Jerald Silverman, DVM, Column Coordinator

Using pets in drug studies

Best America Pharmaceuticals was developing a unique new drug for human patients to treat both the hyperphosphatemia and the hypocalcemia that often accompany chronic renal failure (CRF). There was even preliminary evidence from preclinical work with a surgically induced rodent model that the drug might partially reverse the nephrocalcinosis that can be seen in CRF. Prior to moving forward on the path to a new drug application, Best America decided to investigate the drug's efficacy in pet animals with clinical CRF. Although the rodent model was satisfactory for initial studies, the company wanted to evaluate the drug in spontaneous clinical cases before investing further in its development.

Perhaps Best America was thinking that at some point, it might seek to have the drug approved for veterinary use, but that was not part of the discussion when Best America met with Dr. Harry Reiss, chairman of internal medicine at the Great Eastern University College of Veterinary Medicine. The basic proposal from Best was that the company would sponsor a dose-finding study in laboratory dogs and then move on to a study involving clinical cases of CRF in client-owned dogs who had an urgent need for the new drug. Best would pay for the clients' veterinary fees and would provide a substantial payment to the College itself. The primary stipulations of the proposal were that the animals were to have periodic blood samples and, if able to withstand them, four renal biopsies, at 3-month intervals.

Reiss estimated that the College of Veterinary Medicine's small animal clinic saw at least one new case of CRF a week and often more than that, and so entering the minimum of 20 new cases requested by Best would not be a problem. He was somewhat concerned about the need for kidney biopsies, but the company had said that there could be two biopsies from each kidney. That, he rationalized, was acceptable. The agreement with Best was tentatively completed pending approval from the IACUC, which at Great Eastern served its primary purpose and also approved clinical studies with client-owned animals.

The IACUC understood the potential value of the new drug and the need for the dose-level study, but it could not understand how the four biopsies would benefit the patients. It questioned why Reiss could not use blood samples to assess serum phosphorus and calcium levels. The committee also noted that there are non-invasive procedures to help evaluate kidney function. When pressed for an explanation, Reiss said that the biopsies were to help Best obtain a sequential picture of renal histopathology and tissue enzyme activity, neither of which could be determined without the biopsies. Additionally, Reiss reminded the IACUC that the ultimate goal was to develop a drug for people with CRF, which would likely have a useful application in animals with the same disease. Best America was not willing to sponsor the project without the biopsies, and if the project fell through, he said, both humans and animals would suffer until Best America located another school willing to collaborate in this important study.

There was a heated IACUC deliberation, largely focused on the need for the biopsies in client-owned animals. Do you believe the proposed study should be done under the general conditions prescribed by Best America? Or should the IACUC withhold its approval of the study?

RESPONSE

Forget Fido

Laura E. Noll, BS, RLAT, ILAM

This study lacks appropriate scientific controls and provides no net benefit to the client-owned animals it professes to help. Thus, our IACUC would not approve it as presented.

One problem with this protocol is the lack of scientific validity in the absence of any experimental standardization or controls in the study. There is no requirement for any uniformity in breed, age, initial cause of kidney disease or any underlying conditions that may affect the subject and its disease process. The number of applicable patients seen by the College of Veterinary Medicine is not enough to overcome this bias, nor should a larger number of animals be exposed to this procedure to attempt to overcome this bias.

Benefits to the clients' animals are far outweighed by the risks. The drug may provide clinical benefits; however, the request for kidney biopsies in client-owned dogs with kidney disease, not for the benefit of the animal but rather for that of the company, would be unacceptable to our IACUC. The short-term and long-term risks of the procedure are too great to the clients' pets. These risks to dogs with CRF include the following: anesthesia complications, including respiratory depression and biochemical changes; intraoperative and postoperative biopsy complications; and long-term risks of scarring already compromised kidneys.

Additionally, our Committee understands and accepts that financial gain should not be the primary reason to approve a study. Our Committee would furthermore find it curious that Best America Pharmaceuticals is so adamant about the biopsies, despite potential negative health effects on privately owned animals, when other diagnostic laboratory and imaging modalities could be used. The company seems to think that cash