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SURGICAL RESEARCH GUIDELINES

Guidelines for Training in Surgical Research with Animals

Academy of Surgical Research

Guidelines for Training in Surgical Research in Animals was first published by the Academy of Surgical Research (ASR) in April 1989. The Board of Directors for the Academy recommended that these guidelines be reviewed and updated to reflect current practices and the additional levels of certification. A committee was formed to draft revised guidelines for review by the Board. The committee included Jan Bernal, DVM, Teresa Gleason, BS, LVT, SRS, Steve Kuhlman, VMD, DACLAM, John Long, DVM, DACLAM, and Michael Talcott, DVM, DACLAM. These guidelines were presented to the Board at the 2008 Annual Meeting and approved for publication.

The Academy of Surgical Research is an international organization that promotes the advancement of professional and academic standards, education, and research in the arts and sciences of experimental surgery. The Academy interfaces with medical and scientific organizations, and governmental agencies in establishing and reviewing ethics, theories, practices, and research pertaining to surgical research and promotion of the results for clinical application. Part of the mission when ASR was founded in 1982 was to encourage, foster, promote, and advance professional and academic standards, education, and research. That original purpose holds true today as the Academy expands its certification program for persons without professional degrees to include the two new levels of anesthetist (SRA) and technician (SRT), in addition to the established surgical research specialist (SRS). The need for education and training is critical to ensure that qualified personnel are available to perform anesthesia and surgery on laboratory animals.

The purpose of this document is to assist institutions in establishing a training and education program to ensure that surgical procedures performed on laboratory animals are conducted with skill and compassion. It includes expanded sections on animal welfare, anesthesia, pain management, alternatives to animal use in training, and post-training evaluation. It is recommended that these voluntary guidelines be established at institutions performing experimental surgery to ensure compliance with current laws, regulations, and standards. Ultimately it is the responsibility of the Institutional Animal Care and Use Committee in conjunction with the attending veterinarian to assure the competency of the individuals involved in surgical research at any given facility or institution.

GUIDELINES IN TRAINING

Most research institutions performing experimental surgery have and conform to regulations, laws, and standards that required personnel be trained when performing surgery on animals. The Public Health Service Policy on Humane Care and Use of Laboratory Animals require institutions receiving funds to follow the National Research Council's Guide for the Care and Use of Laboratory Animal Care (National Research Council (NRC), 1996). In addition, the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International is a nonprofit organization that accredits institutions in many countries. This organization uses the *Guide for the Care and Use of Laboratory Animals* (the *Guide*) as one of the standards to assess an institutions' program. The *Guide* states, "Investigators, technical personnel, trainees, and visiting investigators who perform animal anesthesia, surgery, or other experimental manipulations must be qualified through training or experience to accomplish these tasks in a humane and scientifically acceptable manner." In the *Guide* a number of options are discussed for training technicians, including educational programs (colleges, American Association for Laboratory Animal Science (AALAS), Animal Welfare Information Center (AWIC), and Institute for Laboratory Animal Resources (ILAR)) as well as guidelines from other countries including the Canadian Council on Animal Care. The *Guide* also cites the previous ASR publication on training program guidelines that this document is intended to update.

There are few regulations that discuss in detail the manner in which surgical training or how a qualification process for surgery personnel is to be performed. In the United States, the Animal Welfare Act regulations provide some guidance as to specific topics related to training for surgery. The regulations require guidance in proper preprocedural and postprocedural care of animals, aseptic surgical methods and procedures, and proper use of anesthetics, analgesic, and tranquilizers. These requirements are useful for the development of an institutional surgical training program and further recommendations of components to include in this training program are outlined below.

PERSONNEL REQUIRING TRAINING

Very little has changed over the last 20 years with regard to the type of individuals who perform surgery on animals for biomedical research. They are people with varying backgrounds in education and experience who may have doctorates (physicians, veterinarians, dentists, and PhDs) or may be non-doctoral individuals (graduate students, medical students, and technicians). Assessment of the surgical skills and knowledge of persons performing surgery on animals in biomedical research is difficult due to the vast array of procedures that are performed. There are, however, basic tenets of surgical technique to which all individuals must adhere and demonstrate competence prior to initiating procedures undertaken for the benefit of biomedical research. Responsible individuals planning to perform surgical procedures on animals must demonstrate a proficiency in proper sterile technique, tissue handling, hemostasis, and closure techniques (obliterating dead space, skin sutures, etc.). In addition, often times these individuals are responsible for perioperative care including anesthesia, analgesia, and postoperative care which may require additional knowledge and proficiency in areas such as drug dosages, administration techniques, and pain assessment. Regardless of their background, all of these individuals have a responsibility for the well-being of the animal and must have adequate training and experience in surgical techniques to assure the animal's well-being.

In the past, one of the more controversial aspects of this issue was whether to automatically consider persons with an earned degree in health sciences (MD, DDS/DMD, DVM/VMD) competent in experimental surgery regardless of experience or training. While this issue is not fully resolved, over the years most institutions assess degree holders based on their experience and background and they are not automatically assumed to be competent based solely on their degrees. In recent years it has become more commonplace for increased numbers of non-doctoral-level persons (technicians, students, etc.) to perform biomedical research-related surgical procedures on animals. In academia, this may occur because clinical and administrative responsibilities placed on physicians can reduce the amount of time dedicated in the lab leaving non-doctoral persons to assist or perform these procedures. In industry, the need for surgically induced models has greatly increased and many of these procedures are performed by non-doctoral degree persons.

The following is a list of personnel categories that may be encountered in a biomedical research setting and the training that may be associated with these degree and nondegree levels. Individuals should be assessed independently based on their experience, background, and previous training prior to being allowed to perform surgery on laboratory animals.

1. MD

   All physicians have had some didactic or observational training in human surgery and should have an understanding of basic sterile surgical techniques. In addition, physicians trained in surgical specialties should be considered competent in their field of expertise and the basic tenets of surgery. For example, training a board-certified orthopedic surgeon in basic surgical procedures or sterile technique would be inappropriate. However, most physicians are not trained in comparative anatomy, animal behavior, or veterinary anesthesia and analgesia, and training in interspecies differences or anatomy may be necessary. In addition, many medical schools have dropped live animal surgical training programs opting instead for inanimate models and in recent years fewer physicians have actual hands-on experience with live animals. Because societal changes have mandated greater oversight over biomedical research, carte blanche training exemptions of these individuals is no longer adequate or acceptable.

   Current training recommendations for most physicians therefore should include basic didactic training which may include unique aspects of anatomy for their chosen animal model, animal handling/basic techniques such as blood collection and injections, anesthesia, analgesia, and postoperative care. Federal, state and local (Institutional Animal Care and Use Committee/IACUC) regulatory requirements also continue to evolve and the didactic training should include an overview of laws and regulations governing animal use in surgical and biomedical research.

   Physician's experience and background should be taken into consideration when assessing hands-on training requirements. Surgically trained physicians undertaking procedures in their field of expertise and/or who have demonstrated competence in the

described procedures should be exempted from additional training. Documentation of competency may include a review of the morbidity/mortality rates for the procedures (or similar procedure) and complications that have been experienced. Proficiency in these areas should be documented prior to these individuals being solely responsible for the performance of these procedures.

Surgical residents and interns, however, may not have the experience necessary to perform complicated animal surgical procedures without some additional training by the principal investigator (PI), veterinary staff, or other experienced personnel. Physicians trained in nonsurgical specialties may also need hands-on training in basic surgical techniques, drug administration, recordkeeping, and postoperative care as well as hands-on training in the specific surgical procedure.

2. DVM/VMD

All veterinarians have didactic and hands-on training in veterinary surgery, anesthesia, analgesia, and comparative anatomy as part of their core veterinary training. These individuals should have a working knowledge of the basic tenets of surgery, standard veterinary surgical procedures, comparative anatomy, anesthesia, analgesia, and postoperative care of animals and further training should not be necessary. Few veterinarians are trained in complex experimental surgical procedures or in working with laboratory animal species. Veterinarians expected to perform complex surgical procedures (organ transplantation, thoracic, orthopedic, or neurosurgery) may require additional training by experienced surgeons or may be asked to document their relevant experience prior to performing complex surgical procedures. In addition, veterinarians not trained in laboratory animal medicine may need additional training on interspecies differences in anatomy, physiology, anesthesia, analgesia, animal handling, and general care of the species being used. IACUC regulatory requirements governing animal use in surgical and biomedical research should also be included in this didactic training. Veterinarians who are certified or trained in laboratory animal medicine, surgery, or anesthesia should be considered competent in their field and should not require additional training.

3. PhD

Few individuals with postgraduate degrees are trained in the basic tenets of surgery or have formal training in experimental surgery in laboratory animals. Similar to physicians, these individuals are not trained in comparative anatomy, animal behavior, veterinary anesthesia, or analgesia. Most often, PhDs have experience in one discipline or sometimes one procedure and a documented history of successful procedures should be taken into consideration when determining their training requirements.

Current recommendations for PhD scientist training should include didactic and hands-on training in the basic tenets of surgical techniques including sterile technique, proper tissue handling, hemostasis, and closure techniques. Alternatively, demonstrated proficiency in these areas could be used in lieu of formal training. Additional didactic training should include unique aspects of anatomy for their chosen animal model, animal handling, and basic techniques, such as blood collection and injections, anesthesia, analgesia, and postoperative care. IACUC regulatory requirements should also be included in this didactic training with an overview of laws and regulations governing animal use in surgical and biomedical research. Finally, scientists expected to perform complex surgical procedures should be required to provide a documented history of success with procedures, demonstrate proficiency with these procedures, or undergo additional training under the supervision of an experienced human or veterinary surgeon. Scientists who can demonstrate that they have adequate training or who have documented experience in particular surgical procedures should be recognized as competent in those procedures. Documentation of competency may include a review of the morbidity/mortality rates for each surgical procedure and complications encountered. Proficiency in these areas should be observed or documented prior to these individuals being solely responsible for the performance of these procedures.

4. DDS/DMD

Dentists and oral surgeons are trained in human dental and oral surgical procedures and may be familiar with sterile or aseptic techniques. They should be recognized as competent in the procedures in their field of expertise. However, similar to MDs and PhD scientists, these individuals generally do not have experience using laboratory animals for surgical research and may need additional didactic training in laboratory animal medicine and surgery. Dentist or oral surgeon training should include didactic and hands-on training in the basic tenets of surgical techniques including proper tissue handling, hemostasis, and closure techniques. Alternatively, demonstrated proficiency in these areas could be used in lieu of formal training. Additional didactic training should include unique aspects of anatomy for their chosen animal model, animal handling, and basic techniques, such as blood collection and injections, anesthesia, analgesia, and postoperative care. IACUC regulatory requirements should also be in this didactic training with an overview of

the laws and regulations governing animal use in surgical and biomedical research. Dentists or oral surgeons expected to perform complex surgical procedures outside their field of expertise should be required to provide a documented successful history with the procedures, demonstrate proficiency with these procedures, or undergo additional training under the supervision of an experienced human or veterinary surgeon. Individuals who can demonstrate that they have adequate training or who have documented experience in particular surgical procedures should be recognized as competent in those procedures. Documentation of competency may include a review of the morbidity/mortality rates for the procedures (or similar procedures) as well as complications that have been experienced. Proficiency in these areas should be documented prior to these individuals being solely responsible for the performance of these procedures.

5. Technical staff

   Non-doctoral degree personnel usually perform surgical procedures under the direction of investigators with doctoral degrees as part of an IACUC-approved protocol. These individuals have varying backgrounds and levels of experience including technical certification in various fields.

   Registered veterinary technicians have had formal training in aseptic preparation, sterile techniques, anesthesia, drug administration, and postoperative monitoring. These individuals should be considered competent in these areas but may need additional didactic and hands-on training in the basic tenets of surgery including tissue handling, hemostasis, and suturing/closure techniques. Alternatively, demonstrated proficiency in these areas could be used in lieu of formal training.

   Certification programs exist that provide verification of competency in anesthesia (SRA), minor surgical procedures (SRT), and more complex surgical procedures (SRS) through the ASR. Individuals are required to maintain logs demonstrating proficiency, submit surgical narratives and outcomes that are reviewed and verified by a trained person familiar with their work, and pass a certifying examination. Persons with these or equivalent certifications should be considered competent in the areas of expertise associated with the certification. Non-doctoral degree persons without these credentials may require additional didactic and hands-on training in anesthesia and surgical procedures in addition to basic training in animal handling, techniques, and regulations. They may also require training in the basic tenets of surgery (tissue handling, hemostasis, suturing, etc.) and are required to demonstrate proficiency in these procedures. Persons in this category should not be considered competent in experimental surgery without documentation of previous training and experience, demonstration of proficiency in sterile techniques, proper tissue handling, and documented history of performing a particular procedure with minimal operative and postoperative complications.

Ideally, a multidisciplinary team approach to performing investigative surgery should be used. This should include protocol review by a veterinarian, preoperative consultation with the surgeon, veterinarian, and support staff, and utilization of trained veterinary technicians or personnel for anesthesia, analgesia, intraoperative monitoring, and postoperative care. Preoperative consultation between the surgeon and veterinarian may help to identify potential complications or unique anatomical or physiological aspects of that species. Anesthesia, intraoperative monitoring, and postoperative care utilizing trained veterinary technicians can greatly improve the outcome of survival surgical procedures and potentially reduce the training requirement for the surgeon.

Non-doctoral degree personnel can be an integral part of a multidisciplinary team approach and can provide assistance in many ways based on the expertise of an individual. Depending on the level of experience or certification, these individuals can provide preoperative surgical support, intraoperative anesthetic monitoring, surgical assistance, primary surgical support, and/or postoperative care, including analgesic administration and pain evaluation. Many times the role and expertise these individuals provide can reduce the activities and training requirements of the primary researcher.

ETHICAL TRAINING

Consistent with other medical disciplines, it is incumbent on the surgeon to demonstrate a working knowledge of the ethical considerations and laws that govern the performance of experimental surgery in animals. In addition, it is paramount that the surgeon demonstrates proficiency in all facets of the procedure to be performed. Each institution should develop some mechanism to document training and proficiency as a safeguard to prevent untoward consequences.

The basis of ethical training in experimental animal surgery stems from the current existence of a strong acceptance of fundamental moral and ethical considerations related to the use of animals in biomedical research. In many countries, governmental agencies and institutional policies govern the type and extent of training/certification necessary for individuals to perform experimental surgery on research animals. Each institution's animal care and use program description should outline and define the essential components of

a training program, and this should be reviewed by the attending veterinarian and the IACUC. Each institution's training program should provide the necessary training and oversight to ensure compliance with accepted policies and guidelines. Insufficient training can have dire consequences toward research objectives as well as animal care and welfare.

The use of animals for surgical training, demonstration, and/or research applications should only be used in those instances where suitable alternatives are not available. In 1959, British scientists William M. S. Russell and Rex L. Burch wrote *The Principles of Humane Experimental Technique*, wherein they introduced the concept of the 3R's (replacement, refinement, and reduction) as the framework for considering humane use of animals in research, including experimental surgery. It is important that the 3R's be considered before any animal is subjected to any experimental surgical procedure. The adoption of "alternative" approaches or methods should be viewed as complementary to the use of animal model and should be actively encouraged for both scientific and humane reasons.

Research personnel with professional degrees in varying specialties may not require additional training outside the one that was provided in their predoctoral training. Physicians, veterinarians, dentists, and some technical specialties may have a component of ethical training as part of their background. This ethical training should, at a minimum, emphasize that individuals seek training to develop expertise in areas, including such areas as experimental surgical protocols, with which they are unfamiliar prior to performing such a procedure.

Research personnel without such background in their training may have developed expertise in experimental surgical protocols through either experience or formal training. This experience, if documented, should be taken into consideration when selecting individuals for formal training in experimental surgery. It is also important to emphasize that ongoing continuing education is an important part of training and certification of professionals. Continuing education should be included in the judgment of a person's qualifications.

Another important consideration for ethical training in experimental surgery is the issue of pain management. Surgeons and anesthesiologists/anesthetists play a vital role in laboratory animal pain control and management. Position statements from numerous regulatory agencies (i.e., Office of Laboratory Animal Welfare (OLAW), U.S. Department of Agriculture (USDA)) and laboratory animal organizations (American College of Laboratory Animal Medicine (ACLAM), American College of Veterinary Anesthesiologists (ACVA), American Association for Laboratory Animal Science (AALAS), and American Veterinary Medical Association (AVMA)) support, in general, that pain and distress must be minimized or avoided at all, if possible. Research personnel engaging in activities that may result in more than momentary pain or distress, must be appropriately trained and have a strong working knowledge of the animal species and the efficacy of the anesthesia/analgesia being employed. Numerous references exist to guide surgeons and anesthetists to indicated and accepted anesthetic/analgesic protocols for pain control and management in most commonly used laboratory animal species.

SUGGESTED COMPONENTS OF A TRAINING PROGRAM

In the past, developing a comprehensive surgical training programs was time-consuming and expensive involving the development of didactic courses and, when appropriate, live animal laboratories. Many institutions have surgical training programs as part of a medical school curriculum but these are focused on human medicine and not directed at biomedical research training or the variety of animal models being used. However, the present advent of Internet access and web-based interactive learning and digital materials has provided numerous available options that can be incorporated into institutional surgical research training programs either at no or minimal cost.

Part of a successful surgical outcome relies upon the support staff of the surgeon, including a surgical anesthetist. Training for these individuals is crucial and often overlooked by many research institutions. Because of the complex procedures that are often undertaken for research and development, these individuals must be qualified to manage these specific cases. Anesthetic management, including patient monitoring, equipment maintenance, and emergency treatments should, therefore, be included in the overall program.

Accordingly, the areas that could be included in a comprehensive training program or in evaluating the background of personnel performing experimental surgery on animals are as follows:

Regulatory/Ethical Considerations

USDA regulations (Animal Welfare Act (AWA)) or other applicable national regulations (CCAC etc.)
Guide for the care and use of laboratory animals

Public Health Service Policy and Government Principles Regarding the Care and Use of Laboratory Animals
Local IACUC guidelines
Good Laboratory Practice regulations
Proper recordkeeping and documentation
Ethics and animal welfare

Facility Requirements

Functional areas needed for rodent vs. nonrodent surgeries
Maintenance/setup of surgical areas
Maintenance/use of equipment
Safety training for equipment, procedures, and specific species (i.e., gas scavenging, fluoroscopy, use of nonhuman primates)

Presurgical Planning

Model/species selection/literature search
Anatomy and physiology
Individual subject selection (health evaluation)
Handling, restraint, dosing, and sampling techniques (blood collection etc.)
Special equipment needs and operation (fluoroscopy, ultrasound, endoscopy, etc.)
Instrument identification/handling/cleaning/care
Surgical pack preparation and sterilization techniques
Identification and coordination of appropriate personnel

Analgesia

Agents/dosage calculations/routes of administration
Controlled substance regulations
Adverse interactions
Knowledge of preemptive, intraoperative, and postoperative options and techniques
Multimodal anesthesia and analgesia
Pain recognition/assessment

Anesthesia

Preanesthetic health evaluation of patient (body weight, physical examination, vital signs, nutrition status, etc.)
Species specific differences
Stages of anesthesia
Injectable agents, mechanism of action, dosages, and calculations for premedication, induction of anesthesia, maintenance of anesthesia, and emergency drugs
Inhalant anesthesia including agents, delivery techniques, scavenging system
Local and regional anesthesia
Tracheal intubation
Breathing circuits
Anesthesia machine use and maintenance including ventilators
Principles of respiration and ventilation
Anesthesia monitoring parameters for rodent and nonrodent species, vital signs/reflexes/support of normal body temperature,
ECG/SPO_2/CO_2/blood pressure monitoring devices,
arterial blood gasses—acid/base balance
Fluid therapy
Emergency care
Recovery
Recordkeeping

Aseptic Technique

Sterilization vs. disinfection
Sterilant, disinfectants, and antiseptics
Operating room personnel conduct
Personnel scrubbing, gowning, gloving
Surgical pack handling—opening packs, sterile field
Animal preparation—skin preparation, placement on surgical table, drape techniques
Addressing breaks in sterility

Surgical Technique

Presurgical planning to minimize surgery time
Minor and major procedures
Knowledge of healing process
Principles of good surgical technique
Tissue handling
Hemostasis techniques
Suture types—materials, uses, and needle types
Suture patterns
Suture techniques and wound closure
Species consideration
Proper instrument handling

Postoperative Care

Immediate postoperative care
Analgesics and pain recognition (pain scale scoring)
Health monitoring—body condition scoring
Postoperative emergencies and treatment
Nutrition (basic and supplemental)
Incision care
Bandaging techniques
Housing
Environmental enrichment

Implementation of the above-listed components should encompass a variety of training methods. For example, topics such as regulatory/ethical considerations and facility requirements lend themselves well to a didactic approach, whereas surgical techniques will require

both didactic and hands-on training before proceeding to the animal model.

For hands-on training, programs should include the use of all resources available, including inanimate and interactive training tools. Inanimate training aids, such as anatomic phantom models or "dummies," simulators, and virtual hands-on surgical training, are commercially available for learning based upon surgical specialty and type of procedure or technique. Advances in computer technology have made interactive simulations for operating anesthesia machines and virtual patient monitoring available and these should be considered when developing a comprehensive surgical training program. Alternatively, less expensive options with easy accessibility, such as oranges, chicken breasts, or pigs feet purchased from a grocer, have been used for injections and suturing. In addition, cadaveric tissues, such as harvested arteries and veins for microsurgical training, have been successfully utilized for many years. Most of the inanimate models focus on a particular task (suturing, vascular access, tissue handling) and provide surgical trainee a fantastic tool to develop these skills. However, there is currently no acceptable substitute for performing the specific surgical procedure of interest on an animal. In an ideal program, the surgical research trainee has a stepwise process of learning from didactic course to skill development using inanimate or cadaver models and finally live animal training under the supervision of a qualified instructor.

The goal of the training program is to assure that persons responsible for these procedures are competent in their duties. Competency should be evaluated and documented after the completion of training modules/laboratory courses. This evaluation should include testing and observation of the individual performing the tasks by an experienced professional (physician, veterinarian) or certified individuals (surgical research specialists etc.).

Post-training education and reevaluation is a necessity in a training program to avoid procedural drift and ensure that the trainee is apprised of advances in the field of surgical research. This should be accomplished by a periodic review of trainee's technique and compulsory continuing education through journal review and professional meeting attendance.

Reevaluation of the training program is also necessary. The program must be reviewed and updated periodically and should be a part of institution's IACUC program review process to ensure that it includes and is compliant with the most current advances in surgical research, standards of veterinary care and animal welfare. The goal of the review is to achieve the highest level of technical training while maintaining the highest level of animal care.

RECOMMENDATIONS

- It is the responsibility of the institution to ensure that all personnel performing survival or terminal surgical procedures on research animals be qualified by experience, education, and training to perform such procedures. The institution is responsible for supporting the training and providing the necessary resources for the program. If personnel are not qualified to perform these procedures, either education and training must be provided or collaborative arrangements be made with qualified personnel before performing the surgery.
- Training courses should be conducted by qualified instructors and must adhere to all applicable regulations, laws, and standards. The topics listed earlier comprise the ideal requirements included in a course. A team or multidisciplinary approach should be considered and a qualified veterinarian should be included in the training process. The training should consider aspects beyond merely performing the mechanics of the surgery, but should also focus on the overall impact of the procedure on the animal's well-being.
- There should be a tier approach to determine the training required for a person, depending on their education, experience, and background. The education level suggested in the "personnel requiring training" section can be used as a foundation for that decision.
- Because animals are sentient creatures and we have a responsibility for minimizing their pain and distress during research, a stepwise approach to surgery must be taken. A person should be able to demonstrate proficiency in a technique using nonliving alternatives before being allowed to perform it on a live animal. The training should include the minimum number of animals necessary to achieve the objective and consideration should be given to start with a less sentient animal.
- There must be a mechanism in place to monitor the competency of a person performing surgery to ensure that the training was adequate. Continuing education should be required so that less invasive techniques might be utilized when they become available.

SUMMARY

This document is meant as a guideline to assist research institutions in adhering to best surgical practices and regulatory requirements. It is the hope of the Academy of Surgical Research that institutions will utilize this document to develop a surgery training program that improves the results of a procedure for the benefit of both the science and the welfare

of the animal. There is a variety of resources that can be found, both published and online, to support a quality training program. It is in the best interests of the institution to be proactive in training and aim for improved quality for both the animal and the research.

FURTHER READING

http://old.cvm.msu.edu/courses/vm557/surgery/index.html
http://cal.vet.upenn.edu/
http://grants.nih.gov/grants/OLAW/TrainingVideos.htm#rodent
http://www.ahwla.org.uk/site/tutorials/
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Pain Management

AALAS Position Statement for recognition and alleviation of pain and distress in laboratory animals; (2003). Available at http://www.aalas.org/pdf/Recognition_and_Alleviation_of_Pain_and_Distress_in_Laboratory_Animals.pdf

ACLAM Position Statement on pain and distress in laboratory animals. Available at http://www.aclam.org/print/position_pain-rodent-rabbit.pdf

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