



ANIMAL TRACKS



A newsletter for the Duke research community

September 2007

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

OESO Review

The Occupational and Environmental Safety Office (OESO) reviews all animal protocols for compliance with safety requirements for working at Duke. The review is based on hazards identified in the protocol, as well as compliance with safety training requirements and completion of an annual laboratory audit. To ensure the timely approval of protocols, OESO recommends that PIs have all personnel on the protocol, either new additions or existing personnel, check their safety training status prior to submitting a protocol.

Safety training requirements and training status are available to employees on the OESO web-site at www.safety.duke.edu. Information regarding suggested training for research laboratory employees is also available on this web-site under the Services and Resources section, "Safety Training Requirements for Research Laboratory Personnel" link. If an employee does not have all requirements displayed on their requirements page, they may still take the recommended training by clicking on the "Courses Available On-Line" link on the left side of the screen.

To review training requirements and training status go to www.safety.duke.edu and click on On-Line Training on the left side of the screen. You will be asked to enter your Duke NetID and password. Once your password has been validated, you will be directed to your training requirements page. This page will list training requirements and the due date for the training. To access training, click on the course name. Note: The list of requirements is subject to change based on the hazardous materials being used in the laboratory. If you know that you will require a certain training that is not displayed on your requirements page, i.e. formaldehyde, you should go ahead and take the training through the "Courses Available On-Line" link.

The OESO can provide PIs, or their designees, access to a protocol page that lists all employees on a particular protocol. Training requirements and training status for employees on the protocol can be accessed from this page. Checking the training status of your employees and having them complete their safety training requirements PRIOR to submitting a protocol will help the protocol clear faster. If you are interested in accessing the protocol page, please contact Cackie Joyner at 684-2794.

Tips for the New Protocol Preparation and Submission

Tip Number 1: Use Adobe Acrobat version 6, 7, or 8, (available at the Duke store) or Adobe Reader 8 (this is a free program from Adobe.com). The protocol template was designed using Adobe 8, but will work equally well using Adobe 6, 7, or 8.

Tip Number 2: Use a computer that has at least 512 MB RAM (1GB is better). The protocol file is large, using an older or slower computer will work, but will work slowly.

Tip Number 3: Every application for animal use MUST include all of PART I; BUT ...you will ONLY complete those SECTIONS of PART II that are applicable. Download Part I (consist of Section A-G) and only those Sections of Part II that you need. NOTE: SECTION A6 (in PART I) will help you identify which SECTIONS of PART II you will need to complete.

Tip Number 4: Submit your application PART I & SECTIONS by one of the following methods:

- * Email the completed PART I & SECTIONS to: IACUC@DUKE.EDU (this is the preferred method); or
- * Print off a hard copy of the completed PART I & SECTIONS and FAX to: 919.668.6725; or
- * Print off a hard copy of the completed PART I & SECTIONS and hand carry to: Hock Plaza Building; Suite 1104.; or
- * Print off a hard copy of the completed PART I & SECTIONS and mail to: Office of Animal Welfare Assurance; 2424 Erwin Road, Suite 1104; Durham, NC 27705

Tip Number 5: Documents emailed from the PI's Duke Email account do not need to be signed. The PI's Duke Email account is considered an 'electronic signature.'

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Upcoming Dates & Deadlines

| | |
|--------------|---------------------------------------|
| September 6 | Significant Change Meeting |
| September 10 | New Protocol Deadline |
| September 10 | Significant Change Deadline |
| September 20 | Brown Bag Seminar: New Protocol Hints |
| September 20 | Significant Change Meeting |
| September 24 | Significant Change Deadline |
| September 27 | IACUC Meeting |
| October 4 | Significant Change Meeting |
| October 8 | New Protocol Deadline |
| October 8 | Significant Change Deadline |
| October 18 | Significant Change Meeting |

Deadlines are 5 PM on the date listed! No exceptions!

REGULATORY WATCH

(NIH/OLAW Q&A)

Question: May an investigator transfer animals and research to an institution different than the grantee institution?

OLAW Answers: The transfer of PHS-supported research to a different institution requires the prior approval of the funding component. The proposed new grantee institution must have or obtain an Animal Welfare Assurance and possess all the resources necessary to fulfill the conditions of the grant, and its IACUC must review and approve the animal activities. The original IACUC approval is void when the original grantee formally relinquishes the award. The receiving institution must provide verification of IACUC approval prior to receiving funding. Note that the conditions of approval by the IACUC at the receiving institution may differ from those required by the original grantee's IACUC.

Question: May investigators use expired pharmaceuticals, biologics, and supplies in animals?

OLAW Answers: The use of expired pharmaceuticals, biologics, and supplies is not consistent with acceptable veterinary practice or adequate veterinary care. Euthanasia, anesthesia and analgesia agents should not be used beyond their expiration date, even if a procedure is terminal. Other expired materials should not be used unless the manufacturer verifies efficacy beyond the expiration date, or the investigator is able to document to the satisfaction of the IACUC that such use would not negatively impact animal welfare or compromise the validity of the study. The veterinarian and IACUC must maintain control over the use of expired medical materials in order to meet their responsibilities to avoid or minimize discomfort, pain or distress to animals.



Are you missing a form you used to be able to find on the web? Well, actually it is still there ... but

With the large number of forms people are using, there was a need to separate those that are WORD VERSION forms from PDF VERSION forms. *Almost* all, but not quite all of the forms are in both versions, WORD and PDF. But, if you cannot find the form you are looking for, use the third link from the top of the page and go to the other version (if on the WORD VERSION page, the link says click to go to PDF VERSIONS; if on the PDF VERSION page, the link says click to go to WORD VERSIONS).

The ultimate goal is to convert ALL forms to a PDF 'fillable' form, but that will take time. Until then, maybe this little tip will help you find the animal form you need.

DLAR Pharmacy Scripts

Many of the medications and drugs that are regularly used by DLAR and research groups at Duke are maintained in the DLAR pharmacy including those for analgesia and anesthesia. Requestors should submit an IR form to the Pharmacy drop box at the front desk of the vivarium or fax a copy to 668-1642.

Orders for non-controlled drugs will be filled within 48 hours; requestor will be contacted and the drugs left at the front desk. Orders for controlled drugs and substances can only be picked up directly from the pharmacy technician on Tuesday and Thursday afternoons between the hours of 2-4 pm. Please submit the IR request at least 24 hours in advance of desired pick up time.

SPECIAL REMINDER!!!

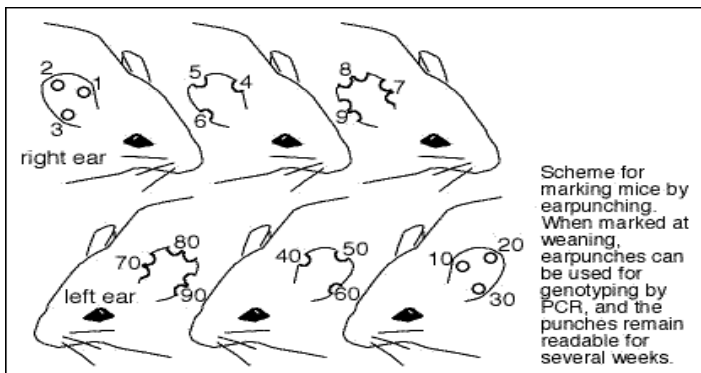
**ALL NEW PROTOCOLS MUST BE
SUBMITTED USING THE
NEW PROTOCOL TEMPLATE**

AFTER OCTOBER 9, 2007!

Guidelines for Rodent Identification

All the following techniques are acceptable forms of identification; some require IACUC approval. Individual identification of animals plays a critical role in accurate record keeping. There are several optional methods of identification of rodents. Proper restraint plays an important role in most of these techniques.

- ◆ **Metal ear tags** are inexpensive and don't require anesthesia for application (although this may facilitate proper placement) but the animal must be securely restrained. The tags need to be appropriate size for the species and should be applied to the distal 1/3 of the pinnae. If placed correctly they generally last for at least 6 months. There is a possibility of local infection and implantation sites should be monitored occasionally.
- ◆ **Ear notch punch** is another identification option. It is inexpensive and permanent, the animal must be securely restrained but no anesthesia is required if the animal is less than 3 weeks of age. Ear clipping remnants can usually provide enough DNA for an initial PCR screening.



- ◆ **Tattoo** is an acceptable technique and offers a permanent means of identification. Disadvantages include initial cost of equipment, some skill and experience is needed and the need for anesthesia. Good for long term studies, especially in rats.
- ◆ **Electronic Transponders** are a recent option. Anesthesia is not required, but may facilitate placement, as this only requires a subcutaneous injection. Initial cost for reader is high but this is useful method for accurate identification. Toe clipping is a traditional method of identification and has the added benefit of high quality tissue sample for analysis. However, the IACUC discourages toe clipping because it has the potential to cause pain and distress and might alter the gait, weight-bearing ability of a limb, and ability to feed.
- ◆ **Toe clipping** can be considered under the following conditions: 1) Alternative methods of identification must first be considered. 2) A written explanation of why it is necessary is required, including a discussion of why alternate methods are unsatisfactory. This will be considered and must be approved by the IACUC. 3) It should only be performed when mice are less than 12 days of age and is generally limited to only one digit per extremity. Mice should be anesthetized, but topical anesthetics are acceptable. Sharp sterile scissors should be used and the foot should be cleaned with a dilute betadine solution.



Guidelines for Alternatives Searching

Federal regulations require researchers attempt to avoid the use of animals, to improve the quality of their research, and to utilize advances in technologies as new methods of doing research are developed. Some 'new methodologies' avoid the use of animals, reduce the number of animals required to attain the intended results and lessen the impact on the animals used. Alternative methodologies should be adopted as they become available.

Alternative searches are difficult for many researchers to perform, so let's look at the alternative for animal use search part of the animal application.

The Legal Requirements: The **Public Health Service (PHS)** policy on humane care and use of animals requires adherence to the **US Government Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research, and Training**. Principle III says in part "Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered." Principle IV states in part that "Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative." The PHS Policy has no additional guidance on how the institution is to assure compliance with the Principles other than to hold the Animal Care Council (the IACUC) responsible for it.

The federal **Animal Welfare Act** is more specific regarding the alternatives requirement. In Subpart C, section 2.31 the USDA standards state "...the IACUC shall determine that the proposed activities or significant changes in ongoing activities meet the following requirements: (ii) The principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources, e.g. the Animal Welfare Information Center, used to determine that alternatives were not available." There is also a requirement in section 2.32 that the institution assure that personnel are trained in utilization of services providing information about alternatives [2.32 (c)(5)(ii)].

The Meaning of Alternatives: The concepts involved in "alternatives" to animal research were originally put forth in a 1959 publication, *The Principles of Humane Experimental Technique* by Russell and Burch. Alternatives encompass three broad categories that are commonly called the "3 R's": replacement, reduction, and refinement. In a 1995 article titled: *The 4th R of Research*, the author argued the addition of 'responsibility' to the original three R's of Russell and Burch. Recommended for the new era of 'performance based outcomes,' the 4th R reflects integrity, honesty, and scientific correctness in appropriate and reasonable use of laboratory animals.

Continued on the Next Page (See Alternative Searching)

Continued from page 3:

The Search for Alternatives - Defining the Goal:

The search for alternatives is not simply a literature search to show that the animal use is unique. A search for alternatives is also not a search of the literature to show that the animal use has scientific validity. Searches for unnecessary duplication and scientific validity are required; however, those searches have the wrong focus and would not be sufficient to adequately assess the possibilities for alternatives to the use of animals. The alternatives search begins after the search has been assured. The alternatives search is best approached by necessity of techniques used in the research. The "causes" of the events and it is avoided or minimized. Therefore, the alternatives search is an effort to find methods of accomplishing the goals of the research with less or no animal impact.

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Pain and distress can be quite difficult to assess in animals that can not verbally describe their experiences. In practice, familiarity with normal behavior and critical observation of the animals are essential for making a reasonable appraisal of the animal's experience. More importantly in the search for alternatives, pain and distress are legally defined. Procedures that would reasonably be expected to cause pain or distress in a human if performed on a person must be considered potentially painful or distressful in other animals. The most obvious approach to reducing pain or distress is through the use of anesthetics and analgesics. However, the USDA standards define painful procedures such that the use of pain relieving drugs do not make the procedure definable as "nonpainful". Therefore, use of pain relieving drugs is a practical way of reducing the impact of the procedure on the animals but it does not change the requirement for an alternatives search.

Conceptualizing the Search: The search, therefore, must focus on techniques that may cause pain. There may be several techniques used and each may need to be considered separately in the alternatives search. For instance, a research project may involve surgery to implant an aortic artery catheter and infection to induce pneumonia. These techniques are quite different and the opportunities for using alternative techniques may present themselves in entirely different places. A concurrent search for both would severely limit the search. Of further note in this example is that the surgery is unique to neither a specific species nor a specific research field. Thus the search must be designed to avoid artificial limitations such as would be imposed if "hamster" or "immunology" were search words. Techniques should be viewed as an avenue to a goal, as many techniques can be adapted to different species and research areas. For instance, the example above must consider the purpose of the catheter. If it is used to monitor blood oxygenation as an indication of disease progression, then techniques that measure this transcutaneously may be a useful alternative. In some cases, the techniques are unique to the research field. In the example, the infection procedure may be to study a specific lung infection. An alternatives search to this technique may be most appropriately done in the literature of the specific topic.

Conducting the Search: There are a variety of sources that can be explored for alternatives to animal research. The USDA has indicated their expectation that an alternatives search includes searching a literature database. There are many literature databases available and information on useful alternatives may appear in databases quite distinct from those where the goals of the experiment would be published. Assistance with determining which databases to search and the specific search strategies for those databases is best sought from a library information specialist.



What Resources Are Available:

A very good place to start the process is with ALTBIB (Bibliography on Alternatives to the Use of Live Vertebrates in Biomedical Research and Testing). ALTBIB is a searchable bibliographic collection on alternatives to animal testing. It includes citations from published articles, books, book chapters, and technical reports from 1980 to 2000. Citations were selected manually after searching various National Library of Medicine (NLM) bibliographic databases. The bibliography features citations concerning methods, tests, assays, and procedures that may prove useful in establishing alternatives to the use of intact vertebrates. ALTBIB has not been updated since 2001 because new features were added to PubMed®/MEDLINE® to assist users in searching and retrieving directly from the file. Search strategies for some animal alternatives have been developed and incorporated in the ALTBIB search interface. ALTBIB is accessible, free of charge, via TOXNET® at: <http://toxnet.nlm.nih.gov/altbib.html> Users can search ALTBIB (1980 to 2000) by term or by one of these 16 categories: General; Carcinogenesis; Cytotoxicity; Dermal Toxicity; Ecotoxicity; Genotoxicity and Mutagenesis; Hepatic and Renal Toxicity; Immunotoxicity; Neurotoxicity; Ocular Toxicity; Pharmacokinetic and Mechanistic Studies; Pulmonary Toxicity; Quantitative Structure Activity Relationships; Reproductive and Developmental Toxicity; Tissue and Organ Toxicity; and Miscellaneous.

Users can also search PubMed/MEDLINE from the ALTBIB page using the animal alternative search strategy provided. The search strategy can be limited by date, animal alternative (MeSH) or toxicology subset. Search strategies incorporated in the ALTBIB search interface can be seen by clicking on the detail button in the result page. Strategies can be modified or written de novo.

Users can easily link to additional resources on the 3Rs (reduction, refinement, replacement) and animal testing alternatives, as well as other NLM databases.

For detailed information about ALTBIB or TOXNET, contact:

Two Democracy Plaza, Suite 510
6707 Democracy Boulevard, MSC 5467
Bethesda, MD 20892-5467
Telephone: (301) 496-1131
FAX: (301) 480-3537
e-mail: tehip@tehip.nlm.nih.gov
URL: <http://sis.nlm.nih.gov>
National Library of Medicine
Specialized Information Services



OAWA's Brown Bag Seminar

Monday, September 17th, 2007

Noon – 1 p.m.

Bryan Research Building: Room 103

Dr. Ron Banks

Director of the Office of Animal Welfare Assurance will be presenting:

Now On-line and Ready for Submission: The New Duke IACUC Protocol Template, The “How To’s” for the new system

**This is a repeat of the previous session,
for those who were unable to attend last month
or have questions since using the application.**

The Duke IACUC has been working for over a year to develop a new animal use protocol template. The new template has several goals:

1. To develop a 'back-bone' document for the soon-to-be-coming web-submission for animal use applications;
2. To have a protocol that asks the questions necessary for the IACUC to make an informed decision;
3. To have a protocol that is easier for researchers to follow;
4. To decrease the number of clarification questions required; and
5. To allow reviewers to be able to review efficiently and completely.

At this seminar, the Office of Animal Welfare Assurance will give a preview of the animal use protocol template and discuss how to use it. The protocol template has a core document that will be completed with each new protocol submission, and then additional sections will be completed and submitted as they apply to the proposed research plan and procedures. We will discuss:

1. General overview of the purpose of a protocol template;
2. General overview of the Duke IACUC's actions in developing the new template; and
3. General overview of the structure of the new template and the concept of how it will work, by Part and Section.

Hard copies of the template core will be available at the seminar with a web-link for the various appendices for specific sections of the protocol. Dr. Banks will briefly touch on each of the appendices of the template. P.I.s, laboratory managers, and research associates are strongly encouraged to attend to minimize speed bumps during the transition to the new template.

The presentation will be on **September 17th, 2007** 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. The session will begin promptly at noon. Please arrive early to sign-in and find a seat.

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>