



OFFICE OF
RESEARCH COMPLIANCE
INDIANA UNIVERSITY

Institutional Animal Care and Use Committee (IACUC)

Use of Anesthesia, Analgesics and Sedatives in Research Animals

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Responsible University Office:
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Policy Owner:
Bloomington Institutional Animal Care and Use Committee (BIACUC)

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Policy Statement

Relief of postoperative pain is mandated by the *Guide for the Care and Use of Laboratory Animals* and the *Public Health Service Policy* and is a major objective of laboratory animal medicine. Animals experiencing more than momentary or slight pain or distress require appropriate sedation, analgesia or anesthesia unless suitable, scientific justification is provided. Assessment of pain and distress in animals can be difficult, challenging and subjective. As such, and in accordance with the *US Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*, unless the contrary is established, it should be considered that procedures that cause pain or distress in humans may also cause similar effects in animals. This policy has been created to provide guidance on the use of analgesics in various procedures including surgery. The Attending Veterinarian is responsible for ensuring that adequate anesthesia, analgesia or sedation is provided.

Reason for Policy

The IACUC has ultimate responsibility for ensuring that pain and distress in research animals is limited to that which is necessary in the course of approved experimentation. This includes review and approval of methods and agents used for prevention and alleviation of pain and distress. Committee decisions on the use of anesthetics, analgesics or sedatives will be based on regulatory requirements as well as advice from the veterinary staff and the Principal Investigator (PI). The IACUC will periodically review (at least every 3 years) protocols that involve pain or distress. The review will specifically assess methods and agents being used and any deviation from this policy. Within this assessment of methods and agents used for prevention of pain and distress, the IACUC also has the responsibility to verify that anesthesia vaporizers actively used in animal research are fully serviced and certified at least every 1-3 years.

Role of the Laboratory Animal Resources (LAR) and Clinical Veterinary Staff

The proposed methods and use of agents to prevent or alleviate pain or distress in experimental animals must have the approval of the veterinary staff. The LAR veterinary staff will review animal care and use protocols to determine if proposed methods and agents for anesthesia and analgesia are appropriate. The veterinarians consult with PI's as needed, to determine appropriate treatments that meet the clinical needs of the animals, while not compromising the scientific integrity of the experiments.

In the event of unanticipated pain or distress that is protocol-associated or arises from spontaneous illness or injury, LAR veterinarians are responsible for determining the cause of pain and then establishing ameliorative therapy consistent with established veterinary medical and nursing procedures. The Attending Veterinarian has authority to make independent emergency decisions concerning the treatment regimen of animals experiencing unalleviated pain or suffering. This authority is delegated to veterinarians overseeing the animals under the IUB Animal Care and Use Program. These animals must be provided with appropriate veterinary care or be humanely euthanized, unless an exception has been justified within an IACUC approved protocol.

Every effort will be made to consult with the Investigator prior to initiating treatment or euthanasia. However, the welfare of the animal will be the primary consideration in all cases.

Role of the Investigator

When animals experience more than momentary or slight pain or distress, the Investigator must provide in the animal care and use protocol a detailed description of how pain or distress will be assessed and how agents will be used to alleviate pain and distress. To meet this requirement, and depending on procedures to be performed, PIs can use a post-operative monitoring scale designed to objectively assess pain or distress in animals and provide precise instruction regarding analgesic use and euthanasia. Post-operative monitoring forms are available on the LAR website for labs to download and edit to suit the surgeon's individual needs. When animals are subjected to major survival surgery, post-surgical analgesia is usually required. If the Investigator seeks to withhold sedatives, analgesics, or anesthetics, or asks to deviate from the

recommendations of the veterinary staff, the PI must provide the IACUC with scientific justification for consideration. Justification should include the rationale or evidence that demonstrates how agents would compromise the scientific aspects of the study. Investigators are highly encouraged to consult with veterinary staff during protocol planning and to reach an agreement about the appropriate use of drugs for controlling pain and distress.

Definitions

Pain: an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

Anesthesia: Total loss of sensation in a body part or in the whole body; induced by a drug that depresses the activity of nervous tissue either locally (peripherally) or generally (centrally).

General anesthesia: a state of unconsciousness and insusceptibility to pain, produced by administration of anesthetic agents by inhalation, intravenously, intramuscularly, rectally or via the gastrointestinal tract.

Local anesthesia: drug acting directly on nervous tissue to block the conductive nerve impulses either at the surface or deeper tissues in contact with the drug so that there is a loss of sensation.

Analgesia: Loss of sensitivity to pain.

Sedative: Substance that produces a mild degree of CNS depression in which the patient is awake but calm; a term often used interchangeably with tranquilization; with sufficient stimuli the patient may be aroused; produces a dose-dependent depression of the cerebral cortex. A sedated animal can still perceive pain.

Procedures: Use of Anesthetics, Analgesics and Sedatives

1. Animal welfare regulations require that experimental procedures involving animals avoid or minimize discomfort, distress, and pain to the animals. If procedures involve more than momentary or slight pain and discomfort to animals, as is often the case in surgery, regulations require the appropriate use of analgesics, unless withholding of such agents is scientifically justified in writing and approved by the Institutional Animal Care and Use Committee (IACUC).
2. The LAR *Anesthesia & Analgesia Guidelines* specified for each species (accessible at <https://lar.indiana.edu/drug-formularies/index.html>) should be consulted prior to submission of the protocol to determine the species-specific recommendations on analgesic use. The above website also offers species-specific behaviors and circumstances indicative of pain and suggesting the need for analgesics. Any questions regarding behavioral signs indicative of pain in a particular species, the choice of agents, dose range, etc. should be directed to the LAR veterinary staff.
3. This IACUC Policy requires that investigators follow the recommendations made in this document and specified in their approved IACUC protocol when performing surgical procedures. Surgical procedures are divided into three categories for the purpose of this document: Type I, II and III.
 - a. **Type I:** Surgical procedures performed with appropriate anesthesia that do not require the use of additional analgesics.

- b. **Type II:** Surgical procedures that require the use of preemptive analgesics. Additional analgesics might also be indicated for postoperative pain relief.
- c. **Type III:** Surgical procedures that require analgesia. Animals must be medicated preemptively and for a minimum postoperative time period as specified in the attached tables, and then as needed by the animal for pain relief.

For each of these categories, the *minimum* analgesic requirements are included in the tables at the end of this document. For surgical procedures where analgesics are required, the investigator can request approval to withhold analgesics but *scientific justification must be provided* to the IACUC. **If the IACUC approves the withholding of analgesics for Type II or III surgical procedures, the procedure will automatically be elevated to Humane Use Category E** meaning it will include procedures that expose animals to pain or distress without administration of appropriate analgesic medications. The procedure(s) will also be included as such in an annual report to the USDA, for species covered by the AWA.

- 4. For the purposes of this document, **preemptive analgesia** is defined as analgesia administered shortly before or immediately after an animal is anesthetized, but prior to initiation of a painful stimulus, such as the skin incision. Some anesthetics also have analgesic properties (i.e.: ketamine/xylazine, neurolept-analgesia, etc.). Additional preemptive analgesia may not be indicated for some procedures or in some species with the use of such anesthetics. Please consult an LAR Veterinarian if you have questions as to the analgesic value of your anesthetic agent.
- 5. If an analgesic approved in the protocol as required by this document appears to be contributing to adverse consequences and a PI wishes to alter the analgesic regimen as a result, the investigator must consult with an LAR veterinarian to discuss possible alteration of the analgesic regimen as specified in the approved protocol.
- 6. A veterinarian can suggest or prescribe that an alternate analgesic be tried without it being listed in the protocol if it is administered under his/her supervision. If the suggestion concerning an alternate analgesic regimen results in a permanent change with regard to the administration of analgesics for the protocol, an amendment must be submitted through the IACUC to include the change in the approved protocol.
- 7. Finally, every effort has been made to include in this document a comprehensive list of the types of surgical and non-surgical procedures frequently performed on research animals at the university. However, the recommendations herein should be considered the minimum acceptable for procedures listed, and veterinarians reviewing protocols may determine a need for analgesics beyond the recommendations of this document based on professional judgment and clinical monitoring of the animal.
- 8. Anytime an animal is administered an anesthetic, whether it is to conduct surgery, to restrain an animal or to prevent an animal from moving so that a procedure can be conducted, the person performing the anesthesia should monitor the animal while it is on supplemental heat until body temperature returns to normal and the animal is sternal and able to ambulate about the cage. If the animal appears to be taking a prolonged time to recover, the body temperature should be taken and a LAR Veterinarian should be called to determine what is best for the animal.

**INDIANA UNIVERSITY - BLOOMINGTON
POLICY ON THE USE OF ANALGESICS IN ANIMAL SURGERY**

Surgery classification for MICE AND RATS:

If your procedure is not listed below, Veterinary Staff is available for consultation.

	Type I Surgery	Type II Surgery	Type III Surgery
Definitions	Surgical procedures performed with appropriate anesthesia that do not require the use of additional analgesics.	Surgical procedures that require the use of preemptive analgesics . Additional analgesia might also be indicated for postoperative pain relief.	Surgical procedures that require analgesia. Animals must be medicated preemptively, for a minimum of 48 hours postoperatively , and then as needed by the animal for pain relief.
Procedures	Skin incision without deeper tissue manipulation e.g., Skin biopsy Subcutaneous implant Tracheal injection Tail biopsy*	Skin incision and deeper tissue manipulation e.g., Muscle incision Muscle biopsy Vessel cannulation Vessel incision Vessel biopsy Castration Vasectomy Oral tissue manipulation	Any surgical procedure not included as Type I or Type II e.g., Penetration of a major body cavity Direct manipulation of a joint, nerve, or bone

*Analgesia may be required in some instances. For more detailed information, see *Tail Biopsy Guidelines*, available on the IACUC website.

Sanctions

Failure to comply with IACUC policies may result in noncompliance reports to the Institutional Official (IO), 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.

Additional Contacts

Subject	Contact	Phone	Email
Veterinary Concerns	LAR Veterinarians	855-2356	lar@indiana.edu
Policy	IACUC Manager	855-5138	biacuc@indiana.edu

References

1. *U.S. Government Principles for the Care and Use of Animals Used in Testing, Research, and Training* (1983)
2. *Guide for the Care and Use of Laboratory Animals* (NRC, 1996)
3. *Animal Welfare Regulations* (9 CFR, chapter I, subchapter A)