ANIMAL CARE AND USE STANDARD

The Animal Care & Use Standards are designed to provide guidance regarding good practice to institutional animal users and carers, as well as animal ethics committees, on the care and use of animals for scientific purposes such as research and teaching. The Standards are evidence-based, reflecting current or accepted good practice and allow for the flexibility that is required in research and teaching activities using animals.

BREEDING OF NEW MOUSE STRAINS

This standard has been developed by the University of Melbourne Animal Care & Use Standards Committee, and endorsed by the University of Melbourne Animal Welfare & Ethics Committee.

V1 Date of Approval:	21 December 2015	**Date of Review:**	21 December 2018

1. ASSOCIATED STANDARDS

This Standard should be read in conjunction with the following University of Melbourne Animal Care & Use Standard:

- Monitoring

2. SUMMARY

New strains of mice can be generated by the mating of existing strains or by direct genetic modification. Documentation of the phenotype and genotype of novel strains created at the University is required to enable appropriate monitoring of animal welfare.

3. BENEFITS & RISKS

- New strains can allow advances in scientific research including elucidation of genes and pathways involved in various disease conditions.
- A disadvantage of generating new strains by breeding is being reliant upon specific mouse strains to be available, which may not be the case. Gene modifying technology, such as transgenics or CRISPR, used to artificially create strains can overcome these limitations.
- A potential complication of working with new strains is the uncertainty relating to welfare impacts and scientific outcomes.

4. PROCEDURE/PROTOCOL

4.1 Breeding to create new strains

- Animal Ethics Committee approval must be obtained for breeding of new mouse strains
- A male of one strain is placed together with one or more females of a different strain and allowed to mate.
- Successful mating can be monitored by the presence of a vaginal plug.
- Females are monitored for signs of pregnancy including increase in body weight and body shape/size.
- Viable pups are born and the litter remains with the mother until ready to be weaned.
- If pups are not born then this could suggest an embryonic lethal phenotype, which can be investigated by assessing embryos at different time points post-vaginal plug.

- Health status of the pups must be monitored and recorded.
- If required, the genotype of the new strain is determined, typically by taking a tail or ear clip for molecular analysis.
- Where surgical embryo transfer is performed this should be done under aseptic technique by a competent person.

4.2 Mouse Passport

- A Mouse Passport, which documents genotypic and phenotypic details of the new strain, must be completed once these are known. The University of Melbourne Mouse Passport template is the recommended format for record keeping. Once completed, the Mouse Passport must be submitted to the Animal Ethics Secretariat who will maintain a database of new strains. Prior to creation of new strains, researchers must check that any relevant information is not already held in this repository.
- Information includes: coat colour, litter sizes, mortality rates, any physical abnormalities including motor function and seizures, immune status, behavioural traits (aggression, tremor, over-grooming etc.), effects on body weight and growth rate, lifespan, specific phenotype changes expected based on genetic changes, post-mortem assessment, and any other relevant welfare measures.
- The Mouse Passport should include the mouse strain name based on Jax Laboratory strain naming nomenclature.
- The completed Mouse Passport is to be approved by the Animal Welfare Officer (AWO) and relevant Animal Ethics Committee.
- Based on the Mouse Passport, if special husbandry requirements are identified, such as specific barrier requirements, diet, specific monitoring, these are to be implemented for all subsequent breeding and use of this strain.

5. MONITORING & INTERVENTION

- Animals must be monitored and recorded at least weekly, which is done by animal facility staff prior to transferring animals to the researchers. A monitoring sheet similar to Appendix 2 in the NHMRC Guidelines (2007) in addition to a tailored intervention sheet may be used and must be submitted to the Animal Ethics Committee for approval.
- The mother must also be monitored more closely for any pregnancy or parturition welfare impacts.
- New strains that are expected to exacerbate a disease or physiological phenotype must have a tailored monitoring schedule and intervention points for early identification and actions relating to any adverse impact on animal health or behaviour.
- Unexpected deaths and abnormalities in physical or behavioural traits must be reported immediately to the AWO and Animal Facility Manager for independent assessment of impact on the animal's welfare.
- Inappropriate monitoring may result in animals with undetected abnormalities.

6. ADDITIONAL INFORMATION

- The University of Melbourne Mouse Passport template can be downloaded from the Forms, Templates & Guidance documents webpage.
- NHMRC (2007) example monitoring sheets in Appendix 2: http://orei.unimelb.edu.au/content/gm-and-cloned-animals

7. ENFORCEABLE REQUIREMENTS

- Use of an Animal Ethics Committee approved monitoring and intervention sheet for new strains
- Frequency of monitoring at least weekly.
- Frequency of monitoring for new strains that may exacerbate a disease or physiological phenotype to be tailored for early identification of adverse impact on animal health.
- Completion of a Mouse Passport and its approval by the Animal Ethics Committee/AWO.
- Unexpected adverse events, unexpected deaths, abnormalities in physical or behavioural traits to be

reported immediately to AWO and Animal Facility Manager.

8. EXEMPTIONS

Where adherence to this Standard conflicts with proposed work, the University's Animal Ethics Committees may grant exemptions to all or part of the Standard. To seek exemption, applications should clearly outline how the proposed work deviates from the Standard, and justify the need for this. Before seeking exemption, it is recommended that you consult with the University's AWO.

9. UNEXPECTED ADVERSE INCIDENTS

An unexpected adverse event is any event, which impacts negatively on the wellbeing of animals, and which was not anticipated, or has occurred at a frequency or severity in excess of what was anticipated in line with the AEC approval. This can be a single or cumulative event, and will normally involve unexpected mortality, morbidity or injury. Anyone identifying an unexpected adverse event must act to remove and/or minimise any immediate risk to animals. Immediately thereafter, the University's AWO and relevant Animal Facility Manager must be notified of the event. The AWO will advise researchers of the appropriate response.

10. GLOSSARY

Scientific Term	Lay Description
Strain	A group of animals that is genetically uniform.
CRISPR	CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats. It is a method for editing the genetic sequence of an organism.
Transgenic	An organism that has been genetically modified by transferring another gene.

11. REFERENCES & RESOURCES

The following source material contributed to the development of this Standard:

- NHMRC (2013). Section 2.4.26-27. Australian Code for the Care and Use of Animals for Scientific Purposes
- NHMRC (2007). Guidelines for the Generation, Breeding, Care and Use of Genetically Modified and Cloned Animals for Scientific Purposes.

MOUSE PASSPORT

Mouse Passports are designed to provide welfare, husbandry, background and administrative information to assist in the development and maintenance of new mouse strains.

Passports are intended as summaries only. Full details of strain development should be outlined in the associated animal ethics application, and be in accordance with the University of Melbourne *Breeding of New Strains* Animal Care & Use Standard.

Standards should be submitted as attachments to the associated animal ethics application, for review by the relevant animal ethics committee, and completed standards should be lodged for with the University's Animal Welfare Officer.

[COMMON STRAIN NAME]

First Submitted:	DD/MM/YY	**Last Updated:**	DD/MM/YY

1. STRAIN SUMMARY

Exact Nomenclature	[]Use JAX labs nomenclature.]
Working Name	[Common strain name]
Origin of Strain	[Location of development]
Date of Development	
Background Strain	
Details of Modification	[Include type, gene affected, inheritance pattern, etc…]
Immune Status	
Genotyping Protocol	[Type of tissue sample]

2. ADMINISTRATIVE DETAILS

Contact Name	[Project Supervisor, as named on associated animal ethics application ID]
Contact Email	
Department	
Application ID/s	

3. WELFARE

General Appearance	[Where possible, include images as attachments]
Behavioural Traits	[Description of any abnormal behaviour]
Physical Abnormalities	
Location/s of Housing	[Name/s of animal facility where housed]
Other Abnormalities	[Include any post-mortem findings]
Lifespan	[Indicate whether a welfare assessment has been conducted for the full period for which the strain is normally maintained]
Growth Rate	[Where possible, include data as attachments]
Phenotypic Testing	[Where possible, include results as attachments]
Required Actions	[Details of any actions required to manage welfare concerns]

4. HOUSING & HUSBANDRY

Location/s of Housing	[Name/s of animal facility where housed]
Details of Housing	[Include details of environmental enrichment]
Diet	
Current No. of Backcross/Generations	
Current breeding strategy	
Average Litter Size	
Breeding Lifespan	
Pre/Post-Weaning Mortality	
Required Actions	[Details of any actions required to manage housing and husbandry concerns]

5. UNEXPECTED ADVERSE EVENTS

An unexpected adverse event is any event, which impacts negatively on the wellbeing of animals, and which was not anticipated, or has occurred at a frequency or severity in excess of what was anticipated in line with the AEC approval. This can be a single or cumulative event, and will normally involve unexpected mortality, morbidity or injury. Anyone identifying an unexpected adverse event must act to remove and/or minimise any immediate risk to animals. Immediately thereafter, the University's AWO and relevant Animal Facility Manager must be notified of the event. The AWO will advise researchers of the appropriate response.

6. GLOSSARY

Scientific Term	Lay Description

**Add more rows as necessary*

7. ADDITIONAL INFORMATION & REFERENCES

The following source material contributed to the development of this passport:

- [List any source material used in developing the passport]

The following additional or supplementary material is attached:

- [List any attachments]