Subject: Policy for Substance Administration and Blood Collection

IACUC 03/09/20

Source: Institutional Animal Care and Use Committee (IACUC)
Effective Date: 03/09/20
Replaces: 11/13/17
Applies to: Personnel involved in research or teaching studies involving animals
Reference: Animal Welfare Act; PHS Policy on Humane Care & Use of Laboratory Animals; Guide for the Care & Use of Laboratory Animals

Introduction

The Institutional Animal Care and Use Committee (IACUC) maintains oversight review for federally mandated rules and regulations with regard to animal research, ethics, misconduct and biomedical research for the University of Colorado Denver | Anschutz Medical Campus (UC Denver | Anschutz).

Policy Statement

This policy is intended to provide guidance and parameters for the administration of substances and establish limits on safe blood collection in laboratory animal species.

Maximum Injectable Volumes by Route of Injection in Adult Animals*

Species	IP	IM	SC	IV	ID	ROS
Mouse	2 mL	0.05 mL	3 mL	0.2 mL	N/A	0.15 mL
Rat	5 mL	0.1 mL	5 mL	0.5 mL	0.05 mL	N/A
Guinea Pig	10 mL	0.3 mL	5 mL	0.5 mL	0.1 mL	N/A
Hamster	4 mL	0.1 mL	3 mL	0.3 mL	0.05 mL	N/A
Gerbil	3 mL	0.1 mL	3 mL	0.3 mL	0.05 mL	N/A
Rabbit	50 mL	1.5 mL	100 mL	5.0 mL	0.1 mL	N/A

(Abbreviations: IP=intraperitoneal; IM=intramuscular, SC=subcutaneous; ID=intradermal; IV=intravenous, ROS = retro-orbital sinus)

* Volumes listed above are based on the administration of isotonic saline. Experimental compounds that vary in osmolarity, viscosity, pH, etc. may not be appropriate at the volume listed above. All administered substances will be reviewed by the IACUC at the time of protocol review.

Common Parenteral (Inject or Infusion) Routes of Administration

Mouse: IP, IM, SC, IV, ROS
Rat: IP, IM, SC, IV, ID
Guinea Pig: IP, IM, SC, IV, ID
Chinchilla: IP, IM, SC, IV, ID
Hamster: IP, IM, SC, IV, ID
Gerbil: IP, IM, SC, IV, ID
Rabbit: IP, IM, SC, IV, ID
Cat: IM, SC, IV
Pig: IM, SC, IV
Sheep: IM, SC, IV

(Abbreviations: IP=intraperitoneal; IM=intramuscular, SC=subcutaneous; ID=intradermal; IV=intravenous, ROS = retro-orbital sinus)

Common Venous Access Points for Injection or Blood Collection
Mouse: submandibular vein, submental vein, retro-orbital sinus, lateral saphenous vein, lateral tail vein, tail tip snip (< 0.5 mm) and scab removal
Rat: sublingual vein, jugular vein, retro-orbital sinus, lateral saphenous vein, lateral tail vein
Hamster: jugular vein, retro-orbital sinus, lateral saphenous vein
Gerbil: jugular vein, retro-orbital sinus, lateral saphenous vein, lateral tail vein
Guinea pig: jugular vein, lateral metatarsal vein
Chinchilla: jugular vein, cephalic vein, lateral saphenous vein
Rabbit: jugular vein, cephalic vein, lateral saphenous vein, lateral ear vein, central ear artery
Cat: jugular vein, cephalic vein, medial saphenous vein, ear tip prick
Pig: jugular vein, cephalic vein, medial saphenous vein, peripheral ear vein
Sheep: jugular vein, cephalic vein, medial saphenous vein, peripheral ear vein

Blood Collection Volumes
The total blood volume in an adult mammalian laboratory animal species is approximately 7% of body weight. The volume of blood that can be removed at one collection should not exceed 10% of total blood volume without further care. [Example: 25 g mouse = 0.175 mL, 200 g rat = 1.4 mL, 75 g hamster = 0.52 mL, 4 kg rabbit = 28 mL].

- 15% of blood volume can be removed at one time if collected slowly, and warm replacement fluids are administered SQ, IP, or IV to replace the blood volume collected.
- For repeated blood sampling, up to 7.5% of the total blood volume can be taken per week, or 10% of the total blood volume may be removed every two weeks.
- To collect blood at a more frequent interval or in larger volumes, a higher level of physiologic monitoring will be required, and approved by the Institutional Animal Care and Use Committee.

Oral Administration (ORL, PO, Per os)
Commonly performed with non-sterile solutions in all species. Experimental compounds should not be caustic to mucus membranes. Confirmation of complete consumption is difficult using this route.

Oral-Gastric Gavage
Oral gavage is the administration of fluids directly into the lower esophagus or stomach using a feeding needle introduced into the mouth and threaded down the esophagus. Feeding needles can be made of plastic or stainless steel.

- Stainless feeding needles are autoclavable, and thus reusable. They have a stainless steel ball-tip that makes them atraumatic on delicate oral and esophageal tissues and reduces the chance of introducing the ball-tip into the trachea.
- Plastic feeding needles are typically pliable (bend) and disposable. Plastic models also have a rounded plastic tip to decrease trauma. Typically, plastic models can only be used for a limited number of animals before cuts from teeth make the shaft friable and rough which can cause irritation to the oral cavity and esophagus.
- The guideline for volume of administration are:
    - 10 mL/kg (10 uL/g) body weight for mice

    - 20 mL/kg (20 uL/g) body weight for rats.
    - Repeated oral gavage in mice and rats should not be repeated more frequently than every 6-8 hours to allow for gastric emptying.
- For information on oral gavage volume limitations in other species, please contact the veterinary staff.

Inhalational Administration

Intranasal (IN) – Administration of fluids or fluid suspensions of particulates into the nasal cavity

- May require anesthesia to facilitate restraint and mitigate sneezing
- Substances should be nonirritating to minimize sneezing and rhinitis
- Systemic absorption is rapid across nasal mucous membranes
- The recommendations for volume of administration are:
    - 30 – 50 µl per nostril for mice and rats

Intratracheal (IT) - Administration of fluids or fluid suspensions of particulates into the trachea via the oral cavity or directly into the lungs by intubation or tracheotomy

- This route of administration requires anesthesia
- Care should be taken to minimize trauma to the tongue and oral structures
- The recommendations for volume of administration are:
    - 50-75 µL per injection for mice
    - 200 µL per injection for rats

Note: IACUC approval for fluid administration and blood collection that falls outside of the above parameters will be reviewed and considered for approval by the IACUC on an individual basis.

References

1. Hrapkiewicz K, Medina L, and Holmes D. Clinical Laboratory Animal Medicine: An Introduction. 2nd Ed. Iowa State Press, 1998.
2. Hawk CT, Leary S, Morris T. Formulary for Laboratory Animals. 2nd Ed. Iowa State University Press, 1999.
3. Wolfensohn S, and Lloyd M. Handbook of Laboratory Animal Management and Welfare. 2nd Ed. Blackwell Science, 1998
4. Hulin M. et al. Laboratory Animal Data: Quick Reference Guide For Researchers. American Association of Laboratory Animal Science, 2002.
5. www.citiprogram.org; downloaded 9/22/2010
6. www.aalaslearninglibrary.org; downloaded 10/4/2010
7. Turner PV, Brabb T, Pekow C, Vasbinder MA. 2011 Administration of Substances to Laboratory Animals: Routes of Administration and Factors to Consider. *Journal of the American Association for Laboratory Animal Science*. 50(5): 600-613.
8. Morton DB. 2001 Refining Procedures for the Administration of Substances. *Laboratory Animals*. 35(1): 1-41.
9. Driscoll KE, et al. 2000 Intratracheal Instillation as an Exposure Technique for the Evaluation of Respiratory Tract Toxicity: Uses and Limitations. *Toxicological Sciences*. 55(1): 24-35.
10. Costa DL, Lehmann JR, Harold WM, Drew RT. 1986 Transoral Tracheal Intubation of Rodents Using a Fiberoptic Laryngoscope. *Laboratory Animal Science*. 36(3): 256-261.