

**Survival Surgery** – Issues involved performing surgery on animal subjects are numerous and varied. Survival surgery, regardless of the species, requires aseptic technique; non-rodent mammalian surgery must be performed in dedicated facilities. Procedures may be considered *major* or *minor*. The use of animals in multiple survival surgical procedures must be justified scientifically. During the planning of surgical protocols, pre-, intra-, and post-operative practices must be outlined. An RRF staff veterinarian should be consulted during the planning stages of survival surgery to assist in ensuring appropriate techniques, anesthesia methods, and post-operative care.

**Euthanasia** (Gr. *eu* – good; *thanatos* – death) – Guidance for appropriate methods of performing euthanasia in animals is provided by the “2000 American Veterinary Medical Association (AVMA) Panel on Euthanasia” (*JAVMA* **218**, 5: 669-696, 2001), which categorizes methods as acceptable, conditionally acceptable, and unacceptable. Methods listed as conditionally acceptable (e.g., all physical methods) **require** scientific justification in an IACUC-approved *Proposal*. Other considerations include ensuring adequate training, the absence of other animals, methods to ensure death.

**Humane Endpoints** – Research protocols, especially those with the potential for systemic disease and associated pain/distress (e.g. neoplasia, sepsis) should outline specific criteria for removing animals from study (i.e., euthanasia). Death or mortality is rarely justified as a scientific endpoint and requires extensive justification.

**Occupational Health and Safety** – All individuals exposed to animals at UofL must enroll in the Occupational Health and Safety Program for the UofL ACUP. For Project Participants, or Associates, there are two major components to this Program: training and individual risk assessment via a “Periodic Animal Contact Health Survey.” For research “assistants” (those who have only completed “Level I Training,” enrollment in the OHSP consists of receipt and familiarization with the contents of the brochure entitled, “Occupational Hazards Associated with the Care and Use of Laboratory Animals.” Assistants are encouraged to seek the advice of a medical professional to assess their personal risk in working with research animals.

**“Whistle-blowers”** – The UofL IACUC continues to develop policies regarding important aspects of the ACUP. One critical IACUC policy describes the process of reporting *perceived* deficiencies in the Program. Concerns should be reported to the IACUC, either through the Chair, a committee member, or an RRF veterinarian. Written reports should be addressed to the Chair or a specific member c/o the IACUC Office, Research Resources Center, Room 102, HSC, and marked “Private and Confidential,” if desired. An IACUC Subcommittee will immediately investigate and subsequently prepare a report for presentation to the IACUC, including recommendations for resolution. Note that this policy states that persons “generating a deficiency report *shall not be discriminated against or be subject to any reprisal*. Individuals who desire anonymity may be certain that the IACUC will handle a deficiency report in confidence to the extent permitted by law.”

**Take-Home Message #1:** Animal research models must be as free from pain and distress as possible to yield the most robust research data.

**Take Home Message #2:** Replacement, Reduction, Refinement. If the Three R’s are continually kept in mind when planning a project involving animals, most other welfare issues will follow.

**Take Home Message #3:** If you don’t KNOW, then ASK.

#### **Local Contact Information:**

**Office of Research Services**  
Attending Veterinarian  
502/852-5268

**Institutional Animal Care and Use Committee**  
502/852-7307  
[IACUC@louisville.edu](mailto:IACUC@louisville.edu)



University of Louisville

Office of Research Services

## **The Use of Animals in Biomedical Research at the University of Louisville**

### **Introduction and Purpose**

- ◆ This brochure is written to provide one-time users of UofL research facilities (“assistants”) with basic information regarding the use of animals in research and the UofL Animal Care and Use Program (ACUP).
- ◆ Reading this brochure is considered “Level I Training” by the Institutional Animal Care and Use Committee (IACUC), and entitles the individual to limited activity with research animals.
- ◆ Activities with research animals by individuals who have only completed “Level I Training” must be monitored by an individual who has completed “Level II Training.”
- ◆ “Level II Training” is required for authorization of unmonitored access into UofL research animal facilities.

### **“The Three R’s”**

One of the most important references discussing the welfare of research animals is WMS Russell and RL Burch’s, *The Principles of Humane Experimental Technique* (1959). This book introduced the concepts of “The Three R’s,” which have been used as a basis for essentially all policies, procedures, guidelines, and laws governing the use of animals in research and teaching.

- **Replacement** – animal use should be replaced with non-animal use whenever possible.
- **Reduction** – scientists and educators have a moral obligation to use the minimal number of animals necessary to accomplish their goals. The assurance of a lack of unnecessary duplication is an important consideration.

- **Refinement** – studies, experiments, and procedures should be refined as much as possible to accomplish the scientific and educational goals with minimal animals and minimizing potential pain and distress. This may be accomplished by increasing the skills of animal handlers and improving techniques of experimentation. The use of an appropriate pain-relieving method may also be considered a refinement.

## Regulatory Overview

In 1984, the Interagency Research Animal Committee (IRAC) produced the *U.S. Government Principles for the Utilization and Care of Vertebrate Animal Used in Testing, Research, and Training*, to summarize the U.S. Government’s overall policy on the use of animals in research. The resulting “IRAC Principles” (reproduced below) have been subsequently used by all major regulatory bodies in developing specific guidelines, and provide a useful summary of the spirit of animal welfare regulations. Comments pertinent to the UofL ACUP follow each principle in italics.

- I. The transportation, care and use of animals should be in accordance with the Animal Welfare Act (7 U.S.C. 2131 *et seq.*) and other applicable Federal laws, guidelines and policies. *The UofL IACUC maintains a policy on the appropriate transport of animals.*
- II. Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.
- III. The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and *in vitro* biological systems should be considered. *The consideration of alternatives to animal studies, especially those that are associated with potential pain and/or distress, is one of the single most important aspects of a Proposal submitted to the UofL IACUC.*
- IV. Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.
- V. Procedures with animals that may cause more than momentary or light pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgical or other painful procedures should not be performed on un-anesthetized animals paralyzed by chemical agents.
- VI. Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedures, or, if appropriate, during the procedure.

- VII. The living conditions of animals should be appropriate for their species and contribute to their health and comfort. Normally the housing, feeding, and care of all animals used for biomedical purposes must be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied. In any case, veterinary care shall be provided as indicated. *The Research Resources Facilities (RRF) is the administrative and operational oversight unit responsible for managing and directing animal care for the UofL research program. The RRF Veterinary Care staff employs three veterinary specialists and two veterinary technicians.*
- VIII. Investigators and other personnel shall be appropriately qualified and experienced for conduction procedures on living animals. Adequate arrangements shall be made for their in service training, including the proper and humane care and use of laboratory animals. *Although this brochure provides some basic information, attendance at a “Level II Training” session is mandatory for all participants in an IACUC-approved Proposal.*
- IX. Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned by should be made, with due regard to Principle II, by an appropriate review group such as the institutional animal research committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.

The UofL is registered with the is **United States Department of Agriculture** (USDA), which has US Congressional authority to implement the *Animal Welfare Act* (Public Law 89-544, 91-579, 94-279, 99-198, 101-624). As such, the research program is subject to unannounced inspections by the Animal and Plant Health Inspection Service (APHIS) to ensure compliance with “Animal Welfare Regulations” (CFR, Title 9). UofL also maintains an “Assurance of Compliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals” with the **Office of Laboratory Animal Welfare** (OLAW) so that it is eligible to receive funding through the National Institutes of Health. *PHS Policy* requires that all vertebrate animals used in UofL research and teaching be included in the regulatory process. Furthermore, the UofL ACUP is accredited by the **Association for the Assessment and Accreditation of Laboratory Animal Care, International** (AAALAC). In fact, UofL has been recognized as one of two institutions that has maintained continuous accreditation since the organization was founded in 1965. Both AAALAC and the *PHS Policy* use the *Guide for the Care and Use of Laboratory Animals* (the “*Guide*”, ILAR, NRC) as their primary reference. It is through the *Guide* and the USDA Regulations that the ACUP receives most of its direction in developing institutional policies and procedures.

Institutional regulatory authority is relegated by the Institutional Official (Executive Vice President for Health Sciences) to the Institutional Animal Care and Use Committee (IACUC), which is comprised of researchers using animals, laboratory animal veterinarians, and non-affiliated members (community representatives). ***All proposed use of animals in research and education must be reviewed and approved by the IACUC prior to their acquisition.*** The IACUC also performs a semi-annual assessment of programs and facilities, reviews all animal welfare concerns, suspends non-compliant activities, and makes recommendations to IO concerning issues associated with the UofL ACUP.

## Issues for Special Consideration

**Pain and Distress** – Clearly, a primary goal of all refinements is to minimize pain and distress. In order to accomplish this goal, the researcher must be familiar with the pathophysiology and consequences of discomfort, distress, and pain. Recognition of signs of pain in the species in question is vital. The use of agents to relieve pain requires that the researcher is familiar with the use of anesthetics (which produce unconsciousness, analgesia, muscular relaxation), tranquilizers/sedatives (which reduce anxiety), and analgesics (which alleviate pain without loss of consciousness). Product selection must keep in mind species-specific and animal-to-animal variability.

**Anesthesia** – Projects requiring a loss of consciousness for surgery or immobilization rely on a thorough understanding of the stages of anesthesia (I-IV) and the ability to assess anesthetic depth. Proper monitoring of anesthetized animals includes assessment of reflexes and cardiovascular function.

**Use of Pain-Relieving Agents** – The UofL IACUC requires that all animal undergoing major survival surgery receive post-operative analgesics for at least 48 hours unless specifically and scientifically justified in an IACUC-approved *Proposal*. Many analgesics are controlled by the Drug Enforcement Agency (DEA). DEA regulations require strict control over the use of these agents, including user registration, storage, and appropriate recordkeeping. It should be noted that the use of neuromuscular blocking agents (paralytics) is strongly discouraged because of the difficulty in monitoring the depth of anesthesia and retention of unconsciousness.