This document has been developed by The Australian National University's (ANU) Research Ethics Office. It has been endorsed by the ANU Animal Experimentation Ethics Committee (AEEC). It is designed to provide guidance regarding current best practice to institutional animal users and carers on the care and use of animals for scientific purposes. It has been prepared in consultation with the Australian code for the care and use of animals for scientific purposes 8th edition 2013.

Document 001: Procedure for Managing & Reporting Unexpected Adverse Events Involving Animals Used in Research & Teaching V2.0

Quick Contacts & Important Information

Reporting of Unexpected Adverse Events is mandatory, not voluntary.

ANU Veterinarian On Call Number: **612 51130**

Please note this number is diverted to a mobile phone. If your call is not answered please leave a name and phone number for returning your call and a brief message. The mobile phone does not always display a phone number and therefore you must leave a return number.

Unexpected Adverse Event Form	Click Here
ANU Animal Ethics Team	Animal.ethics@anu.edu.au 612 55325.
Vet Services Email	vetservices.rsd@anu.edu.au

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Background

This procedure applies to all ANU research or teaching activities that involve the use of animals as approved by the ANU Animal Experimentation Ethics Committee (AEEC). It applies only to unexpected adverse events (UAEs), not events detailed and approved within a current animal ethics approval. It is a condition of approval on all animal ethics protocols that in accordance with sections 2.4.18 (ix) and 2.4.34 (ii) of the Code, investigators must promptly notify the ANU Animal Experimentation Ethics Committee (AEEC) of any UAEs that have or have the potential to impact on animal wellbeing.

Reporting of UAEs **in a timely manner is mandatory** in order to ensure timely investigation and provision of veterinary support to prevent further occurrences and improve animal welfare outcomes. Reporting is critical to identifying where improvements can be made, positively contributing to the continuation of the research. Early reporting also assists with recall accuracy of the event. There is an expectation that reasonable care and due diligence will be undertaken at all times where research involves the use of animals.

Information provided in UAE reports will be circulated to the AEEC in accordance with the Code and the ANU UAE Procedure. Once the UAE has been reviewed by the AEEC the PI will receive communication as to whether any further action is required.

Definitions

The Code: The NHMRC's *Australian code for the care and use of animals for scientific purposes 8th Edition 2013.*

Adverse Event (as per the Code): *Any event that has a negative impact on the wellbeing of an animal*

Unexpected Adverse Event (UAE) (as per the Code): *An event that may have a negative impact on the wellbeing of any animals and was not foreshadowed in the approved project or activity. A UAE may result from different causes, including but not limited to:*

- *death of an animal, or group of animals, that was not expected (e.g. during surgery or anaesthesia, or after a procedure or treatment);*
- *adverse effects following a procedure or treatment that were not foreshadowed in the approved project;*
- *the sudden death of any animal under an approved animal ethics protocol;*
- *adverse effects in a larger number of animals than predicted during the planning of the project or activity, based on the number of animals actually used, not the number approved for the study;*
- *a greater level of pain or distress is evident, beyond what was predicted during the planning of the project or activity;*
- *power failures, inclement weather, emergency situations or other factors external to the project or activity that have a negative impact on the welfare of the animals.*

Animal (as per the Code): *Any live non-human vertebrate, that is, fish, adult decapod crustaceans amphibians, reptiles, birds and mammals, encompassing domestic animals, purpose-bred animals, livestock, wildlife, and also cephalopods such as octopus and squid.*

Animal Experimentation Ethics Committee (AEEC) (as per the Code): *A committee constituted in accordance with the terms of reference and membership laid down in the Code.*

Investigator (as per the Code): *Any person who uses animals for scientific purposes. Includes researchers, teachers, undergraduate and postgraduate students involved in research projects, and people involved in product testing, environmental testing, production of biological products and wildlife surveys.*

Animal Carer (as per the Code): *Any person involved in the care of animals that are used for scientific purposes, including during their acquisition, transport, breeding, housing and husbandry.*

Facility Manager (as per the Code): *Person responsible for the overall management of a facility used for the breeding and holding of animals.*

Nominated Delegate: A representative nominated by Research Services or the AEEC.

Veterinarian: A person with veterinary training and registered as a veterinarian with the relevant Veterinary Surgeons Board in the relevant State or Territory. May or may not be an ANU employed veterinarian.

General Information and Considerations

What is an Unexpected Adverse Event (UAE)?

A UAE occurs when there is an event that has had, or may have had, a negative impact on the wellbeing of animals, or affected the intended usage of animals, which was not foreseen in the approved animal ethics protocol.

Some examples of situations that are defined as unexpected adverse events include:

- More deaths or complications than described in the approved animal ethics protocol, e.g. 10% of animals died following surgery when a 5% fatality rate was expected and justified in the approved animal ethics protocol. The number or percentages of animals may refer to a single cohort or across a group of experiments. Some judgement may be required in interpretation of numbers e.g. if one animal dies as a result of surgical complications from a group of 5 animals, this may not be considered a UAE, even if the 'expected' rate is <5%. However if an animal dies every cohort of 5 animals, or two to three animals die in a single cohort then a UAE is likely to be required. Where there is any question as to whether an incident is a UAE, the ANU vets must be consulted for additional advice and interpretation.
- Death of animals not described in the approved animal ethics protocol, e.g. an animal found dead the day after surgery, or death of an animal post trapping.
- Complications not described in the approved animal ethics protocol, e.g. one or more animals have allergic reactions to a treatment, the type of anaesthetic doesn't provide

adequate pain relief (analgesia) or restraint, animals die during or after anaesthesia, animals develop abscesses at the surgical or treatment site, or unexpected predation of animals in the field.

- Facility or equipment failure compromising or possibly compromising animal welfare or the success of the activity, e.g. power loss to a facility means ventilated mouse cages don't receive fresh air, therefore animal exposure to ammonia levels could reach adverse levels; inability to irradiate animals on a particular day means that this critical part of the activity is not undertaken when animals are the right age, so there may be no justification to continue using these animals.
- Animal wellbeing is compromised due to a deficiency in routine husbandry practices, such as the provision of suitable food, water, bedding and housing conditions; for further definitions see Appendix I.
- An unexpected event that leads to termination of an ongoing animal experiment without the ability to collect useful data. For example, a tumour model where the tumour does not behave as expected or as detailed in the ethics protocol, or essential reagents run out during a long-term drug treatment resulting in use of animals without collection of data.
- Additional field work examples, including but not limited to:
    - Thrown/injured pouch young that is either euthanased or brought into care
    - Birds abandoning nests due to intervention by investigators e.g. to place monitoring equipment
    - Death due to tracking equipment issues e.g. collar too tight or collar gets caught on a branch
    - Animal injured/dies during handling and processing
    - Traps left out and not checked resulting in death of animal
    - Animals dying in traps due to temperature extremes.

If there is any uncertainty around whether an event should be reported, then advice should be obtained from one of the ANU Vets on 02 612 51130 as soon as possible.

For events that impact animal welfare but are not classed as UAEs, there may be a requirement to lodge an event as an 'incident' or to report the event in your annual review to allow for tracking and management of such cases. Direction to lodge an incident will be given by the RSD Animal Ethics Team or by one of the ANU Vets.

Proactively discussing any concerns is more likely to result in a continuation of your research and improve the welfare outcomes for animals under your care.

How to Report an Unexpected Adverse Event?

The ANU *AEEC Unexpected Adverse Event Report* form must be completed and submitted via email to animal.ethics@anu.edu.au **within 72 hours** of the occurrence of an UAE (this time frame includes weekends and public holidays). The form can be found on the *ANU Animal Ethics Forms* web page. Investigators working in remote locations must make every effort to notify the ANU Vet as soon as possible and submit a written report to the AEEC within 10 days.

The procedure in this document outlines the steps for appropriate action to be taken and reporting of UAEs.

When is an Unexpected Adverse Event Report NOT required?

A UAE report is not required if the event was foreshadowed in the approved animal ethics protocol. Animal users are required to provide details of the type and frequency of possible adverse events in their protocol application. If the events happen as expected (i.e. as approved and outlined in the approved animal ethics protocol), they do not have to be reported as a UAE, unless additional reporting is required as a condition of AEEC approval.

Furthermore, events which are unexpected and impact the research and the project but no live animals are affected, for example loss of stored samples from a historical experiment, due to a freezer breakdown do not have to be reported as an UAE. If these events require additional experimental repeats and additional animals or greatly alter the progress of research they must be reported in an amendment and/or annual report.

Pilot Studies and Unexpected Adverse Events

Pilot studies, by definition, are likely to be of greater risk to animal health and welfare, and are at risk of greater variability in results and success. Pilot studies are strongly advised for new experiments, use of new drugs and/or dose rates, and where the impact(s) on the animals are not known.

The AEEC requires that the investigator provides a description of what type of incidents/risks may exist with regards to any proposed pilot experiment in the animal ethics protocol. The risks should be clearly identified along with appropriate risk mitigation measures which must be implemented prior to starting the pilot experiment. These predicted risks and mitigation measures will be assessed by the AEEC as part of the application review process. Any event that occurs outside the stated and approved risks must then be reported as an UAE. Any error on the part of the investigator or incident that results in the death of an animal or compromises its welfare is also deemed an UAE. This may include incorrect drug reconstitution or administration, poor planning that results in animal wastage or inadequate monitoring or intervention.

Example: An investigator would like to trial a new type of drug compound that has not been used in animals before. They have approval for a pilot study which states that up to 100% of animals in the high dose range will require euthanasia due to drug toxicity but only 50% of the animals in the lower dose range. During the experiment, 25% of the animals in all cohorts die without human intervention (i.e. euthanasia does not occur) in the first hour post drug treatment. This would be considered an UAE as it was not consistent with the predicted risk.

Procedure for managing and reporting UAEs

The formula is Act, Inform and Report (AIR)

1. **ACT**

   Act quickly to:

   a. Determine and remove obvious hazards while responding to the immediate needs of sick or at-risk animals.

   b. Alleviate immediate unexpected pain and distress in the animal. The immediate welfare of the animals is paramount. This may include euthanasia.

2. **INFORM**

   Reporting of UAEs is mandatory, not voluntary. You must ensure that:

   a. **An ANU Vet is contacted as soon as practically possible**. Timely treatment, post mortem examination, testing or further risk minimisation strategies may be required. The ANU Vets Team is available 24/7 by dialling 612 **51130.**

   b. **Samples must not be taken from the animal until you have spoken to one of the ANU Vets** and they have provided advice on the next actions.

   c. Carcasses need to be placed in the fridge (in case post mortem is required) NOT in the freezer unless instructed by the ANU Vet.

   d. The Primary Investigator is contacted.

   e. The Animal Facility Manager (where relevant) is contacted. The animal facility manager **must** be contacted if the UAE is related to animal husbandry in an animal facility scenario.

   f. If an external vet and/or vet clinic is listed on the approved animal ethics protocol for field work, the ANU Vet must also be contacted via the emergency phone number as soon as possible about the UAE. If the animal is being taken to a vet clinic, the ANU Vet needs to be advised prior to arrival at the clinic. The ANU Vet may contact the clinic to confirm the animal is covered by an ANU ethics approval.

3. **REPORT**

   All UAEs must to be reported to the AEEC.

   a. The ANU *AEEC Unexpected Adverse Event Report* form is available on the ANU Animal Ethics Forms web page. It must be completed and emailed to animal.ethics@anu.edu.au.

   b. Reports must be received by the AEEC **within 72 hours**.

   Investigators working in remote locations must submit a written report to the AEEC within 10 days.

Minimum Requirements

Investigators must:

- Act to alleviate unanticipated significant pain and distress in their research animals as immediately as possible. This may require euthanasia even if the planned endpoint has not been reached. Where the investigator determines there is a benefit to maintaining the animals or collecting samples for research purposes, you must ensure that the welfare of the animal(s) is the primary concern and the veterinarians are consulted to ensure this does not interfere with any necessary investigation of the cause of the UAE. If the investigator feels that an animal should be euthanased immediately and cannot wait for veterinary advice then this should be done so. All instructions regarding sample and carcasses preservation should be adhered to. Carcasses must be placed in a fridge and any samples collected must be done with the authority of the ANU vet (see above).
- For severely injured or ill wildlife, if euthanasia is not possible (due to species and availability of a suitable method), all efforts must be made to immediately transport the animal to a suitable location/person for euthanasia. The requirements for euthanasia of wildlife in the field are outlined in the ANU AEEC Approved Document_016 Field Euthanasia of Wildlife Guidelines.
- As soon as practically possible contact the ANU Vet via the emergency number 612 **51130** and the Primary Investigator of the approved ethics application (or their nominee).
- Promptly advise the animal facility manager (where appropriate).
- Promptly notify the AEEC by completing the ANU AEEC Unexpected Adverse Event Report form (see above 3.a).
- Ensure that for any animals that die unexpectedly, a post mortem is performed by a vet or suitably qualified person as directed by a vet and that the results are recorded. Carcasses must be stored in accordance with veterinary instruction. Carcasses must be placed in a fridge unless advised by the vet (in case a post mortem is required).

Animal facility managers must:

- Immediately contact relevant investigators, preferably by phone where possible. (NB it may be appropriate to call the ANU vet first in some circumstances where animal welfare is at risk).
- Immediately contact the ANU Vet via the emergency number 612 **51130**.
- Provide prompt review and treatment under direct veterinary supervision for any animals that are ill or injured or show unexpected abnormalities or behaviour.
- When an animal dies unexpectedly, is euthanased due to unforeseen complications, or where a concerning pattern of disease is found, a post mortem and/or investigation should be performed by a vet or a person with appropriate qualifications and/or experience as directed by a vet and the AEEC must be notified promptly.
- Carcasses must be placed in a fridge unless advised by the vet (in case a post mortem is required).

Promptly notify the AEEC by completing the ANU AEEC Unexpected Adverse Event Report form (see above 3.a).

Animal carers must:

- Take all reasonable steps to first contact the responsible investigator. However, the welfare of the animal must be the priority at all times and may necessitate immediate intervention including euthanasia. Please note a phone call is required to the investigator if animals are at immediate risk or require immediate euthanasia.
- Ensure that the ANU vets are contacted and advise the animal facility manager and/or your area manager.
- Contact the investigator, if not already done, and advise them of the actions taken and why they were taken.
- When an animal dies unexpectedly, is euthanased due to unforeseen complications, or where a concerning pattern of disease is found, a post mortem and/or investigation should be performed by a vet or a person with appropriate qualifications and/or experience as directed by a vet and the AEEC must be notified promptly.
- Before any post mortem an ANU Vet must be consulted with via the on call number 612 **51130**.
- Carcasses must be placed in a fridge unless advised by the vet (in case a post mortem is required).

AEEC Responsibilities & Processes

The AEEC must take appropriate action in response to an UAE to ensure animal wellbeing is not compromised and the issue is addressed promptly. This may include requesting that activities that have the potential to adversely affect animal wellbeing, cease immediately.

UAE reports are received by the ANU Research Services Division's Animal Ethics Team at animal.ethics@anu.edu.au and are passed on to the AEEC and ANU Vets. Research Services will send an acknowledgement of receipt on behalf of the AEEC to the person lodging the report. The UAE report, along with any follow up correspondence including post mortem and/or vet reports, will be filed with the relevant animal ethics protocol records.

The AEEC and Animal Ethics Team will liaise with the Primary Investigator and/or Facility Manager as appropriate to determine the appropriate course of action. For all AEEC decisions a quorum is required or where this cannot be reached, the Chair may defer to a majority decision as per the Code's requirements and the ANU's AEEC Operating Procedures.

Depending on the seriousness or urgency of the event, the AEEC, in consultation with one of the ANU Vets, may undertake one or more of the following:

- Request further information from the primary investigator or other staff involved.
- Request immediate veterinary intervention if this has not already occurred.

- Request that an ANU Vet or nominated person visit a specific animal holding facility or site, or animals on a project to make an assessment.
- Require that the experiment or that part of the experiment cease until the matter has been investigated further especially where there are ongoing perceived risks to animal welfare.
- Defer the matter to the next scheduled AEEC meeting.
- Call a special AEEC meeting to discuss the event.
- Suspend or withdraw approval for the project or activity either temporarily or permanently as required.
- The AEEC will provide a written response to the Primary Investigator outlining any further action required. AEEC instructions must be followed.

Veterinary Responsibilities & Involvement

In most cases one of the ANU Vets or a nominated delegate will investigate the event and any action taken. The aim of the investigation is to determine the cause of the UAE and to minimise the risk of future UAEs. The Primary Investigator, project supervisor (where appropriate) and relevant staff must cooperate with the vet during this investigation.

An ANU Vet or a nominated delegate:

- Will determine if further veterinary or clinical intervention is required; if the project should be temporarily suspended pending the results of further investigations or if any other action should be taken to protect the welfare of the animals involved.
- Has the authority to take samples from other animals if required to determine the cause of the UAE.
- Using their authority as afforded to them by the Code and in their position by the ANU Executive, can immediately remove animals from experiments and may temporarily suspend part or all components of a project if there is potential risk identified to the welfare of animals or the quality of research pending AEEC review and decision.
- Will provide an update on the progress of the investigation of the UAE(s) to the AEEC in a written format.
- Together with the AEEC, will keep the Primary Investigator and other relevant parties updated on any actions taken, investigations findings and decisions made pending further discussion.

Complaints

Any complaints regarding the management and response of a UAE will be managed as per the AEEC Operating Procedures and/or ANU Policy.

Responsible Officer

The Deputy Vice-Chancellor (Research and Innovation) is responsible for the development, compliance monitoring and review of this policy and any associated schedules, procedures and guidelines.

Implementation Officer

The Director, Research Services Division (RSD) is responsible for the implementation of this policy.

References and Resources

ANU. Form for reporting Unexpected Adverse Events

ANU. Research Integrity https://services.anu.edu.au/research-support/ethics-integrity/raising-concerns

NHMRC. Australian code for the care and use of animals for scientific purposes 8th Edition 2013 (Section 4.4.3) https://www.nhmrc.gov.au/about-us/publications/australian-code-care-and-use-animals-scientific-purposes

NHMRC. Best practice methodology in the use of animals for scientific purposes 2017 https://www.nhmrc.gov.au/about-us/publications/best-practice-methodology-use-animals-scientific-purposes

NHMRC. Australian Code for the Responsible Conduct of Research 2018 https://www.nhmrc.gov.au/about-us/publications/australian-code-responsible-conduct-research-2018

ANU. Code of Research Conduct https://policies.anu.edu.au/ppl/document/ANUP_007403

ACT Government. Animal Welfare Act 1992 https://www.legislation.act.gov.au/a/1992-45/