



# Indiana University

Office of the Vice President for Research  
Office of Research Compliance

## Institutional Animal Care and Use Committee (IACUC) Office of Research Compliance (ORC)

---

# IACUC Policy for Dose Volumes in Laboratory Animals

### FULL POLICY CONTENTS

Policy Statement  
Reason for Policy  
Procedures  
Sanctions  
Contacts

#### ADDITIONAL DETAILS

References

**Effective:** May 23, 2017  
**Last Updated:** --

**Responsible University Office:**  
*Fred H. Cate*  
*Vice President for Research*

**Policy Owner:**  
*Bloomington Institutional Animal Care and Use Committee*

**Policy Contact:**  
*IACUC Administrator*

---

## Policy Statement

This document is designed to provide information about the volume or amount of a substance to be given to laboratory animals depending on route of administration. All procedures must be approved by the Institutional Animal Care and Use Committee (IACUC). The method of administration to be performed, the intervals between substance administration, and the volume to be given must be listed in the approved protocol specific to each study. Contact the LAR office (ext. 5-2356) or email [lar@iu.edu](mailto:lar@iu.edu) if training is needed on these techniques.

---

## Reason for Policy

In conducting studies that utilize laboratory animals, various compounds or substances may be administered to the animal to observe its response to the treatment. Table 1 provides ideal maximum dose volumes to be used by species and route (the bolded numbers). The guidelines also provide an indication of the maximum volume that may

be administered to an animal by route. If dosing beyond the recommended volume up to the maximum volume, IACUC approval **must** be obtained before dosing.

## Procedures

### Abbreviations Used in Tables 1 and 2:

Orally (**PO**)- per os- given by mouth alone or in food or water  
 Intra-gastric- given via a gastric gavage needle for rodents or stomach tube for larger species  
 Intravenous (**IV**)- administered through a blood vessel directly into the blood stream  
 Subcutaneous (**SC**)- administered under the skin  
 Intradermal (**ID**)- administered directly into the dermal layer of skin  
 Intramuscular (**IM**)- administered into the muscle  
 Intraperitoneal (**IP**)- administered into the abdomen for exposure by the peritoneal cavity and lymphatic system  
 Intranasal (**IN**)- administered into the nose  
 Intratracheal (**IT**)- administered into the trachea

Please use the following volumes (in bold) for the maximum dose volumes and routes of administration.

**Table 1: Maximum Volumes to be used for dosing of species by route of administration (All volumes are ml/kg unless otherwise noted)**

Species	PO gavage/intra-gastric	IV* (bolus)	IV** (ml/kg/h)	IP <sup>@</sup>	SC <sup>@</sup>	IM <sup>***@</sup>	IN <sup>***</sup> IT <sup>***</sup>	ID <sup>***</sup>
Mouse	<b>10</b> (20)	<b>5</b> (10)	<b>1</b> (4)	<b>10</b> (20)	<b>5</b> (20)	<b>0.03</b> (0.05) <sup>§</sup>	<b>0.05</b>	<b>0.05</b> (0.1)
Rat	<b>10</b> (20)	<b>5</b> (10)	<b>1 or 2</b> (4)	<b>10</b> (20)	<b>5</b> (10)	<b>0.1</b> (0.2) <sup>§</sup>	<b>0.1</b>	<b>0.05</b> (0.1)
Hamster	<b>10</b> (20)	<b>5</b> (10)	--	<b>10</b> (20)	<b>1</b> (10)	<b>0.05</b> (0.1) <sup>§</sup>	<b>0.05</b>	<b>0.05</b> (0.1)
Guinea pig	<b>10</b> (20)	<b>1</b> (5)	--	<b>10</b> (20)	<b>5</b> (10)	<b>0.1</b> (0.2)	<b>0.1</b> (0.2)	<b>0.05</b> (0.1)
Rabbit	<b>2</b> (10)	<b>1</b> (5)	<b>1</b>	Not recommended	<b>2.5</b> (10)	<b>0.25</b> (0.5)	<b>0.2</b> (0.5)	<b>0.05</b> (0.1)

**Ideal maximum dose volumes are bolded, absolute maximum dose volumes are (smaller in parenthesis)**

\*An IV bolus injection is typically dosed in less than 1 min.

\*\*Continuous IV infusions are typically dosed over 3-10 minutes. Solution properties such as tonicity, pH, etc. must be taken into account when approaching the volume limits or determining the volume to be infused IV. The recommended working range for pH is 4.5-8.0. The order of degree of tolerance of pH for different dosing routes is oral>intravenous>intramuscular>subcutaneous>intraperitoneal. Animal health must also be taken into consideration, such as kidney function and cardiovascular function. These systems must be normal to handle increased fluid volume.

\*\*\*The values listed in this column are the total volume in ml per site, total of 2 sites/day.

<sup>@</sup>When administering a solution IP, SC, or IM, the viscosity, concentration, tonicity and pH of the solution need to be taken into account.

<sup>§</sup>IM dosing in mice, rats, hamsters and voles is **NOT** recommended.

**Table 2: Recommended locations for administration of substances by listed route of administration**

	<b>Mouse, Rat, Hamster, Voles</b>	<b>Rabbit</b>
<b>PO gavage</b>	Oral, intragastric (gavage needle)	Oral, intragastric (nasopharyngeal tube)
<b>IV</b>	Tail, saphenous	Ear, cephalic
<b>IP</b>	Lower right abdominal quadrant	Not used
<b>SC</b>	Intrascapular, neck, shoulders, flank, lower back	Intrascapular, neck, shoulders, flank
<b>IM</b>	Not recommended	Triceps, quadriceps, dorsal lumbar, semimembranosus, semitendinosus
<b>IN*</b>	Nose	Nose
<b>IT*</b>	Trachea	Trachea
<b>ID</b>	Skin	Skin

*\*Usually requires sedation or anesthesia for administration*

1. The first dose listed in **bold** is the **ideal maximum dose volume**. However, the dose can range up to the second value given in parentheses. Volumes up to or less than the ideal dose volume should be used. Dose volumes should be the minimum compatible with compound formulation and accuracy of administration. **If dose volumes are between the ideal and maximum volumes, this needs to be noted in the protocol along with justification for the higher dose and then approved by the IACUC.**
2. Dosing volumes for **voles** should be the same as for mice.
3. If dosing parenterally toward the maximum quantities listed, ensure that the dosing solution is isotonic, close to physiologic pH (6.8-7.2), stable, not viscous, has appropriate osmolality, biocompatibility, sterility, and does not contain quantities of diluent that could be toxic when dosed. Dosing solutions given parenterally can have a pH range of 4.5-8; however, when given intravascularly, solutions should be administered through a central (jugular v., femoral v., etc.) rather than a peripheral (cephalic v., saphenous v.) vessel. When substances are given by IV infusion, the volume should not exceed 5% of the circulating blood volume over 2 hours or 4 ml/kg/h.
4. The **maximum recommended injection volume** for a dosing solution that is given **rapidly IV is 1 ml/kg body weight** for most laboratory animal species. If dosing a larger quantity of solution is necessary, infusion of the dose IV over greater than 5 minutes should be considered and should not exceed 10% of the circulating blood volume over 2 hours. Rats may be given daily IV injections of isotonic saline at up to 80 ml/kg at 1 ml/min. for 4 days. Intra-arterial administration should be avoided since it can result in blindness, cerebrovascular stroke, permanent motor deficits and limb gangrene.
5. When administering large volumes subcutaneously, 2-3 sites of administration should be used.
6. No more than 2 IM sites should be used per day. In small rodents (mice, voles and hamsters) the IM route is not preferred because of the mouse's small muscle mass and possibility of side effects, such as paresis, paralysis, muscle necrosis, localized muscle sloughing and self-biting of injected areas.
7. The anatomy of the pharynx in the rabbit and guinea pig species makes gavaging difficult. Nasogastric tubes 3-8 French soft rubber pediatric feeding tubes can be

used instead. Please contact LAR to learn about or obtain assistance with this technique.

8. The **smallest volume possible** is recommended for the oral route of administration, 5 ml/kg or less should be administered via the oral or gastric route to avoid gastric distension especially in species unable to vomit (such as rodents). Limitations of oral dosing may include slower onset of action compared with parenteral delivery, potentially significant first-pass effect by the liver resulting in reduced efficacy, lack of absorption due to chemical polarity or interference with absorption by ingesta, poor compliance with voluntary consumption because of poor palatability or local irritation, lack of systemic absorption from the digestive tract, degradation of substances by digestive enzymes and acid, and inability to use this route in animals that are unconscious or have clinically significant diarrhea or emesis.
9. The intraperitoneal (IP) route of administration is **not used in rabbits**.
10. All substances given **parenterally (not by the oral route) must be sterile**. If the preparation is not a commercially manufactured solution, it should be mixed in a laminar flow hood or biosafety cabinet and filtered through a 0.2 µm filter.
11. If a route or species being considered is NOT on this list, please consult the veterinary staff.
12. In all cases, consult the veterinary staff if you have questions about your dosing material, dose route, or technique.
13. The following routes of administration are acceptable but there are no current recommendations on dose volumes. Information may be obtained from the literature or by contacting LAR veterinarians.
  - Epicutaneous/transcutaneous/topical/percutaneous**- delivered onto or across the skin
  - Transcorneal**- administered onto the eye.
  - Intraocular**- administered into the eye
  - Intracerebral** (or other structures of the brain)- administered into the brain
  - Epidural**- administered into the space surrounding the dura mater
  - Intrathecal**- administered into the space surrounding the spinal cord (subarachnoid space)
  - Intraosseous**- administered into the bone marrow cavity
  - Inhalation**- administered into the lungs
  - Enteral**- administered into the mouth, in the diet or food, orogastric or nasogastric gavage, per rectum

## Sanctions

Failure to comply with IACUC policies may result in noncompliance reports to the Institutional Official, the Office of Laboratory Animal Welfare (OLAW), the U. S. Department of Agriculture (USDA), and/or the suspension of animal use privileges. In addition, the availability of sponsored research funds may be affected when an investigator is found to be in violation of these policies.

---

## Contacts

<b>Subject</b>	<b>Contact</b>	<b>Phone</b>	<b>Email</b>
Veterinary Concerns	LAR Veterinarians	855-2356	lar@indiana.edu
Policy	IACUC Administrator	855-5138	buiacuc@indiana.edu

---

## References

1. Bauck L, Bihun C. Basic anatomy, physiology, husbandry and clinical techniques. In Ferrets, Rabbits, and Rodents: Clinical Medicine and Surgery. Hillyer EV, Quesenberry KE Eds. W. B. Saunders Company, Philadelphia, PA, 1997, p. 303.
2. **Diehl KH. et. al. A good practice guide to the administration of substances and removal of blood including routes and volumes. *J. Appl. Toxicol.* 2001 21:15-23.**
3. Donkin H, Zeoli A, Crewell C, Fetrow N, Johnson DK, Kinter LB. A maximal rapid intravenous injection volume in dogs (*Canis familiaris*). Dept. of Biological Sciences, Nycomed, Inc. Wayne PA.
4. Fanton JW, Cosgrove DJ, Golden JG. Gastrin levels and gastric emptying times in rhesus monkeys with a history of acute gastric dilatation. *J. Med. Primatol.* 1995; 24: 243-245.
5. Flecknell PA, Waynforth HG. Experimental and Surgical Techniques in the Rat. Second Ed. Academic Press. San Diego, CA 1992.
6. Fowler JSL, Ruttby DA. Methodological aspects of acute toxicity testing. *ACTA Pharmacol. Toxicol.* 1983; 52(511): 20-30.
7. Gad SC, Spainhour CV, Shoemaker C, et. Al. 2016. Tolerable Levels of Nonclinical Vehicles and Formulations Used in Studies by Multiple Routes in Multiple Species with Notes on Methods to Improve Utility. *International J Toxicol.* Jan. 2016; 1-84.
8. Hawk CT. et. al. Formulary for Laboratory Animals. Third Ed. Blackwell Publishing, Ames Iowa. 2005.
9. Holmberg A, Pelletier R. Automated blood sampling and the 3 r's. NC3R's #16 Automated blood sampling and the 3R's. April 2009: 1-8.
10. Hull Rm. Guideline limit volumes for dosing animals in the preclinical stage of safety evaluation. *Human & Exp. Toxicol.* 1995; 14: 305-307.
11. Joslin JO. Blood Collection Techniques in Exotic Small Mammals. *J Ex Pet Med.* April 2009; 18(2): 117-139.
12. Li P, Zhao L. (2007) Developing Early Formulations: Practice and Perspective. *International J. Pharma.* 341: 1-19.
13. Mann WA, Kinter LB. Characterization of maximal intravenous dose volumes in the dog (*Canis familiaris*). *Gen. Pharmacol.* Mar 1993; 24(2): 357-66.
14. Morton DV, Abbot D, Barclay R, Close BS, Ewbank R, Gask D, Heath M, Mattic S, Poole T, Seamer J, Southee J, Thompson A, Trussell B, West C, Jennings M. Removal of blood from laboratory mammals and birds. First report of the BVA/FRAMWE/RSPCA/UFAW joint working group on refinement, *Lab Animals.* 1993; 27: 1-22.
15. **Morton DB, Jennings M, Buckwell A, Ewbank R, Godfrey C, Holgate B, Inglis I, James R, Page C, Sharman I, Verschoyle R, Westfall L, Wilson AB. Refining procedures for the administration of substances. Report of the BVA/FRAM/RSPCA/UFAW Joint Working Group on Refinement. *Lab Animals.* July 2000; 35: 1-41.**
16. Morton D, Safron JA, Rice DW, Wilson DM, White RD. Effects of infusion rate in rats receiving repeated large volumes of saline solution intravenously. *Lab An Sci.* Dec. 1997; 47(6): 656-59.
17. Recommended Dose Volumes for Common Laboratory Animals. IQ 3R's Leadership Group- Contract Research Organization Working Group.
18. Rowan AN. Refinement of animal research technique and validity of research data. *Fundamental and Applied Toxicol.* 1990; 15: 25-32.
19. Synapse (American Society of Laboratory Animal Practitioners Publication), 24: 1, March 1991.

22. Turner PV, Brabb T, Pekow C, Vasbinder MA. Administration of Substances to Laboratory Animals: Routes of Administration and Factors to Consider. *JAALAS*. Sept. 2011; 50(5): 600-13.
23. Turner PV, Pekow C, Vasbinder MA, Brabb T. Administration of Substances to Laboratory Animals: Equipment Considerations, Vehicle Selection, and Solute Preparation. *JAALAS*. Sept. 2011; 50(5): 614-27.