This document has been developed by The Australian National University's (ANU) Research Ethics Office. It has been endorsed by the ANU Animal Ethics Committee (AEC). 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 (updated 2021).

Document 010: ANU Position Paper – Use of Non-Pharmaceutical Grade Discovery Compounds in Animals V2.0

Background

The use of non-pharmaceutical grade compounds (non-PGCs) may compromise animal welfare, as well as impact the quality of research produced, as outlined by The National Research Council's (US) Guide for the Care and Use of Laboratory Animals. Due to these reasons, and others, it is considered best practice to only use pharmaceutical grade compounds (PGCs) in animals.

The ANU requires the use of best practice methodology at all times as per the NHMRC Best Practice Methodology in the Use of Animals for Scientific Purposes and the Australian Code for the Care and Use of Animals for Scientific Purposes. The ANU, therefore, requires that where possible, only compounds of pharmaceutical grade are used in animals.

Discovery compounds are, for the purposes of this standard, defined as chemicals or substances that are non-PGCs, and which have not previously been used in animals, or drugs that are currently under development and not yet available in a pharmaceutical grade preparation. The justifications for the use of discovery compounds in animals differs from the use of non-PGCs for anaesthesia and euthanasia, and as such, two separate standards have been developed.

General Information and Considerations

Where a researcher requests to utilise a non-pharmaceutical grade compound for discovery purposes (i.e. a potential new drug), they must specifically justify what steps they have taken to minimise any impact on animal welfare.

Where non-PGCs are requested to be utilised under a protocol, they must be clearly identified as a non-PGC, and it is the researcher's responsibility to appropriately mitigate the risks of using such a compound.
The following factors must be considered;

- Has the compound been used in any animal species previously, and if so, what dose rates and routes of administration were found to be safe and effective?

- If the compound has not been used in any animal species previously, has any *in vitro* work been completed?
- If safe protocols have not been established, how will an appropriate treatment protocol be developed to determine safe doses and administration routes?
- Is the chemical properties and route of administration appropriate for the aims of the study (this includes the purity, grade, stability in and out of solution, vehicle properties, pH, osmolality etc.)
- Are protocols available for the method of preparation, appropriate storage, and labelling (including expiry) of the compound?
- What monitoring protocols will be put in place to ensure adverse events and poor animal welfare outcomes are minimised?

Monitoring, Intervention and Reporting

Adverse Events

Any approval given for the use of non-PGCs will be conditional on any individual adverse event (i.e. a single mouse death or complication that Impacts the ability to utilise the data from an animal). Any adverse event related to the use of a non-PGC must be immediately reported via the University's Unexpected Adverse Event reporting mechanism. There is no acceptable complication rate for the use of non-PGCs.

If a complication is found to be due to, or is potentially attributed to, the use of the non-PGC, a review of the protocol and its approved procedures will be undertaken. While the review is being undertaken, the use of the non-PGC may be suspended at the discretion of the AEC and ANU veterinarians or their delegates.

Any investigator that does not follow their AEC approved procedure for the use of non-PGCs will have their approval immediately revoked.

Minimum Requirements

- Where non-PGCs (discovery compounds) are requested to be utilised under a protocol, they must be clearly identified as a non-PGC
- Animal ethics applications using non-PGCs (discovery compounds) must outline the possible risks to animal welfare and the strategies proposed to address these
- Any adverse event related to the use of a non-PGC must be immediately reported via the University's Unexpected Adverse Event reporting mechanism. There is no acceptable complication rate for the use of non-PGCs

References and Resources

ANU Training and Support

The ANU Veterinary Services Team are available to provide advice on the use of novel or discovery compounds, and help researchers develop protocols that ensure appropriate experimental and animal welfare outcomes.

Related Documents

Information Paper January 2020: *Use of Non-Pharmaceutical Grade Compounds (Non-PGCs) and Discovery Compounds in research animals*

ANU Position Paper: Use of Non-Pharmaceutical Grade Compounds for Anaesthetising & Euthanasing Animals

Procedure for Managing & Reporting Unexpected Adverse Events.

References

The Australian code for the care and use of animals for scientific purposes 8th edition. 2013 (updated 2021)

Best practice methodology in the use of animals for scientific purposes (2017)