Low and Negligible Risk Research

Summary This Guideline clarifies the requirements for Low and Negligible Risk Research under the National Statement on Ethical Conduct in Human Research (2007).

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Audience Research Office Staff;Researchers;Health Professionals;Heads of Departments Hosting and Supporting Research

NSW Health

GUIDELINE

Low and Negligible Risk Research

GUIDELINE SUMMARY

This Guideline represents NSW Health's interpretation of the *National Statement on Ethical Conduct in Human Research (2007)* [National Statement] as it applies to low and negligible risk (LNR) research.

It is intended to provide consistency amongst Human Research Ethics Committees (HREC) and others in applying the low and negligible risk concepts contained in the National Statement, which enables the processing of research projects according to the same low and negligible criteria.

KEY PRINCIPLES

This Guideline is based on the principles described in the National Statement. It has been developed to clarify the requirements of low and negligible research under the National Statement.

It promotes standard processes in determining the risk and appropriate level of review of low and negligible risk projects with consistency per the National Statement. Matters of detail and precise procedure may be subject to particular local needs.

NSW Health Organisations may adopt this Guideline or incorporate them into their existing local guidelines. 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.

REVISION HISTORY

Version	Approved By	Amendment Notes
GL2023_007 April-2023	Deputy Secretary, Population and Public Health & Chief Health Officer	New Guideline

CONTENTS

1. BACKGROUND

1.1. About this document

This Guideline forms NSW Health's interpretation of the National Statement on Ethical Conduct in Human Research (National Statement) as it applies to low and negligible risk (LNR) research.

It is intended to provide greater consistency amongst NSW Human Research Ethics Committees (HRECs) and other relevant parties in interpreting and clarifying the LNR concepts contained in the National Statement.

1.2. Key definitions

Clinical Trial	A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trials include but are not limited to: • Surgical and medical treatments and procedures • Experimental drugs • Biological products • Medical devices • Health-related service changes • Health-related preventative strategies • Health-related educational interventions.
Human Research	Research conducted with or about people, or their data or tissue as described in the *National Statement on Ethical Conduct in Human Research (2007)*.
Human Research Ethics Committee (HREC)	A committee constituted in accordance with the *National Statement on Ethical Conduct in Human Research (2007)* to review and, where appropriate, approve and monitor the ethical and scientific aspects of human research.
Low risk research	Research where the only foreseeable risk to the participant is one of discomfort. Discomforts may include minor side-effects of medication, discomforts related to measuring blood pressure or anxiety induced by an interview. Where the risk, even if unlikely, is more serious than discomfort, the research is not low risk.

Negligible risk research	Research where there is no foreseeable risk of harm or discomfort, and any foreseeable risk is not more than inconvenience to the participants. Inconvenience is the least form of harm that is possible for human participants in research.
NSW Health Organisations	Public Health Organisations established under the *Health Services Act 1997* (NSW) and NSW Ambulance.
National Statement (NS)	*National Statement on Ethical Conduct in Research Involving Humans (2007)* released by the National Health and Medical Research Council (NHMRC). Reference to specific paragraphs of the National Statement will be in the format NS 2.2.6.
Research	An original investigation undertaken to gain knowledge, understanding and insight as described in the *Australian Code for the Responsible Conduct of Research (2018)*.

1.3. Legal and legislative framework

This Guideline should be read in conjunction with the following NSW Health Policy Directives and Guidelines.

Document Number	NSW Health Policy Directive and Guidelines
(PD2010_055)	Research - Ethical & Scientific Review of Human Research in NSW Public Health Organisations
(PD2010_056)	Research - Authorisation to Commence Human Research in NSW Public Health Organisations
(GL2010_014)	Operations Manual: Human Research Ethics Committee Executive Officers
(GL2010_015)	Operations Manual: Research Governance Officers
(GL2013_009)	Human Research Ethics Committees: Standard Operating Procedures for NSW Public Health Organisations

2. 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.

Table 1. The types of harm that may be encountered when research is conducted (adapted from the National Statement).

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.

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:

Table 2. Research risk categories (adapted from the National Statement).

Research Risk Category	Definition
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 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 several factors including the study's methodology and design, participant characteristics and the research activity.

In some cases, the requirement for full review may be mandated by Australian law (for example Commonwealth or state privacy legislation, the *Therapeutic Goods Regulations 1990* (Commonwealth) and the *Research Involving Human Embryos Act 2002* (Commonwealth). 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 Human Research Ethics Committee may wish to undertake/confirm that an 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

The handling of findings that may have health implication 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.

Participants' 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

Whether the research aims to expose illegal activity or involves active deception or planned concealment.

The risk to researchers or staff

Research assessing emergency services or research requiring home visits

The nature and context of the test/ procedures/ measure

- 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. National Statement Section 3.1.6[1] should be considered.

3. PROJECTS THAT MUST BE REVIEWED BY A HUMAN RESEARCH ETHICS COMMITTEE

According to the National Statement (NS), if the project includes any of the following types of research and/or participants and/or approaches to consent, it will require Human Research Ethics Committee review[2] regardless of the level of risk:

- Waiver of consent (NS 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 (NS 3.2.14)
    - Genomic research (NS 3.3.14)
    - The sharing of genomic data or information (NS 3.2.24b)
- Research involving the derivation of embryonic stem cell lines or other products from a human embryo (NS 3.2)
- Research involving *prospective collection* of human biospecimens including establishment of a biobank (NS 3.2.1)
- Exportation of bio-specimens for research in accordance with institutional policy (NS 3.2.9b)
- 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 (NS 3.2.15)
- Research including genomics (NS 3.3)[3]
- Animal-to-human xenotransplantation (NS 3.4)[4]

[1] 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.

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

[3] 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 (NS 3.3).

[4] Xenotransplantation research must also be ethically reviewed and approved by an institutional animal ethics committee.

- Research on women who are pregnant, research on the human foetus in utero, and research on the separated human foetus or on foetal tissue (NS 4.1)[5]
- Research involving people highly dependent on medical care who may be unable to give consent (NS 4.4)[5]
- Research involving people with a cognitive impairment, an intellectual disability or a mental illness (NS 4.5)[5]
- Research that is intended to study or expose, or is likely to discover, illegal activity (NS 4.6)[5]
- Research with Aboriginal and Torres Strait Islander Peoples (NS 4.7).

4. PROJECTS THAT MAY BE SUITABLE FOR REVIEW BY NON – HREC LEVELS OF ETHICS REVIEW

These examples were generated in consultation with NSW Health Organisations.

4.1. Examples of projects involving the collection, storage and disclosure of data

Surveys or questionnaires where the data is not identifiable or potentially identifiable to the researcher (such as returned anonymously) and 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:

- 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.

4.2. 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).

[5] 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.

4.3. 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.

5. 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 are exempt from ethics review are likely to review this sub-set of research under their established low risk review processes.

6. JOURNAL REQUEST FOR ETHICS REVIEW

If required by a journal as a condition of publication, a Human Research Ethics Committee or other ethics review bodies 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.

7. APPENDIX

1. Decision tree for low and negligible risk review

7.1. Decision tree for low and negligible risk review

Decision tree for the low and negligible risk review, including stepwise considerations to help institutions determine the appropriate level of review.