TOP TIPS FOR SUCCESS IN ANIMAL ETHICS APPLICATIONS

UQ RESEARCH AND INNOVATION







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UQ's innovations have, and continue to make, life-changing advances. The University is committed to maintaining the highest standards of ethical decision-making, animal husbandry and care as a contribution to achieving quality research and teaching outcomes.

For research that involves the study of animals in the wild or in agriculture, or the use of animal models of human disease, the University's Animal Ethics Committees review proposals to ensure that animal welfare is fully considered before the commencement of any project activities. Similarly, the Committees must consider teaching activities that directly involve animals, such as veterinary science or marine biology.

As part of Top Tips Series produced by UQ Research and Innovation (UQR&I), this brochure provides applicants with helpful advice for ensuring high quality applications and maximising success in the Animal Ethics Committee review process.



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INTRODUCTION

The University of Queensland (UQ) has five Animal Ethics Committees (AECs) that review ethics submissions from UQ staff and students, as well as some external organisations. Timely approval of applications depends on providing the information needed by the AEC to reach a consensus decision. If an AEC requires more information, that additional detail is often reviewed at their next meeting - one month later.

Delays in AEC approval are not usually related to poor experimental design or concerns that animal welfare is not being considered, but because the information required by the Committee to evaluate and approve an application is either not provided, or not clearly presented. AEC meetings often last many hours; therefore, increasing the number of approved applications at first review by the Committee benefits both researchers and the AECs, whilst simultaneously maintaining the highest commitment to the humane care and use of animals at the University.

This Top Tips brochure provides advice to researchers preparing ethics applications and is based on common application errors and/or omissions UQ AECs have encountered.

01 PROVIDE THE RIGHT INFORMATION

The animal ethics applications are designed to inform the AEC of the reasons for animal use and for consideration of the wellbeing of animals during the course of a project. Its core function is to enable the AEC to determine if the use of animals is justified and outcomes of the project outweigh the potential impact on animals. This is called the 'cost versus benefit' consideration, that is, the cost to the animal versus the benefit to other animals or to humans.

Providing the right information in the right format to enable decision making, is vital. For example, cutting and pasting text verbatim from other documents, such as grant proposals can introduce unnecessary information that detracts from what the AEC needs to consider. Documents such as grant proposals also have a very different purpose to an animal ethics application.

Ensure your application clearly and concisely informs the AEC:

- Why the work is necessary
- Why the use of animals for the work is necessary (addresses the 3Rs Replacement, Reduction, Refinement)
- What will happen to the individual or groups of animals over the course of the project
- What impact will the project have on the wellbeing of animals
- How animals will be monitored for pain and distress
- How will pain and distress be avoided or minimised
- Why your assembled team is the right one, with the right experience, for the project
- If you are working with laboratory animals the officer in charge of your animal facility should be part of the team and be consulted before submission

It is essential that ethics applications provide sufficient evidence that the use of animals is fully justified. This puts animal welfare at the forefront of your application.



02 WRITE PLAINLY AND ACCESSIBLY

The AECs are comprised of four categories of membership:

- Category A (veterinarian)
- Category B (senior scientist)
- Category C (external animal welfare advocate)
- Category D (external independent/layperson)

Please note that Category D and most Category C members are not likely to have a scientific background. Each member is responsible for making their own judgement on matters that come before the Committee.

This means that when writing applications the language should be plain, avoid scientific jargon and complex descriptions, and avoid using abbreviations or acronyms. Committee members should not need an 'acronym buster' to understand your proposal. In particular Section A of UQ's research application must be written using language that will be understood by lay people on the Committees to ensure they are able to make their own judgement on the application. Using ambiguous language should be avoided at all times. For example, terms such as 'should' and 'might' are better replaced with definitive terms such as 'will' or 'will not'. Lengths of time should be exact (e.g. blood will be collected several days later, should be written as blood will be collected three days later). Exact volume doses, sites and frequency of any substances injected should be given rather than approximate values, or ranges.

Your application will not be rejected by an AEC for incorrect spelling and grammar; however both may lead to misunderstanding and/or ambiguity, sometimes resulting in an inability for the AEC to understand and (hence) approve the application. Ensure that you are using the correct terms; for example an error commonly found in applications is use of 'anaesthesia' when the researcher really means 'analgesia'.

Always read through your applications, use spelling and grammar checkers where possible, and get others (particularly those named on the application) to read through and make corrections before submission.



In order to determine the effect of the proposed project on animal wellbeing all information about the use and care of animals from the beginning of the experiment until the end must be clear to the Committee. This includes

- Where the animals come from
- Transport
- Acclimatisation procedures
- Details of experimental procedures
- The number of procedures used on any animal
- The time between any procedures
- The potential effect on the animal after each procedure
- How pain will be monitored and, where necessary, relieved over the course of the project
- What will happen to the animal at the conclusion of the project

The AECs find the use of timelines and/or flow charts exceptionally helpful in understanding the impacts on animals, especially for projects where animals undergo several procedures and/or may be used for more extended periods. Timelines and flow charts are also useful when submitting modifications to projects, so that the Committee can clearly see how the modification relates to the original, approved application as well as to any other modification that has been made (ensuring the primary aims of the application remain clear to the AEC).

The use of timelines and flow charts will enhance your applications: they are a highly effective tool to provide an overarching structure, to avoid inadvertent omissions in the detailed description of project activities, and to ensure consistency across the various sections of the application.



04

JUSTIFY AND MINIMISE NUMBERS

This aspect of the application is vital to get right, but often may be unclear to Committee members in reading your proposal. As long as you have fully justified the need for using the animals, and have justified the number of animals you need for the project, the Committee will not ask you to use less animals than you request. However, the strength of your defence and reasoning is important.

Where possible, use appropriate statistical power analysis; consult a statistician if at all possible. Justify the number of animals required in terms of the experiment, not in terms of how many people are available to work on the project or its economics. For example, when killing animals to collect tissue for culture, the number of animals requested should be based on the number of cells obtained from each animal, and how many cells are required for each assay. Requesting a certain number of animals to produce enough cells for 5 students to use each week, is not justifying the number of animals in the terms required by the Committee and does not consider animal welfare impacts.

Also consider a pilot study. In some cases it is not possible to determine how many animals should be in an experimental group because it is not yet known. Instead of submitting a full application, in the first instance you could request a pilot study using a smaller number of animals. A pilot study can be used to determine the effects of the research on animal wellbeing when it may otherwise be unknown. Use of pilot studies is a valuable approach when planning projects, by helping to refine the protocol, and to reduce potential impact on animals before a larger study is performed. Pilot studies may be used to determine the variation in results from animals after a particular procedure or in a test. This can then be deployed in statistical justifications making it easier to justify the number requested per experimental group for the full study, once the pilot study is complete. Pilot studies can be one experiment that is part of a larger application, or the pilot study can be a stand-alone ethics application.

The '3Rs' (Refinement, Replacement and Reduction) are at the heart of the animal ethics processes. It is important to let the Committee know that you have given thorough consideration to the 3Rs. Progress in areas of work that do not use animals is of interest to the Committee, as well as the reasons why those methods will not address the research question at hand. Discuss ways in which you have modified procedures to either replace animal use, or improve outcomes for animals, or have refined procedures to reduce the number of animals required.



All AECs encounter applications where a lack of detail in methods or inconsistencies in methods across the application makes it impossible for the Committee to approve a project. This is often the case for administration of drugs and for blood sampling. The following information must be provided to the AEC for each drug used:

- Route of administration
- Site of administration
- Dose rate
- Infusion rate where appropriate
- Frequency of administration
- Volume
- Needle gauge
- A brief, lay description of the mechanism of action
- A brief description of the anticipated effect on the animal
- For new compounds, the class of the compound type and a description of quality control in their production that will avoid adverse side effects.

These details also need to be justified in terms of best practice. For example, volumes injected intraperitoneally may be too large for the animal and could be reduced. Needle gauges should be the most appropriate for use with the species of animals or in specific circumstances (such as injection of cells where a larger needle gauge may be required to limit cell damage).

Similarly, information related to drawing blood samples is often incomplete. The AEC requires the following information:

- The site from which blood is taken/the method used
- The volume of blood sampled. Volumes must not exceed the recommended amount that considers the species from which blood is taken
- The time between sampling, if multiple samples are taken

- If animals have already undergone other experimental procedures, how long after these procedures is blood sampled?
- Who is taking the blood samples and are they appropriately trained for generic or highly specialised techniques?
- Is fluid replacement required and how will it be provided?
- Is anaesthesia required? If so provide the details.

Also explain why the volumes and number of samples requested are appropriate for the project and necessary for downstream analysis and interpretation.

The Guidelines to promote the wellbeing of animals used for scientific purposes: The assessment and alleviation of pain and distress in research animals (2008) is a document that provides this type of information for several species. www.nhmrc.gov.au/ guidelines-publications/ea18.

Where there is doubt about current best practice seek advice from the UQR&I Animal Ethics Unit Coordinator and/or the UQR&I Consultant Veterinarian Officer (CVO), who are there to help you.



06 USE PRE-APPROVED UQ STANDARD OPERATING PROCEDURES

The Animal Ethics Unit website has a number of preapproved UQ standard operating procedures (SOPs) for commonly used protocols/procedures. Before being made available as a resource, the relevant AEC/s consider and approve the SOPs, which are then reviewed every three years. Use of SOPs can streamline your application by reducing the amount of information to enter, and by using procedures that the AECs are familiar with and which are already endorsed in a standard format. When using SOPs:

- Provide both the number and full name of the SOP (e.g. AHT 21; Rotarod test for rodents, April 2015).
- Read the SOP and make sure that no other information is required. For example if the SOP uses an 'anaesthetic of choice' provide details of the anaesthetic including dose, route, volume, gauge needle and frequency of administration.
- If your requirements are very similar to the SOP but you need to make minor modifications, provide the SOP number and title, but also provide details of any deviation from the SOP you will need to make.
- If the SOP states 'operator must be experienced', outline the person/people performing the procedures and their experience. If further training is required, then state who will provide the training.

Please note that the use of SOPs in this manner only refers to those approved by UQ AECs and published on the UQR&I website. SOPs from your own laboratory do not fall into this category. Each application is stand alone, and so even if you use the same protocol on more than one application, unless they are University SOPs, the full procedural details will need to be provided on each application you make. You are encouraged to contribute to UQ SOPs if you use generic protocols and procedures and would like for these to be added to the University's approved SOP website.

Please contact the UQR&I Consultant Veterinary Officer for help in preparing SOPs for submission to the AEC for approval.

UQ's standard operating procedures can be found at: www.uq.edu.au/research/integrity-compliance/ inclusion-and-use-of-sops-in-applications



Monitoring score sheets are an important element for the ethical treatment of animals during their use for scientific and teaching purposes. Appropriate monitoring provides a means to recognise signs of pain and distress and to apply criteria for deciding when intervention or euthanasia is applicable.

Template monitoring score sheets are available from the UQR&I AEU website (www.uq.edu.au/research/ integrity-compliance/score-sheets). It is recommended that you seek assistance from the CVO prior to submission to ensure these are adapted to the specifics of each individual project. Score sheets should also include the frequency of monitoring. AECs frequently receive non-customised scoresheets that are not fit for the specific purpose, or applications without any score sheets or appropriate information about the intended monitoring procedures. All information regarding monitoring of animals should be described within the experimental methodology component of the application, so that it is clear when and how often the animals are monitored, and by whom. For experiments, where pain relief in controls is not possible ensure the minimisation of their pain and suffering is also addressed.

The animal ethics application requires the score sheets used for monitoring be attached to the application for approval by the AEC. For those using genetically modified organisms (GMOs) consider how the genetic modification affects the wellbeing of the animal. Many animal models of human diseases produce that disease in the model organism. These animals should not be left to suffer unnecessarily and score sheets should be tailored to monitor for the specific symptoms. For new GMOs monitoring should include screening newborns for neonatal lethality. A scoresheet for a genetically modified organism should include the age at which monitoring for symptoms of the disease occur, the types of symptoms likely to occur, and clear points at which intervention or euthanasia will occur. When GMOs undergo experimental procedures, the effect of the genetic modification should also be taken into account, and be reflected in the score sheet by appropriate monitoring.

For newly created GMOs appropriate monitoring is essential for identifying expected as well as unexpected phenotypes. It is a requirement of the *Australian code for the care of animals for scientific purposes (current edition) (the Code)* that records of monitoring are maintained, and both regular reports on the monitoring of a new line and a final report be submitted to the AEC. *The Guidelines for the generation, breeding, care and use of genetically modified and cloned animals for scientific purposes* outlines ethical considerations and monitoring procedures and contains example score sheets for assessment of GMOs.

www.nhmrc.gov.au/_files_nhmrc/publications/ attachments/ea17.pdf

The UQR&I Animal Ethics Unit Coordinator or Consultant Veterinary Officer are available to give advice on all issues relating to monitoring arrangements and documentation.



08 USE THE HINTS PROVIDED WHEN FILLING OUT APPLICATIONS

The University's online Animal Ethics Application form contains many functions aimed at helping you complete your application successfully.

For example, there are tips embedded within the online form, at most of the key questions. For any question where you see a symbol () underneath the question number, hints for answering that question can be obtained by clicking on the symbol.

The text in the pink 'hints' box is not visible until you click on the symbol. The information may include details and/or helpful examples of what is required for the question.





A common challenge with animal ethics applications is in using the terms 'replicates' and 'repeats'. Using these terms interchangeably and ambiguously makes it impossible for the AEC to follow the application. *The Australian code for the care and use of animals for scientific purposes* (the Code, current edition) states:

1.23 Activities involving the use of animals must not be repeated within a project or between projects unless such repetition is essential for the purpose or design of the project (e.g. sound experimental design, statistical analysis, corroboration by the same or another investigator).

'Replicates' should be used to describe multiple animals within an experiment for the purpose of sound experimental design. The number of replicates should be expressed as n=3, n=10 etc. For some non-quantitative experiments a minimum of duplicate observations (e.g. n=2) or triplicate (n=3) is required. The number of animals used should, of course, be justified as described above. 'Repeats' on the other hand are a second, third or subsequent conduct of an entire experiment, or part of an experiment. According to *the Code* repeats are permitted when:

- it is necessary that the same investigator confirm a result (e.g. where biological variability imposes a requirement to ensure a result is not a 'one-off'); or
- it is necessary to confirm a result by another investigator (e.g. where it is important to ensure that a result is genuine or does not rely on a specific researcher or participant).

If repeats are requested in your application, the request should be accompanied by a suitable justification mindful of the requirements of *the Code*. In cases where a third repeat is requested, AECs will usually approve the application minus the animals required for the third repeat. The investigator will be asked to request additional animals for the third study when required, accompanied by strong justification for the need.



Consistency across all key elements of your application is a key factor in facilitating the work of an AEC.

Ensure that when you enter the total numbers of animals you are requesting that the number is the same as you have justified. Where there are inconsistencies the AEC will need to clarify if your justification needs reworking, or if you just made a typo. The AEC cannot make interpretations of inconsistencies on your behalf.

Inconsistencies in applications have been observed by AECs where incorrect numbers, strain names or even species are 'copied and pasted' that do not make sense with the rest of the application. If copying and pasting from other applications it is recommended that you exercise caution and make sure all of the details are relevant to the current application.

If you use animals with strain names, keep the naming consistent throughout your application. An example of inconsistent naming often encountered on animal ethics applications is with the mouse strain, C57BI/6, often shortened to C57 or BI/6. On many occasions a single application contains a variety of names for the same strain. The application form has a drop down list. Select the strain from this list before entering a new strain name.

The UQR&I Animal Ethics Unit staff cannot interpret what you mean on an application. If you are consistent

- a. The chance the Committee will get confused is reduced
- b. Your approval certificate will make more sense
- c. You will reduce confusion when preparing your annual reports

Furthermore, if you are working with laboratory animals and keep track of your animals using Genotrack, the strain information is entered from what is on the AEC certificate. If the strain names are consistent, then when it comes to generating annual reports the information exported will be clear and writing your annual report will be a breeze! Of course this doesn't only apply to c57BI/6 mice; naming fish, production animals or other species can have similar problems. If you work with laboratory animals, using the same naming on your breeding application, research application, teaching application and then in Genotrack, will provide clarity for you, the people in your group, the Animal Facility Staff and UQR&I Animal Ethics Unit staff.

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