

## 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 (AECs), 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.

## Use of Antibiotics

*This standard has been developed by the University of Melbourne Animal Care & Use Standards Committee, and approved by the University of Melbourne's Animal Ethics Committees.*

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**1. ASSOCIATED STANDARDS**

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

- Injections and microchipping
- Holding and restraint of rats and mice
- Administration of substances by oral gavage in mice and rats

**2. SUMMARY**

2.1 Antibiotics are an important part of human and veterinary medicine. These drugs can be integral in the effective treatment of diseases which can lead to subsequent improvements in animal health and welfare. Additionally, to maintain their maximum efficacy and prevent antimicrobial resistance, the prudent use of antibiotics is of utmost importance. Therefore antibiotic usage standards have been developed to ensure animal welfare standards are maintained and the efficacy of antibiotic treatment continues into the future.

**3. BENEFITS & RISKS****3.1 Benefits**

- 3.1.1 Animal welfare can be improved through the use of appropriate antibiotic treatments in sick animals.
- 3.1.2 Antimicrobial resistance can be reduced through the appropriate choice and usage of antibiotic treatments.

**3.2 Risks**

- 3.2.1 Antibiotics can cause mild to severe side effects, including nausea, appetite loss, anaphylaxis or death.
- 3.2.2 Any antibiotic usage can unintentionally select for antibiotic resistant bacteria and therefore reduce future efficacy.
- 3.2.3 Incorrect or excess antibiotic usage can exacerbate and expedite the selection for antibiotic resistant bacteria.
- 3.2.4 Antibiotic treatment may cause experimental interference.

## 4. PROCEDURE/PROTOCOL

- 4.1 Any prescription antibiotic may only be administered to animals with the approval of a veterinarian and must only be used as prescribed.
- 4.2 The delivery of antibiotic drugs must be undertaken by competent investigators or trainees under the direct supervision of competent investigators.
- 4.3 Antibiotic selection should be based on an accurate diagnosis of a bacterial pathogen and the appropriate spectrum of activity which should be subsequently verified by microbial culture with antibiotic sensitivity testing. The duration of antimicrobial action, administration methods, side effects and toxicity, concurrent drug interactions and any interference with the experimental study and outcomes must also be considered.
- 4.4 Selection of antibiotics must also consider the species and age as well as the immunological, reproductive, gestation and concurrent disease status of the animal. Many antibiotics can cause severe and lethal side effects in different species of animals and their offspring, therefore appropriate selection is critical to animal welfare and safety.
- 4.5 Drug withdrawal times for any food producing animals must be strictly adhered to and recorded. Some classes of antibiotics cannot be used in food producing animals (e.g. Chloramphenicol).
- 4.6 Drug withdrawal times for any competition animals must be strictly adhered to and recorded. Some classes of antibiotics cannot be used in competition animals.

### 4.7 Types of Antibiotics

#### 4.7.1 Beta-Lactams

4.7.1.1 Penicillins – Bacteriocidal by inhibiting cell wall formation in bacteria. Resistance is known to be an issue and many formulations are combined with another antimicrobial agent. Can be used for skin infections, respiratory tract infections and genito-urinary tract infections. Common generic drug formulations: Penicillin, Amoxicillin, Amoxicillin Clavulanate.

4.7.1.2 Cephalosporins – Bacteriocidal by inhibiting cell wall formation in bacteria. Resistance is known to be an issue and several new generations of cephalosporin drugs have been developed (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>). Each generation may have a broader spectrum of activity. Can be used for skin infections, respiratory tract infections, ear infections (otitis media and externa), genito-urinary tract infections, oral infections, bone infections and surgical prophylaxis. Common generic drug formulations: Cephalexin (1<sup>st</sup>), Cefazolin (1<sup>st</sup>), Cefaclor (2<sup>nd</sup>), Ceftiofur (3<sup>rd</sup>), Cefovecin (3<sup>rd</sup>)

4.7.2 Macrolides – Bacteriostatic derived from Streptomyces bacteria with a macrocyclic lactone chemical structure. Can be used for respiratory tract infections, gastrointestinal tract infections, genital tract infections, mycoplasma infections and skin infections. Common generic drug formulations: Erythromycin, Tylosin, Azithromycin.

4.7.3 Fluoroquinolones – Synthetic, bacteriocidal and broad-spectrum drug. Spectrum of activity is known to vary depending on the generation of fluoroquinolones (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>). Can be used for respiratory infections, genito-urinary tract infections and mycoplasmal infections. Common generic drug formulations: Enrofloxacin, Marbofloxacin, Ciprofloxacin.

4.7.4 Tetracyclines – Broad-spectrum bacteriostatic derived from Streptomyces bacteria with a four ring chemical structure. Can be used for skin infections, respiratory infections, otitis media infections, gastrointestinal tract infections, tick-borne diseases, oral infections, anaerobic infections and genito-urinary tract infections. Common generic drug formulations: Oxytetracycline, Doxycycline, Tetracycline.

4.7.5 Aminoglycosides – Bacteriocidal, more narrow in spectrum towards aerobic gram-negative bacteria. Cannot be given orally and have a low therapeutic index. Can be used for genito-urinary tract infection, mammary gland infections (mastitis), topical infections (skin, otic and ophthalmic preparations) and other aerobic gram-negative infections. Common generic drug formulations: Amikacin, Gentamicin, Neomycin, Streptomycin.

4.7.5 Sulphonamides and Potentiated Sulphonamides – Broad-spectrum bacteriostatic derivatives of sulphanilamide. Resistance can occur, thus the development of potentiated sulphonamides. Can be used for many types of infections including respiratory, genito-urinary, bone, skin, gastrointestinal, toxoplasmosis and coccidiosis. Common generic drug formulations: Trimethoprim/sulfadiazine, Sulfadiazine, Sulfathiazole.

4.7.6 Lincosamides – Bacteriostatic or bacteriocidal depending on the concentration with limited activity against aerobic bacteria and broad-spectrum activity against anaerobic bacteria. Can be used in anaerobic, bone, genito-urinary tract, oral and respiratory tract infections. Common generic drug formulations: Clindamycin, Lincomycin.

## 5. MONITORING & INTERVENTION

- 5.1 The animal must be correctly identified and identification recorded. Body weight must be monitored and recorded prior to calculation and administration of antimicrobial drugs. Drug dose, route of administration, and time of administration must be recorded and adhered to as per the drug prescription. Animals should be monitored for both signs of improvement, any new signs and potential side effects with these results recorded along with the initials of the person(s) administering the antibiotic treatment(s).
- 5.2 In addition to the above monitoring, other monitoring criteria should include: diarrhoea, vomiting, skin tenting, water and feed consumption, REI sample monitoring sheet criteria and any additional experimental criteria.

## 6. ADDITIONAL INFORMATION

- 6.1 REI Sample Monitoring Sheet: <https://staff.unimelb.edu.au/research/ethics-integrity/animal-ethics/forms-examples-and-training/forms-and-templates>

## 7. ENFORCEABLE REQUIREMENTS

- 7.1 Adherence to the prescribed drug dose, frequency of treatment, and any other usage instructions as per the prescription instructions or AEC approved administration.
- 7.2 Adherence to the monitoring guidelines described above.
- 7.3 Performance of animal handling, oral gavage and injections by competent personnel or those under the supervision of competent personnel.
- 7.4 Acceptable skill level must be demonstrated on at least two occasions before people are permitted to handle animals or administer antibiotics by oral gavage and/or injection.

## 8. EXEMPTIONS

Where adherence to this Standard conflicts with proposed work, the University's AECs 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 AWO.

## 9. UNEXPECTED ADVERSE INCIDENTS

An unexpected adverse event is any event which impacts negatively on the wellbeing of animals and 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 AWO and relevant AFM must be notified of the event. The AWO will advise researchers of the appropriate response.

In addition, a necropsy must be performed on any animal whose illness or death constitutes an unexpected adverse event. The body of an animal found deceased, or humanely killed as a consequence of an unexpected adverse event, must be refrigerated and the necropsy performed in a timely manner to provide for accurate and reliable results. A full necropsy report as well as any relevant photographs and external laboratory results should be submitted to the AWO alongside the adverse event report.

## 10. GLOSSARY

Scientific Term	Lay Description
Breakpoint	The concentration of an antimicrobial drug at which the population of bacteria can be split into susceptible (can be killed by the drug) or resistant (no effect by the drug) groups.
Antimicrobial	Any agent, including drugs or disinfectant chemicals, that can kill or slow the growth of microbes.

Aerobic bacteria	Bacteria that grow well in environments with oxygen
Anaerobic bacteria	Bacteria that grow well in environments without oxygen
Antibiotic	A drug used to kill or slow the growth of bacteria. Antibiotics are a type of antimicrobial.
Bacteria	Single celled microscopic organisms
Efficacy	The ability of a drug to produce a desired result
Gram negative bacteria	Bacteria that are negative to a Gram stain test and appear pink under a light microscope
Gram positive bacteria	Bacteria that are positive to a Gram stain test and appear purple under a light microscope
Microorganism	Refers to microscopic organisms such as bacteria, viruses or fungi
Microbe	A micro-organism, especially a bacteria that may cause disease
Therapeutic Index	A measurement of the relative safety of a drug
Virus	An infective agent that typically consists of a nucleic acid molecule in a protein coat, is too small to be seen by light microscopy, and is able to multiply only within the living cells of a host:
Fungus/ Fungi	Any of a group of unicellular, multicellular, or spore-producing organisms feeding on organic matter (includes moulds, yeast, mushrooms, and toadstools)
Bacteriostatic	Describes the mechanism of action for an antibiotic drug that works by arresting the growth or multiplication of bacteria
Bactericidal	Describes the mechanism of action for an antibiotic drug that works by destroying the bacteria, causing its death
Broad Spectrum	Antibiotics used to treat a wide range of bacteria
Narrow Spectrum	Antibiotics used to treat a narrow range of bacteria

## 11. REFERENCES & RESOURCES

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

- <http://www.merckvetmanual.com/mvm/>
- [Lab Anim.](#) 1995 Jan; 29(1):16-36. Antibiotic therapeutics in laboratory animals. [Morris TH](#)<sup>1</sup>. Accessed 8/7/16 from <http://lan.sagepub.com/content/29/1/16.long>
- Federations of Veterinarians of Europe “Antibiotic Resistance and Prudent Use of Antibiotics in Veterinary Medicine”. Accessed 7/8/16 from <http://www.fve.org/news/publications/pdf/antibioen.pdf>