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Reactivation of a suspended protocol

The hammer came down harder than Les Redmond had expected. He knew he was in trouble for being noncompliant with his IACUC protocol but for a change—and a change it would be—his noncompliance was inadvertent. Redmond had a poor track record with the Great Eastern University IACUC, having received IACUC-imposed sanctions twice before for protocol noncompliance incidents. However, neither of those sanctions included a protocol suspension. This time the IACUC wasn't interested in whether or not the problem was intentional; Redmond's protocol was suspended at a meeting of the full committee until the committee felt assured that the current and similar problems would not recur.

No matter how much Redmond ranted, threatened legal action against the IACUC

and protested to the Institutional Official, the IACUC would not retreat from its position. Finally, Redmond gave up and asked Larry Covelli, the IACUC chairman, what he would have to do to get his protocol reinstated. "You have to understand," said Covelli, "the ball is in your court. You have to develop a plan to bring your research back into compliance and convince the IACUC that it will not see another noncompliance problem in the future. That's when a final decision will be made."

Redmond developed a plan that he thought would meet the demands of the IACUC. He presented it to the IACUC office and asked how long it would take before a decision was made. "I really don't know," said the IACUC's secretary, "but I'll ask Dr. Covelli and get back to you this afternoon."

After Redmond left, the secretary called Covelli and said, "Larry, every time the IACUC has reactivated a protocol, it just seems to happen, but I really don't know how it happens. What should I tell Dr. Redmond?"

Covelli replied that he would review Redmond's plan, and if it seemed adequate, he would send it to the IACUC by e-mail. If there were no questions or dissents, he would approve reactivating the protocol. However, if there were any questions or dissents, the decision would have to wait until the next full committee meeting so that Redmond's plan could be discussed and subsequently put to a formal committee vote.

Is the process described by Covelli appropriate to reactivate a suspended protocol?

RESPONSE

Plan ahead for reactivation

Betty R. Theriault, DVM, DACLAM

The appropriate process for IACUC suspension of protocol activities is well described in both the Animal Welfare Act and Animal Welfare Regulations (AWARs)¹ and the Public Health Service *Policy on Humane Care and Use of Laboratory Animals (PHS Policy)*². Although these documents do not specifically address reactivation of a suspended protocol, one can extract guidance on the steps the IACUC must take for protocol reactivation by examining the process for initial suspension.

Owing to the inherent gravity of a decision to suspend a protocol given the types of non-compliance that may lead to protocol suspension, both the AWARs and PHS *Policy* require that protocol suspensions be reported. Reporting to APHIS is required when the suspended activities involve

USDA-covered species, and reporting to OLAW is required if the protocol covers federally funded research. Additionally, both regulations require that any federal funding agencies financially supporting the research also be notified. At the time of reporting, it is expected that the Institutional Official (IO), in consultation with the IACUC, has reviewed the reason for suspension, that appropriate corrective action has been prescribed and that there are follow-up measures in place to ensure these corrective actions are sufficient and completed.

It appears that the IACUC of Great Eastern University has fallen short of its oversight obligations. It appears as though the IACUC did not discuss and agree upon a plan of corrective action or requirements for reactivation when it voted to suspend Redmond's protocol. Appropriate requirements could include training sessions for the principal investigator (PI), documentation of protocol compliance by the PI and his staff, a plan to ensure future compliance and possibly protocol

amendments to address any unapproved or inadequately described activities in which the PI was engaged. At the time of protocol suspension, the IACUC should have discussed these measures and agreed that the PI submit all requested information and documentation before a scheduled convened quorum meeting for review and further action. At this meeting, the IACUC would have the opportunity to review protocol amendments (if indicated), training activities and documents from the PI and to then decide whether these measures satisfy the IACUC's requirements for protocol reactivation.

It is unclear from the scenario whether the protocol suspension was reported to Great Eastern's Institutional Official (IO) and to what extent the IO was involved in the corrective action process.

Without a plan of corrective action, the IACUC lacks defined expectations for the PI's actions, for the time line for completion of these actions and for how it will review and evaluate the corrective actions. This

means that both the IACUC and the PI lack a good understanding of what is required for protocol reactivation.

Covelli's intention to send out Redmond's plan by e-mail to the IACUC to see whether any members had questions or dissents appears to fall far short of what would be expected of the IACUC in such situations.

1. Animal Welfare Act and Animal Welfare Regulations. 9 CFR 2.31 (C)(6), (C)(7) & (C)(8).
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* Section IV, Part C 6, 7 & 8. (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).

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RESPONSE

Do it by policy

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Given the seriousness of the repeated noncompliance, it is important for the IACUC to take all measures necessary to avoid future violations by Les Redmond (the principal investigator; PI) at Great Eastern University. Redmond's protocol had been suspended at a meeting of the full committee and was not to be reactivated until the committee was assured that the current and similar problems would not recur. The Great Eastern University IACUC should have an established policy regarding the suspension and reactivation of protocols to assure that the committee follows set procedures in such circumstances. The PHS *Policy on Humane Care and Use of Laboratory Animals* (PHS *Policy*; Section IV.C.6)¹ and the Animal Welfare Act and Regulations (AWARs; §2.31,d,6)² state that a vote to suspend an animal activity can occur "only after review of the matter at a convened meeting of a quorum of the IACUC and with the suspension vote of a majority of the quorum present." It appears that the Great Eastern University IACUC followed this requirement. However, the PHS *Policy* and the AWARs are somewhat silent on the

exact mechanism for IACUC reactivation of a suspended protocol. The IACUC should have a set policy to provide guidance for the reactivation of a suspended protocol and should only reinstate a suspended protocol with the assurance that the animal activity is, or will be, in full compliance with the PHS *Policy*, the AWARs, the *Guide for the Care and Use of Laboratory Animals* (the *Guide*)³ and the Great Eastern University Animal Welfare Assurance. If the suspension is open-ended (and not for a finite period) until a particular outcome occurs, the IACUC can vote (at the time of animal activity suspension) for the IACUC chair to make the decision to reactivate the protocol at his or her discretion. The IACUC can also require, according to set policy, a committee vote to reactivate a suspended animal activity. It all depends on the established IACUC policy that must be followed in these circumstances.

We believe that the Great Eastern IACUC should have requested mandatory retraining for the PI and his research staff; regular meetings of the PI and his staff with the attending veterinarian and IACUC chair (or designees) to discuss animal use protocols; and ongoing post-approval monitoring of the animal research and any future husbandry and clinical matters pertaining to the animal research. Furthermore, to avoid future noncompliance issues, the IACUC could have placed the PI on probation for a specified amount of time (e.g., 6–12 months) during which the use of animals and procedures would be closely monitored by animal care personnel and the IACUC. This would allow the PI to continue his animal research while at the same time sending a clear message that further noncompliance must be prevented. The IACUC should have also discussed ways to improve the program to prevent such instances of noncompliance from occurring again and assessed the adequacy of the IACUC-administered institutional animal care and use training program for training PIs and their research staff in appropriate policies and procedures, proper handling and restraint, and basic biotechnology and experimental techniques.

In summary, Covelli and the Great Eastern University IACUC may indeed reactivate a suspended animal protocol when it is confirmed that the PI, the

research staff and the animal protocol are in full compliance with all animal care and use standards as required by the PHS *Policy*, the AWARs, the *Guide* and the Great Eastern University Animal Welfare Assurance. Once compliance and documentation that all IACUC-mandated retraining and monitoring stipulations have been met and adequately addressed by the PI and research staff, protocol reactivation is appropriate. However, the reactivation of a suspended protocol should follow established procedures and IACUC policy.

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 Part 2, Subpart C 2.31(d)(6).
3. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Research Council, Washington, DC, 2011).

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RESPONSE

Appropriate reactivation process

Benjamin C. Datiri, PhD, RLATG

All research activities must conform to the statutes of the Animal Welfare Act¹ and the guidelines of the Public Health Service as issued in the *Guide for the Care and Use of Laboratory Animals*². For an approved protocol to be suspended, an investigator must have violated the regulations in these documents by making significant changes to the IACUC-approved protocol. The IACUC *Guidebook*³ states that "significant changes to an IACUC-approved protocol must be reviewed and approved before they occur (PHS *Policy* IV.C.1; and AWR §2.31[d][1])." Perhaps Redmond had made significant changes to his IACUC-approved protocol that warranted its suspension, since he had received IACUC-imposed sanctions twice previously for

protocol noncompliance incidents without suspension of the protocol.

Redmond must now officially submit any significant protocol changes that he had made to the IACUC for review (by the full committee or by a designated member) and approval before he continues his research. Since Redmond developed a plan that he thought would meet the demands of the IACUC and submitted it to the IACUC office, it is appropriate for the committee to expedite the review process. In my opinion, it was with this in mind that Covelli developed his plan to review Redmond's plan, send it to the IACUC members by

e-mail if it seemed adequate and, if there were no questions or dissents, approve the reactivation of the protocol.

Apparently Covelli made himself the designated member for review of Redmond's plan but also e-mailed other committee members to ensure they had an opportunity to assess the adequacy of Redmond's plan, cross-checking it and accepting the significant changes to the protocol before giving his final approval as a designated reviewer. If there were any objections, then the IACUC would have to meet to review and reach an appropriate decision. This, in my opinion,

is an appropriate process to reactivate a suspended protocol.

1. Animal Welfare Act and Animal Welfare Regulations. 9 CFR Ch.1 §2.31[d][1].
2. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Research Council, Washington, DC, 2011).
3. Office of Laboratory Animal Welfare. *Institutional Animal Care and Use Committee Guidebook* 2nd edn. (US Department of Health and Human Services, Bethesda, MD, 2002).

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A word from OLAW and USDA

In response to the questions 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:

In the scenario, the specific reason for suspension of the protocol by the IACUC is not described. In OLAW's and APHIS's experience, repeated noncompliance, implementing significant changes without IACUC approval or other noncompliance with the Animal Welfare Act and Regulations (AWARs)¹, the *Guide for the Care and Use of Laboratory Animals*² or the institution's Animal Welfare Assurance are all reasons for an IACUC to suspend an approved protocol.

The IACUC may only suspend an activity during a convened IACUC meeting with a quorum present and a majority vote for suspension^{1,3}. If the IACUC does suspend an activity involving animals, the Institutional Official (IO) in consultation with the IACUC shall review the reasons for suspension, take appropriate corrective action and report that action with a full explanation to OLAW, APHIS and the funding agency supporting the award^{1,3,4}. The suspension must be reflected in the minutes of the IACUC meeting and in the semiannual report to the IO^{1,2}. During the period of suspension, charges are not to be made to the grant for any research activities involving animals covered by the suspended protocol. However, funding components may allow expenditure of NIH grant funds for maintenance and care of animals on a case-by-case basis⁵.

The suspension may only be lifted by the IACUC. The IO may independently suspend a protocol, but only the IACUC may reinstate or approve an animal activity. IACUCs are at liberty to set stricter institutional requirements for reinstatement than those required by the PHS Policy on Humane Care and Use of Laboratory Animals (*PHS Policy*)³ and the AWARs¹ but cannot set less restrictive procedures. The AWARs and the *PHS Policy* provide no specific procedure for protocol reinstatement. APHIS and OLAW expect that the suspended protocol, along with any amendments added as a result of the suspension, will be reinstated only by review and approval according to the IACUC protocol approval process^{1,3}.

The PI may suggest corrective actions, which the IACUC may or may not accept. The IACUC may require additional actions such as staff retraining, enhanced IACUC oversight or protocol changes. It may not be necessary for certain corrective actions to be completed by the time of protocol reinstatement, but it is required that a plan and schedule be developed prior to lifting the suspension. The IACUC may set a time for completion and carry out continued protocol monitoring as necessary until requirements are met^{1,3}. Corrective and preventive measures are to be included in the report of the suspension to OLAW and APHIS.

1. Animal Welfare Act and Regulations. 9 CFR Ch. 1, Part 2, Subpart C.
2. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Research Council, Washington, DC, 2011).
3. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
4. Office of Laboratory Animal Welfare. Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals. Notice 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>>
5. 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. Notice NOT-OD-07-044. (National Institutes of Health, Washington, DC, 26 January 2007) <<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-044.html>>

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