

Protocols for pets: what authority does an IACUC have?

E-2400, an anti-neoplastic drug, was to be used in a clinical trial for dogs with osteosarcoma, a bone tumor often seen in large breeds such as Irish wolfhounds. The proposed plan was for the dog's affected limb to be totally amputated and then the drug would be administered intravenously, once every two weeks for four treatments. The control group of dogs would also have the limb amputated but postoperatively would receive the antineoplastic drug carboplatin, the standard treatment for dogs with osteosarcoma that were seen at Great Eastern University, College of Veterinary Medicine.

The study's principal investigator was Dr. Sheila McCrae and the work was funded through an NIH grant. On her IACUC protocol form McCrae carefully described the general mechanism of action of E-2400, qualifications required for a dog to be entered into the trial, number of animals receiving either E-2400 or carboplatin, blinding procedures, details of

the intravenous infusion, observations to be made, possible side effects of E-2400, a copy of the information sheet and consent form to be given to the owner, and so forth. The protocol was destined for full committee review and per the standard procedure of the school's IACUC, it was pre-reviewed by a laboratory animal veterinarian and another member of the committee. The reviewers were impressed by the amount and quality of the details provided by McCrae, but one item was conspicuously missing: a description of the amputation procedure. When she was asked to add it to the protocol, McCrae replied that the surgical procedure is the veterinary hospital's standard of care for dogs with osteosarcoma and it would be performed on all osteosarcoma patients, whether they would receive E-2400 or carboplatin. This response was deemed unsatisfactory by the IACUC administrative office and the pre-reviewers, and they again asked McCrae for a detailed description of the surgery

and all perioperative procedures, including anesthesia and analgesia. McCrae, who was usually a very non-confrontational and compliant researcher, believed that the IACUC had overstepped its authority and was asking to review a standard oncological procedure used at the veterinary school. She lodged a formal complaint with the IACUC chairperson, alleging that the requested additional information exceeded the authority of the IACUC.

The McCrae protocol and her complaint were discussed at the next full committee meeting. Do you believe that the IACUC exceeded its authority and how should the IACUC proceed to resolve this issue?

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Published online: 23 April 2018

<https://doi.org/10.1038/s41684-018-0049-0>

Details necessary for IACUC assessment?

Although the animals under this study are privately-owned, there is no distinction in terms of regulations between the PHS Policy¹ and the Animal Welfare Act and Regulations (AWAR)² when compared to animals owned by the institution. As such, pets used in research must be covered under an IACUC-approved protocol. Additionally, given that this study is PHS-funded, all applicable IACUC approval is required for research activities. This includes endorsement of the "U.S. Government Principles"³, compliance (where applicable) with the Animal Welfare Act, and requires institutions to use the *Guide for the Care and Use of Laboratory Animals (the Guide)*⁴ for the basis of assessment and development of institutional policies.

It is important to note that the question of appropriate training and qualifications of Dr. McCrae, correctly, do not appear to be a topic of disagreement for the IACUC. The Academy of Surgical Research's "Guideline for Training in Surgical Research with

Animals"⁵, which is referenced in *the Guide*, states that "Veterinarians who are certified or trained in laboratory animal medicine, surgery, or anesthesia should be considered competent in their field and should not require additional training." However, the point of debate between the IACUC and the PI concerns the provision of detailed surgical procedures and perioperative procedures and monitoring to the IACUC for review.

As per *the Guide*, "the IACUC is responsible for assessment and oversight of the institution's Program components...". The Program is specifically defined as "all activities conducted by and at an institution that have a direct impact on the well-being of animals, including animal and veterinary care...". As the limb amputation procedure certainly has a direct impact on the well-being of the study animals, it is directly within the purview of the IACUC to request a detailed description of the amputation procedure and all perioperative procedures.

Additionally, the provision of these details will provide both the IACUC and the attending veterinarian with the necessary information to assure that pain and distress is minimized in these patients, as well as the appropriate use of analgesic, anesthetic, and tranquilizing drugs—as is emphasized in the PHS Policy, US Government Principles, *the Guide*, and the AWAR.

Dr. McCrae may be advised that citing an IACUC-approved Standard Operating Procedure (SOP) for amputation in the IACUC protocol is also feasible. IACUCs may approve SOPs that can be cited by investigators in their protocols⁶. The IACUC approval and incorporation of SOPs into IACUC protocols helps reduce regulatory burden for investigators, while providing the IACUC the necessary details of the procedures performed.

Rather than questioning Dr. McCrae's expertise as a veterinarian and oncologist, the IACUC simply needs to be provided with all the appropriate information to evaluate the protocol to the standards of federal regulations.