LAB_026 Intranasal Delivery in Mice and Rats (Expiry: March 2026)

I. OBJECTIVE

To describe the intranasal delivery procedure in mice and rats that is used within the UQBR facilities.

NB: The use of (*) indicates this statement is dependent on the facility procedures
NB: The use of (**) indicates this statement is dependent on AEC Approvals

II. COMMENTS / RECOMMENDATIONS

- The volume of substance to be administered should be determined by the target site of delivery. The following relates to mice:
  - Small volumes (~5uL) when targeting the upper respiratory tract and central nervous system
  - Larger volumes (e.g. 35-50uL) when targeting the lower respiratory tract
- The requirement for anaesthesia is determined by the volume of substance administered (small volumes may be administered under conscious restraint, while larger volumes require anaesthesia). It is not appropriate to administer large volumes to conscious animals as they are more likely to expectorate the substance and experience inappropriate levels of stress.
- The volume administered cannot exceed 50uL without specific justification (and AEC approval). (**)

In relation to human safety:

- Facility and procedure appropriate PPE use is essential when handling laboratory rodents
- All accidents, injury or near misses are to be reported immediately to the Facility Manager and recorded on a UQ OHS Incident Report Form. This procedure has particular risk of:
  - rodent bite injury – take appropriate care.
  - Splash back into the face or eyes – take/apply appropriate care and PPE.
  - musculoskeletal injury when performed regularly – consider suitable ergonomic design wherever possible
- In the event of a spill follow facility emergency spill procedures relative to SDS details.

III. EQUIPMENT

- PPE *
- Disinfectants *
- P20 Pipette
- Micro-pipette tips
- Sharps container
- Substance for administration**
- Change station/Bio-safety cabinet *
- Vaporous anaesthetic and associated delivery apparatus

(e.g. isoflurane vaporiser induction chamber or methoxyflurane bell-jar)

- Oxygen supply

IV. PREPARATION

1. Turn on Change station or Biosafety Cabinet *
2. Clean surfaces and relevant equipment with disinfectant
3. Organise all equipment and ensure its good working condition
4. Prepare substance for administration, confirming volume and concentration**
   Refer to UQBR Guideline 6 Preparation for Injection

V. PROCEDURE

Intranasal Delivery Procedure – anaesthetised animals

Anaesthesia must be used if administering ≥20uL (total), see table 1.
Wherever possible, supplementary oxygen should be provided from anaesthetic induction, through the procedure, until the animal has recovered from anaesthesia.

1. Correctly identify the rodent and induce anaesthesia with a vaporous anaesthetic via an induction chamber (for isoflurane) or a bell-jar (for methoxyflurane) (**)
2. Once anaesthetised, check the animal is at an appropriate depth of anaesthesia, then collect the animal from the anaesthetic delivery apparatus and position them so that you are able to gently restrain the head.
   When appropriately anaesthetised the rodent has lost its righting reflex and withdrawal reflexes.
3. Place the end of the pipette tip near the rodent's nostril
4. Slowly push the plunger to form a small droplet at the end of the pipette tip
5. Place the droplet near the rodent nostril allowing the rodent to inhale the solution
6. Repeat above steps for remaining volume, alternating nostrils for each drop inhaled
   Steps 2-6 must be done with consideration that the animal could start to regain consciousness. For this reason these steps must be done without being wasteful of time. If the rodent is becoming "too light" in the anaesthetic plane (i.e. regaining consciousness), gently place it back into the anaesthetic delivery apparatus and recommence the intranasal dose delivery from step 2.
7. Discard the pipette into the sharps container (*)
8. Place the rodent into holding cage and continuously monitor the animal until it is able to perform deliberate conscious movements (e.g. able to walk, eat, drink and toilet normally). If any abnormal behaviour is observed (e.g. increased respiratory sounds) establish a plan for ongoing management (e.g. on-going oxygen supplementation and monitoring or immediate euthanasia) and consult a UQBR veterinarian, as required.
9. Complete all record keeping requirements e.g. updating the cage cards and animal monitoring records

Intranasal Delivery Procedure – conscious animals

When administering small volumes (e.g. <5uL), conscious restraint may be more appropriate considering the additional impact anaesthesia can have on the animal. Conscious restraint (without anaesthesia) may only be used when administering <20uL (total), see table 1.

1. Correctly identify the rodent and appropriately restrain the animal by the scruff. It is imperative that the animal cannot freely move its head: if it is able to move its head you may inadvertently injure the rodent during the procedure.
   Refer to LAB_006 Handling and Restraint in Mice
2. Place the end of the pipette tip near the rodent's nostril
3. Slowly push the plunger to form a small droplet at the end of the pipette tip
4. Place the droplet near the rodent nostril allowing the rodent to inhale the solution
5. Repeat above steps for remaining volume, alternating nostrils for each drop inhaled
6. Discard the pipette into the sharps container (*)
7. Place the rodent into holding cage and continuously monitor the animal for 5 minutes. If any abnormal behaviour is observed (e.g. increased respiratory sounds) establish a plan for ongoing management (e.g. on-going oxygen supplementation and monitoring or immediate euthanasia) and consult a UQBR veterinarian, as required.
8. Complete all record keeping requirements e.g. updating the cage cards and animal monitoring records

Monitoring of animal condition

- If there are any concerns relative to the animal's ability to breath, immediately discontinue the procedure, release restraint, and provide supplementary oxygen and refer to LAB_022 UQBR Veterinary Care Protocol
- If the animal's ability to breath has been affected by the intranasal delivery, the volume was likely incorrectly calculated (i.e. >60uL) or it was administered too rapidly
- In the unlikely event that respiratory distress is observed, immediately perform euthanasia of the animal
  Respiratory distress characterised by irregular, laboured breathing that causes significantly reduced activity in the animal and is unresponsive to intervention (e.g. releasing the animal from restraint and providing oxygen supplementation does not resolve the symptoms). Animals in respiratory distress sometimes have blue discolouration of the skin.

VI. REFERENCE INFORMATION

Table 1. Recommended maximum volumes and their relative targets from intranasal delivery of substances to mice and rats.
Being a larger animals, rats may tolerate slightly larger volumes than mice. If larger volumes are required, specific justification must be made within the application to the AEC for approval.

	Conscious rodent	Anaesthetised rodent

Maximum volume, via intranasal delivery	20uL total (10uL to each nares)	50uL (25uL to each nares)
Target site of delivery (generalised)	Upper airway and central nervous system (small volumes)	Lower airway (larger volumes)

VII. BIBLIOGRAPHY

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Conditions:

- Investigators named in an animal ethics application, relative to this SOP, must be competent to implement the SOP
- Any variation to this SOP must be described in the relevant animal ethics application
- If this SOP has not been reviewed and approved by a UQ AEC within the last three years it is no longer valid and cannot be used in animal ethics applications until reapproved (see "AEC Reviewed/Approved" date in this document's header).