Review pathways - quality assurance (QA), low and negligible risk (LNR), full ethical review

Public

Purpose

This guidance document aims to give a brief overview of the review pathways available to those seeking ethical review for human research, quality assurance (QA) activities, and low and negligible risk (LNR) research.

Definitions

Quality assurance (QA): An activity where the primary purpose is to monitor or improve the quality of service delivered by an individual or an organisation is a QA activity. Terms such as 'peer review', 'quality assurance', 'quality improvement', 'quality activities', 'quality studies' and 'audit' are often used interchangeably. In this document the term 'quality assurance' is used to include all of these terms. QA activities are exempt from the ethical approval process. Researchers may seek acknowledgement from Bellberry that an activity is QA and exempt from ethical review."

Low and negligible risk (LNR): Research is 'low risk' if the only foreseeable risk to participants is discomfort. If the research poses even the slight chance of a more serious risk, the research is not low risk. (National Statement 2.1.6). Research is 'negligible risk' if the only foreseeable risk to participants is inconvenience (National Statement 2.1.7). LNR activities require ethical approval.

Full ethical review: Research involving humans, with more than a low level of risk (as defined in National Statement 2.1.6), must have ethical and relevant site approval prior to commencement. Research involving humans may include any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data with the intent to generate new knowledge, in which human beings:

- are exposed to manipulation, intervention, observation, or other interaction with investigators either directly or through alteration of their environment; or
- become individually identifiable through investigator's collection, preparation, or use of biological material or medical or other records.

ARTG: Australian Register of Therapeutic Goods.

IVD: In vitro diagnostic device.

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).

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".

TGA: Therapeutic Goods Administration.

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.

Quality assurance (QA)

Many QA activities can be part of routine clinical practice or service delivery and may not pose additional ethical risks. However, in the same way as clinical research must be reviewed for risks, QA activities must be reviewed for potential risks, burden, inconvenience or breach of privacy.

QA projects are generally in-house activities that aim to determine if a particular treatment or procedure at an institution is meeting expected standards. If deficiencies are detected, changes may be required to clinical practice, local guidelines or staff training. QA findings are typically specific to the institution or health service in which the activity was conducted, so the results are usually disseminated only within that institution or service. Data from a QA project may be published (e.g., in a peer-reviewed journal) if the findings have ramifications for the broader community.

QA activities may be based on individually identifiable, re-identifiable or non-identifiable data. Some could generate or illuminate information of a sensitive nature, such as HIV status, genetic disease or social issues relating to a particular demographic, so it is essential that privacy and participant anonymity needs are considered.

While QA activities typically involve minimal risk, they must still be conducted ethically. Consideration should be given as to whether the participants and staff may be exposed to harm, and how consent will be obtained (if applicable) and privacy protected. Ethical issues should be explicitly identified and a plan to manage them included in the QA project plan.

Researchers seeking advice on whether their proposal meets the National Health and Medical Research Council (NHMRC) 'Ethical Considerations in Quality Assurance and Evaluation Activities (March 2014)' criteria, may contact Bellberry via email (bellberry@bellberry.com.au) for guidance. The Operations Manager / delegate and HREC Chair will review the application and, by consulting the QA checklist, determine whether the study is a QA activity and is exempt from ethical review, or requires full review. QA projects must obtain all necessary institutional/site approvals. If requested, the Bellberry HREC can provide a letter of exemption in relation to their QA assessment.

The QA checklist can help the researcher and/or the HREC in determining if the QA activity should be subject to ethical review.

Quality assurance (QA) reviews

Bellberry delegates QA reviews out of session, to reviewers with specialised knowledge and understanding of the guidelines governing QA. Reviews are conducted by the Committee Chair and/or the QA Review Sub-Committee.

The reviewers may use the QA checklist while considering issues including consent, privacy, relevant legislation, professional standards and whether an ethical review is required. If the project is determined QA,

the applicant will be notified. Applications that do not meet the NHMRC 'Ethical Considerations in Quality Assurance and Evaluation Activities (March 2014)' criteria will be redirected to the full ethical review process.

Low and negligible risk (LNR) research

Responsibility for reviewing research involving low or negligible levels of risk has been delegated to the Committee Chair and/or the LNR Review Sub-Committee (National Statement 5.1.18 – 5.1.21).

1. An investigator may request LNR review of their research proposal by submitting their application through the eProtocol application form. The investigator will be notified of any outcomes/comments via eProtocol.
2. The Operations Manager or delegate and Committee Chair will review the study to determine the level of risk. The Operations Manager or delegate and the Committee Chair will 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.
3. If the Sub-committee decides that further review is required, the investigator will be notified that the project will be redirected to the full ethical review process, and the study will be assigned to an HREC meeting. The Sub-committee will provide its report to the HREC for consideration.
4. After approval, the investigator must submit any amendments to the project protocol or study documentation, an annual progress report, and a report when the project is completed.

Full ethical review

Any research that does not meet the QA or LNR criteria must be reviewed by a convened HREC. Such research may not be reviewed by expedited review or exempt review. Additionally, research involving the following populations must be reviewed by a convened HREC, regardless of the level of risk:

- women who are pregnant and the human foetus
- children and/or young people not of the legal adult age in the jurisdiction where the research is undertaken
- people highly dependent on medical care who may be unable to give consent, including those in neonatal intensive care; in terminal, emergency or intensive care; or who are unconscious
- people with a cognitive impairment, intellectual disability or mental illness
- Aboriginal and Torres Strait Islander individuals or communities.

Additionally, only a HREC can review and approve research involving active concealment, planned deception, or researching aiming to expose illegal activity.

Bellberry HRECs are comprised of members with expertise in both clinical and non-clinical trials. For clinical trials where research is regulated by the TGA, research means any use of an unapproved therapeutic good. 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.

An 'unapproved' therapeutic good is:

- 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.

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.

If comments are received regarding the review process the Committee Chair will consider face to face meetings to resolve issues that have been unresolved by written or telephone communication.

In the event that issues are unresolved, the complaints procedure may be followed.

In some circumstances, the committee may grant approval 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.

Taking over ethical oversight of approved research

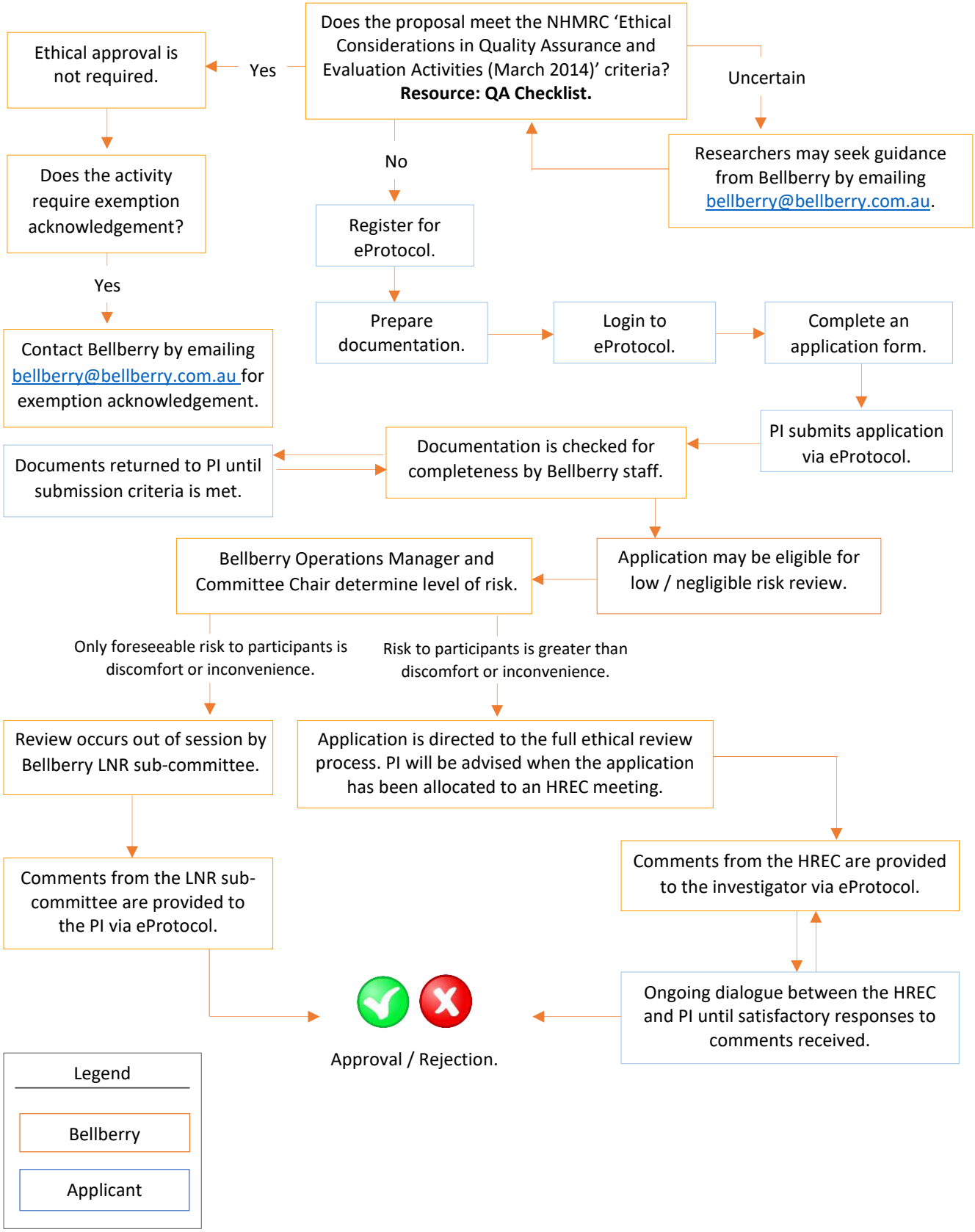
Any request by an Investigator for Bellberry to take over ethical oversight of a research proposal which has been approved by another HREC will be treated as a new application. Bellberry will require a full submission via eProtocol. It will be subject to full ethical review by a Bellberry HREC. This may occur where the original HREC is no longer going to operate, or where the Investigator/Sponsor decides to transfer the study from another HREC.

Approval by Bellberry will not be guaranteed. Transfer of the study cannot take place until Bellberry has provided ethical approval.

References

Ethical Considerations in Quality Assurance and Evaluation Activities 2014
National Statement on Ethical Conduct in Human Research (2007 incorporating all updates)
LER SOP1.1 HREC review process
LER F1.1.1 Quality Assurance (QA) checklist
LER F1.1.2 Low and Negligible risk (LNR) checklist
LER F1.1.3 Triage checklist
LER F1.1.4 Reviewers checklist (primary and secondary)
LER F1.1.6 Study decision considerations
LER F1.1.7 Review of protocols for devices
LER F1.1.8 National statement updates checklist
LER F1.1.10 Quality Assurance exemption register

Appendix


Does the proposal meet the NHMRC 'Ethical Considerations in Quality Assurance and Evaluation Activities (March 2014)' criteria? **Resource: QA Checklist.**
Yes
Ethical approval is not required.
Uncertain
Researchers may seek guidance from Bellberry by emailing bellberry@bellberry.com.au.
No
Register for eProtocol.
Does the activity require exemption acknowledgement?
Yes
Contact Bellberry by emailing bellberry@bellberry.com.au for exemption acknowledgement.
Prepare documentation.
Login to eProtocol.
Complete an application form.
PI submits application via eProtocol.
Documentation is checked for completeness by Bellberry staff.
Documents returned to PI until submission criteria is met.
Application may be eligible for low / negligible risk review.
Bellberry Operations Manager and Committee Chair determine level of risk.
Only foreseeable risk to participants is discomfort or inconvenience.
Risk to participants is greater than discomfort or inconvenience.
Review occurs out of session by Bellberry LNR sub-committee.
Application is directed to the full ethical review process. PI will be advised when the application has been allocated to an HREC meeting.
Comments from the HREC are provided to the investigator via eProtocol.
Comments from the LNR sub-committee are provided to the PI via eProtocol.
Ongoing dialogue between the HREC and PI until satisfactory responses to comments received.
Approval / Rejection.
Legend
Bellberry
Applicant