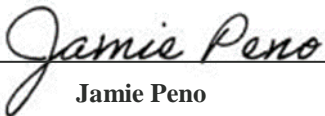
 <div> <div>DIVISION OF RESEARCH & INNOVATION</div> <div>Research Integrity & Compliance</div> </div>		Institutional Animal Care and Use Committee Standard Operating Procedures	
Title: Routes of Administration			
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REVISION HISTORY			
Date	Section	Author	

PURPOSE

This procedure is intended to provide guidelines about administration of substances to laboratory animals. All procedures must have prior IACUC approval. The route of administration, intervals between substance administration, dose range, and volume to be administered should be carefully chosen and listed in the approved protocol specific to each study.

SCOPE

It is the responsibility of the Principal Investigator to consult with Veterinary Staff to ensure the appropriate methods and routes of administration are described in their approved animal use protocols.

It is the responsibility of the Principal Investigator to ensure staff have appropriate training in the methods and routes of administration as they pertain to their approved protocols.

DEFINITIONS AND ABBREVIATIONS

UNT- University of North Texas, Denton

IACUC- Institutional Animal Care and Use Committee

NPGS(s)- Non-Pharmaceutical Grade Substance(s)

SOP/SOP's- Standard Operating Procedure(s)

AUP- Animal Use Protocol

PI- Principal Investigator

AV- Attending Veterinarian

PROCEDURES

I. Parenteral Administration of Substances

A. These routes administer substances outside of the gastrointestinal tract.

1. Substances administered parenterally should be isotonic (the same concentration of solute as the blood) and close to physiologic pH (6.8 – 7.2). If the pH is outside of the physiologic range, administer the substance through a central vessel (such as the jugular or femoral vein) or buffer the solution such that pH is appropriate.
2. All substances given parenterally must be sterile and should be delivered aseptically. If the preparation is not a commercially manufactured solution, it must be mixed in a laminar flow hood or biosafety cabinet and filtered through a 0.2-micron filter.
3. Routes of parenteral administration are listed below.
 - a) Intravenous (IV) – administration of substances into venous circulation.
 - i. Substances can be administered as a bolus or as an infusion. Infusions are often administered with specific equipment (precision pumps or microdrip infusion sets).
 - ii. Substances must be free of particulates that may induce foreign body emboli; and minimally irritating to vascular endothelia, to prevent vasculitis and thrombosis, and to erythrocytes, to minimize lysis
 - iii. Site selection for venous access is species-specific. The following are common sites:
 - (i) Rodents: lateral tail vein, saphenous vein, or retro-orbital venous sinus (injection volume for retro-orbital injection is limited to 200 µl)
 - (ii) Rabbits: lateral ear, jugular, or cephalic vein
 - (iii) Other larger species: jugular, cephalic, femoral, or saphenous vein
 - (iv) Consult with veterinary staff for recommendations on refinements to improve animal comfort during repeated IV dosing.
 - b) Intraperitoneal (IP) – Administration of substances into the abdominal cavity.
 - i. Injections are administered into lower abdominal quadrants. Aspirate before injecting to avoid inadvertent administration into the bladder or gastrointestinal tract.
 - ii. Repeated daily intraperitoneal dosing for up to one month is well-tolerated in rodents. Doses should be administered to alternating sides of the abdomen.
 - iii. Administration of irritating substances may cause ileus (stasis of the gastrointestinal tract) and peritonitis (inflammation of the abdominal cavity).
 - iv. This route is not recommended for rabbits.
 - c) Topical (epicutaneous) – The application of substances directly to the skin for topical effect.
 - i. Avoid application of caustic or irritating substances unless you have prior approval on an IACUC protocol.
 - ii. Apply substances to skin that is unbroken and free of hair.
 - iii. Avoid application of substances to sites that animals can reach during grooming.
 - d) Transdermal (percutaneous) – The application of substances directly to the skin for systemic effect.
 - i. Transdermal dosing is typically accomplished by application of a patch impregnated with the substance of interest.
 - ii. Apply the patch so as to avoid inadvertent ingestion or removal by the animal.
 - iii. Systemic absorption is not immediate. Patches should be applied prior to the time of anticipated need according to manufacturer's instructions.
 - iv. Do not cut patches to reduce dose size. If an appropriate dose of patch is not

commercially available, consider an alternative route of administration or cover the un-needed portion with surgical tape.

- e) Subcutaneous (SC) – Administration of substances into the subcutaneous space.
 - i. Tent the skin. Holding the syringe parallel to the animal, direct the needle into the subcutaneous tissue (beneath the skin). Aspirate and inject.
 - ii. When administering large volumes subcutaneously, 2-3 different sites of administration should be used
 - iii. The rate of absorption from the subcutis may be slower than with other parenteral routes.
 - iv. Subcutaneous infusions can be administered with the use of an oily depot or osmotic mini-pump. Consult veterinary staff for additional information.
- f) Intradermal (ID) – Administration of substances into the dermis.
 - i. Use a small, sharp needle (25-27G).
 - ii. Tent the skin. Holding the syringe parallel to the animal, direct the needle into the dermis. Aspirate and inject. A “bleb” should be visible if the substance is in the intradermal tissue.
 - iii. Inadvertent subcutaneous administration is common. Consult ARC veterinary staff for assistance or training.
- g) Intramuscular (IM) – Administration of substances into the muscle.
 - i. IM dosing is best used in larger species with greater muscle mass and is not recommended in rodent species.
 - ii. In smaller animals, use the gluteal or quadriceps muscles.
 - iii. In larger animals, use the gluteal, quadriceps, biceps, or epaxial muscles.
 - iv. Take care to avoid the sciatic nerve, which runs along the caudal aspect of the femur.
 - v. Inadvertent injection into nerves can result in paralysis and localized muscle necrosis.
- h) Intranasal (IN) – Administration of substances into the nose.
 - i. May (often) require(s) sedation or anesthesia.
 - ii. May be used for local or systemic delivery of substances.
 - iii. Due to high vascularization of nasal mucosa, results in rapid absorption.
 - iv. Always use the smallest volume possible to avoid suffocation
- i) Intraosseous (IO) – Administration of substances into the marrow of a bone.
 - i. Generally requires sedation or anesthesia.
 - ii. Substances must be delivered aseptically and be free of particulates.
 - iii. Can be used in some hypovolemic patients with inaccessible or collapsed veins.
 - iv. IO administration of substances requires highly trained personnel. Consult with veterinary staff before attempting this technique.
- j) Intratracheal (IT) – Administration of substances within the trachea to deliver substances to the lungs.
 - i. Requires sedation or anesthesia.
 - ii. Requires familiarity of intubation of the species being used.
- k) Intracranial – Administration of substances into the brain.
 - i. Intracranial injections require anesthesia (and stereotactic equipment when appropriate). Injections can be administered through a surgically implanted cerebral cannula, direct injection, or an osmotic pump catheter.
 - ii. Animals must be heavily sedated or anesthetized for cannula or catheter placement and for direct injections
- l) Epidural (ED) – Administration of substances into the epidural space.
 - i. Epidural administration of substances requires highly trained personnel.

- Consult with veterinary staff before attempting this technique.
- ii. Animals must be heavily sedated or anesthetized.
- m) Intrathecal (IT) – Administration of substances into the subarachnoid space (in the spinal canal but not within the spinal cord).
 - i. Intrathecal administration of substances requires highly trained personnel. Consult with veterinary staff before attempting this technique.
 - ii. Animals must be heavily sedated or anesthetized.
- n) Inhalation (INH) – Administration of substances into the lungs.
 - i. Inhalational delivery typically uses vapors or aerosols of nebulized particles in solution.
 - ii. Animals are conscious with this delivery method and are restrained with or without a specialized nose mask to optimize delivery.
 - iii. Complex technique requiring specialized equipment and knowledge. If vapor chambers are used, the investigator must contact ARC and EHS staff prior to use to ensure correct installation for animal and human safety.

II. Enteral Routes of Administration of Substances

A. This route administers substances into the gastrointestinal tract.

1. Routes of enteral administration are listed below:
 - a) Per os (PO) – Administration of substances by mouth through voluntary consumption.
 - i. Substances are typically mixed with the daily diet, flavored water, or other palatable items to encourage consumption.
 - ii. Care should be taken to maintain an appropriate daily caloric intake and to habituate animals to any novel food items before adding drugs.
 - iii. Care should be taken to ensure animals consume all agent offered. Laboratory personnel are responsible for ensuring that food and water intake is adequate.
 - iv. Food or water containing additives should be clearly labeled and disposed of properly.
 - b) Gavage – Administration of substances via a tube that is passed through the nose or mouth into the esophagus or stomach.
 - i. Gavage is often used to administer an exact PO dose.
 - ii. The anatomy of the pharynx in the rabbit and guinea pig species makes gavaging difficult
 - iii. Administration of gavage volumes greater than 5 ml/kg may cause distress in species that are unable to vomit such as rodents, rabbits, chinchillas, etc.
 - iv. The gavage tube size should be appropriate for the species being dosed. Contact veterinary staff for assistance.
 - c) Rectal – Administration of substances into the rectum.
 - i. This technique is not frequently used in laboratory animals.
 - ii. Substances can be administered via an enema or a suppository.

REFERENCES

1. The Guide for the Care and Use of Laboratory Animals.
2. Animal Welfare Act
3. Turner PV, et al. 2011. Administration of substances to laboratory animals: Routes of administration and factors to consider. JAALAS. 50(5): 600-613.
4. Turner PV, et al. 2011. Administration of substances to laboratory animals: Equipment considerations, vehicle selection, and solute preparation. JAALAS. 50(5): 614-627
5. Content adapted from University of Texas at Austin procedure: Guidelines for Use of Drugs and Chemicals in Animal Research

APPENDICES

IACUC Standard Operating Procedures