

IACUC Guidelines

Routes of Administration Guidelines: for Research and Teaching Animals

IACUC #: N/A

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A. PURPOSE

This document aims to guide personnel administering substances to laboratory animals on an approved protocol. It is the responsibility of the researcher and IACUC to ensure that substance administration techniques are performed with the least pain and distress to the animal, while meeting the needs of the experiment. Route of administration, intervals between substance administration, range and volume of doses of medications or drugs should be listed on the approved protocol.

B. DEFINITIONS/ Abbreviations

- **Parenteral:** Administration of substances outside the gastrointestinal tract (that is not through the mouth of alimentary canal). Specific considerations for parenteral routes should be:
 - Isotonic substances- should be the same concentration of solute as the blood
 - Close to physiologic pH (6.8-7.2). If outside this range, should be administered through central vessel (jugular or femoral vein) or buffered to appropriate pH.
 - Sterile, endotoxin free and delivered aseptically
- a. Intramuscular (IM)- into the muscle
- b. Intravenous (IV)- into venous circulation
- c. Intradermal (ID)- into the dermis
- d. Transdermal/ percutaneous- into the skin for systemic effect
- e. Topical- applied onto the skin
- f. Intraperitoneal (IP)- into the abdominal cavity
- g. Subcutaneous (SQ or SC)- into the subcutaneous space
- h. Intra-tracheal (IT)- into the trachea
- i. Intranasal (IN)- into the nostril/s

- j. Intracranial- into the brain
 - k. Epidural (ED)- into epidural space
 - l. Intrathecal (IT)-into subarachnoid space (not within the spinal cord)
 - m. Retro-orbital (RO)- into ophthalmic venous sinus or plethys
- **Enteral:** administration of substances into the gastrointestinal tract. Specific considerations for enteral routes include:
 - If voluntary consumption - mix with daily diet, flavored water or other palatable substance to encourage consumption
 - Ensure maintenance of appropriate daily caloric intake, and habituate animals to any novel foods before adding in the drug or medication
- a. Per os (PO)- by mouth
 - b. Gavage- via a tube or feeding needle through the nose or mouth into the esophagus or stomach
 - c. Rectal- into the rectum
- **Bolus:** administering a large volume of a substance by injection (less than 1 minute).
 - **Infusion:** administration of substance over time (more than 5 minutes) depending on the drug or diluent.

C. NEEDLE SIZE, MAXIMUM VOLUMES TO BE ADMINISTERED and EXTRA CONSIDERATIONS

The following table provides guidance on administration of substances' dose volumes. If different species are being used, please follow up with OLAC and the Attending Veterinarian. If the volumes noted are to be exceeded, consult with the Attending Veterinarian for further guidance. Dose ranges and volumes are to be approved by IACUC.

ROUTE	MOUSE	RAT	NOTES
IV bolus (~1min)	1-5ml/kg	1-5ml/kg	-large volumes to animal's blood supply may cause hemo-dilution, changes in acid-base balance, potential increase in respiratory and heart rate, as well as diuresis and potential pulmonary edema -for slow injections or continuous infusions, a butterfly needle or indwelling venous catheter is advised -common IV sites in rodents: lateral tail vein, saphenous vein, retro-orbital venous sinus
IV infusion (max rate 3ml/min)	2-4ml/kg/hr	2-4ml/kg/hr	
Needle size	25-28G	23-27G	
IM needle size	0.05-0.1ml/site 25-30G	0.05-0.2ml/site 25-30G	-animals should be properly restrained -irritating substances may cause tissue necrosis and/or pain at injection site -smallest possible volume should be used, since volume can physically distend the muscle and

			<p>force the substance into fascial or subcutaneous space</p> <ul style="list-style-type: none"> -minimum number of sites should be used per day, sites should be rotated; muscle atrophy and nerve damage are possible -rodents, use gluteal or quadriceps muscle -large animals, use gluteal, quadriceps, biceps or epaxial muscles -avoid the sciatic nerve- can result in paralysis and localized muscle necrosis
IP needle size	1-10ml/kg 25-30G	1-10ml/kg 23-27G	<ul style="list-style-type: none"> -administered into lower abdominal quadrants. -aspirate before injections to avoid inadvertent administration into bladder or gastrointestinal tract. -repeated daily IP dosing up to one month can be well tolerated in rodents. Alternate sides of the abdomen. -Administering irritating substances may cause ileus and peritonitis.
ID needle size	0.05-0.1ml/site 25-30G	0.05-0.1ml/site 25-30G	<ul style="list-style-type: none"> -Tent the skin, hold syringe parallel to the animal, direct the needle into dermis. Aspirate, then inject. -Inadvertent SQ administration is not uncommon.
PO gavage needle size	5-20 ml/kg 18-24G	5-20ml/kg 18-20G	<ul style="list-style-type: none"> -Gavage needle or tube size should be appropriate for the species and size of the animal. -Tubing or Needle should have a rounded tip to prevent sharp edges from causing trauma
SC needle size	1-40ml/kg 25-27G	5-20ml/kg 25-27G	<ul style="list-style-type: none"> -Tent the skin, hold syringe with needle parallel to animal, direct needle into the SQ. Aspirate, then inject. -should be done no more than 3 sites per day -not >1ml per site in mice; not >5ml per site in rats -Rate of absorption may be slower than with other parenteral routes
RO Needle size	150ul (max one/eye) 25-30G	n/a	In anesthetized mice, with topical ophthalmic anesthetic
IT	75ul (max)	75ul (max)	
IN	0.03-0.05 ml/inj	0.03-0.05ml/inj	Care for proper administration to avoid aspiration pneumonia, suffocation, inaccurate dosing due to sneezing

Abbreviations G: gauge

Reference: Diehl KH, Hull R, Morton D et al: A Good Practice Guide to the Administration of Substances and Removal of Blood, Including Routes and Volumes. J Appl Toxicology 21: 15-23, 2001.

D. ADDITIONAL CONSIDERATIONS

- These guidelines apply to normal healthy animals. For dehydrated, aged, neonatal, or sick animals or for more guidance, please contact the veterinary staff.
- Both the substance and the associated vehicle must be appropriate for the species, route of administration, and purpose of the experiment.

- The smallest possible needle size (highest gauge) should be used, while accounting for the dose volume, species, route of administration, viscosity, and speed of injection, to limit the amount of trauma to the surrounding tissue.
- Needles and syringes used for parenteral injection must be from a sterile source and should be limited to one needle use per animal. Use of the same needle on multiple animals can spread infection and lead to adverse outcomes.
- Re-use of single-use supplies (needles/ syringes), must be described and approved on the IACUC protocol. If done, a single, initially sterile needle may be used for IP, SQ, or IM to five rodents from any single cage. Additionally,
 - The same product is to be used for all injections
 - Any damaged or blunted needles are to be discarded
 - If any blood or other fluids is aspirated into the needle, it is to be discarded
- Once a needle is inserted into an animal it should not be re-inserted into stock container of solution.
- Substances should be room or body temperature prior to administration, especially when large volumes are to be delivered.
- Syringes should be of the locking type in order to prevent accidental dislodgement which may result in autoinoculation or back spray.
- Used needles and syringes must be disposed of properly and needles should not be re-capped before discarding
- Subcutaneous implants including microchips and osmotic pumps must be sterilized prior to implantation.
- Prior to parenteral injection, the injection site should be free of visible contamination. The intended injection site may require preparation including shaving and skin disinfection.
- When using animals for training exercises, it is recommend to use the minimal volume necessary for each procedure.