

Jerald Silverman, DVM, Column Coordinator

## Which protocol deviations require preapproval?

Both the Animal Welfare Act regulations and the Public Health Service Policy make it clear that prior IACUC approval is required for research procedures using animals. Carrying out procedures that have not been approved can potentially be considered a serious deviation from the approved protocol, requiring notification of an appropriate federal agency. But consider a case where part of an approved protocol is *not* carried out. Is this also a deviation requiring notification of the proper federal agency?

Dr. Mike Sanchez studied cytokines, proteins that facilitate cell-to-cell communication. As part of his research on cytokines and bone-fracture healing, he was approved to radiograph his rats at 10, 20, 40, 60 and 80 days post-fracture. Each radiograph required the rat to be anesthetized for approximately 10 minutes. Sanchez followed his protocol and imaged the rats; however, after viewing the results of the day-40 images, he decided that the day-60 imaging was unnecessary, so he skipped that

time point and completed his study on day 80. He thought nothing of this and mentioned the dropped time point to a colleague who was also on the IACUC during a casual conversation about his research. She asked Sanchez if he had reported the dropped time point to the IACUC, and Sanchez, looking surprised, asked if he should have done so. She said that she believed that he should have, and that she would bring it up for discussion at the next IACUC meeting.

At the IACUC meeting, she asked the group whether Sanchez should have informed the IACUC that he left out one imaging time point. Larry Covelli, the chairman, said that he wasn't certain but he was pretty sure that it wasn't necessary because Sanchez didn't do anything he wasn't approved to do. "This is just a minor issue. It's not a significant change." Covelli said. "I can understand it being important if somebody was supposed to give pain relief and he never did, but what Sanchez did was immaterial to animal welfare. In fact, it

helped the animals because they didn't have to be anesthetized."

"Well, maybe," said Joan Roth, another IACUC member, who also was on the Institutional Review Board (IRB, the human subjects review board). "If this was an IRB-approved study, it would have to be reported as a deviation from the approved protocol."

"And would you have to report it to the funding agency?" asked Covelli.

"I'm not sure about that," she said, "but I'm sure you always have to report any proposed change in a research activity to the IRB before it happens. It's like an amendment to an IACUC protocol. You have to get approval before you make the change unless you have to make the change immediately for the safety of the animal."

In your opinion, should Sanchez have requested a protocol amendment before omitting the day-60 imaging? Are there times in which non-emergency protocol changes should be allowed without prior IACUC approval?

### RESPONSE

#### Communication is the key

Carole R. Baskin, DVM, MS &  
Dale DeNardo, DVM, PhD

This case illustrates the importance of excellent and ongoing communication between the research investigators, the animal support staff, and the compliance office. Having functioned in all these capacities ourselves to some extent, we can sympathize with the various and sometimes seemingly conflicting concerns of the different parties involved. Most researchers understand the necessity for preapproval of animal research activities, particularly given that such approval is often necessary for funding. But post-approval compliance can be more ambiguous to interpret and

therefore more difficult to maintain, in part because additional communications tend to be postponed because some people may see them as optional.

According to the *ARENA/OLAW IACUC Guidebook*, "after the IACUC has approved a protocol, it has a responsibility to ensure that procedures are carried out in the laboratory or classroom as described in the protocol." The *Guidebook* also outlines what constitutes a significant change to an approved protocol, and that includes a "change in duration, frequency or number of procedures performed on an animal." In some institutions, this statement is modified to pertain to only an increase in the number or duration of procedures. Notwithstanding specific institutional policies, however, the guidelines are general enough to include a decrease in the number of radiographs taken under anesthesia.

This alteration may ultimately benefit the animals, but the situation raises the pertinent question of whether a researcher is qualified to make such a judgment in the context of animal welfare.

In this case, the radiographs are part of a protocol to monitor the rate of bone healing. Sanchez's conclusion that there are no substantial changes between day 40 and 80 may be correct, but they could also be premature or erroneous, depending on the number of animals he observed. Additionally, there could be complications at that stage of bone repair that would be difficult to observe in a timely manner by any other methods, particularly if such complications were to occur in a very small proportion of animals. Because this is a departure from the approved protocol, Sanchez should not have made the decision on his own. If in doubt, he should have contacted the IACUC.