html
7. *International Conference on Harmonization E-6 Guidelines for Good Clinical Practice (ICH-GCP-E6)* https://ichgcp.net/
8. *NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods.* https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods