**IACUC Training Exercise #2- 2015**

The following exercise may be useful in stimulating discussion regarding compliance with PHS Policy and VA Handbook 1200.07. To facilitate discussion, page 1 of the exercise may be distributed to the IACUC members prior to a meeting. After a few minutes of discussion about the exercise during the meeting, the remaining pages of the exercise may be distributed to provide ideas for the committee’s consideration.

Dr. Zauberfinger is performing a surgical procedure on a rat, and everything is proceeding smoothly, exactly as described in the protocol that was approved by the IACUC. He has just taken a biopsy, which has been sent to his laboratory for examination, and is waiting for confirmation that the sample contains the histological areas of interest before continuing with the surgery. The confirmation typically takes 5-10 minutes, so he takes the opportunity to double-check the level of anesthesia, and injects a small supplementary dose of the approved ketamine/xylazine rodent cocktail. At 20 minutes, he gets word that there’s a problem with the microscope in the lab, and his technician is changing a part, but expects to have results for him in 10 more minutes. Dr. Zauberfinger administers another small supplementary dose of ketamine/xylazine, according to the protocol, which was wisely written to allow adjustments of the doses and frequency of administration “as necessary to maintain an appropriate level of surgical anesthesia”. Forty minutes after sending the biopsy off to the lab, he learns that the microscope is still not functional, and efforts are now being made to find another microscope to use. He is reluctant to give yet another supplementary dose of injectable anesthetic, but is concerned that the level of anesthesia is likely to become too light before he will be able to finish the procedure, so he asks his assistant to contact the veterinarian, Dr. Tierartzt. Fortunately, Dr. Tierartzt answers the call immediately and agrees that administering more ketamine is likely to result in delayed recovery from anesthesia. He directs Dr. Zauberfinger to switch to isoflurane anesthesia, administered by nose cone.

Questions to consider:

1. Can Dr. Zauberfinger do this, given that his IACUC-approved protocol makes no mention of using isoflurane?
2. What if Dr. Zauberfinger wants to be able to switch to isoflurane during future procedures on this protocol, and is concerned that the veterinarian might not be available every time when the decision is to be made?
3. What if the IACUC decides that this is generally a good option to allow for most protocols?

Question 1): Is it compliant with regulatory requirements for Dr. Zauberfinger to switch to isoflurane anesthesia for this animal, when his IACUC-approved protocol makes no mention of isoflurane?

It is the veterinarian’s responsibility “to oversee the well-being and clinical care … and promoting animal well-being at all times” (Guide, p. 105). The change to isoflurane in this example is

* for the well-being of the animal, and
* according to the professional judgment of the veterinarian.

So, no IACUC approval is required.

Question 2): What if Dr. Zauberfinger wants to be able to switch to isoflurane routinely, without having to ask the veterinarian, if any animal on the protocol turns out to need more than 2 anesthetic supplements?

This is a significant change and requires IACUC approval. IACUC approval can be granted after review by DMR or FCR, as in the past.

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| **Significant Changes in an Approved Protocol** (require IACUC approval) | **Other Changes in an Approved Protocol** (do not require IACUC approval) |
| These are generally changes that will have, or have the potential to have, negative impacts on animal welfare or personnel safety | These are mainly changes that only have to do with documentation or project management |
| Examples:* Procedures (including changes in anesthesia)
* Locations
* Species
* Objectives
* PI
* Increased numbers
 | Examples:* Corrections of typos/grammar
* Updates of contact information
* Personnel other than PI
 |

Question 3): What if the IACUC determines that it is generally acceptable for protocols that involve ketamine/xylazine anesthesia to be modified to allow switching to isoflurane after two supplementary doses of the injectable anesthetic?

In addition to DMR and FCR, OLAW recently approved of another mechanism by which some significant changes can be approved by the IACUC, **V**eterinary **V**erification & **C**onsultation (**VVC**). In this method, approval is granted by the IACUC when it votes to approve a policy allowing specific changes (such as the change from ketamine/xylazine to isoflurane, in this example) to be made in approved protocols. The role of the veterinarian is not to grant the approval, but to verify that the change requested is consistent with the change covered by the policy that was approved by the IACUC, and that it is appropriate for the animals in the protocol in question. When the veterinarian deems that the IACUC-approved policy is appropriate to apply to the protocol, the change is considered approved by the IACUC. If the veterinarian has concerns about the change, and deems that the IACUC-approved policy should not be applied, the investigator will only be able to make the change after submitting a formal modification for review and securing IACUC approval by DMR or FCR.

Mechanisms for Handling Significant Changes That Require IACUC Approval

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| **DMR or FCR is required**(An amendment must be submitted to the IACUC for review) | **Eligible for Veterinary Verification & Consultation (VVC)**(Only if DMR/FCR is not specifically required, and if an IACUC-approved policy is in place) |
| * Nonsurvival → Survival surgery
* ↑ pain, distress, invasiveness
* Move to housing not already under IACUC oversight
* Δ species
* Δ study objectives
* Δ PI
 | Categories:* Δ anesthesia, analgesia, sedation, or experimental substances
* Δ euthanasia to method approved by AVMA
* Δ duration, frequency, type, or number of procedures
 |

Important points to keep in mind …

* **VVC** may be used for some significant changes in an IACUC-approved protocol. The flowchart on Page 5 may be helpful in making determinations.
* There must be an IACUC-approved policy in place for the specific change requested -- It’s up to the IACUC to decide what policies to establish, so draft carefully to make sure that the IACUC still gets to review changes for which it considers committee review necessary.
* The veterinarian determines whether the IACUC-approved policy is applicable. The “veterinarian” may be any veterinarian acceptable to the IACUC (doesn’t have to be the Attending Veterinarian, or even a member of the IACUC), as the role of the veterinarian is simply to confirm that the policy that was approved by the IACUC applies to the protocol in question. The approval for the change is granted by the IACUC, through its policy, not by the veterinarian.
* The veterinarian may decide that the policy should not be applied to a given protocol. In this case, the change must be submitted to the IACUC for review.
* Any changes in any approved protocol must be documented.

References:

1. Not-OD-14-126 Guidance on Significant Changes to Animal Activities, August 26, 2014.
2. OLAW Special Seminar on “Guidance on Significant Changes to Animal Activities”, presented August 21, 2014, transcript at <http://grants.nih.gov/grants/olaw/140821_seminar_transcript.pdf>

**Veterinary Verification & Consultation Flowchart**

