Jerald Silverman, DVM, Column Coordinator

Tissues from privately owned dogs

Dr. Lisa Archer, a board-certified veterinary oncologist at the Great Eastern University College of Veterinary Medicine, had a particular interest in canine mast cell tumors. Before she began treating an affected animal, which usually included surgically removing the tumor, she would ask her client to sign a release allowing part of the tumor tissue to be used for her research. The release also stated that the identity of the owner and the animal would be removed from the tissue sample. Her research, which was done entirely *in vitro* using the tumor tissue, was funded by a grant from the National Institutes of Health. Other than asking clients to sign the release, Archer did not solicit subjects for the study, because the clinic's case load almost guaranteed that she would obtain a large enough sample size. The college's Clinical Research Committee (CRC), but not the IACUC, had approved the study because the animals involved were privately owned, were brought to the school for clinical treatment and received exactly the same treatment as did animals whose owners chose not to participate in the study.

A client whose dog had a mast cell tumor was talking to Archer and mentioned that he was a physician at the Great Eastern University School of Medicine. He said that at the medical school, a study like Archer's would require approval by the Institutional Review Board (a committee that oversees the protection of human subjects). Archer knew that the Public Health Service *Policy on Humane Care and Use of Laboratory Animals* did not draw distinctions between privately owned and institutionally owned animals, but she did not want to rock the boat and make more work for herself. Nevertheless, some discrete inquiries on her part revealed that at one time, the Great Eastern IACUC did require that similar studies obtained its approval, but over time decided that its approval was not truly required and ceded the responsibility to the CRC.

What is your opinion? Does Archer's study require IACUC approval, or is approval from only the CRC appropriate for her research?

RESPONSE

IACUC approval required

Sylvia Allen, AS, RLATG

Archer's study needs IACUC approval in addition to the CRC approval she received from her institution. Her research is funded by a grant provided by the National Institutes of Health; by accepting this funding, Archer is obligated to follow the guidelines set forth in the Public Health Service *Policy on Humane Care and Use of Laboratory Animals* (PHS *Policy*)[1].

Archer's research is being done *in vitro* (meaning in a test tube or in culture medium); she is collecting samples of canine mast cell tumors from client-owned animals that are brought into her institution's animal clinic for treatment; and she obtains a signed release from the owners of the animals allowing her to use the samples in her research.

Privately owned or not, live animals being used in research are covered under the Animal Welfare Act and the *Guide for the Care and Use of Laboratory Animals* (the *Guide*)[2] as described in the PHS *Policy*[1].

We do not know what conditions or circumstances contributed to the Great Eastern IACUC's decision to cede responsibility for similar studies to the CRC. There is some precedent regarding privately owned agricultural animals in the *Institutional Animal Care and Use Committee Guidebook*[3], which allows an institution's IACUC to decide whether such animals need to be covered by an IACUC-approved protocol. I appreciate that Archer made discrete inquiries about this particular situation, but I wonder what role the institution's CRC played in this scenario.

In my opinion, IACUC approval is needed in addition to CRC approval for Archer's study. Archer should be made aware of this requirement and should halt her studies until she gets IACUC approval. Perhaps the IACUC could grant conditional approval so that she could continue her research and still be compliant. I feel that the CRC bears some responsibility as well. The CRC should have told Archer that using live animals (client-owned or not) would require her to write and submit a protocol to the IACUC for approval. When an institution accepts funding from the National Institutes of Health, it must become familiar with the conditions that must be followed as outlined in the PHS *Policy*[1].

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
2. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* (National Academies Press, Washington, DC, 1996).
3. Office of Laboratory Animal Welfare. *Institutional Animal Care and Use Committee Guidebook* 2nd edn. (US Department of Health and Human Services, Washington, DC, 2002, reprinted 2008).

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RESPONSE

CRC is correct

Jody Swain, DVM, MS &
Lori R. Hill, DVM, DACLAM

We must answer two questions to determine whether IACUC approval of Archer's study is required. First, are the dogs in question ever considered to be research animals? Second, what are the requirements for the use of tissue removed from a privately owned dog and then used in research?

The *Guide for the Care and Use of Laboratory Animals*, which provides the basis for accreditation by the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC International), describes an animal as any vertebrate animal used in research, teaching or testing[1]. The Public Health Service *Policy on Humane Care and Use of Laboratory Animals* defines an animal as any live vertebrate animal used or intended for use in research, research training, experimentation or biological testing or for related purposes[2]. The US Department of Agriculture (USDA) Animal Welfare Act and Animal Welfare Regulations classify animals as any live or dead, warm-blooded animal being used or intended for use for research, testing, experimentation or exhibition purposes[3].

According to these documents, the dogs in this scenario are not used or intended for use in research. These dogs are undergoing a surgical procedure that benefits them (removing the mast cell tumor) under a recognized client–patient–veterinarian relationship. The dogs will undergo the surgery regardless of whether the clients consent to allow their tissue to be used in Archer's study. The excised tissue, not the dog, is being used in the study. If the tissue was harvested specifically for the study, then the dog would be considered a research animal. In that case, the study would require IACUC approval.

In addition, the dogs are not housed as research animals at any time during their treatment. Because the animals are at the veterinary school for treatment and not for research, AAALAC International would not look at them during a site visit. If the dogs were enrolled in a research project

A word from OLAW and USDA

In response to the question posed in this scenario, the Office of Laboratory Animal Welfare (OLAW) and the United States Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care (USDA, APHIS, AC) offer the following clarification and guidance:

The Public Health Service *Policy on Humane Care and Use of Laboratory Animals* (PHS *Policy*) covers live vertebrate animals used or intended for use in research, research training, experimentation or biological testing activities conducted or supported by the PHS[1]. The Animal Welfare Act defines an animal as "any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or any other warm-blooded animal, which is being used, or is intended for use for research, teaching, testing, experimentation, or exhibition purposes, or as a pet"[2]. The term 'dog' includes all dogs, including those used for hunting, security or breeding purposes. The PHS *Policy* and the Animal Welfare Regulations (AWRs) do not distinguish between animals owned by the institution and privately owned animals. In this scenario, the determining factor as to whether the PHS *Policy* and the AWRs are applicable to the dogs receiving clinical care is whether the animals are at the veterinary clinic and being handled in response to the requirements of the NIH grant or as routine patients at the University College of Veterinary Medicine. If the actions of the client owners and the treatment of the dogs are not influenced in any way by the study parameters (*i.e.*, the treatment of an animal included in the study would be identical to that of an animal whose tissue would not be used for study), then the disposition and subsequent research on the discarded tissue would not fall under the jurisdiction of the PHS *Policy* and the AWRs and would not require IACUC approval. However, if the surgery is conducted as a custom request or the animal is handled in a different manner to support the study, then IACUC approval would be required.

Animals in a veterinary client–patient relationship are not considered regulated animals by USDA. A veterinary client–patient relationship is one in which animals undergo procedures that are medically justifiable for the health and well-being of the animals. In this scenario, Archer is surgically removing mast cell tumors as part of a diagnostic and treatment plan for the health and well-being of the patient animals. The tissues are used for research purposes only after surgical excision, and the animals themselves have no role in the research protocol. Thus, IACUC review and approval for this study would not be required. If the animals were to undergo procedures that were intended solely for experimental purposes (as opposed to treatment and diagnosis), the animals would be subject to USDA regulation, and IACUC review and approval would be required.

The PHS *Policy* does not affect applicable state or local laws or regulations, which impose more stringent standards for the care and use of laboratory animals[1]. The institution is at liberty to have the procedure reviewed by the IACUC for the reasons stated by one of the reviewers. Also, as noted by one reviewer, NIH will not make an award for research involving live vertebrate animals unless the applicant organization and all performance sites are operating in accordance with an approved Animal Welfare Assurance and provide verification that the IACUC has reviewed and approved those sections of the application that involve use of vertebrate animals in accordance with the requirements of the PHS *Policy*[1]. The PHS *Policy* recognizes that the IACUC may approve, require modifications or withhold approval of a proposed animal activity[3]. The PHS *Policy* does not recognize 'conditional approval' and OLAW discourages the use of these terms.

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
2. Code of Federal Regulations, Title 9, Chapter 1, Subchapter A - Animal Welfare: Part 1 Definitions (§1.1).
3. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals –Frequently Asked Questions.* Protocol Review, Question No. D.4. (US Department of Health and Human Services, Washington, DC, 2006, revised 2009).

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and housed at the university, however, then AAALAC International would look at them[4]. The clients maintain ownership of the dogs who participate in Archer's study, and the Great Eastern College of Veterinary Medicine does not at any point possess ownership of the animals. These dogs are treated as client-owned animals. The USDA monitors only those animals owned by licensed dealers and exhibitors or registered research facilities. Because the dogs are privately owned and housed, they are not covered by the USDA regulation[3].

Over the years, the Great Eastern College of Veterinary Medicine has decided to refer these types of studies to the CRC for approval. A client consent form is signed to help address issues of liability and public relations. Consent forms are not required but are recommended[5]. Archer has approval from the CRC to conduct her study. Archer has received funding for her study from the National Institutes of Health, confirming that an IACUC-approved protocol is not needed for this study. The National Institutes of Health requires documentation of IACUC approval for studies involving animals in research[2]. In conclusion, I believe Archer is following the appropriate channels for approval of her study.

1. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* (National Academies Press, Washington, DC, 1996).
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
3. Animal Welfare Act and Animal Welfare Regulations.
4. AAALAC International. *Contracts, Collaborations and Co-Ownership: Roles and Responsibilities of the Institution* (2005). <https://www.aaalac.org/resources/Contracts_Collaborations_Co-Ownership.ppt>
5. Silverman, J., Suckow, M.A. & Murthy, S. *The IACUC Handbook* 2nd edn. (CRC Press, Boca Raton, FL, 2007).

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RESPONSE

Don't rock the boat!

Kari Koszdin, MS, DVM DACLAM

Archer does not need IACUC approval for this study, because she is harvesting the mast cell tumors that she is studying in the course of providing clinical care for patients. Because she does not collect any extra tissue or samples from the animals whose owners consent to the use of the tumor tissue, she is not doing any research on the dogs; rather, she is using only the tissues she collects from them in her research. According to the Public Health Service, the use of parts of animals for research purposes is not a regulated activity, unless animals are killed for the purpose of obtaining the tissues or project-specific antemortem manipulations are done on the animals[1]. Even though the Animal Welfare Act defines an animal as "any live or dead dog"[2], it does not specifically address the issue of research carried out on animal tissues. Additionally, the USDA does not regulate veterinary care for dogs in a private-practice setting.

Her client is correct that a medical school's Institutional Review Board would be required to review this study. According to the Office for Human Research Protections[3], the study would be exempt from review by the Institutional Review Board only if the samples had been collected before the initiation of the research and if the information about the subjects was recorded such that there was no possible way to link the tissue sample to the patient. Archer's research seems to comply with the second part of this requirement but clearly does not comply with the first part. However, her study does not involve any human research subjects, and one must only peruse the sections of the Code of Federal Regulations that pertain to the protection of human research subjects to realize that the regulations governing research on human subjects are quite different than those governing research on animals.

In the end, it is strictly Great Eastern University's decision whether or not to require IACUC review for this study. There are a few good reasons that an institution may decide to require IACUC review for studies using tissues collected from dead animals or in a clinical setting. Tissues from wild animals, nonhuman primates and unconditioned pets may contain zoonotic pathogens, and so the institution must have some mechanism in place to address potential occupational health and safety issues that may arise in research that utilizes animal tissues. The IACUC review process is often a good means to address these types of issues, as the veterinarian on the committee has the expertise needed to evaluate them. Tissue studies may involve collection of tissues from sources that could lead to public relations problems for the institution's animal research program, and so the institution must have some oversight for these studies. Finally, the IACUC review process would ensure that the study parameters are clearly defined and that the investigator understands exactly which animal activities are approved (and which are not approved) in advance of the study. If the institution can assure that all of these issues can be addressed by its CRC, then IACUC review would be redundant, as it is not required by any regulations. If no CRC exists at an institution that conducts research on animal tissues collected from dead animals or in a clinical setting, then IACUC review would be a good idea.

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
2. Animal Welfare Act and Animal Welfare Regulations. 9 CFR.
3. Public Welfare (Title 45) and Protection of Human Subjects (Title 46). CFR. Department of Health and Human Services. 2005. <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.101>

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