

Jerald Silverman, DVM, Column Coordinator

## Refusal to renew an expiring protocol

"I'm really sorry, Connie, but I don't have the authority to extend your protocol's expiration date. The NIH/OLAW policy is pretty clear about that. The IACUC sent you three notices that it was nearing its expiration date, but a renewal application was never received. In the meantime, you can work on your other protocols, but this one is now a holding protocol. You have to stop all work on this protocol until you get it renewed."

"You must be kidding, Larry," was the response from Dr. Connie Linder. "We're talking about a week, maybe less, and you're making me jump through bureaucratic hoops and stop funded research?"

"I understand why you're upset," answered Larry Covelli, the IACUC Chair, "but you're the one who stopped it. The IACUC has no choice in this. The IACUC office will send you a letter saying you have 30 days

to submit a new protocol, and during that time, Lab Animal Resources will care for your animals, but no research or breeding can be done, and you're going to have to pay for the care of the animals."

"And what happens if I don't submit one in 30 days?" queried Linder.

The answer came slowly but clearly: "The animals are now under a holding protocol, with the IACUC as the investigator. Nothing will be done other than providing husbandry and any needed medical care. The IACUC will determine their fate, which can include euthanasia, donation to other investigators, etc."

Hearing that, Linder hung up her phone and complained, to no avail, to all of her colleagues.

Thirty days later, there still was no protocol renewal from Linder. Covelli was unsure what to do, because in similar

past instances, the investigators had always submitted their protocol renewals as quickly as possible. Covelli decided to send an ultimatum to Linder, in which he warned her that if a protocol renewal application was not received within 30 days, the 172 mice that were on the holding protocol would be euthanized. Thirty days passed again with no renewal submission. Covelli finally discussed the issue with the IACUC, and the committee's decision was to euthanize the animals if other investigators could not use them. That was not what Covelli wanted to hear, although he didn't know what he did want to hear.

Do you think that the IACUC's initial action and Covelli's subsequent actions were ethical and permissible under policies of the National Institutes of Health and Office of Laboratory Animal Welfare? How would you approach the problems faced by Covelli?

### RESPONSE

#### Cruel to be kind

**Alison D. Pohl, MS, RLATG, CPIA & Ron G. Wallace, PhD, CIH, RBP**

Both the Chair (Covelli) and the IACUC were caught unprepared. This situation may have been avoided by having a cohesive Animal Care Program supported by IACUC policies and procedures. The principal investigator (PI) was given adequate warnings that her protocol was expiring, but the Chair and IACUC didn't know what to do if the warnings went unheeded. When people don't know what to do, particularly in high-pressure situations, they may improvise in ways that are counterproductive.

Other than sending the warning letters, the uninformed IACUC seems to have taken no initial actions. Covelli's initial action of granting 30 days to submit a protocol application was acceptable; however,

additional actions should have been taken at that time, such as securing the animals, notifying the Grants Office and setting up weekly reminders to the PI. Because a renewal protocol was never submitted, one wonders whether Linder, acting in bad faith, might have just finished off the week's work she needed to do after the expiration of her protocol. This argues that animals on holding protocols should be secured or at least closely monitored. In addition, the IACUC should have been notified at the point of expiration that the PI was no longer authorized to use the animals.

The Chair's actions in granting the second 30-day period seem to be compliant with both the Public Health Service *Policy on Humane Care and Use of Laboratory Animals*<sup>1</sup> and the Animal Welfare Act and Regulations<sup>2</sup> because the animals from the expired protocol were covered under an approved holding protocol. But his actions seem to have exacerbated the problem. Granting the second 30-day period, without

IACUC involvement, sets a bad precedent and weakens the perceived authority of the IACUC. Attention needs to be paid to a nuance like this where 'public' perception is involved. In the end, the Animal Care Program is hurt by the Chair's attempt to soften the blow to the PI. Ethically, the Chair is caught between helping the PI and upholding institutional standards.

This situation should have been addressed programmatically. PIs should be trained to understand that IACUC-approved protocols cannot be extended and must not lapse unless there are extenuating circumstances; that they will not be able to work with their animals after the protocol expires; and that expenses for the animals during that period of time cannot be supported by the PI's Public Health Service funding (*i.e.*, funds used during periods of non-compliance have to be reimbursed to the federal source, which involves further unpleasant procedures between the institution and the PI).

The IACUC should have instituted policies outlining an exact set of procedures for expired protocols. These should include the following: (i) written notification to the PI that he or she cannot use animals until a protocol is approved and that if the renewal is not received within 30 days of the protocol expiring, the animals will be euthanized or transferred; (ii) a definite time period during which animals can be housed on a holding protocol; (iii) notification to the IACUC that the PI's protocol has expired; (iv) post-expiration reminders to the PI to submit a renewal protocol; (v) a procedure for transferring animals from a research protocol to the holding protocol; (vi) a way to ensure the animals are not used experimentally; and (vii) a procedure to inform the Grants Office upon expiration of the PI's protocol.

It is important to develop programmatic ways of addressing IACUC issues that promote consistency, efficiency and compliance with federal, state and institutional regulations. In order to have a quality animal care program that functions smoothly, the institution must spend time completing this kind of 'foundational' work. It may be difficult, in the fray, to find time to improve the program when it seems barely possible to keep up with it, but to end the cycle of 'barely keeping up', programmatic measures must be taken.

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 Regulations, 9 CFR (Chapter 1).

*Pohl is Research Compliance Monitor and IACUC Coordinator, and Wallace is Biological Safety Officer and IBC Coordinator at the University of Connecticut Health Center, Farmington, CT.*

## RESPONSE

### Three strikes; PI's out!

**Matthew Panarella, DVM**

I think a baseball analogy perfectly describes the clear lack of responsibility on the part of the principal investigator (PI) Linder. The IACUC, as reported, gave her three chances to respond to notices that

her protocol was nearing expiration. As PI, Linder is solely responsible for making sure that she is compliant with all regulations. Unfortunately for IACUC Chair Covelli, the 'pain' does not end here.

Because Linder did not respond promptly to the IACUC notification, her protocol is no longer approved. If her research is federally funded, then her non-compliance must be reported to the Office of Laboratory Animal Welfare (OLAW) in accordance with the Public Health Service *Policy on Humane Care and Use of Laboratory Animals* (section IV.F.3)<sup>1</sup>. In addition, Covelli is incorrect in calling the protocol a holding protocol with the IACUC as PI. This is not an acceptable interim solution. An individual (possibly the facility director or veterinarian) can submit a new protocol to maintain the animals until a decision can be made about Linder's animals, in the hope of salvaging the mice as part of the research study.

Covelli acted ethically but not swiftly enough. He should have brought the issue to the IACUC immediately after the protocol expired to address the non-response by the PI and the possible reassignment of the mice to another individual PI. I also think that Covelli should be in contact with the Institutional Official (IO), as Great Eastern now needs to contact OLAW and the funding agency. Linder has shown disregard for the IACUC, the institution and the animals themselves. She was given ample opportunity to submit a revised protocol; by ignoring the IACUC, she has created a completely unnecessary and avoidable situation. The IO should be concerned about Linder's commitment to ethical research, compliance training and responsibility to the university and granting agency. The probable euthanasia of the mice (loss of precious research resource) should be a large motivator for Linder; she, Covelli and the IO should meet to discuss a solution.

Research is a collaborative process that includes the PI, the IACUC, the animals and all the staff caring for them. All participants, especially the PI in this case, must accept responsibility and act ethically, or the process may break down. One could argue that IACUC did not do enough to notify the PI (possibly a phone call was warranted in addition to the three notices, warning Linder of the consequences of her inaction), but PIs must be held

responsible for their obligations. Maybe for the future, Covelli, the IACUC and the IO could include training for PIs to inform them that non-compliance can have negative consequences for the animals, the university and the people involved.

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).

*Panarella is President, Research Consulting Services, Hampton, NJ.*

## RESPONSE

### IACUC acted appropriately, but...

**Joan T. Richerson, DVM, MS, DACLAM**

The Great Eastern University IACUC seems to have an established procedure for addressing expiring protocols, which is consistent with policies of the National Institutes of Health (NIH) and Office of Laboratory Animal Welfare (OLAW). OLAW guidance states unequivocally that IACUCs do not have the authority to administratively extend approval beyond 3 years<sup>1</sup>. The IACUC sent Linder three notices of pending protocol expiration, but it is unclear how much advance notice she actually received. Submitting and obtaining approval of a renewal protocol well in advance is essential, because a protocol expires even if it is under review by the IACUC on the expiration date<sup>2</sup>.

Linder's statement that "[w]e're only talking about a week, maybe less, and you're making me jump through bureaucratic hoops and stop funded research?" suggests that her grant period may be ending very soon. Consequently, she doesn't see the need to renew her protocol. Nonetheless, NIH and OLAW policy is clear: "continuation of animal activities in the absence of valid approval is a serious and reportable violation of PHS [Public Health Service] Policy [*Policy on Humane Care and Use of Laboratory Animals*]"<sup>1</sup>. Therefore, Covelli, the IACUC Chair, is correct to state the IACUC must ensure that research manipulations stop and to point out that

PHS funds may not be used in support of unauthorized activities<sup>2</sup>.

The PHS *Policy* stipulates that only the IACUC may approve activities involving animals but does not dictate which administrative actions may or may not be taken after approval has lapsed<sup>3</sup>. Actions taken by the IACUC Chair or the committee should be consistent with the institution's approved Assurance and internal policies. One wonders whether the Chair was authorized by the Assurance or internal policies to take these actions. This potential concern is supported by the facts that the mice were not euthanized when Linder failed to meet the second deadline and that Covelli did not involve the IACUC until fairly late in the process.

The committee members' decision was to euthanize the animals if other investigators could not use them. Unfortunately, this decision may result in additional animals being used if Linder later decides to seek approval to resume her project. In keeping

with the spirit of the principle of reduction, the decision to euthanize animals should be made with due diligence.

In general, Great Eastern University's IACUC has acted in accordance with NIH and OLAW policy, but the IACUC Chair may have exceeded his authority. Most Great Eastern University investigators seem to be adequately informed about the policy on protocol expiration, because they do not appear to readily support Linder's position. To avoid this situation in the future, the IACUC should first re-examine its procedure for handling protocols that are approaching expiration to ensure that PIs are given adequate notice and response time to continue IACUC approval. Next, the IACUC should refine its policy for handling a lapse in protocol approval in order to specify the maximum amount of time that animals may remain on the holding protocol; the justification needed to keep animals on the holding protocol beyond the specified time period; and

those actions that are delegated to the Chair versus those that require majority vote of a quorum. Finally, the IACUC should amend its Assurance as needed and publicize the revised policy among investigators.

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals — Frequently Asked Questions*. Protocol Review, Question D-2. (US Department of Health and Human Services, Washington, DC, 2006; revised 2010). <<http://grants.nih.gov/grants/olaw/faqs.htm#d2>>
2. National Institute of Health Office of Policy for Extramural Research Administration. *Transcript of OLAW Online IACUC Staff Seminar: When Terms and Conditions Are Not Met*. 4 December 2008. <[http://grants.nih.gov/grants/olaw/081204\\_seminar\\_transcript.pdf](http://grants.nih.gov/grants/olaw/081204_seminar_transcript.pdf)>
3. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals — Frequently Asked Questions*. IACUC Composition, Functions and Authority, Question B-10. (US Department of Health and Human Services, Washington, DC, 2006; revised 2010). <<http://grants.nih.gov/grants/olaw/faqs.htm#b10>>

*Richerson is the Assistant Chief Veterinary Medical Officer with the Department of Veterans Affairs Office of Research and Development in Nashville, TN.*

## A word from OLAW

*In response to the issues raised in this scenario, the Office of Laboratory Animal Welfare (OLAW) offers the following clarification and guidance:*

OLAW has previously commented on a similar situation concerning administrative extension of an expired animal study protocol<sup>1</sup>. For animal activities funded by the Public Health Service (PHS), the PHS *Policy on Humane Care and Use of Laboratory Animals (Policy; section IV.C.5.)* states that "the IACUC shall conduct continuing review of each previously approved, ongoing activity covered by this *Policy* at appropriate intervals as determined by the IACUC, including a complete review in accordance with IV.C.1.-4. at least once every three years"<sup>2</sup>. In order to extend the project, the IACUC must carry out a complete review and approve the protocol either at a full committee meeting or by designated member review<sup>2</sup>. If a protocol expires, all animal activities conducted under that protocol must cease. Continuation of animal activities in the absence of a valid approval is a serious violation of both the PHS *Policy* and the terms and conditions of the grant<sup>3</sup>. These violations must be reported to OLAW and the funding component<sup>3</sup>. If the project is PHS-supported, funds may not be drawn from the grant for any animal activities during the expired period<sup>4</sup>.

If an approved research protocol expires and animals are held under a holding protocol under which no research work is done, then reporting is not required. Use of a holding protocol, though permissible, should be viewed as an emergency stopgap and should not be a regular practice. Institutions should have policies and procedures in place to ensure that protocols are reviewed in a timely fashion. By allowing the investigator to keep animals on a holding protocol for an extended period of time without a compelling reason, Great Eastern University's IACUC is encouraging disregard for its authority and oversight of the animal care and use program. The IACUC needs to carry out a comprehensive review of its policies and procedures and to communicate them clearly to all investigators.

1. Brown, P.A. A word from OLAW. *Lab Anim. (NY)* **36**, 14 (2007).
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. Office of Laboratory Animal Welfare. Guidance on Prompt Reporting to OLAW. NOT OD-05-034. (National Institutes of Health, Washington, DC; 24 February 2005; updated 15 April 2010). <<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-034.html>>
4. Office of Laboratory Animal Welfare. Guidance Addressing the NIH Policy on Allowable Costs for Grant Activities Involving Animals when Terms and Conditions are Not Upheld. NOT OD-07-044. (National Institutes of Health, Washington, DC; 26 January 2007; updated 15 April 2010). <<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-044.html>>

**Patricia Brown, VMD, MS, DAACLAM**

*Director  
OLAW, OER, OD, NIH, HHS*