National Mutual Acceptance
Single Ethical Review of Multi-centre Human Research Projects

STANDARD PRINCIPLES FOR OPERATION

Version: January 2022

Scope

These Standard Principles for Operation (Principles) describe the common principles for the National Mutual Acceptance of single scientific and ethical review of multi-centre human research projects (National Mutual Acceptance) in publicly funded health organisations.

The acceptance of scientific and ethical review of multi-centre human research projects will be referred to as National Mutual Acceptance.

The Principles are designed to inform the process of single ethical review for multi-centre human research projects. These principles should be applied to all types of research, with due consideration, for the differences in the ethical and governance review processes for the research.

These Principles provide general guidance for investigators, trial coordinators, sponsors, Contract Research Organisations (CRO) and other parties undertaking human research projects within public health organisations. Scientific and ethical review should be in accordance with the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007).

For more detailed operating procedures in each State or Territory, the relevant jurisdictional websites should be referred to and are available in the Fact Sheet and at Appendix 4.

For queries regarding these Principles, or the processes for ethical approval and site authorisation of multi-centre human research projects nationally, please contact the relevant jurisdiction listed on the Fact Sheet and in Appendix 4.

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Glossary

ACT	Australian Capital Territory
AHEC	Australian Health Ethics Committee
AHREC	Aboriginal Health Research Ethics Committee
ARPANSA	Australian Radiation Protection and Nuclear Safety Agency
Code	Code of Practice - Exposure of Humans to Ionizing Radiation for Research (2005) published by ARPANSA
CPI	Coordinating Principal Investigator
CRA	Clinical Research Associate
CRO	Contract Research Organisation
FSS-HREC	Forensic and Scientific Services - Human Ethics Committee
HREC	Human Research Ethics Committee
HREA	Human Research Ethics Application
MOU	Memorandum of Understanding for mutual acceptance of scientific and ethical review of multi-centre human research projects undertaken in Public Health Organisations
National Statement	National Statement on Ethical Conduct in Human Research (NHMRC)
NHMRC	National Health and Medical Research Council
NMA	National Mutual Acceptance
NSW	New South Wales
NT	Northern Territory
PI	Principal Investigator
PICF	Participant Information and Consent Form
Principles	Standard Principles for Operation
RGO	Research Governance Officer
SA	South Australia
SSA	Site Specific Assessment (includes research governance review/institutional authorisation)
SUSAR	Suspected Unexpected Serious Adverse Reaction
TAS	Tasmania
USADE	Unanticipated Serious Adverse Device Event
WA	Western Australia

Principle 01 National Mutual Acceptance of single scientific and ethical review of multi-centre research projects

Implementation

1. All Australian jurisdictions are participating in NMA.

2. NMA is the framework for single scientific and ethical review of multi-centre human research projects in publicly funded health organisations of participating jurisdictions.

   There are exceptions to single scientific and ethical review and details can be found on jurisdiction health websites in the NMA Fact Sheet and in this document.

Multi-centre research

Under NMA multi-centre research means research to be conducted at more than one centre. Some examples can be found in Appendix 1.

Scope of research to be considered under the NMA

3. The scope of NMA includes any form of human research as defined in the *National Statement on Ethical Conduct in Human Research* 2007, for which an application must be made to a HREC for the purpose of being conducted at a public health organisation. This includes low and negligible risk research review by a full HREC using a national ethics form (e.g. HREA).

4. The NMA single ethical review process applies to public health organisations; however, private health organisations may accept the review of a NMA proposal reviewed by a NHMRC certified HREC. Some jurisdictions may have certain requirements to provide ethical approval for private health organisations. Investigators should contact the respective State or Territory health department representatives and ensure these requirements are followed.

5. Participating jurisdictions are required to sign an inter-jurisdictional Memorandum of Understanding (MOU) to:
   - Enable publicly funded health organisations within their jurisdictions to accept the scientific and ethical review of a NHMRC certified reviewing HREC and ensure that these organisations will not undertake any further review by the organisation's HREC, acknowledging there are some exceptions in jurisdictions;

- Apply a 60 calendar day (with stop-clock capability) benchmark[1] for scientific and ethical review and decision making by a certified reviewing HREC;
- Provide consistency of HREC review according to the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007);
- Ensure that a process of research governance review/institutional authorisation/site specific assessment (referred to collectively as SSA) is undertaken by a participating site at a publicly funded health organisation. A research governance process should be practiced at non-public health organisations as part of research governance responsibilities; and
- Ensure that a human research project does not commence at a site until approval from a certified reviewing HREC has been received and site authorisation has been endorsed at the site where the research is to be conducted.

[1] Sixty calendar days are allowed for the single scientific and ethical review of an application. Where a valid application is received, the clock starts on the submission closing date for the HREC meeting at which an application will be reviewed. The clock stops when a request for further information or clarification is requested from the applicant. The clock recommences when the requested information or clarification has been received. The clock is stopped when the HREC provides a final decision.

Principle 02 Transition to National Mutual Acceptance

1. The initiative for interstate mutual acceptance of single scientific and ethical review between New South Wales Ministry of Health, Queensland and Victorian Health Departments operated from October 2011. It was superseded by NMA in November 2013.

2. Clinical trials that were granted ethical approval under the interstate mutual acceptance process will continue under those prior arrangements.

3. There will not be retrospective inclusion of approved research projects under the NMA process. However, additional sites from newly joined jurisdictions may be added to projects approved under the NMA process, by way of amendments.

4. The expansion of NMA to all human research projects commenced on 14 December 2015 and will apply in States and Territories that are signatories to the national MOU. There will not be retrospective inclusion of approved research projects (non-clinical trials) that pre-date 14 December 2015.

Principle 03 Types of human research projects excluded from single scientific and ethical review

For research conducted in Australian Capital Territory Health

Phase 0 and Phase I (first time in human) clinical trials will not be accepted under the single ethical review system for institutions under the ACT public health system and must be reviewed by ACT Health HREC.

All human research projects requiring access (including linkage) to territory data collections owned or managed by the ACT Government must be reviewed by the ACT Health HREC.

All human research projects involving persons in custody in the ACT and/or staff of ACT Justice Health require review by the ACT Health HREC.

Research projects involving access to coronial material must be reviewed by the ACT Health HREC Approval from the ACT Health HREC is required where the research project involves research in, or concerning:

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

For research conducted in New South Wales

All human research projects involving persons in custody in NSW and/or staff of NSW Justice Health require review by the NSW Justice Health HREC.

Approval from the Aboriginal Health and Medical Research Council Ethics Committee is required where the research project involves research in, or concerning, NSW and any one of the following applies:

- The experience of Aboriginal people is an explicit focus of all or part of the research;
- Data collection is explicitly directed at Aboriginal people;
- Aboriginal peoples, as a group, are to be examined in the results;
- The information has an impact on one or more Aboriginal communities; or
- Aboriginal health funds are a source of funding.

All human research projects requiring access (including linkage) to statewide data collections owned or managed by NSW Health or the Cancer Institute (NSW) must be reviewed by the NSW Population and Health Services Research HREC.

Early Phase Clinical Trials (EPCTs) (definition provided on NSW OHMR website, but includes Phase 0 (first time in human) and Phase 1 clinical trials) will not be accepted under the NMA scheme for clinical trials for New South Wales Public Health Organisations, except in the following circumstances:

- EPCTs involving adult participants will be required to be submitted to the Bellberry Ltd HRECs;
- For EPCTs involving paediatric participants:

- Where the lead site is located in NSW, these applications will be required to be submitted to the Sydney Children's Hospitals Network HREC;
- Where the lead site is located in other NMA jurisdictions, approvals will be accepted from a certified HREC hosted by a specialist paediatric health organisation operating under the NMA scheme,

In addition to any research governance (site specific assessment) requirements.

For research conducted in the Northern Territory

Please refer to the requirements at the Menzies School of Health Research website – NMA application process, and complete the requested documents:

- Cover letter describing the study and its NT context including naming the NT sites and NT co-investigators.
- Ethics application that was previously approved by the lead NMA-certified HREC, including all supporting documents e.g. HREA, protocol, PIS/CF
- Approval letter from lead NMA-certified HREC; and correspondence from lead HREC acknowledging ethical oversight of NT sites if applicable and if not included on original approval letter
- Part D attachment to HREA NMA – Aboriginal and Torres Strait Islander Research.

For research conducted in Queensland

Research projects involving access to coronial material must be referred to the Queensland Health Forensic and Scientific Services Human Ethics Committee (FSS-HEC) for ethical and legal approvals.

For research conducted in South Australia

Phase 0 (first time in human) and Phase 1 clinical trials will not be accepted under the single ethical review for clinical trials for South Australian public health organisations. 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 ethically by the appropriate HREC in South Australia in addition to any research governance/site specific assessment/institutional authorisation requirements.

Approval from the Aboriginal Health Research Ethics Committee (AHREC), South Australia, will be required where:

- The experience of South Australian Aboriginal and Torres Strait Islander people is an explicit focus of all or part of the research; or
- Data collection is explicitly directed at South Australian Aboriginal and Torres Strait Islander people; or
- Where it is proposed to separately identify South Australian Aboriginal and Torres Strait Islander people in the results; or
- The information has an impact on one or more South Australian Aboriginal and Torres Strait Islander communities; or
- The geographic location of the research is such that a significant number of the population are likely to be of Aboriginal and Torres Strait Islander origin (based on 4.7.6 of the *National Statement*, 2007); or

- Where terms such as ‘resilience’; ‘well-being’; ‘cultural safely’; ‘cultural health’; and ‘language and culture’ are used in the description and design of the project indicating that the project has important health implications; or
- South Australian Aboriginal and Torres Strait Islander health funds are a source of funding.

For research conducted in Tasmania

All human research projects will be accepted under the single ethical review for clinical trials in a Tasmanian publicly funded health service, where the HREC providing the ethical review is certified appropriately for the category of research in which the HREC approval is sought.

For research conducted in Victoria

Research projects involving access to coronial material must be referred to the Victorian Institute for Forensic Medicine HREC.

Research projects involving persons in custody require review by the Justice HREC of Victoria.

For research conducted in Western Australia

All research projects, where Aboriginality is a key determinant or is explicitly directed at Aboriginal people, must be reviewed by the Western Australian Aboriginal Health Ethics Committee (WAAHEC). That is, where the clinical trial involves the following categories:

- Aboriginality is a key determinant;
- data collection is explicitly directed at Aboriginal people;
- Aboriginal people, as a group, will be examined in the results;
- the information has an impact on one or more Aboriginal communities; or
- Aboriginal health funds are a source of funding.

All research projects that require access to coronial samples, data or information must be reviewed by the Coronial Ethics Committee, WA.

All research projects that require the use and disclosure of personal information from the Department of Health data collections or data linkage must be reviewed by the Department of Health WA HREC.

Principle 04 Submission for scientific and ethical review

Coordinating Principal Investigator (CPI) and Principal Investigator (PI) responsibilities

Coordinating Principal Investigator

- Takes overall responsibility for developing the HREC application in consultation with accepting sites (participating PIs).
- Takes overall responsibility for the research project and submits the project for scientific and ethical review;
- Is responsible for the ongoing communication with the reviewing HREC and passing on information from the HREC to the sponsor and the PI at each site conducting the research; and
- Takes on the responsibilities as the PI at their own site (as outlined below).

Principal Investigator

- Takes responsibility at their own site for the conduct, management, monitoring and reporting of the research project;
- Is responsible for submitting the site specific assessment documents for site authorisation and liaises with the site Research Governance Officer (RGO) throughout the life of the research project; and
- Is responsible for relevant communication with and reporting to the CPI with respect to all information related to the research that requires submission to the reviewing HREC.

The CPI and PI may delegate some responsibilities to research staff to manage communication during the project.

CPI Declaration on the Human Research Ethics Application (HREA)

1. The CPI must sign the declaration section of the HREA. PIs are not required to sign the declaration as they will make a declaration in the SSA form.

2. Single ethical approval will be provided through NMA; however, a human research project cannot commence until authorisation is provided by the participating site. The PI is responsible for obtaining this authorisation. The site Chief Executive or a delegate (as determined by that organisation) will have the responsibility for providing authorisation for the commencement of a human research project at their site.

Reviewing HRECs

3. The single scientific and ethical review of a multi-centre human research project is to be conducted by an appropriately NHMRC Certified HREC (reviewing HREC) in a participating jurisdiction.

4. The *HRECs, RGOs and Organisations* NMA document lists participating jurisdiction HREC information. There are different areas of certified review. The majority of reviewing HRECs are certified to review adult research projects. Some HRECs are certified to review paediatric research projects and some are certified to review both adult and paediatric research projects. This document is available on jurisdictional websites (refer to Appendix 4).

How to submit an ethics application in each jurisdiction

5. Applications by the CPI for ethical review of multi-centre human research projects are to be made as follows:
   - Australian Capital Territory use REGIS at: https://regis.health.nsw.gov.au
   - New South Wales use REGIS at: https://regis.health.nsw.gov.au/how-to/
   - Northern Territory, the HREA may be prepared using the NHMRC portal https://hrea.gov.au/
   - Queensland use ERM at: https://au.forms.ethicalreviewmanager.com/Account/Login?ReturnUrl=%2fHome%2fIndex
   - South Australia use Research GEMS at: https://gems.sahealth.sa.gov.au/
   - Tasmania – Investigators from Tasmania wanting to submit an ethics application for review of multi-centre human research projects should refer to the relevant reviewing HREC jurisdiction for more detailed instructions.
   - Victoria use ERM at: https://au.forms.ethicalreviewmanager.com/Account/Login?ReturnUrl=%2fHome%2fIndex
   - Western Australia use RGS at: https://rgs.health.wa.gov.au/Pages/Home.aspx

   The applications should be to the certified HREC associated with the site at which the applicant is conducting the research project and if this is not applicable, the researcher should identify a suitable HREC.

Principle 05 Ethics application forms

1. A Human Research Ethics Application (HREA) is to be used for submission of a research proposal to a reviewing HREC for scientific and ethical review.

2. Each jurisdiction, through the reviewing HREC, may require additional forms to be submitted aside from the HREA. Additional forms to be reviewed by the HREC are required as follows:

    - For projects in NT, specific forms must be completed and further ethical and scientific review may be triggered
    - For projects in Victoria, the Victorian Specific Module must be completed and the CPI must submit this form, in addition to the HREA, to the reviewing HREC.
    - For projects in Western Australia, the Western Australian-Specific Module (WASM) must be completed in addition to the HREA.

Principle 06 Master participant information and consent form

1. The NHMRC templates are the recommended Master Participant Information and Consent Forms (PICFs).

2. The CPI is responsible for submission of the Master PICF to the reviewing HREC following appropriate consultation with participating sites.

3. A PICF with site-specific wording may be submitted by a participating site, via the CPI, and must be based on the Master PICF with addition of specific site requirements or policies relating to the conduct of the research. The Site PICF should be on the letterhead of the site with an appropriate footer, referencing the Master PICF and version.

4. For sites which function in accordance with the Catholic Health Australia's "Code of Ethical Standards for Catholic Health and Aged Care Services in Australia" 2001 ("the Catholic Code") a recommended Catholic statement is available at Appendix 2. However, it should be noted that a Reviewing HREC is not required to accept Catholic wording on a PICF if it is deemed not appropriate for that particular research project.

Principle 07 Notification of a HREC decision and post approval of a human research project

Duration and conditions of scientific and ethical approval

1. Scientific and ethical approval for human research projects will be for up to a five year period or rolling approval for the life of the project.

HREC approval letters

2. HREC approval letters should clearly:
   - List all organisations (or sites) that have been approved through single ethical review;
   - State the HREC approval anniversary date;
   - Specify the date(s) on which the CPI submits to the reviewing HREC, a progress report which includes reporting from all approved sites;
   - List documents, with version identification, associated with the research project that was reviewed and approved by the reviewing HREC;
   - Indicate that the research cannot commence until site authorisation has been endorsed by the participating site;
   - Specify the duration of ethical approval.

Annual/progress reports

3. Annual or more frequent progress reports to the reviewing HREC should be provided by the CPI to maintain the approval for the designated approval period. Continuing HREC approval will be contingent upon receipt of an annual (or more frequent) report to the reviewing HREC.

4. An annual progress report will be due on the **anniversary date of HREC approval** (not on the anniversary date of site authorisation or project commencement).

5. The CPI is responsible for submitting a collated annual progress report to the reviewing HREC. The CPI should submit reports to the reviewing HREC by the required date. If a site PI has not provided the CPI with the appropriate annual report information, it will be at the discretion of the reviewing HREC whether to suspend ethical approval at that participating site until a report is submitted.

Amendments

6. Modification of an approved human research project must be submitted to the reviewing HREC as an amendment. This may include, but is not limited to, a change to the protocol or an approved document or addition of a new site.

7. In cases of immediate safety concerns not covered under usual monitoring or a risk to participant safety, the reviewing HREC should receive a report from the responsible investigator as soon as possible. The reviewing HREC can then be fully informed and an ethical decision made, before a formal amendment process occurs.

8. A HREC amendment must not be implemented at a site until ethical approval is provided and the RGO at the site has been consulted and has confirmed that site authorisation is current.

9. A site RGO(s) should provide a timely response to PIs regarding the amendment, to avoid undue delay of the project.

Extension of HREC approval

10. Extension of the HREC approval period may be requested and the reviewing HREC must be consulted for information on the process and period of the extension prior to expiry of the current approval period. In some jurisdictions, a new ethics submission, review and scientific and ethical approval will be required. The process to be followed will depend on the decision of the reviewing HREC in the relevant jurisdiction.

Monitoring of approved human research project

11. The reviewing HREC and the site conducting the human research project is responsible for monitoring the ongoing conduct and safety of approved research as stated in the *National Statement on Ethical Conduct in Human Research* (NHMRC, 2007).

12. The *Monitoring and Reporting Framework* and *Monitoring and Reporting Tables* for NMA should be referred to and are available on participating jurisdiction websites (see Fact Sheet and Brochure). The *Monitoring and Reporting Tables* are a guide for CPIs, PIs, reviewing HRECs and Research Governance Officers (RGOs) involved in multi-centre human research projects.

13. Safety (adverse events, SUSARs/USADEs) reporting is the responsibility of the research project's sponsor and submission of appropriate safety reports should be guided by *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods* (NHMRC, 2016) available at https://www.nhmrc.gov.au/guidelines-publications/eh59.

14. For safety (adverse events, SUSARs/USADEs) reporting refer to the *Monitoring and Reporting Tables* for NMA on jurisdictional websites (at Appendix 4).

Principle 08 Requirements for a multi-centre human research project involving use of ionising radiation

1. The reference document for research involving the use of ionising radiation is the *Code of Practice - Exposure of Humans to Ionizing Radiation for Research* (2005) published by ARPANSA (2005) (Code). The Code applies to research involving humans who are exposed to ionising radiation which is additional to that received as part of normal clinical management.

2. Jurisdictional websites may be referred to for guidelines and further information on research involving the use of ionising radiation.

Principle 09 Guidance for reviewing Low or Negligible Risk studies under NMA

Background

NMA SOPs have previously required Low and Negligible Risk (LNR) research to be reviewed by a full HREC using a national ethics form (e.g. HREA).

Following consideration by the NMA Inter-Jurisdictional Working Group, it has been agreed to modify the NMA SOPs (and Fact Sheet) to support the acceptance of LNR research that has been reviewed using non-HREC levels of review, in accordance with the provisions in the *National Statement*.

The following statement has been developed following consultation with all States and Territories regarding their preferred process and stance.

Position Statement for all States and Territories except South Australia

As with all NMA applications, projects meeting the Low or Negligible Risk (LNR) criteria for a non-HREC level of review according to the *National Statement on Ethical Conduct in Human Research 2007 (updated 2018)* (*National Statement*) will be reviewed under the NMA scheme only if they are submitted on the Human Research Ethics Application form (HREA).

An LNR project will be accepted under the NMA scheme if the project has been ethically reviewed using a non-HREC level of review described in the *National Statement*.

South Australia only

Non-HREC levels of review will not be accepted for projects being submitted to South Australian public health organisations under NMA.
Acceptable forms of review may include:

(i) review by a full NMA-participating HREC from another jurisdiction
or
(ii) re-review by a NMA-participating HREC from South Australia.

Guidance on NMA LNR review Process (excluding South Australia)

- Institutions with NMA-participating HRECs will have non-HREC levels of review that are consistent with the *National Statement* (5.1.20) for reviewing and approving LNR projects.
- As per the *National Statement*, those reviewing research at a non-HREC level must refer to an HREC any research they identify as involving more than low risk [5.1.21].
- In order to facilitate consistency in LNR review, referral may be made to the set of NMA-endorsed guidelines on LNR review, that are consistent with the *National Statement* (see Appendix 3).

Appendix 1 Definition and examples of multi-centre research for NMA

Multi-Centre Research

Human research conducted at multiple sites within more than one State and Territory public health system.

Some examples:

- The project is at your centre and in **public** hospitals of other jurisdictions participating in NMA.
- The project is to be carried out at more than one centre within different jurisdictional Health districts (relevant in some jurisdictions only) in Mental Health, Community Dental Services, etc.

Multi-centre research not included in NMA

Multi-centre research within **one** jurisdiction (State or Territory) should be reviewed according to the relevant jurisdiction's requirements.

Appendix 2 Catholic recommended wording

If the research project involves a site which functions in accordance with the Catholic Health Australia's *Code of Ethical Standards for Catholic Health and Aged Care Services in Australia* 2001 (the *Catholic Code*), then this must be addressed, particularly with respect to the type of research and Patient Information Sheet/Consent Form content. The investigator must contact the relevant institution(s) for specific advice, especially relating to the content of the Patient Information Sheet/Consent Form.

The Catholic Code is available at the Catholic Health Australia website.

Catholic statement recommended for use by HRECs

The following statement was developed through the deliberations of the Catholic Health Australia working group representing Catholic hospital ethicists and clinicians. This is recommended for use by any human research ethics committee seeking to provide clear communication to potential research participants of child-bearing age and is consistent with Catholic teaching.

Patient Information and Consent Form Statement where pregnancy must be avoided: Recommended Template for Catholic Institutions

The effects of *[Name of investigational product]* on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project. If you are male, you should not father a child or donate sperm for at least *[number]* months after the last dose of study medication.

Both male and female participants must avoid pregnancy during the course of the research and for a period of *[number]* months after completion of the research project. You should discuss effective methods of avoiding pregnancy with your study doctor.

[For female participants] If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You must not continue in the research if you become pregnant.

[For male participants] You should advise your study doctor if you father a child while participating in the research project. Your study doctor will advise on medical attention for your partner should this be necessary.

Appendix 3 NMA Guidelines for Low and Negligible Risk (LNR) Research Review

This Guideline represents an interpretation of the National Statement on Ethical Conduct in Human Research (the "National Statement") as it applies to low and negligible risk research. It is intended to provide greater consistency amongst HRECs and others in interpreting and clarifying some of the concepts contained in the National Statement. It should not be used as a substitute for reading and applying those concepts as directly expressed in the National Statement and other related documents.

Determination of level of risk and appropriate level of review per the National Statement

The National Statement defines risk as "the function of the magnitude of a harm and the probability that it will occur". The types of harm that may be encountered when research is conducted are described below.

Types of harm	**Possible examples**
Physical harm	Including injury, illness, pain
Psychological harm	Including feelings of worthlessness, distress, guilt, anger or fear related, for example, to disclosure of sensitive or embarrassing information, or learning about a genetic possibility of developing an untreatable disease
Devaluation of personal worth	Including being humiliated, manipulated or in other ways treated disrespectfully or unjustly
Social harms	Including damage to social networks or relationships with others; discrimination in access to benefits, services, employment or insurance; social stigmatisation, findings of previously unknown paternity status, reputational harm to a participant, researcher, institution or community
Economic harms	Including the imposition of direct or indirect costs on participants
Legal harms	Including discovery and prosecution of criminal conduct

Adapted from National Statement, 2007 (updated 2018)

The National Statement permits institutions to establish levels of ethics review that are proportionate to the degree of risk involved, and provides the following definitions:

- **Negligible risk research**: Where there is no foreseeable risk of harm or discomfort; and any foreseeable risk is no more than an inconvenience to participants. Examples of inconvenience in human research may include filling in a form, participating in a de-identified survey or giving up time to participate in a research activity.

- **Low risk research**: Where the only foreseeable risk is one of discomfort. Discomforts include, for example, minor side-effects of medication, discomforts related to measuring blood pressure and anxiety induced by an interview.

- **More than low risk research**: Where the risk, even if unlikely, is more serious than discomfort, the research is not low risk.

Researchers, Human Research Ethics Committees (HRECs) and other ethics review bodies are required to determine the existence, likelihood and severity of risk based on a number of factors including the study's methodology and design, participant characteristics and the research activity. In some cases, the requirement for full HREC review may be mandated by Australian law (e.g. Commonwealth or state privacy legislation, the Therapeutic Goods Regulations 1990 and the *Research Involving Human Embryos Act 2002*). Where no such mandate exists, determination of the appropriate review pathway is influenced not only by the risk to participants, but also by a range of other contextual considerations:

- **The level of complexity of the research**: For certain types of research such as complex qualitative research or clinical trials, the HREC may wish undertake/confirm that a rigorous assessment of the methods used to avoid or reduce bias has taken place, as poorly designed research poses risks to data validity and credibility.

- **Whether a research activity raises associated ethical issues**: For example:
  - The handling of findings that may have health implications for the participant and/or their family
  - For research involving the analysis of bio-specimens, the context in which the bio-specimens were acquired or any known limitations the donor(s) placed on their use during the consent process.

- **Participant characteristics**: The National Statement outlines ethical considerations specific to participants in Section 4, which may influence the level of ethics review required. For example:
  - Cultural or religious considerations or the possibility that a dependent relationship may compromise the voluntary character of the participant's decisions
  - Whether participants have the capacity to give their informed consent

- **The intent of the research**: For example,
  - Whether the research aims to expose illegal activity or involve active deception or planned concealment

- **The risks to researchers or staff**: For example,
  - Research assessing emergency services or research requiring home visits

- **The nature and context of the test/procedure/measure**: For example,
  - The frequency of its use
  - The degree of its invasiveness
  - The skill and experience of the person performing it
  - Whether there is adequate supervision of the activity
  - Whether the measure is already part of the standard of care is also relevant to the determination of whether a research project is suitable for review under low or negligible risk processes. Section 3.1.6 of the National Statement should be considered:

    In health research involving an intervention, the risks of an intervention should be evaluated by researchers and reviewers in the context of the risks of the health condition and the treatment or treatment options that would otherwise be provided as part of usual care.

Projects that must be reviewed by an HREC

According to the National Statement, if the project includes any of the following types of research and/or participants and/or approaches to consent, it will require HREC review[1] regardless of the level of risk:

- Waiver of consent (2.3.9 – 2.3.10), including:
  - Use of human biospecimens obtained without specific consent for their use in research, or where the proposed research is not consistent with the scope of the original consent (3.2.14)
  - Genomic research (3.3.14)
  - The sharing of genomic data or information (3.3.24b)
  - Emergency care research (4.4.6)
- Research involving the derivation of embryonic stem cell lines or other products from a human embryo (3.2)
- Research involving **prospective collection** of human biospecimens including establishment of a biobank (3.2.1)
- Exportation of bio-specimens for research in accordance with institutional policy (3.2.9 b)
- Research involving the **use** of human bio-specimens that may give rise to information that may be important for the health of the donors, their relatives or their community (3.2.15)
- Research including genomics (3.3) †
- Animal-to-human xenotransplantation (3.4) ‡
- Research on women who are pregnant, research on the human foetus in utero, and research on the separated human foetus or on foetal tissue (4.1)*
- Research involving people highly dependent on medical care who may be unable to give consent (4.4)*
- Research involving people with a cognitive impairment, an intellectual disability or a mental illness (4.5)*
- Research that is intended to study or expose, or is likely to discover, illegal activity (4.6)*
- Research with Aboriginal and Torres Strait Islander Peoples (4.7)

† As a general principle, research including genomics will require review by an HREC; however, if no information that can identify an individual is used and no linkage of data is planned, the research may be determined to carry low risk (3.3).
‡ *Xenotransplantation research must also be ethically reviewed and approved by an institutional animal ethics committee.*
***** *Except where that research uses existing collections of data or records that contain only non-identifiable data about human beings and involves negligible risk and which, therefore, may be exempted from ethics review.*

Projects that may[2] be suitable for review by 'other ethics review bodies'/non-HREC levels of ethics review dependent on the context of the research

These examples were generated in consultation with public health organisations.

a) Examples of projects involving the collection, storage and disclosure of data

- Surveys or questionnaires where the data are <u>not</u> identifiable or potentially identifiable to the researcher (e.g. returned anonymously) where the questions are not overly sensitive, and they have been satisfactorily peer reviewed to ensure that the questionnaire is likely to achieve the intended outcomes. For example:

1 *HREC review* means review by an HREC that is constituted and functioning in accordance with Section 5 of the National Statement.

- Online and/or anonymous surveys where there is no direct contact with participants (i.e., recruitment is through generic email, mail or a social networking site link.)

- Research interviews/focus groups that do not include highly sensitive topics or where accidental disclosure would not have serious consequence

- Establishment of a data registry using non-identifiable data from existing data sets

b) Examples of projects involving the use of bio-specimens

Research using existing bio-specimens already taken with unspecified (i.e. broad) or extended consent for research:

- Where the research does not involve any risks to the donors, their blood relatives or their community that are more serious than discomfort
- Where the research cannot reveal information that may be important for the health of the donor(s), their blood relatives or their community
- Where specific individuals cannot be identified from the bio-specimens used (i.e. the bio-specimens are non-identifiable to the researcher).

c) Examples of projects involving non-invasive or minimally invasive activities

- Prospective research involving non-invasive or minimally invasive activities may be eligible for low risk review. Examples might include research activities where participants are asked to read materials, review pictures or videos, play online games, solve puzzles, or perform cognitive tasks.

Projects that may be exempt from ethics review

Institutions may choose to exempt from ethics review, research that involves the use of existing collections of data or records that contain only non-identifiable data about human beings and is negligible risk research.

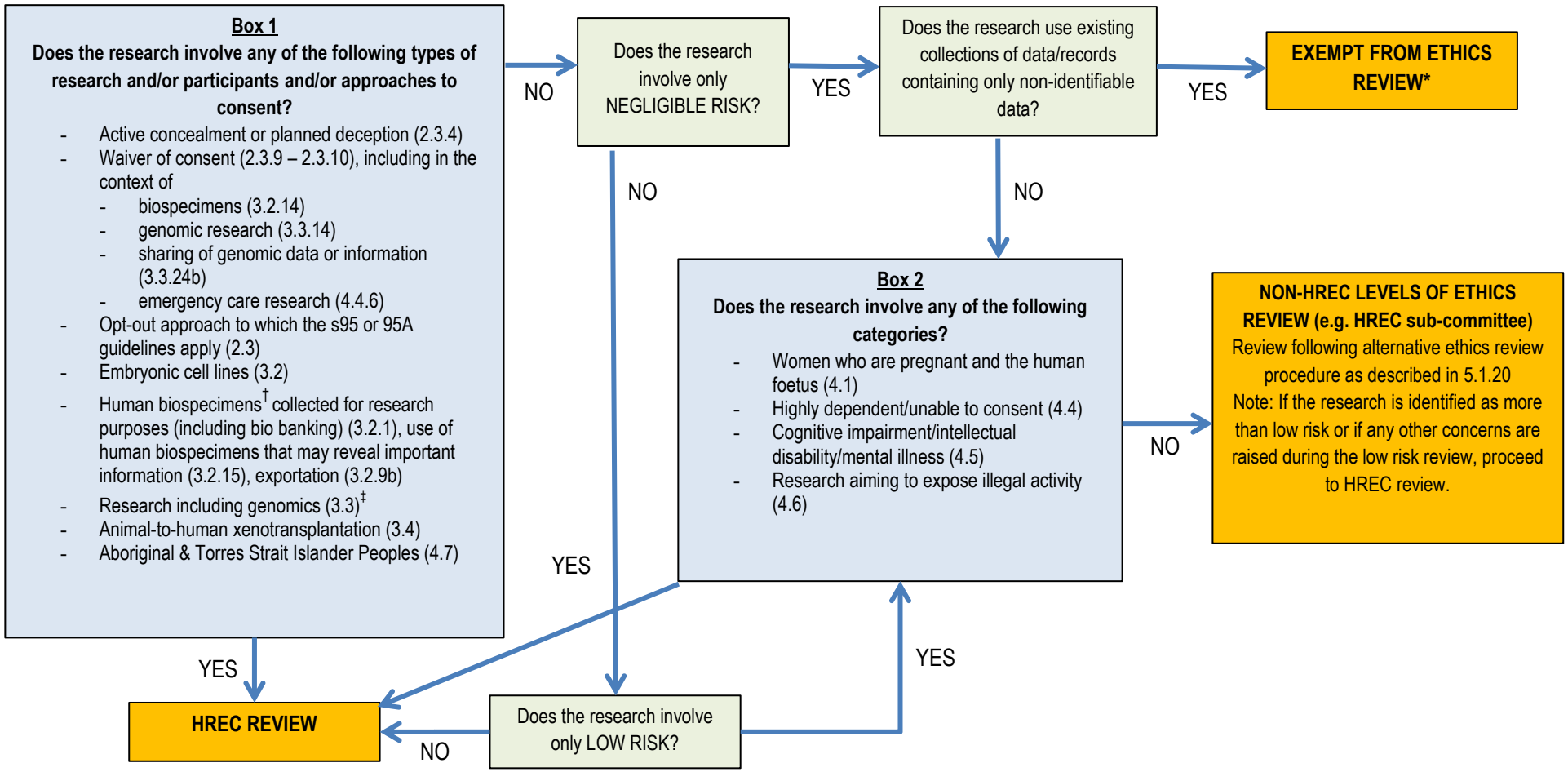
Institutions that do not have separate procedures for reviewing research that is exempt from ethics review are likely to review this sub-set of research under their established low risk review processes.

Journal Requests for Ethics Review
If required by a journal as a condition of publication, an HREC or other ethics review body may be willing to review a study. However, editors of most journals will usually accept a letter from the institution confirming that an appropriate ethics review process was used or that ethics review was not required.

Figure 1 below provides an overview per the National Statement, including step-wise considerations to help institutions determine the appropriate level of review.

[2] Inclusion on this list merely means that the activity is eligible for review through LNR processes when the specific circumstances of the proposed research involve no more than low risk to participants.

Figure 1: Flowchart for Low and Negligible Risk Review



* *Institutions that do not have separate procedures for reviewing research that is exempt from ethics review would review this sub-set of research under their established LNR review processes.*

† *Research involving the **use** of human biospecimens that still meets the definition of low risk after **3.2.2-3.2.3** are considered, may qualify for a non-HREC level of ethics review.*

‡ *As a general principle, research including genomics will require review by an HREC; however, if no information that can identify an individual is used and no linkage of data is planned, the research may be determined to carry low risk (3.3).*

Appendix 4 Jurisdictional Contact Details

Australian Capital Territory
Research Office
Phone: 02 5124 3949
Email: ethics@act.gov.au
Web: www.health.act.gov.au/research/research-ethics-and-governance

New South Wales
The Office for Health and Medical Research
Email: researchethics@doh.health.nsw.gov.au
Website: www.health.nsw.gov.au/ethics/Pages/nma.aspx

Northern Territory
NT Health Research Governance Office
Phone: 08 8922 7764
Email: nthealth.rgo@nt.gov.au
Website: https://health.nt.gov.au/data-and-research/nt-health-research

Queensland
Research, Ethics and Governance; Health Innovation, Investment and Research Office
Phone: 07 3708 5071
Email: hiiro_reg@health.qld.gov.au
Website: www.health.qld.gov.au/hiiro/html/regu/regu_home

South Australia
Office for Research
Phone: 08 8226 4235 or 08 8226 7702
Email: Health.DHAResearch@sa.gov.au
Website: www.sahealth.sa.gov.au/researchethics

Tasmania
Research Governance Office, Clinical Quality Regulation and Accreditation
Tasmania Department of Health
Phone: 03 6166 0395
Email: research.governance@health.tas.gov.au
Website: https://www.health.tas.gov.au/research

Victoria
Coordinating Office for Clinical Trial Research
Phone: 0408 274 054
Email: multisite.ethics@ecodev.vic.gov.au
Website: https://www.clinicaltrialsandresearch.vic.gov.au

Western Australia
Research and Innovation Unit
Department of Health WA
Phone: 08 9222 4222
Email: RIO.DOH@health.wa.gov.au
Website: https://rgs.health.wa.gov.au/Pages/Home.aspx