

Washington State University
Institutional Animal Care and Use Committee

Guideline #10: Drug and Chemical Administration

Approval Date: 8/15/23 (Last approved 11/8/2019)

A. Purpose

The purpose of this policy is to provide researchers with the daily acceptable volumes of fluids or compounds that may be administered to animals. These guidelines apply to healthy, adult animals. When immature or debilitated animals are used, the veterinary staff must be consulted.

B. Background

The administration of excessive dose volumes may produce pain, excitement, and altered physiological parameters (e.g., serum electrolyte imbalance, increased blood pressure, and increased respiratory rate), and cause abnormal compound absorption.

C. Guideline

The following table provides acceptable maximum and absolute maximum daily cumulative volumes in mL/kg body weight for route of administration, unless otherwise specified.

Acceptable **maximum volumes** of administration are **bolded**. These are routine, **acceptable volumes of administration** that typically can be given multiple times to the same animal.

For select species and routes of administration, *absolute maximum* volumes are *italicized* and provided in parenthesis. These *absolute maximum volumes* denote less frequent administration such as one-time dosing.

These volume guidelines must be followed unless otherwise specified in your approved IACUC protocol.

| Species | Oral Gavage* (ml/kg) | SC* (ml/kg) | IP * (ml/kg) | IM* | IV bolus* (ml/kg) |
|--------------------------|--|-------------------------------|---|---|---|
| Mouse | 10 (20) | ≤1-2 mls ^b (40) | 5-10 (20) | 0.05 ^{a,b} (0.1) ^{a,b} <i>Note: this route is not recommended in this species</i> | 5 (25) |
| Rat Hamster Gerbil | 10 (20) | 5-10mls ^b (10) | 5-10 (20) | 0.1 ^{a,b} (0.2) ^{a,b} <i>Note: this route is not recommended in this species</i> | 5 (20) |
| Rabbit | 10 (15) | 1 (2.5) | 5 (10) | 0.25 ^c (0.5) ^c | 2 (10) |
| Guinea Pig | 10 (20) | 5 (10) | 10 (20) | 0.1 ^{a,b} (0.2) ^{a,b} | 1 (5) |
| Ferret | 10 (15) | 2 (5) | 5 (20) | 0.25 ^c (0.5) ^c | 5 (10) |
| Dog | 5 (15) | 1 (2) | <i>Note: this route is not recommended in this species</i> | 0.25 ^c (0.5) ^c | 5 (10) |
| Cat | 10 (15) | 2 (5) | <i>Note: this route is not recommended in this species</i> | 0.25 ^c (0.5) ^c | 5 (10) |
| Swine | 20 | 5 | 10 | 5 ^{b,d} | 5 |
| Sheep/ Goats | 20 | 5 | <i>Note: this route is not recommended in this species</i> | 5 ^{b,d} | 5 |
| Bovine | 20 | 5 | <i>Note: this route is not recommended in this species</i> | 10 ^{b,d} | 5 |
| Horses | | | <i>Note: this route is not recommended in this species</i> | 10 ^{b,d} | |
| Birds (domestic fowl) | 5 | 5 | 10-15ml total per injection (midline, halfway between cloaca and sternum) <i>Note: this route is not recommended in this species</i> | 1-2 ml Total per injection pectoral muscles; divided into multiple sites | 2-3 ml Total per injection (brachial vein) |
| Fish | 2 g/kg | 1 | (10) | (0.05) ^b | 5 |
| Frogs | <i>Note: this route is not recommended in this species</i> | 1 | (10) | (0.05) ^b | 5 (2) |

^a Generally, no more than two intramuscular sites should be used per day, but there may be reasonable exceptions such as for larger species and only when specified in an approved ASAF.

^b Volumes in mls per site

^c *Intramuscular injections should not exceed the following total volumes of injections by species: rabbit, cat, ferret ≤ 1 ml, ; dogs ≤ 3 mls*

^d *Intramuscular injections should not exceed the following total volumes of injections by species: sheep, goats, pigs ≤ 5 ml; horses, cattle ≤ 10 ml*

D. Additional routes, techniques, and volumes of administration:

1. Epidural, intrathecal and intracranial
 - i. Epidural, intrathecal or intracranial should only be performed on heavily sedated animals and by staff trained in these techniques. Epidural, Mammals: 0.15-0.2 ml/kg (6 ml total volume in animals up to 35kg)
Intrathecal, Mammals: 0.075-0.1 ml/kg
 - ii. Intracranial requires additional equipment, training, and specific considerations, please consult Campus Veterinary Services for guidance.
2. Intranasal and intratracheal
 - i. Intranasal should be split into two or more aliquots and administered in alternating nostrils, with a break between each nostril.
 - ii. Maximum intranasal volume per day
Adult rodents: 0.020 - 0.025 ml per nostril
Adult dogs, cats, rabbits, ferrets, swine: 0.1-0.25 ml per nostril
 - iii. Maximum intratracheal volumes:
Adult rodents: 0.5 ml per animal
Adult rabbit: 0.2 ml per animal
3. Intradermal
 - i. Maximum dose for all species is 0.05-0.1 ml/site.
4. Retro-orbital
 - i. Maximum values: adult mice 0.15ml; neonatal mice 0.01 ml
5. Rectal
 - i. Maximum value: mouse <0.5 ml
6. Intraosseous
 - i. Maximum value: mouse 0.20 ml, rat and guinea pig 0.5 ml, rabbit 1-5 ml
7. Footpad Injections
 - i. Acceptable maximum volume of injection is 0.05 ml intradermally into the footpad for mice and up to 0.1 ml intradermally into the footpad for rats.
 - ii. Application of isopropyl alcohol or other appropriate disinfectant over the injection site is recommended.

- iii. Because of prehension of food and manipulation of other environmental implements with the front feed, footpad injections should only be performed in the hind feet.
- iv. Footpad injections should be limited to only one foot to allow for compensatory used of the unaffected contralateral limb.
- v. Multiple injections must be scientifically justified and previously approved in the protocol with an interval of at least 2 weeks between each injection.
- vi. It is recommended that injected animals are housed on soft bedding (ex. ALPHA-Dri, or Diamond Soft).
- vii. It must be ensured that animals are able to reach food and water and the animals are monitored daily for pain or distress.

Procedure

1. For values noted as ml/kg, multiply the appropriate number above times the animals body weight in kg to obtain the acceptable or absolute maximum volume of administration.
2. In addition to the volume of administration, one must also consider the character of the solution. Known irritants such as Freund’s adjuvant must be delivered according to specific approved guidelines.
3. Solutions above pH 8.0 and below 4.5 should be diluted or buffered when given for routes other than intravenous.
4. Injectable products should be formulated as isotonic solutions (osmolality of about 300 mOsm/kg).
5. The highest gauge (smallest) needle size appropriate for volume and material delivery should always be selected. Dull needles use can contribute to pain and discomfort. Best practice is to use one new needle per animal.

If you have any questions about this guideline, need training in one of the above methods, or need the information regarding a species not listed above, please call the Office of the Campus Veterinarian at 509-335-6246 or email at or.ocv.alert@wsu.edu.

| *Abbreviation | Expanded Word |
|----------------------|----------------------|
| PO | Per os (Oral Gavage) |
| SQ | Subcutaneously |
| IP | Intraperitoneal |
| IM | Intramuscular |
| IV | Intravenous |

D. References

1. Diehl, K., et al. 2001, A Good Practice Guide to the Administration of Substances and Removal of Blood, Including Routes and Volumes, *J Appl Toxicol* 21:15-23.
2. Iwarsson K, Lindberg L, Waller T (1994) Common non-surgical techniques and procedures. Chapter 16. Svensen P, Hau J (eds). *Handbook of Laboratory Animal Science*. Volume 1. CRC Press, Inc. Boca Raton, FL
3. *Guide for the Care and Use of Laboratory Animals* 8th edition, 2011 (the Guide) <http://grants.nih.gov/grants/olaw/Guide-for-the-care-and-use-of-laboratory-animals.pdf>
4. Turner, P. et al. 2011, Administration of Substances to Laboratory Animals: Routes of Administration and Factors to Consider, *American Association for Laboratory Animal Science*, Volume 50, 5:600-613
5. Turner, P. et al. 2011, Administration of Substances to Laboratory Animals: Equipment Considerations, Vehicle Selection and Solute Preparation, *American Association for Laboratory Animal Science*, Volume 50, 5:614-627
6. <https://research.ucdavis.edu/wp-content/uploads/IACUC-50.pdf>
7. <https://www.bu.edu/research/forms-policies/administration-of-drugs-and-experimental-compounds-in-mice-and-rats-iacuc/>
8. <http://www.usp.br/bioterio/Artigos/Procedimentos%20experimentais/Routeadministration-4.pdf>