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Purpose

This guidance document aims to give an overview of the review pathways available for human research that involves lower risk or higher risk and those seeking an exemption from ethics review for their research.

Definitions

ARTG: Australian Register of Therapeutic Goods.

Identifiable data: When the identity of a specific individual can reasonably be ascertained the data is referred to as "identifiable data". Examples of identifiers may include name, date of birth, address, postcode (particularly small sets of data or small districts).
IVD: In vitro diagnostic device.

Non-identifiable data: includes the following: data that has never been labelled with individual identifiers; data that has had the identifiers permanently removed in such a way as to ensure no specific individual can be identified.

Re-identifiable data: (potentially identifiable data): data may have identifiers removed and replaced by a code (including but not limited to UR numbers). In such cases it is possible to use the code to re-identify the person to whom the data relates. In these cases, the data are referred to as "potentially identifiable".

Risk: A potential for harm or discomfort. It involves the likelihood that a harm or discomfort will occur, and the severity or magnitude of the harm or discomfort, including their consequences. Risk can apply to an individual research participant, groups, communities as well as to non-participants such as family members. Risk can be associated with the conduct of research or the proposed outcomes of the research (National Statement Chapter 2.1).

TGA: Therapeutic Goods Administration.
Therapeutic goods: Include drugs, devices, and biologics, and are broadly defined as products for use in humans in connection with:

- preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury
- influencing, inhibiting or modifying a physiological process
- testing the susceptibility of persons to a disease or ailment
- influencing, controlling or preventing conception
- testing for pregnancy.

Unapproved therapeutic good:

- Any medicine not included in the ARTG or any medicine already in the ARTG involving a new formulation, strength or size, dosage form, name, indication(s), directions for use, or type of container.
- Any medical device (including an in vitro diagnostic device (IVD)) not included in the ARTG, such as any new sponsor, manufacturer, device nomenclature system code, classification or unique product identifier (for certain classes of medical devices only) of a medical device already in the ARTG.
- Any in-house IVD medical device used for a clinical trial, where the laboratory providing the in-house IVD is unable to comply with the regulatory requirements for in-house IVDs.
- Any biological not included in the ARTG such as:
    - any new applicable standards, intended clinical use, or principal manufacturer of a Class 1 or 2 biological already in the ARTG.
    - any new product name, dosage form, formulation or composition, therapeutic indication, type of container or principal manufacturer of a Class 3 or 4 biological already in the ARTG
    - any use of a therapeutic good already included in the ARTG not covered by the existing entry in the ARTG.

Guidance

Human research is conducted with or about people, or their data or tissue. Human participation in research may include the involvement of humans through:

- participating in surveys, interviews or focus groups
- psychological, physiological, or medical testing or treatment
- researchers observing their responses, actions or behaviour
- researchers having access to their personal documents or other materials
- the collection and use of their body organs, tissues, or fluids (e.g., skin, blood, urine, saliva, hair, bones, tumour or other biopsy specimens) or their exhaled breath
- access to their information (in individually identifiable, re-identifiable or non-identifiable form) in an existing published or unpublished source or database.

For clinical trials where research is regulated by the TGA, research means any use of an unapproved therapeutic good.

Retrospective review

As per the National Statement 5.1.6, Bellberry does not provide counterfactual opinions or retrospective reviews for any work already undertaken.

Assessment of risk level

To determine the level of ethical review required, an assessment of the level of risk involved in the research project must be conducted, referring to the *National Statement on Ethical Conduct in Human Research (2023)* Chapter 2.1.

The risk profile of an individual research project falls somewhere along a continuum. Risk assessment should be based on the following categories.

Lower risk		**Higher risk** (Individual, group, community, societal or global)	
Minimal	**Low**	**Greater than low**	**High**
No risk of harm or discomfort; potential for minor burden or inconvenience*	No risk of harm; risk of discomfort (+/- foreseeable burden)	Risk of harm (+/- foreseeable burden)	Risk of significant harm (+/- foreseeable burden)

Higher risk research

Higher risk research describes research in which the risk for participants or others is greater than discomfort and carries risk of harm. Higher risk research requires full ethics review by an HREC (National Statement Chapter 2.1).

The following non-exhaustive list identifies the types of potential harms in or from research (National Statement Chapter 2.1):

- physical harm: including injury, illness, pain or death;
- psychological harm: including feelings of worthlessness, distress, guilt, anger, fear or anxiety related, for example, to disclosure of sensitive information, an experience of re-traumatisation, 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;
- cultural harm: including misunderstanding, misrepresenting or misappropriating cultural beliefs, customs or practices;
- social harm: including damage to social networks or relationships with others, discrimination in access to benefits, services, employment or insurance, social stigmatisation, and unauthorised disclosure of personal information;
- economic harm: including the imposition of direct or indirect costs on participants;
- legal harm: including discovery and prosecution of criminal conduct.

Any of these types of harm can be experienced individually or collectively.

Full ethics review by an HREC is required for any research that involves greater than low risk and is required for the following types of research as identified by the relevant section and chapters of the National Statement:

- 2.3.4: (a) Research that involves active concealment or planned deception or, (b) Aims to expose illegal activity.

2.3.9: Research proposals requesting a waiver of consent for research using personal information in medical research, or personal health information. Where a waiver is requested and personal

- information in medical research or personal health information is not being used, the application could potentially be reviewed through the Lower Risk pathway.

- Chapter 3.2: Use of biospecimens:
  3.2.1 Where research involves the **prospective collection** of biospecimens for research purposes, a full HREC review is required.
  3.2.2 Where the research involves the use of **stored human biospecimens** for research:
  In determining the level of ethics review appropriate for the research involving the use of human biospecimens, the responsible institution and researcher should consider:
  (a) whether the research involves any risks to the donors, their relatives or their community that are more serious than discomfort (see Chapter 2.1: Risk and Benefit); and
  (b) whether the research may give rise to information that may be important for the health of the donors, their relatives or their community where the identity of the donors will be known to, or can reasonably be ascertained by, those conducting the research or with access to health or research data or information related to donors.
  3.2.3 Where the research involves only the use of **stored biospecimens** and involves **no more than low risk**, then the provisions of 5.1.10–5.1.14 for non-HREC levels of review may apply.

- Chapter 3.3: Where the research involves any genetic testing, a full HREC review is required except where information used cannot identify an individual and no linkage of data is planned, the research may be determined to carry lower risk.

- Chapter 3.4: Animal-to-human xenotransplantation.

- Research involving the following participants:
  - Chapter 4.1: Women who are pregnant and the human foetus
  - Chapter 4.4: People highly dependent on medical care who may be unable to give consent

- Chapter 4.5: People with a cognitive impairment, an intellectual disability, or a mental illness
- Chapter 4.6: People who may be involved in illegal activities
- Chapter 4.7: Aboriginal and Torres Strait Islander Peoples
- Chapter 4.8: People in other countries

Additionally, Bellberry considers research that includes participants under the age of 18 excluded from review via the Lower Risk pathway. Research of this nature will undergo full ethics review by an HREC.

Use of collections of data: Assessment of risk level to be made and consideration of the National Statement Chapter 3.1 Element 4.

General guidance for full HREC review

Bellberry HRECs meet each Wednesday evening. Our submission timelines are as follows:

- An application and documents are required 10 working days prior to the meeting day with submission cut off 5pm every Wednesday. A complete application will be considered at a HREC meeting on the Wednesday two weeks following the submission cut off. Incomplete applications may delay the study's review.
- Generally, at least two meetings are held each week, except between Christmas and New Year; with additional meetings commissioned when necessary.
- An investigator can expect to receive comments detailing the Committee's deliberations 2 working days following the Committee meeting.
- All responses to the Committee's requests/comments are reviewed outside of the meetings and a response will be received generally within a week.
- This meeting date to application decision timeline is dependent on the complexity of the study being reviewed and response time for an investigator to respond to the Committee's questions.

Principal Investigator's/researchers may be invited by the Committee to attend review meetings to present their study, or answer concerns in regard to specific issues either in person or via telephone.

Where issues remain unresolved, the Committee Chair will consider a teleconference upon request from the Principal Investigator. In the event that issues are unresolved, the complaints procedure may be followed.

In some circumstances, the HREC may grant approval of the study on the basis that further information will be required at a later date, for example, where an interim safety report is required prior to the commencement of the second stage of a study. In these instances, the Approval Letter will outline the conditions of approval/caveat.

Following approval of the study by the HREC, the Principal Investigator must submit any amendments to the study documentation, serious breaches, safety reports, annual progress reports and a final report when the project is completed.

Lower risk review

Lower risk research describes research, including some types of clinical trials, in which the only foreseeable risk for participants or others is no greater than discomfort (National Statement Chapter 2.1). Lower risk research may either be reviewed by the Bellberry Lower Risk Sub-committee (National Statement 5.1.12) or may be exempted from ethics review (National Statement 5.1.17).

Discomfort is considered less serious than harm. It can involve physical or psychological impacts, for example, minor side-effects of medication, discomfort related to non-invasive examinations or tests (such as measuring blood pressure), and mild anxiety associated with an interview. However, where a person's reactions might exceed discomfort and become distress, this should be viewed as the potential for harm (National Statement Chapter 2.1).

General guidance for lower risk review

Responsibility for reviewing research involving lower levels of risk has been delegated to the Committee Chair and/or the Lower Risk Sub-Committee (National Statement 5.1.12).

Our submission timelines and processes are as follows:

- An investigator may request Lower Risk review of their research proposal by submitting an application through the eProtocol online platform. Applications can be submitted at any time but submission by close of business each Wednesday will allow for addition to that week's meeting agenda for full HREC review if the research is reassessed as high risk. The investigator will be notified of any outcomes/comments via eProtocol.

The Research Manager or delegate and Committee Chair will review the study to determine the level of risk and determine the appropriate level of review (Committee Chair alone or Sub-Committee), and, if necessary, the composition of the Sub-Committee. The Sub-Committee will be a person or persons with appropriate expertise selected from all Bellberry HREC members, with external expertise sought if needed.

- If the Sub-Committee decides that a full HREC review is required, the investigator will be notified that the project will need to be redirected to the full ethical review process. Upon confirmation from the investigator, the study will be assigned to an HREC meeting. The Sub-Committee will provide its report to the HREC for consideration.

- If reviewed via the Lower Risk pathway the investigator will be notified of the outcome of the review or provided with any comments to be addressed within one week of submission. Ongoing cycles of comments and responses will continue until an outcome has been reached.

- After approval, the investigator must submit any amendments to the project protocol or study documentation, serious breaches, safety reports, an annual progress report, and a report when the project is completed.

Exempted research

Research that carries a lower risk to participants or the community and satisfies one or more of the conditions in (a)-(d), below (National Statement 5.1.15 and 5.1.17) may be exempt from ethical review:

- (a) the research involves the use of collections of information or data from which all personal identifiers have been removed prior to being received by the researchers and where researchers explicitly agree
  - (i) not to attempt to re-identify those with whom the information or data is associated;
  - (ii) to take all reasonable steps to prevent re-identification of the information or data for unauthorised purposes or access to the information or data by those who are not authorised; and
  - (iii) that any sharing of any research data during or after the project will not create any additional risks of re-identification of the information or data;
- (b) the research is restricted to surveys and observation of public behaviour using information that was or will be collected and recorded without personal identifiers and is highly unlikely to cause distress to anyone associated with the information or the outcomes of the research;
- (c) is conducted as part of an educational training program in which the research activity is for training purposes only and where any outcomes or documentation are for program use only;
- (d) the research uses only information that is publicly available through a mechanism set out by legislation or regulation and that is protected by law, such as mandatory reporting information, information obtained from registries of births and deaths, coronial investigations or reports of the Australian Bureau of Statistics.

Examples of research and activities that may be exempt from ethics review include quality assurance or improvement, or clinical audits. In addition to the *National Statement on Ethical Conduct in Human Research (2023)*, please refer to the *NHMRC Ethical Considerations in Quality Assurance and Evaluation Activities (2014)* guidance document.

For research that may be eligible for an exemption from ethics review, and where there is no institution providing oversight of the research, researchers may ask a HREC to grant an exemption from an ethics review (National Statement 5.1.15). Acknowledgement of an exemption from ethics review can be requested by emailing bellberry@bellberry.com.au.

Taking over ethical oversight of approved research

Any request by a Principal Investigator for Bellberry to take over ethical oversight of a research study which has been approved by another HREC will be treated as a new application. These requests may occur when the original HREC is no longer going to operate, or where the Principal Investigator/Sponsor decides to transfer the study from another HREC.

Bellberry will require a full submission via eProtocol to be reviewed by the full HREC. Approval by Bellberry will not be guaranteed. Transfer of the study cannot take place until Bellberry has provided ethics approval.

Review fees

Please refer to BA G6 Application Fees

References

Ethical Considerations in Quality Assurance and Evaluation Activities (2014)
National Statement on Ethical Conduct in Human Research (2023)
LER SOP1.1 HREC review process
LER F1.1.4 Reviewers checklist (primary and secondary)
LER F1.1.6 Study decision considerations
LER F1.1.7 Review of device protocols
LER F1.1.10 Quality Assurance exemption register

Appendix 1. Review flowchart