The Use of S8 Drugs in Animal Studies and their Possible Replacement
A Schedule 8 Controlled Drug is defined in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) as "Substances which should be available for use but require restriction of manufacture, supply, distribution, possession and use to reduce abuse, misuse and physical or psychological dependence." This is published by the Commonwealth under the Therapeutic Goods Act 1989. Possession without authorisation of an S8 drug is a criminal offence unless the holder is a veterinary surgeon, dentist or medical practitioner registered in the ACT.

The Drugs of Dependence Act 1989 (ACT) prescribes that a person wishing to conduct a program of research that would require the possession or use by that person of a drug of dependence or prohibited substance (S8) may apply to the ACT Minister of Health for an authorisation in relation to that drug, and makes it illegal to possess or use drugs of dependence without an authorisation. Part 8 of that Act details storage and recording requirements.

Two drugs that require such authorisation are used for animal studies at the ANU. Buprenorphine, used as an analgesic (pain killer) in some studies is one. Ketamine, used as an anaesthetic component in a number of studies, has been reclassified into this category during 2005. Investigators using either of these drugs will need to apply for authorisation to the Minister.

There are studies at the ANU where the above S8 drugs will be required to be used and where this is the case investigators will need to apply for the appropriate authorisation. There may be studies where alternatives may be used and the ANU Animal Experimentation Committee has delegated its Executive Officer, Dr Simon Bain, to authorise requests to change to other anaesthetics and analgesics that do not fall within the S8 classification. Such requests can be made by e-mail to Dr Bain (Simon.Bain@anu.edu.au). A guide to possible alternatives is outlined below. ANU researchers who wish to surrender S8 substances and move to use alternatives should coordinate the change-over with Simon Bain as soon as possible.

**Additional S8 Drug Information**

A number of other schedule 8 drugs are registered for use in animals. These can be found by accessing the following: [www.apvma.gov.au](http://www.apvma.gov.au) select "search for a product" down left column, then under "Schedule" select "8" and you will have them listed. There are also a number of human preparations which are schedule 8. The schedule which applies to a product is defined by the particular constituent as listed in the SUSDP. The SUSDP is determined by the National Drugs & Poisons Scheduling Committee (NDPSC) and the basis for decisions can be found in the "Record of Reasons" which can be accessed from the NDPSC website [www.tga.gov.au/ndpsc](http://www.tga.gov.au/ndpsc). Recent decisions regarding ketamine and butorphanol can be sought out here.
Alternatives to Buprenorphine

Mice and Rats
1. Tramadol (Available as Tramal). Dose: 10mg/kg to 30mg/kg IP. (Up to 75mg/kg IP has been reported but note that doses over 100mg/kg can be toxic).
   Comments: Can also be given in drinking water at 30 to 50 mg/kg depending on severity of pain. [Mice drink approx 15 ml/100gm body weight per day; for 50mg/kg need a concentration of 0.333mg/ml; dissolve one 50mg capsule in 150ml water.] Available in ampoules (50mg in 1 ml or 100mg in 2 ml; tablets of 50 to 150mg. Has been used in rats repeatedly for several days and much longer (e.g. for arthritis).

2. Metaclopramide (available as Metamide Antiemetic Injection in a 20ml bottle at 5mg/ml) at a dose rate of 5mg/kg i/p is cited in the scientific literature to be effective in rats.
3. Flunixin (available as Finadyne and other proprietary preparations): 2.5mg/kg s/c, i/m at 12 hourly intervals.
4. Paracetamol: 200mg/kg by mouth (in the drinking water).

Sheep and Pigs
1. Flunixin (available as Finadyne and other proprietary preparations): 2mgs/kg i/v or s/c once daily.
2. Carprofen in sheep (available as Norocarp injection) 4mg/kg i/v once daily.

Cats
1. Meloxicam (available as Metacam in 10ml vials): 0.3mg/kg s/c once daily.

Rabbits
1. Flunixin (Finadyne) 1.1mg/kg s/c, i/m 12hourly.
Alternatives to Ketamine

Ketamine is used usually in combination with other agents, but sometimes alone. It is a dissociative anaesthetic agent. Its biggest use at the ANU is in combination with Rompun (xylazine) as an anaesthetic for rodents. Alternatives by species are:

Mice
1. Injectable anaesthetic:
   a. Propofol (Aquafol and Rapinovet X) 26mgs/kg iv will give 5-10 minutes surgical anaesthesia
   b. Tribromoethanol (Avertin) 240mg/kg IP will give 15-45 minutes surgical anaesthesia (must be used freshly mixed).
2. Inhalation anaesthetic:
   a. Isoflurane administered with the appropriate vaporisor.

Rats
1. Injectable anaesthetic:
   a. Propofol 10mg/kg iv will give 5-10 minutes surgical anaesthesia. Follow up intermittent doses of 500µg propofol through i/v cannulation will prolong anaesthesia.
   b. Tiletamine/zolezepam (Zoletil) 40 mg/kg will give light anaesthesia for 15 to 25 minutes.
   c. Alpha-chloralose 55-65 mg/kg will produce light anaesthesia for 480-600 minutes (non-recovery only)
2. Inhalation anaesthetic:
   a. Isoflurane administered with the appropriate vaporisor.

Rabbits
1. Injectable anaesthetic:
   a. At this stage there is no adequate injectable replacement for ketamine 25 mg/kg plus medetomidine 0.5 mg/kg i/m (preferred) or
   b. Ketamine 35mg/kg plus xylazine 5mg/kg i/m.
2. Inhalation anaesthetic:
   a. Isoflurane administered with the appropriate vaporisor.

Pigs
1. Injectable anaesthetic:
   a. Pigs in the JCSMR colony may be given ketamine under the supervision of a veterinarian registered in the ACT.
2. Inhalation anaesthetic:
   a. Isoflurane used in a close circuit system

Cats
1. Injectable anaesthetic:
   a. Propofol 5-8 mg/kg i/v will give 10 minutes surgical anaesthesia;
   b. Alphaxalone/alphadolone (Saffan) 9mg/kg i/v provides about 10 minutes of surgical anaesthesia. Incremental injections of 3mg/kg can be given to prolong anaesthesia;
   c. Alpha-chloralose 70mg/kg i/p or 60mg/kg i/v is suitable for prolonged non-recovery procedures.
2. Inhalation anaesthetic:
   a. Halothane is permitted for use in cats in neuroscience studies providing it is used in a close circuit system and waste gases are scavenged in a safe manner acceptable to the authorities.

Sheep
Ketamine has not been used in ANU sheep studies and i/v administration of thiopentone at 10 to 15mg/kg followed by close circuit use of either halothane or isoflurane will continue.

Wildlife
It is difficult to perceive how the containment requirements for ketamine could be met in field studies. Investigators wishing to use an alternative in wildlife species should discuss this with Dr Bain.