The importance of being 'in charge'

Lila Schope, the Attending Veterinarian (AV) at Great Eastern University, was also the Director of the animal care program. As such, she was always looking for ways to bring in new revenue to help keep down the *per diem* animal care charges. For over three years she had been receiving requests from local startup companies to house mice and guinea pigs. Because animal housing space was available at Great Eastern, she began the process of entering into contractual agreements for animal housing. The companies would provide any technical personnel needed for research procedures. After all legal and National Institutes of Health requirements were in place, the university's attorneys and the Vice President for Research approved the contracts.

Great Eastern had a policy that only a university employee could be a Principal Investigator (PI) on an IACUC protocol, so Schope listed herself as the PI on each individual research protocol that involved work with the contracted companies. Schope felt that this was appropriate because as the AV she had general oversight responsibility for all the animal research performed on campus. The IACUC agreed and it approved her protocols. At first there was no problem, but after two years the IACUC, led by a new Chairperson, told her that she could no longer be PI unless she was "intimately involved with the research." Of course, Schope was upset because the Committee was changing its decision in the middle of work on 12 contract protocols from four different companies. She was trying to help the university and she had no desire to be any more involved in the research than she originally stated to the IACUC. The IACUC said that it was simply complying with federal regulations about the responsibilities of a PI. Schope said that the only regulation that even vaguely touched upon the current issue was the definition of a PI in the Animal Welfare Act regulations (AWRs). Nevertheless, she contended that there was no appropriate regulatory guidance that the IACUC could use to justify replacing her as PI. She also wanted to know what would happen to the research if her PI status was revoked. The Vice President for Research sided with the IACUC.

Was Shope correct to assert that there is no applicable regulatory guidance for either her or the IACUC? Would it be better for everybody if Shope just threw in the towel and discontinued the outside companies' animal housing and research activities? What do you recommend that Great Eastern and Schope do to resolve this conflict?

RESPONSE

A compromise for co-PIs

Harry Rozmiarek, DVM, PhD, ACLAM & Glenn Rall, PhD

It is important to note that the policy on which this issue is based is a university-established regulation at Great Eastern, not a specific federal mandate. While it is the responsibility of the research facility to ensure that all are qualified to perform their duties and that personnel conducting procedures on the research animals are appropriately qualified and trained in those procedures, there is no federal requirement that only a university employee can be a PI on an approved IACUC protocol. Thus, the former arrangement was compliant with federal standards as long as Schope is familiar with the research and qualified to function as the PI. However, because the PI is responsible for all aspects of animal care and use described in the protocol, it would be best for that person to be intimately associated with the experiments described in the protocol. In this particular situation, this is clearly not Schope. The key issue, therefore, is whether a balance can be achieved between appropriate animal oversight and compliance with university policies.

Another important point to consider is that IACUC policies need to be consistent in order to be credible. Reversal of long-standing policies simply because a new chairman deems them no longer acceptable sends a confusing message to the investigators and may prevent valuable research from moving forward. Nevertheless, the new IACUC Chair does have a valid concern in that the PI may not be appropriately familiar with the proposed research, and is listed as PI mainly to comply with a Great Eastern-established policy. One possible remedy that would enable the work to move forward while allowing for someone more familiar with the research to be responsible for the day-to-day monitoring and care of the animals is for the Great Eastern IACUC to consider the idea of co-PIs. Schope could serve as the university representative, along with a non-Great Eastern individual from the contracting company who is actually doing the work. Both would share in the responsibilities of monitoring animal welfare and, in this way, provide adequate surveillance of the animals, while still adhering to the Great Eastern policy.

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A word from OLAW and USDA

In response to the issues raised 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 primary question posed in the scenario is whether there is any applicable regulatory guidance for identifying who can serve as the PI for animal activities approved by an IACUC. As the scenario indicates that appropriate contractual agreements were in place to meet NIH requirements, this commentary assumes the following: that the research projects in question were PHS-supported; that the start-up companies are the primary grantees; and that inter-institutional agreements between the grantee institutions, the performance site, Great Eastern, and OLAW have been signed.

The PHS *Policy for Humane Care and Use of Laboratory Animals* (PHS *Policy*) does not contain specific guidance on who can serve as the senior scientist (often called the PI) responsible for research projects involving live vertebrate animals. The only guideline given by the PHS *Policy* is at IV.C.1.f, where it states that "the IACUC shall determine that personnel conducting procedures on the species being studied will be appropriately qualified and trained in those procedures[1]." Great Eastern requires that the PI for the animal research protocol be "intimately involved with the research," which is not a PHS *Policy* requirement.

The PHS *Policy* (at II) goes on to state that "no PHS support for an activity involving animals will be provided to an individual unless that individual is affiliated with or sponsored by an institution which can and does assume responsibility for compliance with the *Policy*, unless the individual makes other arrangements with the PHS[1]." The relationship and details of the affiliation are left undefined, allowing flexibility for cooperative use of resources and facilities among institutions. The IACUC, as part of its oversight of Great Eastern's program for animal care and use and the institution's animal facilities, should be included in the development of any sub-granting agreements to ensure that they are consistent with provisions of the PHS *Policy*. The veterinarian also must be aware of her involvement and avoid a conflict of interest when her role blurs from veterinary care provider to scientific collaborator. If she continues to serve a role in the collection of the data, then having another veterinarian affiliated with Great Eastern assigned responsibility for institutional veterinary oversight of animal care and use involving those specific protocols is recommended. If she continues as the PI, she has a "conflicting interest," according to PHS *Policy* at II.C.2, and cannot participate in IACUC discussions or reviews (except as invited to respond to Committee inquiries) concerning any of the 12 protocols[1].

The definition cited from the PHS 398 grant application instructions by one of the responders is how the NIH defines who can be named as a PI on a grant application to NIH. This may not necessarily be the same individual listed as the PI on the animal research protocol. As Great Eastern is serving as a sub-grantee (consortium participant) on a PHS-supported award, then the primary grantees (the start-up companies) must have formal written agreements with Great Eastern that address the negotiated arrangements for meeting the scientific, administrative, financial, and reporting requirements, including identification of the PI on each of the grant applications and the individuals responsible for the research activity at Great Eastern, and their roles and responsibilities. Any change in these individuals at Great Eastern is subject to approval by the primary grantee and should be formally acknowledged in the agreements with the primary grantee organization[2,3].

If the research project involves species regulated by the USDA, then the institution must also comply with the Animal Welfare Act (AWA) and regulations (AWRs). The AWRs define the PI as "an employee of a research facility, or other person associated with a research facility, responsible for a proposal to conduct research and for the design and implementation of research involving animals[4]." Again, the relationship and detail of the association is left for the institution to define. The IACUC, however, as the responsible entity for compliance with the AWA, must be satisfied with the relationships created by the veterinarian on behalf of Great Eastern and must ensure appropriate oversight of all aspects of the research being conducted at Great Eastern's facilities by the veterinarian and by researchers from outside institutions.

1. Public Health Service. Policy on Humane Care and Use of Laboratory Animals (US Department of Health and Human Services, Washington, DC, 1986; reprinted 2002).
2. PHS Grants Policy Statement, Part II, Terms and Conditions, Consortium Agreements. http://grants.nih.gov/grants/policy/nihgps_2003/NIHGPS_Part12.htm#_Toc54600259.
3. National Institutes of Health. Office of Extramural Research guidance regarding administrative IACUC issues and efforts to reduce regulatory burden. NOTICE: NOT-OD-01-017 (12 February 2001). http://grants.nih.gov/grants/guide/notice-files/NOT-OD-01-017.html.
4. 9 CFR, Chapter 1, Subchapter A–Animal Welfare, Part 1 Definition of Terms. http://www.nal.usda.gov/awic/legislat/usdaleg1.htm.

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RESPONSE

The buck stops where?

Patricia N. Coan, DVM, PhD, DACLAM & William A. Hill, DVM

Schope was rightfully perturbed that the IACUC changed policies midstream, but changes routinely occur in biomedical studies. For this reason, protocol and program reviews are required to revisit, update, and refine procedures and policies.

Was Schope correct that there is no applicable regulatory guidance? No. The AWRs define PI as an employee of a research facility, or other person associated with a research facility, responsible for a proposal to conduct research and for the design and implementation of research involving animals[1]. Additionally, the Public Health Service (PHS) defines PI as the individual(s) designated by the applicant organization to direct the project or program. According to the PHS, the PI is responsible and accountable for the proper conduct of the project or program and must have the authority and responsibility for leading and directing the project, intellectually and logistically[2].

If Schope became more involved with the studies, as a PI should, the work could continue. Alternately, Schope and an individual from the company could serve as co-PIs. In such an arrangement, Schope would be responsible and accountable for the study but could assign some of the specifics to her counterpart.

As the PI of record, Schope must become more involved in the studies. Additionally, collaborations could be explored. If neither option is acceptable, there may be a faculty member at Great Eastern that would agree to serve as PI on the projects. The studies could continue provided that the new PI was closely involved in the protocol. If there is no interest from the faculty, then the studies must be stopped and the start-up companies forced to find another way to perform their experiments. In this event, Great Eastern should, at a minimum, allow any ongoing studies on animals currently housed at the institution to be completed so as to not waste animal resources or cause future unnecessary duplication of the research.

1. 9 CFR, Chapter 1, Subchapter A—Animal Welfare.
2. US Department of Health and Human Services Public Health Service. Application for a Public Health Service Grant. http://grants.nih.gov/grants/funding/phs398/instructions2/p3_definitions.htm.

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RESPONSE

Increase PI involvement

Jem Scott-Emuakpor, DVM

It is true that there is no clear regulatory guidance on this matter; however, the Organisation for Economic Co-operation and Development's Principles of Good Laboratory Practice state that the PI is responsible for ensuring "that the delegated phases of the study are conducted in accordance with the applicable Principles of Good Laboratory Practice[1]." The AWRs define the PI as "an employee of a research facility, or other person associated with a research facility, responsible for a proposal to conduct research and for the design and implementation of research involving animals[2]," and go on to summarize the PI's responsibilities as (1) to "submit proposed activities and significant changes to activities to the [IACUC] for approval" and (2) to "provide acceptable written justification to the IACUC for areas of noncompliance with the [AWA][3]." These guidelines would indicate that the PI should be involved in monitoring the conduct of his/her studies at a level that goes beyond veterinary oversight.

By listing herself as the PI, Schope has taken on all regulatory responsibility for any studies being run by her 'tenants.' Schope can and will be held fully accountable for any cases of noncompliance under these studies, including of course noncompliance with the Animal Welfare Act. Without understanding exactly what Great Eastern's IACUC Chair means by "intimately involved," it appears that Schope is reluctant to have anything more that a cursory involvement in the research being conducted by her tenants. Schope should rethink her stance, consider assigning someone more involved as PI (probably requiring some modifications to the contracts), or consider terminating the contracts entirely.

It would likely behoove Great Eastern to provide an official (internal) document that clearly defines the role of a PI.

1. Organisation for Economic Co-operation and Development. Principles of Good Laboratory Practice. http://www.oecd.org/env/glp.
2. 9 CFR, Chapter 1, Subchapter A—Animal Welfare.
3. Crawford, R.L. Animal Welfare Act Interpretive Summaries. http://www.nal.usda.gov/awic/legislat/awabrief.htm.

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