Protocols for pets: what authority does an IACUC have?

Although the animals under this study are privately-owned, there is no distinction in terms of regulations between the PHS Policy and the Animal Welfare Act and Regulations (AWAR), 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 protocol is also feasible. IACUCs may approve SOPs that can be cited by investigators in their protocols. 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.

Details necessary for IACUC assessment?

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Oversight depends on how ‘eligibility’ is defined

Dr. McCrae is proposing a trial to evaluate the efficacy of a novel anti-neoplastic drug, E-2400, by comparing it to the standard therapeutic drug, carboplatin, used in the treatment of osteosarcoma. Although limb amputation of the dog’s affected leg is a step in the overall process of treating osteosarcoma, the question is raised as to whether the IACUC must oversee the surgery as part of the drug trial proposed to the IACUC. The answer to that question depends on whether the surgery is described as an animal activity in the grant submission or when the animals are enrolled in the drug trial.

As described in the scenario, the Principal Investigator (PI) has defined the qualifications required for the animal to be eligible for the study, which is the key to deciding whether the IACUC should oversee the surgery. In addition, through the informed consent process (USDA - Veterinary Services Memorandum No. 800.301), the scientist is ensuring the animal owners understand the risks, potential benefits, and alternatives of enrolling their animal in the study, which is also a critical factor.

Regarding the enrolment of an animal in the study, oversight of the surgical procedure should not be under the purview of the IACUC if the criteria for an animal to be eligible to participate in the drug trial is limited to only those that have undergone the first phase of the standard clinical treatment (i.e., the amputation of the affected leg) for osteosarcoma. In this particular scenario, the onus would be on the PI to ensure only those animals satisfying the enrollment criteria would participate in the blind study with a percent of the animals continuing the standard treatment of receiving carboplatin (i.e., the control group), and others the test drug E-2400. In this case, the IACUC should only consider the potential effects of E-2400 on the welfare of the animals.

Alternatively, if eligible animals include all that have been diagnosed with osteosarcoma, the IACUC may have additional responsibilities. For example, let us assume that after osteosarcoma is diagnosed and during the informed consent process, the animal owner learns that the treatment of the disease includes limb amputation followed by chemotherapeutic treatment. At that time, owners are also informed of a trial intended to evaluate the efficacy of a novel chemotherapeutic drug (E-2400) that they believed will increase the chance of the animal being successfully treated for the disease. In addition, and if the surgical procedure is described in the grant, the owners are informed that because the drug trial is sponsored through the NIH all associated expenses relating to the treatment of the animals will be covered as part of the trial.

In this particular scenario, the IACUC must oversee the effects of the drug trials on the animals since that is the overall scope of the study. In addition, the IACUC has some responsibility associated with the surgical procedure especially since the costs associated with the surgery are being covered by the grant. The IACUC can satisfy this responsibility by asking the PI to assure in the protocol that the surgery will be conducted following an established standard clinical practice in a veterinary hospital by a veterinarian with extensive expertise in the standard treatment of osteosarcoma in dogs. Since the findings from the overall study seeks to identify more efficacious drugs for the treatment of the disease, and not methods for improving the associated standard surgical procedures, the IACUC need only concentrate on the drug trial with the consideration that the surgery is a standard of clinical care that ultimately leads to additional drug treatments.

Bill Greer* and Lauren Danridge
University of Michigan Office of Research, Ann Arbor, MI, USA.
*e-mail: wggeer@med.umich.edu
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IACUC overreach, no bones about it

A robust, well-designed pre-review process can be one of the most important steps in the efficient, complete and consistent review of an animal care and use protocol. When properly performed, a pre-review can shorten the IACUC review period, thus reducing administrative burden on the Committee and the investigators. An overzealous review process can accomplish the opposite, increasing the burden of the Committee and frustrating responsible and conscientious scientists1. This seems to be what has occurred at Great Eastern University (GEU)—the IACUC, through its pre-review of Dr. McCrae’s protocol, is requesting information outside of its purview, e.g., the review of standard veterinary care.

In determining the scope of their oversight, GEU research administration and the IACUC should determine (1) whether the Public Health Service (PHS) and or the U.S. Department of Agriculture (USDA) has jurisdiction over the activity, (2) what parts
Complete details for a complete review

The IACUC did not exceed its authority, and is within reason to request additional information from the PI to complete a thorough protocol review as mandated by both PHS Policy1 and Animal Welfare Act and Regulations. These federal regulations do not differentiate between institution- and client-owned animals, and because the work described in the scenario is PHS-funded research, the institution must maintain an OLAW-approved Animal Welfare Assurance covering all performance sites. As written, the scenario indicates that the “proposed plan was for the dog’s affected limb to be totally amputated, indicating that the surgery is clearly being conducted for the purpose of the research, therefore it cannot be solely considered veterinary clinical care of a privately owned animal. If amputation is included in the pre-treatment regimen for the effective use of the study drugs, then the procedure should be described in the protocol for IACUC review.
According to the Guide\textsuperscript{3}, the animal use protocol is a detailed description of the proposed use of laboratory animals, and appropriate sedation, analgesia, and anesthesia, and conduct of surgical procedures should be considered in the preparation of the protocol by the researcher and its review by the IACUC. Specifically, the IACUC is charged with evaluating the surgical procedure, perioperative processes, humane endpoints, and relief of pain or distress. Despite the standard oncological procedure from the veterinary school being used, the IACUC cannot effectively assess the items above to ensure the appropriateness of each element for the study in question without a complete description of the surgical procedure to be utilized.

Additionally, the PHS Policy and the AWRs require research institutions to ensure that investigators have appropriately considered alternatives to procedures that can cause more than slight or momentary pain or distress in animals\textsuperscript{4}. These alternatives are detailed within the “3Rs”: reduction, refinement, replacement. In regards to the study in question, the IACUC needs to evaluate refinement to ensure that current veterinary practices employed at the veterinary school in question reduce or eliminate unnecessary pain and distress in the study animals\textsuperscript{4}.

The IACUC must also be able to assess personnel qualifications, including knowledge of basic principles of laboratory animal science to help ensure high quality science. Staff veterinarians providing clinical support must have the experience, training, and expertise necessary to evaluate the health and wellbeing of the species used in the context of the animal use at the institution\textsuperscript{3}.

The IACUC should request that a description of the surgery procedure be added to the protocol prior to approval. Alternatively, in the spirit of reducing regulatory burden, if Great Eastern University, College of Veterinary Medicine maintains its own IACUC-approved protocol, or Standard Operating Procedure for the amputation, Dr. McCrae's IACUC may request a copy of that document for review instead of requiring that the details be entered into the protocol form. The document could then be attached to or included with the protocol file for future reference.

Courtney P. Nesline* and Emily Weston
Division of Comparative Medicine and Office of Animal Care and Use, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.
*e-mail: cnesline@email.unc.edu

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References
4. ARENA/OLAW. Institutional Animal Care and Use Committee Guidebook. 2nd edn, (OLAW, Bethesda, MD, 2002).