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Animal Ethics Committee

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1. Change History

Version	Author	Description
6	Michael Miller	• Various updates and clarifications throughout the text • Added definition and reporting timelines for Unexpected adverse events regarding EAEC • Added information on multiple surgeries, humane endpoints and studies involving fluid/food restriction • Clarified interval of Animal Research Authority (ARA) issuing • Updated conflict of interest section to require removal of members prior to voting. • Replaced majority decision to consensus • Updated unexpected adverse event reporting lines • Updated requesting an amendment to a study process

2. Purpose

Animal Ethics Committees govern the use of animals in research, teaching and product testing.

The primary responsibility of the Elanco Animal Ethics Committee (EAEC) is to ensure that the care and use of animals by company personnel is in compliance with the *Australian code for the care and use of animals for scientific purposes* (the *Code*), the Animal Research Act 1985 and the Animal Research Regulation 2010.

The EAEC applies a set of principles, outlined in the *Code*, that govern the ethical conduct of people whose work involves the use of animals for scientific purposes. The role of the EAEC is to ensure that the use of animals is justified, provides for the welfare of those animals, and incorporates the principles of Replacement, Reduction and Refinement (the 3Rs).

3. Scope

This Standard Operating Procedure (SOP) describes the operation of the EAEC. The EAEC is established under the Animal Research Act 1985.

4. Procedures

4.1. Terms of Reference

The Elanco Animal Health Animal Ethics Committee (EAEC) has been established to give effect to section 25A of the Animal Research Act 1985. The EAEC is responsible for consideration of applications for animal research authorities and for the supervision of animal supply for research by Elanco Animal Heath (EAH), operating at Yarrandoo.

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The EAEC is responsible to the Site Head of Yarrandoo. Communication with the Site Head may be made directly or *via* the Animal Welfare Officer.

The following sections outline in detail the Terms of Reference of the EAEC.

4.1.1. AEC Responsibilities

The primary responsibility of an AEC is to ensure, on behalf of the institution for which it acts, that all activities relating to the care and use of animals are conducted in compliance with the Legislation and the Australian Code for the Care and Use of Animals for Scientific Purposes (2013) ("The Code"); and that the use of animals in research is justified and incorporates the principles of Replacement, Refinement and Reduction, as set out in the Code.

The EAEC must;

- Review applications for projects and approve only those projects that are ethically acceptable (see 'The Code', clause 1.3) and conform to the requirements of the Code.
- Review applications for activities associated with the care and management of animals in facilities, including procedures applicable to breeding programs integral to the maintenance of an animal line, and approve only those activities that are ethically acceptable and conform to the requirements of the Code.
- Conduct follow-up review of approved projects and activities (see 'The Code', Clause 2.2.32 [ii]), and allow the continuation of approval for only those projects and activities that are ethically acceptable and conform to the requirements of the Code. This review can be conducted by the AWO or delegate and details relayed to the EAEC if concerns are raised. The final project report is part of this review process.
- Monitor the care and use of animals, including housing conditions, practices and procedures involved in the care of animals in facilities.
- Take appropriate actions regarding unexpected adverse events.
- Take appropriate actions regarding non-compliance.
- Approve guidelines for the care and use of animals on behalf of the institution.
- Encourage the reuse of animals but consider any cumulative effects of studies, allow suitable recovery between studies, whether an animal has fully recovered from a previous study and the total time over which an animal will be used.
- Provide advice and recommendations to the institution.
- Submit an annual written report on its operations to the Site Head Yarrandoo advising on;
  - Numbers and types of projects and activities assessed, approved or rejected
  - The physical facilities for the care and use of animals by the institution
  - Actions that have supported the educational and training needs of AEC members and people involved in the care and use of animals
  - Administrative or other difficulties experienced

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  - Any matters that may affect the institution's ability to maintain compliance with the Code and, if appropriate, suitable recommendations.

- Conduct an independent external review, in conjunction with Elanco Australasia Yarrandoo, of its compliance with the Code, at least every 4 years, in accordance with section 6 of the INSTITUTIONAL ACCOUNTABILITY. This review is conducted by ARRP.

The institution must;

- Ensure appropriate animal ethics committee membership, as detailed in section 4.1.2, below (see 'The Code', Clause 2.2.4).
- Ensure that the AEC has Terms of Reference and that they are provided to members of the public, if requested.
- Provide the AEC with adequate resources to carry out its responsibilities and to maintain the AEC, and respond effectively to recommendations from the AEC regarding resources and workloads. Resources will include;
    i. Staffing and administrative assistance
    ii. Orientation and education of AEC members
    iii. Where appropriate, reimbursement of out-of-pocket expenses.
- Establish procedures for the effective governance and operation of the AEC that enable the AEC to comply with the Code and relevant institutional policies, and promote competent and timely ethical review of animal care and use. These procedures will include declarations of interest and management of conflicts of interest, confidentiality, administrative procedures, meeting procedures, communication, complaints and non-compliance, records and documentation.
- Conduct an annual review of the operation of the AEC to ensure the institution's compliance with the Code and institutional policies. This includes an assessment of the AEC's annual report and a meeting with the AEC Chairperson if required.
- Conduct an independent external review, in conjunction with the AEC, of its compliance with the Code, at least every 4 years, in accordance with section 6 of the Code. This review is conducted by ARRP.

Additionally;

- Ensure, through the AEC, that all scientific activities involving the use of animals comply with relevant legislation and the Code.
- Ensure that investigators and staff are aware of their responsibilities under the Code, including by the provision of educational programs, continual training and workshops.
- Respond promptly and effectively to recommendations from the AEC to ensure compliance with the Code.
- Seek comment from the AEC on all matters that may affect the welfare of animals used by Elanco Australasia, including the provision of facilities.
- Ensure the AEC approves relevant SOPs and guidelines and that these are implemented.

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- Provide relevant personnel and AEC members with details on Elanco Australasia confidentiality policy and Freedom of Information legislation.
- Provide personnel and AEC members with information on potential disease hazards and other Work Health and Safety issues associated with the care and use of animals.
- Ensure that there are adequate numbers of appropriately trained and skilled staff to care for the animals including provision of appropriate veterinary services.

4.1.2. Membership

The Site Head Yarrandoo will appoint at least four persons to the AEC, one in each of the following categories.

Category A: A person with qualifications in veterinary science that are recognized for registration as a veterinary surgeon in Australia, and with experience relevant to the institution's activities or the ability to acquire relevant knowledge.

Category B: A suitably qualified person with substantial and recent experience in the use of animals for scientific purposes relevant to the institution and the business of the AEC. This must include possession of a higher degree in research or equivalent experience.

Category C: A person with a demonstrable commitment to, and established experience in, furthering the welfare of animals and who is not currently involved in the care and use of animals for scientific purposes. Veterinarians with specific animal welfare interest and experience may meet the requirements of this category. While not representing an animal welfare organisation, the person should, where possible, be selected on the basis of active membership of, and endorsement by, such an organisation.

Category D: A person not employed by or otherwise associated with the institution and who has never been involved in the use of animals in scientific or teaching activities, either in their employment or beyond their undergraduate education. Category D members should be viewed by the wider community as bringing a completely independent view to the AEC, and must not fit the requirements of any other category.

Before the appointment, all members of the AEC should acknowledge in writing their acceptance of the terms of reference, operating procedures, grievance procedures, confidentiality agreement and the provisions for confidentiality outlined in section 56 of the Animal Research Act 1985.

See section 4.3 for Appointment of new members.

4.2. Off-Site Monitoring

The monitoring of off-site studies initiated by Elanco Australasia and performed by a company or third-party contracted personnel is undertaken by the Elanco R & D AWO or a suitably qualified deputy.

Clinical field studies within NSW or interstate will be monitored by site inspections and the use of CRFs such as the Animal Welfare checklist, observation and communication forms,

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which are maintained in study-specific SMFs. These observations may be performed by farmers or other owners of animals used in off-site studies.

The Elanco R & D AWO or delegate must conduct an Animal Welfare audit prior to the use of a CRO and deem the site as conforming to Elanco Australasia and local standards before any studies can be performed. Monitoring of animal welfare is conducted throughout studies and is described in individual Study Plans/Protocols.

Animal Welfare Reports, that may also include study updates, are presented at EAEC meetings. An EAEC member can request to see any document related to a study being performed off-site at any time and request a site inspection.

4.3. Appointment of members

The Site Head Yarrandoo appoints new members from time to time to enable the EAEC to fulfill its terms of reference. If a position becomes vacant, a replacement must be appointed to ensure at least one member from each category is represented on the EAEC. Details of the new member must be submitted to ARRP for approval prior to them becoming a voting member. New members cannot vote at a meeting until approval from ARRP has been granted. ARRP must be contacted to ensure that all corrected documentation is submitted.

A member of the EAEC is taken to have vacated his or her office if the member:

- Resigns in writing
- Dies, becomes mentally incapacitated or is convicted of an offence punishable by imprisonment
- Absents himself or herself from four consecutive meetings without the consent of the EAEC.

4.3.1. Confidentiality

All Study Protocols/Plans and information coming from Elanco Australasia, and shared with or reviewed by the EAEC are confidential. External members of the EAEC are required to sign a Confidentiality Agreement, and to acknowledge in writing their acceptance of the terms of reference of the EAEC. This will be kept on file in the project office.

4.3.2. Honorarium

External members of the EAEC are paid an annual honorarium in recognition of their time and expenses associated with membership of the EAEC. This clause does not apply to employees of Elanco Australasia (*i.e.* Chair, Elanco Australasia R & D, AWO or associates acting in a Category A or B capacity).

4.3.3. Conflict of interest

The EAEC members must declare any potential conflict of interest in writing prior to their appointment.

When a potential conflict of interest arises because an EAEC member has an interest that may be seen to influence the objectivity of a particular decision, that member must declare their interest as soon as practicable and abstain from voting on the decision and withdraw from the meeting.

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If experts are requested by the AEC to give advice they must remove themselves from the meeting prior to a decision being made on a study.

4.4. Meeting Procedures

- Meetings are convened at least four times a year.
- A senior member of Yarrandoo staff or his/her deputy chairs the meetings. The chair must be approved by ARRP.
- A quorum consists of at least one member from each category. If more than four EAEC members are present, Categories C plus D must represent not less than one third of those members present.
- Members unable to participate in meetings can forward their comments to the Chair or any other committee member prior to the meeting.
- The Elanco R & D AWO or delegate attends meetings as a non-voting committee member, presents an Animal Welfare Report, maintains the EAEC Master Schedule and answers relevant questions from committee members.
- An Animal Research Application form (and any supporting documentation if required) and the documentation provided by the AWO (Master Schedule AEC Study Report and the Animal Welfare Offices Report) is forwarded to each EAEC member approximately 1 week before the scheduled meeting. Proposals must provide the information required under Section 2.2.16 of the *Code*.
- The Investigator/Study Director or delegate presents the Study Protocol/Plan to the EAEC, answers questions and discusses any suggested amendments
- Each committee member will participate in at least three site inspections per year. Records of inspections should include the names of those who attended. Observations and any identified problems will be captured in the meeting minutes. Inspections of remote sites may be performed by the Elanco R & D Animal Welfare Officer or a delegate (refer to Section 4.2).
- The proceedings of each meeting of the EAEC, including decisions regarding research proposals and the reasons for these decisions, will be recorded in written minutes, which will be accepted by the EAEC at the next meeting subject to any required amendments. Minutes and other records must be retained for at least 7 years after the record is made.

4.5. Review and Approval of Study Protocols and Plans

4.5.1. Studies conducted by Elanco Australasia

The EAEC must review and approve studies/plans involving animals for studies to be conducted by company personnel prior to any experimental commencement.

Subject Matter Experts must be made available to the AEC if requested to clarify points of concern. The EAEC must consider the difference between experimental vs humane endpoints. If needed, intervention points should be included in the Study Plan/Protocol. This may need to be included as a condition on the Animal Research Authority.

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The EAEC must consider the justification, study outcomes and monitoring in studies where multiple surgeries are planned.

The EAEC must consider any studies that involve fluid or food restrictions (this does not include routine pre surgical nil by mouth). Animals under such restrictions must be closely monitored, food and water consumption recorded and age/breed/sex of the individuals must be considered.

The EAEC must approve any written information that is to be provided to the owners of privately owned animals (*e.g.* Consent and Animal Agreement Form). Changes to Informed Consent Forms affecting animal welfare must also be approved by the EAEC prior to implementation (*e.g*. they could be sent by mail or email to all EAEC members and then discussed and approved by teleconference or email).

Approval of a Study Plan/Protocol is by consensus decision. Where consensus cannot be reached after reasonable effort to resolve differences, the AEC should explore with the applicant(s) ways of modifying the project or activity that may lead to consensus. If consensus is still not achieved, the AEC should only proceed to a majority decision after members have been allowed a period of time to review their positions, followed by further discussion.

Study Plan/Protocol approval can only be granted at a convened meeting containing a quorum consisting of at least one member from each category and that categories C and D must together represent at least one third of the EAEC members present.

Once approval is granted, an Animal Research Authority (AUKC-FRM-0026) will be issued and signed by the Site Head Yarrandoo or a member of Yarrandoo Leadership Team. Approval is valid for a maximum of 12 months. If a study is likely to run for longer than 12 months, a new application must be submitted to the EAEC prior to the expiry date of the current approval. Any conditions of approval will be recorded on the Animal Research Authority and must be approved by the AWO prior to the corresponding animal procedures commencing.

A study must not commence until written approval has been received in the form of a signed Animal Research Authority or provisional approval is granted.

A final AEC Study Report (AUKC-FRM-0039) should be submitted to the AEC within 3 months of the completion of the study live phase.

Triennial Protocols are protocols that are run for routine procedures involving animals (*e.g.* blood collection, parasite maintenance, training procedures *etc*.) that may form part of a study. Triennial Protocols will be reviewed and approved by the EAEC once every 3 years however an Animal Research Authority must be issued annually for each triennial protocol. The ARA may be issued after review of the annual AEC Study report (see next line). A report using AEC Study Report (AUKC-FRM-0039) must be submitted to the EAEC annually outlining animal use, issues *etc.* that have occurred in the previous year. A final study report using AEC Study Report (AUKC-FRM-0039) must be produced presenting all the animals used during the previous 3 years. This is submitted prior to the protocol being reapproved. Amendments to a triennial protocol must be submitted for approval by the AEC using AUKC-FRM-0155-Request form.

In exceptional circumstances, a Study Plan/Protocol may be submitted for provisional approval before the next scheduled EAEC meeting. The EAEC Chair will determine whether

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this is justified on a case-by-case basis. The rationale for interim approval should be given to the EAEC in each case. The Study Plan/Protocol will be sent by mail or email to all EAEC members and then discussed by teleconference. The teleconference must include a quorum of members. The decision of the quorum must be documented and endorsed at the next formal face-to-face meeting of the EAEC.

4.5.2. Amendments to studies

Any amendment to a study that requires any direct involvement of animals or changes in staff must be approved by the EAEC (*i.e*. increase in numbers, change in sampling frequency *etc*.).

Amendments to planned studies prior to study initiation, where the changes are animal related, must be resubmitted to the EAEC for approval.

Amendments to approved Study Plans/Protocols must be submitted to the EAEC for approval prior to the amendment being implemented. The amendment request must be submitted using AUKC-FRM-0155 and the original Animal Research Application form with the changes highlighted. The amendment request may be handled outside of scheduled meetings by sending appropriate documentation to all EAEC members, followed up by a teleconference or confirmation of approval by email.

In some circumstances, minor amendments can be approved by the AEC Executive without direct approval from the entire EAEC. The AEC Executive must include the AEC chairperson and at least one member from Category C or D. Examples of these can include a short extension of time or a small change in starting time.

4.5.3. Studies conducted by third parties

In situations where a CRO or third-party contracted personnel are used, the organization or individual must obtain approval for conduct of the study from their AEC. Any documentation submitted to the AEC for approval should outline the relevant study activities/details pertaining to the use of animals within the study. A copy of the AEC submitted documentation and any subsequent approval will be filed in the SMF. The EAEC may be used in cases where the organization or individual has no access to their own AEC.

Traceability to any documents approved must be established. The conditions for animal use listed in the final Study Plan/Protocol must be consistent with the conditions approved by the AEC.

Any Consent and/or Animal Agreement Forms that are to be provided to the animal owners should also be approved by the AEC; however, in certain instances where approval cannot be formalized (*i.e.* for privacy or legal reasons) evidence that these forms were presented and discussed by the AEC must be retained in the SMF.

4.6. Annual Report

An AEC Annual Report is created at the end of each year and includes but is not limited to details of AEC meetings, projects, animal use, the 3Rs, animal facilities and compliance. The report must be sent and discussed with the site head of Yarrandoo Elanco Australasia. This report is written by the AWO or delegate.

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4.7. Non-Compliance

Any member of the EAEC may raise concerns regarding activities that are considered non-compliant with the *Code*, either at an EAEC meeting or directly with the Head of Yarrandoo R & D Centre.

The Head of Yarrandoo R & D Centre or the Elanco R & D AWO will investigate and report back to the EAEC on the outcome of the investigation and any remedial action taken. The EAEC may withdraw approval for any study that involves non-compliant activities.

Post approval monitoring is to be undertaken by the AWO or suitably qualified delegate i.e. veterinarian. Any non-compliance noted by the AWO must be raised with the AEC, study personnel and site head. This monitoring can include procedures undertaken, animal observations by animal care staff and examination of housing facilities.

4.8. Unexpected Adverse Events

The code describes an unexpected adverse event as 'an event that may have a negative impact on the wellbeing of animals and was not foreshadowed in the approved project or activity'. In addition, adverse events in non-study animals must be reported to the AEC. This differs from the Elanco where an adverse event is described as any observation in animals, whether or not considered to be product related, that is unfavorable and unintended that occurs after the use of any investigational veterinary product, veterinary product or placebo (off-label and on-label uses). Included are events related to suspected lack of efficacy or noxious reaction in humans after being exposed to the product. The Elanco adverse event reporting to PV is out of scope for this SOP.

Unexpected adverse events can vary in their impact on animals.

Animal attendants or study personnel must contact the AWO or delegate when an unexpected adverse event is noted.

The AWO or delegate will assess the animal and decide if immediate veterinary intervention is required. In addition, the AWO or delegate has the authority to cease study activities if animal welfare is compromised.

The AWO or delegate will promptly (usually within 24 hrs) notify the AEC (usually via email) and outline the issue and any interventions that have occurred. AUKC-FRM-0156 will be filled out by the AWO or delegate and will include details of the event and subsequent actions taken. This will be forwarded to the EAEC at the time of notification.

The EAEC will advise on future actions and launch an investigation if required.

4.9. Grievance Procedures

4.9.1. Complaints and enquiries from the public

Any complaint or enquiry received by Elanco Australasia about the use of animals in studies initiated by Elanco Australasia or about animals maintained at Yarrandoo R & D Centre will be handled immediately by the Head of Yarrandoo R & D Centre and/or the Business Practice Officer, depending on the first point of contact.

- The complaint will be investigated by the Head of Yarrandoo R & D Centre or delegate and remedial action taken. Depending on the type of complaint the

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investigation will involve interviews, sample collection, equipment checks and facility inspections.

- The AWO must be notified immediately if the complaint is an AW issue.
- The AWO will be involved in investigations and will report both the complaint (if AW related) and remedial actions to the EAEC promptly
- Corrective measures will be reported back to the reporting staff member (if known).
- Where complaints involve animal welfare the matter must be documented and forwarded to the EAEC. Where complaints relate to activities that would require EAEC approval, the complaint is referred to the EAEC to investigate whether such activities are conducted in accordance with the EAEC approval.
- If the complaint is about an activity that is likely to adversely impact the welfare of an animal, the activity must cease immediately. The AWO or delegate will coordinate the cessation of the activity.
- Elanco has a strong policy on protecting whistleblowers

4.9.2. Complaints/code noncompliance by staff

Staff are encouraged to constantly observe, consider and propose improvements to the methods of handling, husbandry and research procedures involving animals at Yarrandoo R & D Centre. All staff members are also encouraged to report any incident or practice which they consider to be inappropriate to the welfare and well-being of animals at Yarrandoo R & D Centre.

- It is the responsibility of all staff to bring any matters of concern to the attention of the Elanco R & D AWO, Investigators/Study Directors, the site veterinarian or the Head of Animal Management and Facilities.
- Complaints can be reported to staff line managers, the AWO or delegate or the site head directly. Anonymous complaints can be made by accessing the Elanco internal web page and ‘Report a Concern’
- The complaint will be investigated by the Head of Yarrandoo R & D Centre or delegate and remedial action taken. Depending on the type of complaint the investigation will involve interviews, sample collection, equipment checks and facility inspections.
- The AWO must be notified immediately if the complaint is an AW issue.
- The AWO will be involved in investigations and will report both the complaint (if AW related) and remedial actions to the EAEC promptly
- Corrective measures will be reported back to the reporting staff member (if known).
- Where complaints involve animal welfare the matter must be documented and forwarded to the EAEC. Where complaints relate to activities that would require EAEC approval, the complaint is referred to the EAEC to investigate whether such activities are conducted in accordance with the EAEC approval.

- If the complaint is about an activity that is likely to adversely impact the welfare of an animal, the activity must cease immediately. The AWO or delegate will coordinate the cessation of the activity.
- Elanco has a strong policy on protecting whistleblowers

4.9.3. Serious disagreements between members of the EAEC

The basic premise of the operation of the EAEC is consensus decision, whilst striving to reach unanimity.

In the event of any EAEC member being dissatisfied with a decision, that person should feel at liberty to contact the Country Head, Elanco Australasia and subsequently, if still dissatisfied, to contact the NSW Animal Research Review Panel, and/or the Animal Welfare Unit, NSW Department of Primary Industries.

4.9.4. Serious differences between the EAEC and an Investigator/Study Director

In the event of the EAEC being unable to reach an agreement with an Investigator/Study Director, the matter must be referred by the Head of Yarrandoo R & D Centre to the Country Head of Elanco Australasia for review of the due process.

After such review, the EAEC may need to review its process in reaching the decision regarding the study application and re-evaluate its decision in light of the reviewed process. The ultimate decision regarding the ethical acceptability of an activity lies with the EAEC and must not be overridden.

5. Health, Safety and Environment

From time to time, some or all of the EAEC members conduct site inspections or visit a specific area of the animal housing. In order to comply with the Yarrandoo biosecurity conditions, the following general requirements should be followed:

- Entry to animal housing and treatment facilities should be kept to a minimum.
- Fully enclosed, clean footwear must be worn by all visitors.
- Animals are not to be handled by EAEC members at any time during an inspection.
- Demarcation of designated PPE areas must be observed at all times for reasons of HSE and biosafety. Visitors will be accompanied and supervised at all times by a member of staff who is responsible for the supply and disposal of relevant PPE needed to enter designated areas.
- Known allergies and contact with potentially infectious conditions in humans and animals must be disclosed to the supervising member of staff prior to entering any animal facility.

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6. Definitions & Abbreviations

Term	Definition
AEC	Animal Ethics Committee
ARRP	Animal Research Review Panel
AWO	Animal Welfare Officer
Code	Australian code for the care and use of animals for scientific purposes 8th Edition 2013
CRF	Case Report Form
CRO	Contract Research Organization
EAEC	Elanco Animal Ethics Committee
EAH	Elanco Animal Health
HSE	Health Safety and the Environment
NSW	New South Wales
PPE	Personal Protective Equipment
QA	Quality Assurance
R & D	Research and Development
SMF	Study Master File
SOP	Standard Operating Procedure
3Rs	Replacement, Reduction, Refinement

7. Regulatory Basis and Reference Documents

- Corporate Guidelines and Policies
- OECD Principles of Good Laboratory Practice
- International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) Guideline Series
- Australian Code for the Care and Use of Animals for Scientific Purposes 8th Edition 2013
- Animal Research Regulation 2010
- Animal Research Act 1985.

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8. Annexes/Related Forms

8.1. Forms

No.	Title
AUKC-FRM-0155	Request to amend an approved study
AUKC-FRM-0156	Unexpected adverse event
AUKC-FRM-0039	AEC Study Report

8.2. SOPs

No.	Title

8.3. References
