Continuing Education

All animal users and IACUC members must be satisfactorily trained to accomplish the required approved tasks and participate in on-going continuing education to meet regulatory and oversight obligations, as defined in Duke’s policy.

Required continuing training includes:
1. Animal Handler III (AH III) Annual Refresher Training
2. Periodic re-training on core modules (see Appendix A)

Voluntary opportunities that include:
1. Brown Bag Seminars
2. On-line module training (e.g., AAALAS Learning Library, CITI, OESO <animal related modules>)
3. CE seminars given by DLAR or the Duke Lemur Center
4. IACUC- or animal use-related regional or national conferences
5. Scientific journal articles of particular interest to reduce animal use, improve animal welfare, or refine procedures
6. RAC attendance at IACUC Programmatic Meetings
7. AALAS certification CE modules (e.g., learning library, classes, meetings)
8. Animal Tracks Newsletter
9. DLAR and/or OAWA training, on request

NOTE: Although continuing education is an expectation for all animal users, completion of 3 CEUs per year is no longer a requirement for clearance. Opportunities for CE are available on the Animal Program website.

REPORTING MISSING or ESCAPED ANIMALS

Even under the most controlled circumstances, adverse events may occur. When an animal escapes the holding cage, it is important that measures to capture the animal are engaged immediately! It is not acceptable to consider it returned to the wild or free to roam the building or somebody else’s problem. The goals of recapture are to: a) prevent an injury to an animal unaccustomed to being out-of-the-cage; b) to prevent a transgenic animal from passing their modified genes to other animals; and c) to prevent the spread of potential pathogens (if the animal is infectious).

If you suspect an animal is missing, check the room mortality log to see if an animal has died and the carcass removed for refrigerated storage. If you cannot determine that an animal is missing, or you know it is missing and cannot find the remains, then contact the DLAR supervisor.

Considerations for capturing animals:
- DO NOT handle an escaped rodent by hand. Use a hard container (e.g., a cup or empty cage) when capturing animals.
- Animals found in a trap or on the floor must be placed in a clean cage with food and water. DO NOT mix any caught animals with existing caged animals.
- A label using the word “COMPROMISED” must be affixed to the cage. This denotes that the animals should be handled as if infected.
- Notify a DLAR veterinarian immediately after the animal is captured.
- Notify responsible PI immediately.

NOTE: It is especially important to notify DLAR if the missing animal is transgenic, KO/KI, or an animal with recombinant DNA. Loss of these animals may require notification of the NIH Office of Laboratory Animal Welfare.
Animal Record Requirements: PI and Veterinary

This policy was recently revised to clarify the requirements for animal record keeping.

Who? Any individual performing animal procedures, care or assessments. This policy is applicable to laboratories (PI) and medical records.

What? Documentation of all activities related to animal observation, experimental procedures, surgery, treatment, medication or assessment is required.

Why? Records should convey the necessary information to all people involved in an animal's care and document adequate health care. These records must be made available to internal and external auditors.

How? Records should include the following:

- Analgesic/Anesthetics administered including medication, dose, route, and time of administration
- Details of surgical or research procedures performed on the animal
- Peri-, Intra-, and Post-operative monitoring (e.g., heart rate, oxygen saturation, blood pressures, animal condition, etc.)
- Non-surgical procedures monitoring (e.g., behavioral testing, physiological assessment, animal condition, etc.)
- Fluid/food restriction tracking
- Documentation of preventive medical treatments (e.g., quarantine, vaccinations)
- Descriptions of illness, injury, distress, or abnormal behavior and the resolution of any noted problem
- Treatments, therapies or interventions including dose, route, frequency, and duration, as applicable
- Final animal disposition
- Necropsy records
- Species specific records, as appropriate
- Health certificates
- Environmental enrichment and social housing
- Outdoor housing approval
- Husbandry, environmental, and daily monitoring

Remember! Medical records must be maintained for at least 3 years after final disposition of the animal.
**OLAW** develops and monitors, as well as exercises compliance oversight relative to the Public Health Service Policy on Humane Care and Use of Laboratory Animals (the "PHS Policy"). The following FAQs provide guidance that represents OLAW's current thinking on these topics. This guidance is based on OLAW's experience with the subject matter and draws on best practices followed by the biomedical community regarding the use of research animals.

**IS THE USE OF CO2 AN ACCEPTABLE EUTHANASIA AGENT? (UPDATED 3/2/16)**

Although CO2 is generally considered an acceptable euthanasia agent for small animals when properly administered, its acceptability is predicated on a number of critical factors as described in the [AVMA Guidelines](#) for the Euthanasia of Animals. The Guidelines recommend euthanasia chambers to be filled at a gradual displacement rate of 10% to 30% to minimize aversion and distress. It is important to verify death after CO2 exposure. If an animal is not dead, CO2 narcosis must be followed by a secondary method of euthanasia. Because immature animals are resistant to the hypoxia-inducing effects of CO2 and require longer exposure times to the agent, alternative methods should be considered such as injection with chemical agents, cervical dislocation, or decapitation ([Guide page 124](#)).
Pain Management Tips and Tricks

Reprinted and excerpted from ALN, February 2016, by Mary Ellen Goldberg, BS, LVT, SRA, CCRA

What is Pain?
Pain has been called the “fourth vital sign” after body temperature, heart rate, and respiratory rate, and its potential presence should be evaluated in patients just as other vital signs. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain motivates us to withdraw from potentially damaging situations, protect a damaged body part while it heals, and avoid those situations in the future. It is initiated by stimulation of nociceptors in the peripheral nervous system, or by damage to or malfunction of the peripheral or central nervous systems. Most pain resolves promptly once the painful stimulus is removed and the body has healed, but sometimes pain persists despite removal of the stimulus and apparent healing of the body; and sometimes pain arises in the absence of any detectable stimulus, damage, or pathology. For the purpose of this session we will describe pain as acute, chronic, or neuropathic (maladaptive).

What is the Pain Pathway?
The Pain Pathway = Nociception = processing of harmful stimuli in the nervous system. Nociception refers to the processing of a noxious stimulus resulting in the perception of pain by the brain. The components of nociception include transduction, transmission, modulation, and perception. Transduction is the conversion of a noxious stimulus (mechanical, chemical, or thermal) into electrical energy by a peripheral nociceptor (free afferent nerve ending). Drugs that work well here include:

- NSAIDS (carprofen, meloxicam, robenacoxib, etc)
- Opioids (morphine, hydromorphone, etc.)
- Local Anesthetics (lidocaine, bupivacaine)
- Corticosteroids (dexamethasone, depomedrol, prednisone, etc)

Transmission describes the propagation through the peripheral nervous system via first-order neurons. Nerve fibers involved include A-delta (fast) fibers responsible for the initial sharp pain, C (slow) fibers that cause the secondary dull, throbbing pain, and A-beta (tactile) fibers, which have a lower threshold of stimulation.

- Local Anesthetics (lidocaine, bupivacaine)
- Alpha-2-agonists (dexmedetomidine, xylazine)

Modulation occurs when first-order neurons synapse with second-order neurons in the dorsal horn cells of the spinal cord. Excitatory neuropeptides (including, but not limited to, glutamate, aspartate and substance P) can facilitate and amplify the pain signals in ascending projection neurons. At the same time, endogenous (opioid, serotoninergic, and noradrenergic) descending analgesic systems serve to dampen the nociceptive response.

Drugs that work well here include:

- NSAIDS (carprofen, meloxicam, robenacoxib, etc)
- Opioids (morphine, hydromorphone, etc.)
- Alpha-2-agonists (dexmedetomidine, xylazine)
- NMDA Antagonists (ketamine, amantadine)
- Tricyclic Antidepressants (amitriptyline)
- Anticonvulsants (gabapentin)

Perception is the cerebral cortical response to nociceptive signals that are projected by third-order neurons to the brain.

Drugs that work well here include:

- Opioids (morphine fentanyl, etc)
- Alpha-2-agonists (dexmedetomidine, xylazine)
- General Anesthetics (isoflurane, sevoflurane)
- Benzodiazepines (diazepam, midazolam)
- Phenothiazines (acepromazine) continued p. 5
Pain Management Tips and Tricks (continued)

Pain Assessment
When determining which analgesics should be used, several factors need to be considered:

- What is the likely severity of pain, and what is its anticipated duration?
- Which drug or drugs should be administered, and at what dose rates?
- Are there any special factors that will influence the choice of analgesic, for example, the species of animal, any potential interactions with a particular research protocol, or any particular features of the current condition and the type of pain?
- What facilities are available for management of the animal? What level of nursing care and monitoring of the animal is available? Can staff attend throughout a 24 hour period? Are there facilities for continuous infusion of analgesics?

When left unrelieved, pain in laboratory animals produces a catabolic state, which may lead to wasting of muscles. It also suppresses the immune response, which can lead to infection, and promotes inflammation, delaying wound healing. Pain can also result in increased anesthetic risks, because higher doses are required to maintain a stable plane of anesthesia.

See Table 1 http://www.alnmag.com/articles/2016/02/pain-management-tips-tricks

Assessment of pain or distress may be based on many different criteria including:

- Decreased activity
- Abnormal postures, hunched back, muscle flaccidity or rigidity
- Poor grooming
- Decreased food or water consumption
- Decreased fecal or urine output
- Weight loss (generally 20-25% of baseline), failure to grow, or loss of body condition (cachexia)
- Dehydration
- Decrease or increase in body temperature
- Decrease or increase in pulse or respiratory rate
- Physical response to touch (withdrawal, lameness, abnormal aggression, vocalizing, abdominal splinting, increase in pulse or respiration)
- Teeth grinding (seen in rabbits and farm animals)
- Self-aggression
- Inflammation
- Photophobia
- Vomiting or diarrhea
- Objective criteria of organ failure demonstrated by hematological or blood chemistry values, imaging, biopsy, or gross dysfunction

What About Pain Scoring?

Pain scoring for laboratory animals has evolved since 1985. Being able to recognize pain and score has become commonplace in veterinary practice. Researchers, scientists, and their staff are now required to recognize an animal in pain. Patients should never need to prove that they are in pain. A sound approach to pain management favors anticipation of the severity and duration of pain that is likely to occur with any procedure, condition, or surgery. Pain assessment is currently considered to be an essential part of every patient evaluation, regardless of presenting complaint.

Pain rating scales should include at least three requirements:

1. Minimal inter-observer variability and observer bias.
2. Ability to distinguish varying levels of pain intensity in a particular species and situation.
3. Ability to detect the degree of “importance” of pain to the subject.

Figure 1: VAS pain scale

Pain scales can be visual analog scales (VAS) (Figure 1), numerical rating scales (NRS) (Figure 2), or simple descriptive scales (SDS).

For VAS, a line with no markings is used, numbers are at each end with 0 meaning no pain and 100 being worst. The NRS pain scale uses a number line with individual numerical markings (1-10) which are chosen as the score, and during SDS, numbers are used to assign to descriptions that categorize different levels of pain intensity. continued p. 6
Pain Management Tips and Tricks (continued)

Grimace scales have been developed for several species, notably mice, rats, rabbits, and horses. In the mouse grimace scale, intensity of each feature is coded on a three-point scale. For each of the five features, images of mice exhibiting behavior corresponding to the three values are shown.\textsuperscript{13} The Rat Grimace Scale quantifies pain in the laboratory rat via facial expressions.\textsuperscript{14} The Rabbit Grimace Scale can be used to help recognize subtle expressions of pain in rabbits.\textsuperscript{15} The Horse Grimace Scale was developed to help with recognition of pain after surgical procedures in horses.\textsuperscript{16}

These scales are very helpful however many animals appear stoic. Additionally some animals will actually look better when you directly observe them.

Conclusion
As those working in a research setting we must:

- Have an accurate understanding about what pain is and how it affects an organism
- Be able to communicate intelligently and effectively about pain
- Be able to Recognize Pain
- Be able to Assess Pain
- Be able to Score Pain
- “Think outside the box” where pain is concerned

Let’s make it our mission to reduce pain in research animals.

See References http://www.alnmag.com/articles/2016/02/pain-management-tips-tricks

Mary Ellen Goldberg is a graduate of Harcum College and the University of Pennsylvania. In 2008, she became the Executive Secretary of the International Veterinary Academy of Pain Management. Ms. Goldberg has written several books and contributed to numerous chapters regarding anesthesia, pain management, and rehabilitation.

Applications are now being accepted for 2016-2017 Research Animal Coordinator Certification Course

If you are interested in applying, or know someone who would be a good candidate, please submit an application (signed by the applicant and the PI) to Bill Wade at w.wade@duke.edu

Classes will begin some time in the middle of September 2016. For additional information and to download the application please go to the OAWA website. We look forward to another successful year with another outstanding group of candidates!

REMAINING IACUC SEMIANNUAL SITE VISITS—SPRING 2016

MARCH 31st: CCIF
APRIL 7th: BIOLOGY—FRENCH—GROSS HALL—CIEMAS—DUKE NORTH/SOUTH
APRIL 14th: FOSTER ST—GHRB—VRH-DURHAM
APRIL 21st: VIVARIUM—MSRB1
May 5th: LEMUR CENTER—MSRB2—MESOCOSM

Safeguarding animal welfare is the responsibility of every individual associated with the Duke Animal Program.

REPORT ANIMAL HEALTH EMERGENCIES
to DLAR using the Veterinary Pager (24 hrs/day): 919-970-9410

REPORT OTHER ANIMAL WELFARE CONCERNS
to the Office of Animal Welfare Assurance (24 hrs/day) via the Animal Welfare Hotline: 919-684-3535
The Animal Welfare Information Center (AWIC) is part of the U.S. Department of Agriculture (USDA) National Agricultural Library (NAL) in Beltsville, Maryland. The Center was established in 1986 and is staffed by a two full-time and two part-time information specialists, and one information technology specialist.

A fundamental goal of the Animal Welfare Act and the accompanying regulations is the minimization of animal pain and distress via the consideration of alternatives and alternative methods.

**Mandatory and Regulatory Testing**

*Testing Regulations and Guidelines:*
Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM).

*Regulatory Acceptance of Alternative Methods (ICCVAM)*

*Alternatives:*
- Biologics and Vaccine Testing
- Eye Safety Testing

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**AltTox.org**

*Humane Society of the United States and Proctor & Gamble*

The goal of this website is to advance non-animal methods of toxicity testing through online discussion and information exchange.

**CCAC Three Rs Microsite**

*Canadian Council on Animal Care*

This site provides useful information on the three Rs (replacement, reduction, and refinement alternatives) to those involved with the use of animals in science.

**Alternatives to Animal Testing (Altweb)**

*Johns Hopkins Center for Alternatives to Animal Testing*

A gateway to alternatives news, information, and resources on the internet and beyond.

**US Congress. Office of Technology Assessment**

This 1986 report analyzes the scientific, regulatory, economic, legal, and ethical considerations involved in alternative technologies in biomedical and behavioral research, toxicity testing, and education.

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**What does the IACUC Look for in the Literature Search for Alternatives to Painful or Distressful Procedures?**

At a minimum, the search needs to:
- Include 2 databases
- Cover a reasonable time period (5+ years)
- Include a reproducible search strategy

Could you copy and paste what was submitted and get the same results?

Is it clear how AND, OR, (,), *, ?, etc, were used?

‘Red Flags’ in the search strategies:
- Keywords are not relevant to the protocol
- Is the current submission simply “copy and pasted” from a previous protocol without updating?
- Search strategies don’t include terms for all of the painful or distressful procedures.

Are alternative methods for each potentially painful or distressful procedure included in the search?

**NOTE:** Combining all the procedures with AND is not sufficient and usually produces “0” results.

- **The term ‘alternative’ is used alone**
  - If a search has the term “alternative” in it, it should also have specific terms for alternatives (i.e. cadaver, cell line, imaging, replace, refine, anesthesia, etc.) as well.
- **No Synonyms**
  - Authors don’t always use the exact same term, so searches need to include synonyms, plurals, etc. Using subject headings like MeSH can help with this.
- **Too many (1,000+) or too few (0) results**
  - Too many results may suggest the articles may not be on topic. Too few results may result if too many search terms were combined together.

**For assistance, please contact:**

Emily S. Mazure, MSI, AHIP
Biomedical Research Liaison Librarian
Duke Univ. Medical Center Library & Archives
919-660-1197

**Tools for Biomedical Researchers**