How should the IACUC handle unanticipated deaths?

Jerald Silverman, DVM

Some experimental procedures are more difficult to perform than others. Nevertheless, it is the responsibility of the IACUC to assure that all persons working with animals have been properly trained and can competently perform the procedures for which they are responsible. Proper training was especially important for the success of Dr. Ralph Osterman's cerebral trauma studies which required anesthetized rabbits to remain anesthetized for 12 hours after induced brain trauma. During that time Osterman studied the effect of various therapeutic modalities on brain microcirculation and brain temperature using noninvasive procedures. All animals were then euthanized without recovering from anesthesia.

Osterman's lab had sophisticated animal anesthesia simulation equipment which was used to train the technician-anesthetists who were responsible only for inducing, maintaining, and monitoring anesthesia. The approved anesthesia training had worked satisfactorily for the five years the protocol had been active and the veterinarians who periodically observed the studies had never requested any additional instruction.

In early June there were two experienced anesthesia technicians assigned to a typical 12 hour experiment, each working back-to-back six hour shifts. Two rabbits were anesthetized, one to receive the experimental treatment and one being a control. Unfortunately, the control rabbit died unexpectedly soon after the study began. When the study was repeated a week later with the same two technicians, once again the control rabbit died during the first six hours. This was quite unusual because this problem had never occurred previously with any of Osterman's studies. Osterman reported the two incidents to the IACUC as unanticipated adverse events. The institution's veterinarians had already performed necropsies but could not determine the cause of the rabbits' deaths, either grossly or through histopathology. The anesthesia machines were checked and were working properly. The anesthesia records did not indicate any unusual occurrences until just before death when there was an acute loss of cardiac activity. Osterman was upset but believed that the deaths were unfortunate coincidences and he wanted to move forward with his research. The IACUC discussed the problem but was unsure of what path to take. What do you think would be a proper action for the IACUC?

RESPONSE

Make the leap of faith, but finish looking first

Cheryl A Cheney

Osterman has been fortunate that throughout the five years of his study, the two control rabbits recently lost to cardiac arrest under anesthesia are the first. It is commendable that he promptly informed the IACUC of these untoward outcomes and involved the veterinarians in an investigation into why they occurred. Failing to discover any clear cause for the deaths following an assessment of the anesthesia equipment and necropsies on the bodies, the PI is prepared to chalk it up to bad luck and continue as before, and awaits the IACUC's okay to do so.

The PI and IACUC have equal interest in determining how to prevent future unanticipated mortality; it is unlikely Osterman would have suggested continuing the studies if he wasn't convinced these two deaths were beyond his control. Yet the IACUC first needs to consider whether all reasonable alternative explanations for the complications have been ruled out. A well-formed IACUC will reflect a diversity of expertise and opinion, and by brainstorming together they might identify other study elements to scrutinize. For example, hypothermia can dangerously increase the depth of anesthesia, so they could request confirmation that the thermal support system is also functioning properly.

In the absence of any actionable explanations for what went wrong, and in the interest of maintaining goodwill and an admirably transparent relationship, it is advisable for the IACUC to grant his request.

The Animal Welfare Act requires research facilities to review personnel qualifications with sufficient frequency to ensure individuals are qualified to perform their duties (§ 2.32, b)[1]. Although the two technicians present during the deaths have assisted Osterman on numerous prior study sessions without incident and appear to be maintaining appropriate anesthesia records, it would nevertheless be appropriate for the IACUC to ask for a veterinarian to be present during the next procedure these individuals will support, to assess whether refresher training is warranted and to advise on clinical interventions in the event that further issues arise.

If there is no evidence of noncompliance with the Animal Welfare Act, PHS Policy, or the Guide, there are no grounds to suspend the protocol, so the incidents will not need to be reported to the USDA. Since the deaths occurred under anesthesia, there would be no need to count these animals