RESPONSE

Clinical scoring system and pilot study

Gwenn S. F. Oki, MPH, CIP, Richard W. Ermel, DVM, MPVM, PhD & Robert H. Whitson, PhD

This study was approved as a USDA Category E study, as Smith persuaded the IACUC that there was "ample scientific publication to show that analgesics could potentially interfere with the immune responses" in 6-month-old dogs that had undergone ovariohysterectomy. She further indicated that when the procedure was performed by private practice veterinarians, these animals did not routinely require postoperative analgesia. This information was communicated verbally by Smith but is assumed to have been justified in writing as required by USDA regulations[1] at 9 CFR 2.31(d)(1)(iv)(A) and PHS Policy[2] at IV.C.1..b. The attending veterinarian argued that there "was no reason to perpetuate unacceptable postoperative care," raising questions about whether consultation from the attending veterinarian, as required at 9 CFR.2.31(d)(1)(iv)(B), had been obtained by Smith during the planning phase of this Category E study. In addition, both the USDA regulations[1] (9 CFR 1.1) and U.S. Government Principle IV (ref. 3) indicate that procedures that would normally cause pain in humans would reasonably be expected to cause pain in animals. Ovariohysterectomy is expected to cause pain in humans and, therefore, in animals, regardless of the veterinarian's surgical skills.

Although the first three animals recovered from surgery as predicted by Smith, the fourth animal did not have the same outcome, thereby necessitating veterinary intervention.

The attending veterinarian is responsible for diagnosis and treatment of diseases and injuries and for providing post-procedural care pursuant to currently established veterinary medical practices (9 CFR 2.33(b)(2),(5); PHS Policy at IV.C.1.e). Furthermore, the attending veterinarian, in the provision of adequate veterinary care (which is a research facility or institutional program responsibility), should provide guidance to principal investigators and other animal care and use personnel regarding the proper use of analgesics (9 CFR 2.33(b)(4)). Collins was correct in assuming that the suffering animal required appropriate analgesia to alleviate postoperative pain. Because the animal had been suffering for quite a while ("lying on her side in the corner of her cage and whining long after the other animals were up and walking"), immediate veterinary care was warranted. Waiting for IACUC approval for this deviation would have prolonged this animal's suffering, and Collins had no choice but to obtain morphine to treat the animal right away, opting to deal with the consequences later. Collins did, however, have an obligation to inform Smith of his actions as soon as possible.

This scenario raises several issues that could have been avoided if addressed by early planning and collaboration between the IACUC, Collins and Smith.

Collins, the IACUC and Smith might have saved themselves considerable grief by developing a clinical scoring system to assess post-surgical pain and distress. This scoring system could have been used to determine the disposition of an animal exhibiting more postoperative pain than expected. If the dog met the criterion for removal from the study, Collins could have administered analgesics in a timely manner. In this scenario, it is highly likely that the suffering animal would be a statistical "outlier," necessitating removal from the data set. The clinical scoring system would have provided a mechanism for early intervention.

In consideration of the difference of opinion between Collins and Smith and the Category E designation, a compromise could have been to approve a small 'pilot' study with a limited number of animals, followed by timely IACUC review of the outcomes before proceeding to the larger study. A pilot study in this situation could have been designed to assess the effects of the procedure on the animals, conducted under IACUC oversight, and used to assure appropriate post-procedural care in future studies.

The clinical scoring system, the need for early intervention should animal suffering be observed and the plan of action, including the need to treat or euthanize the suffering animal, should be reviewed and approved by the IACUC before the first surgical procedure is carried out. Clinical scoring systems and pilot studies can be effectively utilized by IACUCs as a means to better assess and monitor experimental procedures that have the potential for pain and distress.

1. Animal Welfare Act. 9 CFR.
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
3. U.S. Interagency Research Animal Committee. U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training. Principle IV. *Federal Register* vol. 50, no. 97 (May 20, 1985).

Oki is Director, Research Subjects Protection; Ermel is Attending Veterinarian and Director, Division of Comparative Medicine; and Whitson is IACUC Chair and Associate Research Scientist at City of Hope National Medical Center and the Beckman Research Institute, Duarte, CA.