



# ANIMAL TRACKS

A newsletter for the Duke research community



February 2009

<http://vetmed.duhs.duke.edu>

## OLAW ADVISEMENT CONCERNING ANIMAL WORK IN YEARS 4 & 5 OF GRANT

The NIH's Office of Laboratory Animal Welfare (OLAW) released a regulatory advisement in early January that clarifies whether the IACUC must review proposed animal research activities at the time of grant award if the animal research activities **will not be conducted until year 4 or 5 of a grant** (animal protocols can only be active for 3 years). OLAW's answer to this question is: YES!

While there are specific exceptions defined in their message ([http://grants.nih.gov/grants/olaw/faqs.htm#proto\\_20](http://grants.nih.gov/grants/olaw/faqs.htm#proto_20)), the take home message is **failure of the IACUC to review and approve activities in year 4 and 5 of the grant (even when recognizing there must be a new protocol for actions occurring beyond year 3), will result in a delay of funds release by the granting agency!**

The IACUC must review the animal protocol for experimental design and reasonable scientific utilization for the entire 5 years. This also includes proposed numbers of animals that would be used in the 5 year study (important point coming) **AS YOU UNDERSTAND THEM** at the time of the protocol submission.

Everyone, including the IACUC and the granting agency, understand that changes in the experimental design (including animal numbers) may be necessary at the 3 year re-write. As long as you stay true to your goals and objectives, you can modify the animal protocol at the 3 year re-write while remaining consistent with your grant.

Wishing you a productive research week,

### Upcoming Dates & Deadlines

February 2	New Protocol Deadline
February 2	Significant Change Deadline
February 3	BB Seminar: Surgical Models & Services
February 23	Significant Change Deadline
	BB Seminar: Preparing Your Lab for an IACUC Inspection
February 26	IACUC Monthly Meeting
March 2	New Protocol Deadline
March 2	Significant Change Deadline
March 23	Significant Change Deadline

*Deadlines are 5 PM on the date listed!*

## A CASE FOR PRE-EMPTIVE ANALGESIA

Pain and distress modifies research outcomes. A simple statement, a true statement, but more thorny when assessing impactful pain or distress, the extent that such conditions may modify the integrity of the research outcomes, and how unnecessary pain or distress may be prevented. Viewed through the core axiom of veterinary medicine 'to prevent or alleviate pain in the animal patient,' the researcher must consider paradoxical, complicated, and frequently self-restrictive options.

How can one perform quality research that is free of outcome modifiers such as animal pain or distress? Sometimes it is not possible, and in those cases it must be recognized and reported. But often, an effective engagement of pre-emptive pain management will allow a strong and stable biologic platform for animal facilitated investigation while eliminating distress or pain in the animal subject. The Duke animal care & use program requires the use of pre-emptive analgesia for animal based activity as an ethical and scientifically sound method of preventing animal pain and maximizing the integrity of research data outcomes. Some of the evidence to support this institutional position follows:

- In a clinical study, titled: Pre-Emptive Analgesia for Post-Operative Pain Relief in Lumbosacral Spine Surgeries: A Randomized Controlled Trial, human patients were evaluated on the effectiveness (or lack thereof) of epidural administration of bupivacaine and tramadol. While not parcel to the objectives of this particular study, the authors reported blinded patient assessments confirmed pre-emptive analgesia was effective in providing a more comfortable and successful patient procedure. An anthropomorphic application would engender a similar outcome in animal patients.
- A report titled: A Qualitative and Quantitative Systematic Review of Preemptive Analgesia for Post-operative Pain Relief: The Role of Timing of Analgesia, notes: "In the perioperative setting, preemptive analgesia can be achieved with NSAIDs, COX-2-selective inhibitors, acetaminophen, and longer-acting opioids such as codeine and propoxyphene."

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While these results also were specific for human clinical assessment, working from a paradigm of anthropomorphism, there remains rational application for animal studies. In this seminal work, the author concludes: 'Understanding of pain mechanisms has revealed the importance of proactive interventions in analgesia that aim to prevent initiation of hyperalgesia and central sensitization through preemptive analgesia. An appreciation of balanced approaches to analgesia has allowed for safer pharmacologic strategies for analgesia.'

- John C. Schofield BVSc, Dip ACLAM, MRCVS and Virginia M. Williams BVSc, MACVSc, Dip Prof Ethics reported to the New Zealand Ministry of Agriculture in their report Analgesic Best Practice for the Use of Animals in Research and Teaching - An Interpretative International Literature Review, noted: "The notion that post-operative pain can be forestalled or even prevented derived from the simple observation of human patients who underwent orthopedic surgery" is worthwhile. Patients who received opiate premedication prior to general anesthesia took four times longer to request pain relief after surgery than those who received a general anesthetic without any premedication; these un-premedicated patients all requested pain relief within 2 hrs. Other authors note that elderly patients receiving pre-emptive analgesia prior to surgical leg amputations for ischemia and diabetes reported no pain at 6 months, whereas 50% of patients who received no premedication reported pain at 6 months.

While arguments supporting pre-emptive analgesia use could continue, it is clear there exists adequate scientific based evidence from the human community to support the use of pre-emptive analgesia for the animal patient. Pre-emptive analgesia should be parcel to a pain management program for animals used in research.

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## OOPS—WHEN LAB ANIMALS ESCAPE FROM PRIMARY HOUSING

Sandra Schenone, BA, RLATG  
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Mike McGarry, PhD  
McG Consulting, LLC, Fountain Hills, AZ

*Ed Note: This article excerpted from AALAS Tech Talk; Vol. 13/No. 5 NOV 08.*

Episodes of lab animals escaping from primary housing are unfortunate and hopefully rare. The Guide is not silent on the subject, noting that "...primary enclosures... provide a secure environment that do not allow escape..." and "...should be kept in good repair to prevent escape...." Although all efforts may be exercised to avoid escapes, it seems only a matter of time before an incident occurs. The situation can present many challenges in the research environment and to the animal care staff. Some matters for concern relate to strategies for recapture without resultant harm to the animal; others are necessarily more focused on the health and safety of the affected staff. Furthermore, the temporary loss of containment, barrier conditions, or just the exercise of unrestricted movement within the animal holding room can result in stress, injury, or contamination that have potential for far-reaching impacts on research, animal health, colony health, room integrity, staff, and even public safety. Strategies to create a workplace culture in which such incidents are reported without fear are critical to open communication. Proactive plans for such events need consideration in advance. Staff needs preparation through education and training on methods, safe strategies, and implements before an incident occurs.

An essential component of orientation and training for new animal care technicians should be procedures to assess and respond to encounters with escaped lab animals, wherever they may occur. Specific standard operating procedures (SOPs) may be developed and include information about the species, hazards involved, and skills necessary to accomplish recapture. Procedures will depend on species-specific natural behaviors, current health status, protocol history (appliances/implants, recent surgery, etc.) and safety issues. Each of these conditions will have a bearing on the methods and urgency of efforts to reconfine the subject animal and the consequent cleanup required for the site.

The majority of animal escapes may not be particularly noteworthy, as they occur within a contained environment, such as a mouse within a transfer station. In fact, some animal care staff may not even consider a mouse that has temporarily "ejected" itself from an open micro-isolator as truly being an escaped animal. However, under some conditions, methods and hazard containment sequellae associated with the replacement of an escaped mouse into its micro-isolator may well present a challenge. Each episode in which an animal becomes loose may need to be addressed and perhaps documented.

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Before an animal is replaced to its primary cage, it must be accurately identified. It may be necessary to have the animal placed into a temporary holding cage until the researcher can confirm its identity and assure the care staff that it is acceptable to replace the animal into its original primary enclosure. This, of course, requires that the incident is reported and the researcher is informed of the event.

**Planning for the Eventual Escapee:** Before animal acquisition or a new program of care is initiated, all aspects of animal care, research use, and housing must be considered. This includes how an animal could escape its primary enclosure. Assessment of primary and secondary enclosures prior to and after an escape is necessary to prevent further incidents. All space, including the primary enclosure, change space, the animal holding room and other accessible space within the animal care and use facility needs review and consideration. Skill in observing the environment needs to be developed.

Not all escapes are observed at the time they occur. With many events, one simply encounters an animal unconfined in its macro environment. How this may occur has any number of possibilities. All aspects of the research protocol should be considered for potential occasions and sites in which an escape may occur. Who has access to the animals? Has it been used recently? Was the animal transported to/from areas for testing, imaging, surgery, conditioning and training, between animal holding rooms (AHR), between AHR and procedure rooms, or between buildings? Escapes that occur outside the AHR present special circumstances that may require particular considerations.

All those working directly with lab animals need hands-on training in proper handling/restraint of the species. If procedures for restraint require collars, handling poles, or other devices, staff needs to be trained in their use.

**After an Escape:** After an event has occurred, several possibilities may be considered regarding the cause—human error, faulty housing, and animal ingenuity.

- **Human Error:** Staff may need to be coached with regard to how they used improper technique and, more importantly, what the proper technique is. Any corrective action should be proportional to the incident, and supportive to an open culture.
- **Faulty Housing:** Close inspection of the caging may reveal the defect that requires repair or modification.
- **Animal Ingenuity:** Hasps and other closure devices can present as manipulata and as tools in which to escape. The strength of other animals is not fully appreciated until they have found ways of forcing their way out of inadequately fastened closures. An unsecured clasp on a transport container provides an ample opportunity for an active animal. Too often, equipment inadequacies are discovered after the fact when it is discovered that the caging was not sufficient to the task.

To help initiate discussion, we present two theoretical cases for the reader's consideration:

**Scenario #1:** While doing a routine change-out of conventionally housed rats, the animal technician is distracted while the cage lid is off an occupied cage. Upon returning their attention to the cage, the tech finds it empty.

**Scenario # 2:** On entry into an AHR, the animal care technician observes a pigeon perched atop of one of the three racks in the room. The room, with a total capacity of 48 birds (3 racks with 16 cages each), has a current census of 39 pigeons. A student had been testing animals previously that day, taking birds to an adjoining room. All testing has been finished for over an hour. One cage of the 48 units is empty and its door is slightly ajar. What should be done?

The reader should contemplate solutions for each of these scenarios if they were to occur in their own facility, and consider methods that would prevent future occurrences.

#### **What to do in an encounter with an escaped lab animal:**

- Alert other personnel in the room.
- Check the cage card to see how many animals were in the cage.
- If an empty cage is the only evidence that the animal is missing, check for other indicators that an animal is loose, hopefully locating it. Look on shelving and in dark places such as under racks or a cart.
- Determine whether help should be requested in locating the animal.
- Once the animal is located, recapture it if it is safe for you and the animal.
- Check for injury to the animal.
- After recapture, notify the PI, the clinical veterinary services staff, and the supervisor.
- Clean all debris, feces, urine, and any other fluids.

#### **Questions to consider when planning for an animal escape:**

- Who is responsible and trained for the capture of a particular loose animal?
- Is there a danger to the animal or staff?
- How is escape handled for each species?
- Is there proper handling equipment available?
- Everyone know where it is kept and how to use it?
- How are procedures affected if more than one animal is loose?

**Conclusion:** Planning ahead for an escaped animal makes dealing with it safer and less dramatic. When taking in all considerations, it is important to include all personnel involved with the animal. This is a team effort that requires cooperation. Remember, when an animal is loose, first and foremost is the need to safely re-secure the animal (s) in the appropriate primary housing.

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# AN ALTERNATIVE METHOD TO RAT RESTRAINT

By Lori Roberts, LVT and Melissa Dyson, DVM  
University of Michigan

**Ed Note:** This article excerpted from AALAS Tech Talk; Vol. 13/ No.6 DEC 08.

Creating comfortable restraint for animals that facilitates efficient accomplishment of procedures while minimizing stress is integral to the success of a research project. Reducing time and manpower are also concerns for research technicians and investigators alike. A novel approach to rat restraint has been employed by our staff for such tasks.

A square, washcloth sized cloth is folded into a triangular shape. The folded cloth is sewn together for approximately half of the length of one of the open sides, leaving a small opening at the tip for air flow to restrained animals. The sewn cloth forms a cone shape.

Place the rat's head into the closed end of the restraint device. Fold the end of the cloth over the rat's back and hind quarters. While maintaining the rat's position by gently pushing forward with a stabilizing hand, carefully place a binder clip over the posterior end of the folded cloth, being careful not to catch the rat's skin. Place a second binder clip on the anterior portion of the folded cloth.

The rat is easily and gently restrained in the soft cloth, leaving the technician with both hands free. Respiratory rate can be easily monitored by movement of the chest wall. The limbs can be removed from slits in the cloth for manipulation. The tail is free to be accessed for injections or blood draws. The tip of the "cone" can be cut to various sizes of rats so the animals can breath freely. The color of the skin and mucous membranes can be assessed through the opening to monitor the animal.

The restraint device is opaque, soft, and gently molds to the animal to provide secure restraint. Most rats quickly become trained and enter the restraint readily. Most rats are also very calm while inside the restraint device. Regular application of this technique by our staff has helped decrease the amount of time and manpower needed to perform injection and blood collection on large numbers of animals. Less experienced personnel are able to learn the restraint technique very quickly. Personnel report that they feel more comfortable completing required tasks while the rat is held safely in a restraint that allows the technician to have both hands free.

## CUSTOM DIETS

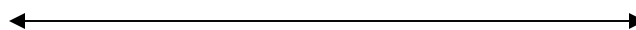
**"What every Pre-clinical Investigator Needs to Know"**  
The Test Diet division of Purina Mills, LLC formulates and produces custom diets for lab animal research around the world. Consult with a world class team of animal nutrition experts to formulate diets for your specific areas of study. For a free copy of the above informative article you can e-mail: [info@testdiet.com](mailto:info@testdiet.com).

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*How can this information be used by the Duke research community? When designing your animal use protocol:*

- *Evaluate an anticipated level of pain or distress for the procedures being proposed. Lacking any clear basis for expectation, asking oneself if the same procedure was performed in a human (and realizing that many research procedures would not be performed in people due to the unethical nature of such), what would be the anticipated pain management plan?*
- *How can the pain management plan (developed above) be applied to the animals proposed for use in research?*
- *How can I employ pre-emptive methodology in my animal studies?*
- *What modifications in medication agent, route of delivery, or dosage should be considered?*
- *What is the MAXIMAL duration of anticipated pain from the procedure I am proposing and have I recommended sufficient duration of coverage to address potentially painful periods?*
- *What signs of distress, specific to the species being used, should be considered as indicators of failed analgesia (observation of these signs is an indication of insufficient frequency of provision of analgesia)?*
- *What humane endpoints should I establish to prevent unnecessary pain or distress, and how will these be monitored?*

*For these or other questions of protocol development, please consult the animal program web site at <http://vetmed.duhs.duke.edu> or call the OAWA (668.6720) or DLAR (684.4204) to schedule a meeting with a Duke veterinarian.*



## FDA ISSUES DRAFT GUIDANCE ON ANIMAL MODELS

The FDA has announced the availability of a draft guidance entitled "Animal Models--Essential Elements to Address Efficacy Under the Animal Rule." This guidance identifies and discusses the critical characteristics of an animal model that should be addressed when developing products for approval under the Animal Rule. When finalized, the guidance will represent the agency's current thinking on animal models when addressing efficacy under the animal rule.

It is important that the FDA hear from research professionals who conduct research using animal models to support approval or licensure of a drug or biological product in cases when human efficacy studies are neither ethical nor feasible, as supported under the Animal Rule. The FDA will accept electronic comments on the draft guidance through March 23, 2009.



**Animal Care & Use Program  
Brown Bag Seminar**

**Tuesday, February 3rd, 2009  
Noon – 1 p.m.  
Hock Plaza Auditorium, Ground Floor**

**Ms. Aimee Coughlin  
Product Manager, Surgical Services  
North American Research Models  
Charles River Laboratories**

**Will be presenting:**

## **Rodent Surgery Overview and Practical Considerations**

**This presentation will cover:**

- ◆ How surgery is set up and executed at Charles River.
- ◆ Basic surgical services offerings (catheterizations, soft tissue, neurological procedures, etc.) What are they and why are they used.
- ◆ Special considerations for catheterized animals (maintaining patency, material types, lock solutions, etc.)
- ◆ Hallmarks of a good surgery program (aseptic technique, quality equipment, diligent operative care).

The presentation will be on **Tuesday, February 3rd, 2009 from Noon to 1 p.m.**

The session will be held in the **Hock Plaza Auditorium**, located on the **Ground Floor of Hock Plaza on Erwin Road**

Attendees are encouraged to bring a lunch. OAWA will provide drinks and desserts.

Please plan on arriving prior to noon in order to get refreshments, sign in, and be seated.

For those who will be coming from off campus, driving directions and parking information can be found at the following link: <http://neuro.duke.edu/Links/map.htm>

**This session will count for 1 CEU of AALAS In-house Training Credit**



**Animal Care & Use Program  
Brown Bag Seminar**

**Monday, February 23<sup>rd</sup>, 2009  
Noon – 1 p.m.  
Bryan Research Building: Room 103**

**Dr. Ron Banks  
Director Office of Animal  
Welfare Assurance**

**Will be presenting:**

## **How to Prepare for an IACUC Semi-Annual Inspection**

**Once again, it is time for the federally required inspection by Duke's Institutional Animal Care & Use Committee of all animal care and use areas on campus. Dr. Banks will discuss the standards used by the IACUC for inspecting your laboratory, procedure room or holding area. Using photographs of good and not-so-good laboratories, the attendees will perform a virtual inspection of the laboratory of Dr. Wool E. Bull at the Great Eastern University. Each attendee will receive a set of 'internal inspection checklists' that can be used to assist the laboratory in preparing for the IACUC inspection.**

The presentation will be on **Monday, February 23<sup>rd</sup>, 2009** from noon to 1 p.m.

The session will be held in room **103 of the Bryan Research Building**, located at 421 Research Drive, on Duke University's West Campus.

Attendees are encouraged to bring a lunch. OAWA will provide drinks and desserts.

Please plan on arriving prior to noon in order to get refreshments, sign in, and be seated.

For those who will be coming from off campus, driving directions and parking information can be found at the following link: <http://neuro.duke.edu/Links/map.htm>

**This session will count for 1 CEU of AALAS In-house Training Credit**