Animal Research Monitoring and Adverse Events Guidelines

Section 1 - Purpose

(1) The Australian Code for the Care and Use of Animals for Scientific Purposes 8th edition (2013) ("the Code"), enacted under the Animal Research Act 1985 No 123 and the Animal Research Regulation 2010 (NSW) requires that institutions develop guidelines to ensure animal wellbeing is monitored by competent people, and that appropriate action is taken when unexpected adverse events occur.

(2) These Guidelines assist University of Newcastle (University) Investigators, as defined in the Animal Research Regulatory Manual, to make decisions regarding animal monitoring and adverse events related to animal research, and in doing so meet legislative requirements.

Section 2 - Audience

(3) This guideline should be read and understood by:

a. Investigators;
b. the University Animal Care and Ethics Committee (ACEC);
c. Research Ethics and Integrity Unit staff; and
d. BioResearch Facilities staff.

Section 3 - Scope

(4) These Guidelines are applicable to all activities involving the use of live animals that are bred, purchased, or captured by the University and any animal selected and/or used for research by a University Investigator.

Section 4 - Related Documents

(5) This document should be read in conjunction with:

a. Animal Research Regulatory Manual;
b. Responsible Conduct of Research Policy;
c. Australian Code for the Care and Use of Animals for Scientific Purposes 8th edition (2013);
d. Animal Research Act 1985 No 123; and
e. Animal Research Regulation 2010 (NSW).

Section 5 - Document specific definitions

(6) In the context of this policy “acclimatisation period” means the length of time that newly received animals are given for physiological, behavioural and nutritional acclimatisation prior to their use in a research project. This period is a minimum of 5 days and a maximum of 7 days, unless otherwise approved by the ACEC.

(7) In the context of this policy “animal welfare check” means the daily process of BRF staff ensuring that animals have food, water and the appropriate environment. Animal welfare checks do not include monitoring for predicted adverse effects or completing a Monitoring Checklist.

Section 6 - Monitoring of Animals

(8) The ACEC requires that all animal ethics applications include information on the monitoring strategy to be used to ensure the wellbeing of animals, including the use of Monitoring Checklist(s).

(9) The ACEC expects that a monitoring strategy will be developed to ensure that abnormalities are detected and acted upon before they result in significant pain, distress or the death of an animal. The frequency of observations should be:

a. increased when animals are in periods of potential impairment; and
b. such that areas of concern and potential problems can be detected and acted upon as early as possible.

(10) All monitoring of animals must be conducted in accordance with the strategy approved by the ACEC. ACEC approval is required for any changes to an approved monitoring strategy and must be obtained before implementing any changes.

BioResearch Facilities (BRF) Monitoring Responsibilities

(11) BRF staff will perform daily animal welfare checks as defined in Clause 7.

(12) BRF staff will notify the project Chief Investigator and a nominated contact person if an animal is found to be unwell during daily animal welfare checks. A veterinarian may be contacted by BRF staff where a Chief Investigator and nominated contact person is not able to be contacted. Any subsequent treatment of research animals will be recorded in the Procedures Record/Treatment folder for the project.

Investigator Monitoring Responsibilities

(13) Chief Investigators are ultimately responsible for the monitoring of wellbeing once an animal is allocated to the project and enters the acclimatisation period, until the animal is no longer required and subsequent provisions are made.

(14) During the acclimatisation period the Chief Investigator is responsible for ensuring that animals are monitored by a project team member at least twice, with the first monitoring event to occur 1-2 days post delivery to ensure that animals are appropriate for the project as per clause 2.4.15 (i) of the Code.

(15) If approved by the ACEC, animals are considered to be in a waiting period after the acclimatisation period has ended and prior to commencement of the project procedures. Animals without known vulnerabilities must be monitored by a project team member at least twice per week during the waiting period. Animals with known vulnerabilities may require more frequent monitoring, which will be considered by the ACEC as part of the initial project application.

Table 1. Summary – Investigator Responsibilities for Monitoring

Period	Period Duration	Monitoring Frequency
Acclimatisation	5-7 days unless approved otherwise by the ACEC.	At least twice during the period with the first monitoring event at least 1-2 days post delivery.
Waiting period for animals without known vulnerabilities	As approved by the ACEC.	At least twice per week.
Waiting period for animals with known vulnerabilities	As approved by the ACEC.	As approved by the ACEC in the project application.
Procedures (project has commenced)	As approved by the ACEC.	As approved by the ACEC in the project application.

Monitoring Records

(16) The Code requires records of the monitoring of animals to be maintained. Standard ACEC approval requires that monitoring records begin at the time that an animal is allocated to an approved project.

(17) The documentation of a monitoring strategy may involve the use of simple checklists for periods when animal welfare is less likely to be impacted (e.g. during the acclimatisation period), and more detailed checklists for periods when an animal's welfare is more likely to be impacted (e.g. following an intervention).

(18) Monitoring Checklists should be:

a. specifically designed for each procedure and species. Clinical signs will differ according to the type of research, as well as between species and individuals. For some projects, several different Monitoring Checklists will be necessary to cover different phases of the work; and
b. developed with input from project members involved with the monitoring of animals. Input can also be sought from the Animal Welfare Officer, Ethics Officer (Animal) or members of the ACEC.

(19) Animals may be monitored individually or in a group. If group monitoring is used and a problem is identified with an individual animal, the monitoring of that animal should be moved to an individual Monitoring Checklist and the original Monitoring Checklist annotated to indicate that this animal is now being individually monitored.

(20) The cages of animals requiring close monitoring should have a Close Monitoring Card to ensure that the need for closer monitoring is readily apparent to BRF staff and Investigators.

(21) Monitoring records used by BRF staff should include:

a. an Initial Examination Form on entry of animals into an BRF animal facility;
b. a Pre and Post-Delivery Monitoring of Central Animal House Animals Sheet, used for animals bred at the Central Animal House; and
c. a University Procedures Record/Treatment Sheet.

(22) Investigators must use a University Procedures Record/Treatment sheet in the following situations:

a. when an animal has been allocated to a project but has yet to enter the research phase;
b. during the research phase if a Specific Monitoring Checklist is not required by the ACEC;
c. during a project when an animal has recovered from a procedure, or when close specific monitoring is no longer necessary; or

d. recording when procedures are performed, with the clinical record then continuing on a specific Monitoring Checklist.

(23) Investigators must use a Specific Monitoring Checklist(s), developed for the project and approved by the ACEC, in the following situations:

a. during the period following an intervention; or
b. when monitoring for specific problems associated with an animal with an inherent condition that affects its health or welfare.

(24) Records associated with the monitoring of animal wellbeing must remain with the animal/s at all times, usually in the red folder provided by the BRF. Specific monitoring records for particular animals may accompany those animals to the laboratory or other examination/ procedure area.

(25) Monitoring records must:

a. be a true and accurate reflection of the monitoring that has occurred. Falsification such as pre- or post- dating records is unacceptable;
b. be completed and signed by the person who has conducted the monitoring;
c. be legible and completed in ink; and
d. only be altered to correct genuine errors by striking through the incorrect information, adding the correct information and including a explanation for the alteration.

(26) The use and effectiveness of Monitoring Checklists are reviewed during inspections of research projects. All monitoring records must be available to members of the ACEC and the Animal Research Review Panel during inspections.

Developing Monitoring Checklists

(27) Examples of Monitoring Checklists are available on the Animal Ethics website.

(28) The effectiveness and relevance of monitoring checklists for specific projects must be reviewed regularly by the Investigator, with a view to improvement.

Use of Pilot Studies

(29) Consideration should be given to the use of preliminary or pilot studies to determine endpoints, particularly when the effects of the treatment are unknown.

(30) Pilot studies using a small number of animals can:

a. help determine the morbidity, time course of effects, and frequency of observations required to set an endpoint;
b. provide an indication of the variance of responses between treatment groups, which can then be used to estimate future group sizes more accurately; and
c. provide the opportunity for project members to become experienced with the procedure and the expected signs and symptoms.

Section 7 - Adverse Events

(31) The immediate welfare of research animals is paramount. If it is discovered that a problem affects animal wellbeing beyond what is planned for in the approved research project, quick actions must occur to remove obvious causes. The reporting of such events is mandatory in accordance with the Code clause 2.4.34 (ii).

(32) Adverse events can be a single or cumulative event, and may be unexpected or predicted.

(33) Examples of adverse events are included in Table 1 and example scenarios of adverse events are available on the Animal Ethics website.

Table 1

Animal related events	Environmental/husbandry related events (potential effect on animal welfare)
Death	Air-conditioning problems
Sickness	Lighting problems
Pain	Access to food/water affected in some manner
Distress	Flooding of cage
Injury	Emergency situation
Abnormal behaviour	Power failure

Unexpected Adverse Events

(34) Unexpected adverse events have a negative impact on animal wellbeing and are:

a. not predicted events in the approved project; or
b. have an incidence rate that is higher than what was predicted in the approved project.

Predicted Adverse Events

(35) Predicted adverse events are events which are adverse, but where the cause is known and the level of incidence/severity is as described in the approved project or supply unit procedures.

Research Related Events

(36) Research related events may impact on research results or the progress of a project, but have no impact on animal wellbeing.

Post Mortem Examinations

(37) A post mortem examination is required if an animal has died or has been euthanased due to its condition, and:

a. the cause of the problem is not defined; or
b. the incidence and severity of the problem is not as expected.

(38) The Animal Welfare Officer must be contacted if the circumstances meet the above criteria and the Investigator proposes that a post mortem should not be conducted. The Animal Welfare Officer's decision to proceed or not

conduct a post mortem remains final.

(39) The ACEC requires that post mortems are conducted by a veterinarian or person approved as competent to do so by the ACEC.

(40) Where the gross examination does not reveal the cause of death, further pathological testing should be undertaken to maximise the chance of determining the cause of the unexpected adverse event.

Actions Required for Adverse Events

Action	Details
Act Immediately:	Determine and remove obvious hazard while responding to the immediate needs of sick or at-risk animals.
Inform:	The Chief Investigator is to immediately contact the Animal Welfare Officer following an unexpected adverse event. If the Chief Investigator is unavailable, the Animal Welfare Officer may be contacted by another member of the research team. Should the Animal Welfare Officer be unavailable, contact the Ethics Officer (Animal).
Inform:	The Associate Director, Research Infrastructure must be advised when an adverse event involves facilities, a disease outbreak, emergency or environmental issue.
Report:	All adverse events involving animals must be reported to the ACEC.

Section 8 - Reporting Adverse Events

(41) Reporting adverse events involving research animals:

a. is an ethical obligation and legally mandatory; and
b. enables timely investigation of the cause/s of the event, and the establishment of prevention strategies to improve animal welfare and research activity outcomes across the University.

(42) The Animal Welfare Officer must be notified of an unexpected adverse event immediately via phone or email. Where it is determined that animal health or welfare is at risk, preliminary written advice must be submitted within 48 hours, so that appropriate action can be taken to remove or minimise the risk. Contact the Animal Welfare Officer for further information if required.

(43) Upon notification the Animal Welfare Officer or Ethics Officer (Animal) will promptly provide the Animal Care and Ethics Committee Chair with the details of an unexpected adverse event. In the absence of the Committee Chair, the Deputy Chair or Animal Care and Ethics Committee Executive will be informed.

(44) A decision flow-chart is available on the Animal Ethics website to assist Investigators in determining the nature of the report required.

(45) Submit all reports to the ACEC in accordance with Animal Ethics application procedures.

Reporting Responsibilities

Table 3 – Responsibilities for Reporting Adverse Events

Situation	Responsibility
Breeding colony	Associate Director, Research Infrastructure or nominee
Stock animals prior to allocation to a project	Associate Director, Research Infrastructure or nominee

Situation	Responsibility
Research breeding colony	Chief Investigator or nominee
Animal supplied or allocated to a project, but experiments have not yet commenced	Chief Investigator or nominee
Animal supplied or allocated to a project, and experimental intervention has commenced	Chief Investigator or nominee

Reporting Unexpected Adverse Events

(46) Adverse Event Reports must be submitted within 14 calendar days of the occurrence of the unexpected adverse event.

(47) Where submissions are incomplete (e.g. post mortem results are not yet available), the completed Report must be re-submitted once results are known or the cause has been identified.

(48) A Separate Variation Application is not required where the adverse event consequently requires currently approved studies to be repeated, and this is detailed in the Adverse Event Report. Studies must not be repeated until the ACEC has approved the Adverse Event Report and an amended Animal Research Authority has been issued.

Reporting Predicted Adverse Events

(49) Predicted adverse events are reported in the Annual Progress Report.

Reporting Research Related Events

(50) Research related events are reported via:

a. a Variation application, to request the use of additional animals if repetition of experiments is required; or
b. the Progress Report/Renewal application for a project, Annual Report for an animal supply unit, or a Specific Report, which can be submitted anytime.

Status and Details

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Responsible Executive	Juanita Todd Pro Vice-Chancellor (Research)
Enquiries Contact	Research and Innovation Division

Glossary Terms and Definitions

"University" - The University of Newcastle, a body corporate established under sections 4 and 5 of the University of Newcastle Act 1989.

"Risk" - Effect of uncertainty on objectives. Note: An effect is a deviation from the expected, whether it is positive and/or negative.

"Research" - As defined in the Australian Code for the Responsible Conduct of Research, or any replacing Code or document.

"Staff" - Means a person who was at the relevant time employed by the University and includes professional and academic staff of the University, by contract or ongoing, as well as conjoint staff but does not include visitors to the University.