Jerald Silverman, DVM, Column Coordinator

Drug menus in protocol applications

The faculty of the Department of Veterinary Surgery had always provided the Great Eastern University IACUC with a list of general anesthetics that might be used in a research project. For example, when Dr. Joyce James submitted an IACUC application that included a major surgical procedure in mice, she listed all of the surgical department's four standard mouse anesthetics (ketamine/xylazine, pentobarbital, isoflurane and tribromoethanol), although once the study began she would use only one of them. Listed along with each drug was the proper dosage to be administered. To complicate matters, James and her colleagues routinely provided an even longer list of analgesics that might be used. This manner of presenting multiple anesthetics and analgesics had been discussed at IACUC meetings, but nobody was willing to speak out strongly against it because none of the protocols reviewed to date specifically required or contraindicated the use

of a particular drug. Furthermore, the committee could not find any regulation that required listing only the drug that would actually be used in the study. In fact, when the topic was last discussed, the IACUC chairman quoted a response to an OLAW "Frequently Asked Question," which stated that IACUCs may approve SOPs that can be cited by investigators in their protocols in order to avoid needless repetition. That, he said, was very similar to what the veterinary school faculty was doing for the IACUC.

So the practice continued. The IACUC believed it was being diligent by assuring that each of the listed drugs was acceptable for the procedure to be performed. The veterinary surgery faculty was pleased with the arrangement because it allowed them to have a ready-made 'pool' of drugs and dosages that could easily be cut-and-pasted into most of their protocols. On semi-annual IACUC inspections there were no problems with surgical records—they properly indicated the actual drugs used, dosages, clinical response and so forth. The

university's laboratory animal veterinarians said that they were unaware of any animal welfare issues arising from the anesthetics or analgesics used by the veterinary surgeons.

Yet, there were issues that could best be described as pertaining to 'comfort levels'. The laboratory animal veterinarians had not detected any problems, but they would have preferred to know prospectively which specific drugs were going to be used so they could do a better job of anticipating possible adverse effects and discussing the same with the surgeons. The IACUC also would have preferred to know the specific drugs being used prior to study initiation, but it could not cite any strong reason to require this. Furthermore, there were no negative comments about this practice when the USDA inspector reviewed protocols that included species covered by the Animal Welfare Act.

What is your opinion about the legality and appropriateness of providing a menu of anesthetic and analgesic drugs that could be used for a research protocol?

RESPONSE

Allow flexibility, with limits

Joseph D. Thulin, DVM, MS, DACLAM

Allowing some flexibility in the animal use proposal is both legal and appropriate, but the IACUC and veterinary staff need to place some limits on the practice.

Because the use of mice bred for research is not covered by the Animal Welfare Regulations¹, I will assume that this animal use is subject to the Public Health Service Policy on the Humane Care and Use of Laboratory Animals². PHS Policy

requires the IACUC to determine that procedures involving animals will avoid or minimize discomfort, distress and pain to the animals and that anesthetics and analgesics will be used appropriately. Therefore, there is no question that the IACUC needs an accurate description of the anesthetics and analgesics to be used in order to fulfill its regulatory and ethical obligations.

If the veterinary responsibilities detailed in the PHS Policy and the *Guide for the Care and Use of Laboratory Animals* (The *Guide*)³ rest with the laboratory animal veterinarians, then they rightfully need to be informed about the selection of the anesthetic and analgesic agents in order to make judgments about anticipated

clinical outcomes. The *Guide* specifies that adequate veterinary care includes effective programs for anesthesia and analgesia, among other considerations. The *Guide* further requires the responsible (or attending) veterinarian to provide guidance to investigators and to ensure appropriate analgesia and anesthesia. These responsibilities do not dissipate simply because the investigators are themselves veterinarians.

Despite the regulatory expectations described above, there is no mandate that the description of animal use must include the exact details of every element of the animal activity. Although the animal procedures performed undeniably need to be described in the proposal,