



ANIMAL TRACKS



A newsletter for the Duke research community

May 2008

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

CONTROLLED SUBSTANCE LICENSING FOR ANIMAL RESEARCHERS: AN UPDATE

Dear Colleagues:

We continue to work with the state and federal agencies to facilitate the necessary controlled substance licensing process for your research efforts. It has been a number of months since this initiative began, and an update is certainly in order.

At present, the state controlled substance agents (NC DHHS) have performed approximately 50 inspections for Duke researchers. Thus far, all inspections have resulted in issuing state controlled substance licenses. However, the state inspection process has not been trouble-free, they were not properly staffed to manage the mandate that they issues. But to the credit of the state agency, the state has added additional inspectors which has improved the speed of inspection and approval. The increased number of inspectors will continue their inspections until all of the initial pool of controlled substance license inspections are completed—it looks like by mid May. For those individuals who have received the state controlled substance license, the next step is the federal approval process.

The federal controlled substance review and inspection is performed by agents of the US Department of Justice, Drug Enforcement Agency (DEA), Diversion Control, Greensboro, North Carolina. While the federal agents MAY perform a physical inspection, this inspection is more often a telephone and/or email review.

Information the DEA inspector will need includes:

- Name of DEA License Holder
- Other names Used (maiden, nicknames, aliases)
- Present Home Address
- City/State/Zip
- Home Phone Number
- Date of Birth
- Place of Birth
- Driver's License Number
- Duke Office Mailing Address
- Duke Phone Number
- Duke Email Address
- NC State License Number
- Protocol Number and Protocol Approval Date
- Location of the Controlled Substance(s) Container
- Person with Direct Responsibility for the Controlled Substance(s)
- State Why Controlled Substances are Required (Note: 2 or 3 paragraphs only; identify whether anesthesia, analgesia, direct experimentation of the controlled substance)
- What Species Will Receive the Controlled Substance?
- What is the Maximum Anticipated Volume of the Controlled Substance You Will Keep in the Cabinet?

Some inspectors have asked for specific animal protocol information. Is this necessary? According to the DEA Chief Agent for our region:

- Schedule I: The approved animal protocol is required for assessment of the controlled substance license. The protocol is used only to confirm appropriateness of the license request, and provides the basis for the inspector's report.. When the report is completed, the protocol is destroyed.

Note: The state DHHS classifies controlled substances in DEA Schedule I as Schedule I or VI. The state agent may also require an approved protocol for these license Schedules.

- Schedule III, IV, and V controlled substances, there is need for the inspector to review the entire protocol, however, the inspector does need sufficient information to make an informed decision about the requirement of, the protection of, and the management of the controlled substance. It is reasonable that the inspector may, while on site, review a copy of the approved animal protocol. You may also refer the inspector to the OAWA for this review procedure.

To assist these inspection request while protecting your proprietary procedural information, the OAWA is creating a new section for the Duke protocol template, which would be completed only if a DEA application is required. This new section will have the necessary information for the state and federal inspectors.

I know how challenging and at times frustrating this new state mandated process has been. The change in the state's interpretation of regulations occurred with less than desirable pre-planning on their support of the process and without clear instruction on the requirements for researchers. Believe me, we have experienced you same distresses in communicating with the agencies, but we will continue to support and facilitate your research as we wish you safe and productive research endeavors,

When Writing a Grant ... (Suggestions for a Smooth Concordance Review)

con-cord-dance: noun: meaning agreement or harmony

Grant and protocol writing is confusing enough without getting caught between the grant regulators and the IACUC's protocol review. Many funding agencies (all NIH divisions) require a 'concordance review and approval letter' from the institution prior to releasing the grant funds. The Duke animal program performs concordance reviews by comparing the grant proposal describing animal procedures with the IACUC approved protocol. Many faculty have had a concordance approval letter delayed due to differences between the grant and the IACUC approved protocol. Most often, the disconnect occurs because researchers have written the grant proposal in a detailed manner that is not matched by the protocol. **A detailed animal protocol application is required by federal law! A less detailed grant provides flexibility for your experiment while allowing for concordance.**



On behalf of the Duke faculty, Dr. James Reynolds, Duke IACUC Chairman, recently requested clarification by the Grants Policy Office at the NIH on the issues of allowable and suggested language in grants concerning animal activities.

In response to Dr. Reynolds' inquiry, the NIH has noted the following:

- ◇ The use of language such as '...appropriate methods of anesthesia, analgesia, and euthanasia will be developed in consultation with our institution's attending veterinarian...' is appropriate, and sufficiently detailed to meet the requirements of the procedure description in the grant.*
- ◇ The grant should also note '... any change from the grant will also be evaluated by the IACUC for implications regarding the effect on the research.' This will allow the IACUC final decision on the appropriateness of the proposed change upon animal welfare, well-being, and grant procedure.

*** This specific language MUST be contained in the 'Animal Use' section of the grant application (for the NIH it is presently Section F). With this specific language in the grant, the IACUC has the authority to employ professional judgment in the concordant assessment.**

The enhanced flexibility offered by this language in the grants should decrease significantly the numbers of concordance approval letters that are delayed due to discordance between the grant and the protocol. Examples where this would be the enhanced ability of the IACUC to make amendment decisions concerning grant described procedures includes:

- ◇ The grant indicated the use of an opioid, but the IACUC determined the use of an NSAID would be more appropriate; or
- ◇ The grant indicated the use of injectable anesthetic overdose, but the IACUC determined the use of CO2 euthanasia would be the preferred euthanasia; or
- ◇ Switching from halothane (listed in the grant) to isoflurane (approved by the IACUC) in response to notification on availability; or
- ◇ Switching from intraperitoneal injections (listed in the grant) to subcutaneous injections (approved by the IACUC in response to veterinary review recommendation).

The 'test' of whether a modification of the grant or protocol is required (or not) will be based upon all of the following:

- ◇ The changed procedure (NSAID for opioid; CO2 for injectable anesthesia overdose; isoflurane for halothane; subcutaneous for intraperitoneal); and
- ◇ Whether the changed procedure still addresses the same base concern (pain relief; humane euthanasia; proper anesthesia; route of administration) listed in the grant; and
- ◇ That the change was, in the opinion of the IACUC, preferred for the well being of the animal; and
- ◇ That the change had no substantive impact upon the outcome of the grant procedures.

If the IACUC can validate each test (above), then the IACUC can determine that concordance does exist, even if the language is not 100% the same.

So, what is the take-home message?

- ◇ **PIs:** Write grants in generic terms using ranges or classes of agents rather than specific doses and routes. Write the Duke protocol with specific language on the agent, dose, and route of administration.
- ◇ **IACUC:** Allow non-substantive differences between the grant and the protocol, as long as those differences pass the 'test' described above.

Ask OLAW (Office of Laboratory Animal Welfare)

Does the IACUC need to require that the investigator submit the grant application, or portions thereof, along with the IACUC animal use protocol form for review by the IACUC? Is the IACUC required to compare the two for consistency?

PHS Policy (IV.D.) requires the institution to verify, before award, that the IACUC has reviewed and approved those components of grant applications and contract proposals related to the care and use of animals. This position is reiterated in NIH Grants Policy Statement under Part II, Terms and Conditions. Most institutions have developed an IACUC protocol form and require investigators to provide detailed information about the proposed use of the animals on this form. The signature of the authorized institutional official on any PHS application or proposal indicates the organization's commitment to comply with the laws, regulations, and policies to which an activity is subject. Institutional submission of IACUC approval, subsequent to submission of the application/proposal, must represent approval of the information originally submitted in the application/proposal, or include notification of any significant changes required by the IACUC.

Although there is no explicit requirement for the IACUC to do a side-by-side comparison of the application/proposal and the IACUC protocol review form, it is an institutional responsibility to ensure that the information the IACUC reviews and approves is consistent with that contained in the application/proposal to be funded. Institutions are free to devise a workable mechanism to accomplish this end. One excellent way to prevent problems of inconsistencies between the information submitted to the PHS and that on the IACUC protocol review form is to implement a procedure for direct comparison. If a procedure of direct comparison is adopted, the individual(s) charged with conducting the comparison should be appropriately qualified to identify inconsistencies. Some institutions have delegated this responsibility to a particular office or position (e.g., sponsored programs office, compliance office); others have asked Departmental Chairs to verify consistency.

You can view OLAW's website at: <http://grants.nih.gov/grants/olaw/>

From the *Institutional Animal Care and Use Committee Guidebook***: Review of Grants and Contracts Submitted to PHS

In order to approve a protocol that involves the use of animals, the IACUC must review the proposed care and use of animals and determine that federal criteria have been met. PHS requires that the project be conducted in accordance with the PHS Policy, the AWA, the Guide, the institution's Assurance, and all other applicable federal statutes and regulations related to animals. The project should also comply with all institutional policies.

Most IACUCs require use of a standardized protocol application form to assist the investigator in providing the information necessary to ensure compliance. While there is no explicit requirement for the IACUC to do a side-by-side comparison of the information contained in the IACUC protocol review form and the information submitted to PHS, it is imperative that the protocol that the IACUC approves is consistent with the information submitted to PHS. Institutions should devise a mechanism to verify that consistency. If the IACUC requires changes to the protocol that are not reflected in the grant application, then the PHS funding component must be notified in the follow-up certification of IACUC approval.

Institutions are required to provide PHS with the date of IACUC approval. There is no provision for providing a contingent approval date; the date provided must signify full approval by the IACUC. If an institution has a PHS Assurance, then in most cases the PHS allows a 60-day grace period following the receipt deadline date during which the investigator may secure IACUC approval; otherwise, the application cannot be peer reviewed. If the IACUC review occurs subsequent to the grant submission, then a letter verifying IACUC approval, and stating any modifications required by the IACUC, must be submitted to the funding agency. This grace period is non-existent for some non-federally funded projects and investigators are required to submit evidence of IACUC approval coincident with the grant or contract submission.

** You can view the entire text of this publication online at <http://grants.nih.gov/grants/olaw/GuideBook.pdf>



OAWA's Brown Bag Seminar

Tuesday, May 13th, 2008

Noon – 1 p.m.

Duke North Central Core Lecture Hall 2001

*** please note the room change to accommodate additional attendees***



**Tom Holder,
2008 Michael D. Hayre Fellow
will be presenting:**

Speaking of Research

The Americans for Medical Progress (AMP), a national nonprofit organization supporting biomedical research, has selected Tom Holder as the inaugural Fellow of the Michael D. Hayre Fellowship in Public Outreach. Mr. Holder, a Pro-Test (U.K. pro-research group) committee member, has begun a U.S. initiative to establish 'Speaking of Research.' This is a campus-oriented group that seeks to provide university students and scientists with accurate information and resources about the importance of animal research in medical science.

During this Brown Bag Seminar, Mr. Holder will discuss the experiences (and part in) the rise and fall of animal extremism in the UK, the value of animal research in medicine, and the importance of standing against the lies, harassment and violence of animal rights groups in the U.S.

As an example, when animal rights militants threatened the Oxford community over the construction of a new research facility, the grassroots group Pro-Test was a fulcrum for an overwhelming change in public opinion toward animal research. Tom's work as Press Officer with Pro-Test included participation in the global media campaign and serving as a lead organizer and spokesman for Pro-Test's historic 2006 march in which hundreds of citizens rallied in support of research and against intimidation by animal rights leaders. Then-standing British Prime Minister Tony Blair cited Pro-Test as an example of the change in public attitudes in the U.K.

The presentation will be on Tuesday, **May 13th, 2008** in the
Duke North Central Core Lecture Hall 2001.

(located directly above the Duke Hospital entrance
at the intersection of Fulton Road and Erwin Drive)

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.

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