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Getting around late protocol renewals

As always, time was running out for Ray Romansky. It was almost a game for him to wait until the eleventh hour before submitting his protocol renewal to the Great Eastern University IACUC. On some occasions he even had to secure a brief extension of time from the IACUC after the protocol had technically expired. So, true to form, he submitted his protocol the day it was due to expire, with a request to keep it active until the IACUC had time to review and approve it.

Naomi Gates was new to the IACUC office and was unaware of Romansky's history. She had been told that every protocol had an expiration date. Beginning 90 days before the expiration date, she sent monthly notices to investigators, reminding them to submit their protocols for renewal well before that date. Once a protocol expired, Gates's instructions were to inform the investigator that no further animal activities could occur until the protocol had been approved.

The following day after Romansky's protocol expired, Gates sent him a perfunctory 'cease and desist' notice, copying the animal facility to ensure that no additional animals could be ordered. Apparently, nobody had told Gates that the committee often flouted federal regulations and policy and allowed investigators to have some additional time before suspending animal activities on a protocol. When Romansky received the notice from Gates he became livid and immediately called the often-hassled Larry Covelli, the IACUC Chairman. Covelli was apologetic, but asked for Romansky's understanding. "The damage is done," Covelli told him, "and there's nothing I can really do."

Then Romansky got an idea. Because all of his protocols used the same basic methodology, he would transfer about 50 mice from his newly expired protocol to one of his active protocols. The 50 animals were less than 5%

of the approved number on the active protocol, so he believed it could be submitted as a minor amendment under Great Eastern's IACUC policy. He would just add them as an additional drug group to those already approved. Then he could continue his drug studies until the suspended protocol was approved, at which time he would transfer the animals back to that protocol. Covelli wanted to redeem himself, so he gave serious thought to Romansky's idea and concluded that he didn't know whether or not he had the authority to grant the request.

By not following federal regulations, the Great Eastern University IACUC seems to have boxed itself into a corner with Romansky. If not ethical, is Romansky's request even legal? If the request is approved by the IACUC as a minor amendment, is it compliant with federal policies to move animals out of a suspended protocol into an active one?

RESPONSE

Still must submit

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It is clear that Romansky does not have any respect for the Great Eastern IACUC. He does whatever he likes irrespective of whether it is lawful or whether the IACUC agrees. Romansky has been lax in the past, as this is not the first time he has requested an extension of an expired protocol. Once his protocol expired, it was proper for the IACUC to send him a 'cease and desist' notice. After receiving that notice, Romansky was within his rights to call and talk with the IACUC Chair and

request an extension of the expired protocol. However, Covelli was right to tell Romansky that he could not reverse the IACUC's decision.

Romansky's request to transfer the mice should be submitted to the IACUC in a protocol amendment and must secure approval before he can actually move the mice from his expired protocol to an active one. However, in approving the amendment and adding the mice to the active protocol—on which a certain number of animals were already approved by the IACUC—Romansky should maintain the same total number of animals on that protocol by reducing the number of previously approved animals by the number of mice added. If Romansky secures approval of his amendment and adds the

animals to the active protocol (reducing the number of animals in the active protocol as described above), then both Romansky and the IACUC will be in compliance with federal policies. If Romansky transfers mice from his expired protocol to the active protocol without securing prior approval from the Great Eastern IACUC, he will have committed scientific misconduct, which should be reported by Covelli to Great Eastern's Institutional Official.

Finally, it appears that the IACUC members and the investigators might want to refresh their training materials in order to comply with all the federal guidelines and avoid any such confusion in the future.

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RESPONSE

A waste of time

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Dr. Romansky’s protocol essentially expired, and therefore, in the eyes of the IACUC, the study came to an end. By setting a historic precedent allowing Romansky to continue activities after his protocol has expired, Great Eastern University has failed to comply with federal regulations. According to federal regulations¹, Ms. Gates was working under the correct assumption and acted appropriately when she notified Dr. Romansky to cease and desist pending renewal of the expired protocol. Furthermore, while Ms. Gates’s letter to Romansky on behalf of the IACUC interrupted the unapproved activities, it does not constitute an official suspension of activities as defined in the Animal Welfare Regulations², which requires a review and decision by a quorum of the IACUC. The protocol simply expired.

While there is no federal regulation that prevents Romansky from requesting to add research animals that were assigned to the expired protocol to an approved one, the IACUC must determine whether or not Romansky’s request constitutes a minor or major amendment to the protocol. Major changes typically include an increase in the number of animals or number of studies or treatment groups. If there is no increase in the number of animals used or procedures performed on each animal, and there is no change in the objectives of the proposed study, then Romansky’s request may be considered a minor change by the IACUC. However, the additional treatment group may very well change the objectives of the study, and therefore will likely be considered a major change. This amendment will require review and approval by the IACUC prior to implementation³. The criteria for categorizing a change to activities proposed to an approved protocol must be delineated in the PHS Assurance for Great Eastern University, and should be in place prior to any further consideration of Romansky’s request.

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:

This scenario raises a number of issues. Can the IACUC administratively extend approval of a project that has expired? No¹. For animal activities funded by the Public Health Service (PHS), the PHS Policy on Humane Care and Use of Laboratory Animals 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”². In order to extend the project, the IACUC must conduct a complete review and approve the protocol either at a full committee meeting or by designated member review². If a protocol is allowed to expire, 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 grant³. These violations must be reported to OLAW and the funding component³. If the project is PHS-supported, funds may not be drawn from the grant for animal activities during the expired period⁴.

Should the IACUC consider the transfer of animals from one project to another as a significant change? This is a more complex question with implications in several areas. The IACUC has some latitude in defining what it considers a significant change, or it can establish a mechanism for determining significance on a case-by-case basis⁵. Significant changes require IACUC approval by either (1) full-committee review by a convened quorum of the IACUC or (2) designated member review by one or more members in accordance with the Policy at IV.C.2. and as previously clarified by OLAW⁵. The IACUC must clearly define its policy and mechanism for determining significance and communicate this to its investigators.

In the scenario described, it is clear that the investigator’s proposal to ‘amend’ an ongoing protocol to accommodate work described in an expired protocol represents a change in the approved objectives of the ongoing study that would require IACUC review⁶. It is also clear that the reason for the investigator’s proposal, including the transfer of mice, has no scientific basis and is actually based on his failure to submit a request for protocol renewal to the IACUC in a timely manner. OLAW expects IACUCs to adhere to the letter and spirit of provisions of the PHS Policy and Animal Welfare Act regulations and recommends that they refuse to consider disingenuous proposals such as the one described. The IACUC has set a precedent for flouting federal regulations by allowing investigators to have additional time before suspending animal activities on an expired protocol. The IACUC needs to conduct a comprehensive review of its practices and revise its policies and procedures so that it is conducting business in accordance with federal requirements.

1. Frequently Asked Questions, Protocol Review, Question No. 2. http://grants.nih.gov/grants/olaw/faqs.htm#proto_2.
2. Public Health Service Policy on Humane Care and Use of Laboratory Animals, Amended August, 2002. <http://grants.nih.gov/grants/olaw/references/phspol.htm>.
3. NOT OD-05-034, Guidance on Prompt Reporting to OLAW. <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-034.html>.
4. NOT OD-07-044, Guidance Addressing the NIH Policy on Allowable Costs for Grant Activities Involving Animals when Terms and Conditions are not Upheld. <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-044.html>.
5. Frequently Asked Questions, Protocol Review, Question No. 3. http://grants.nih.gov/grants/olaw/faqs.htm#proto_3.
6. Frequently Asked Questions, Protocol Review, Question No. 9. http://grants.nih.gov/grants/olaw/faqs.htm#proto_9.

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