

How should the IACUC handle a questionable VVC change to a protocol?

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Dr. Lisa Blackmore's original IACUC protocol approval did not include the use of the school's cold room to house some of her mice, but during the course of experimentation it became necessary to use the room and Blackmore submitted a protocol amendment to the IACUC office for a change in the housing site. Because there was an existing IACUC-approved Standard Operating Procedure for housing mice in the cold room, the IACUC office forwarded the requested change to the attending veterinarian and using the veterinary verification and consultation (VVC) process¹, the veterinarian concurred with the change.

Soon afterwards, during the semi-annual inspection of animal housing areas, an IACUC inspector walked into the cold room that housed Blackmore's cages along with many cages from other mouse studies. All the animals were fine and the studies were being conducted as per the approved

protocols, but the inspector noticed exposed electrical wires that could easily be contacted by anybody working in that part of the room. The wires were above the cages housing Blackmore's mice and due to the other ongoing studies there was no place to relocate the cages. The inspector notified Blackmore and the vivarium of the problem and the vivarium director said that she would call the facilities maintenance department to have the problem remedied. The inspector advised the IACUC office and vivarium that the problem should be considered a significant deficiency because, in the inspector's opinion, it threatened the safety of personnel working in the area.

The exposed wires were quickly put into a proper conduit by the maintenance department which explained that a repair to the cooling unit had not been completed when the inspection occurred. Nevertheless, the IACUC was not entirely sure about how to

handle the inspection finding. There was no question about the safety issue for personnel but the static mouse cages were on a table that was well below the wires. The committee was not sure if a danger to personnel but not to animals constituted a significant deficiency. A second problem was that the Blackmore protocol change was implemented by VVC and NIH guidance on VVC states that changes impacting personnel safety must be approved by either full committee or designated member review¹. The committee was unsure if the inspection finding was a reportable incident to OLAW or if it was just a wake-up call for the veterinarian to be more thorough before approving a change by VVC.

How do you think the IACUC should proceed?

1. National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126.

RESPONSE

Not so simple a scenario

Ellen J. Croxford

At first blush, this scenario appears straightforward, however, several issues come to mind right away. The approval by VVC seemed appropriate according to NOT-OD-14-126 Guidance on significant changes to animal activities¹. The IACUC already had an SOP in place, and Blackmore's change in location had been submitted for approval. But, Blackmore's mice had not been in the cold room prior to the amendment, and in my opinion, despite the existing standard operating procedure, the veterinarian should have made a cursory inspection of the new housing area.

If exposed wires were observed, inquiries could have been made to the vivarium manager to see if there was repairs scheduled that may cause an issue involved with housing the mice in that area.

When the inspection occurred it was obvious that there was a potential danger to people working with the mice and, as stated, in the ARENA² Guidebook the PHS Policy³ places responsibility to ensure a safe working environment with the institution and the "natural point of convergence...at many institutions is the IACUC". In this instance, it was a definite safety issue for the personnel. The IACUC took the proper steps and notified the vivarium manager who promptly called facilities maintenance and the situation was quickly remedied. Was it a significant deficiency? Yes, to a point due to danger to personnel. However,

the definition of significant is unresolved or repeated deficiencies except this situation was attended to immediately by both the vivarium manager and facilities maintenance. In this case, the IACUC need not report it to OLAW since no animals were harmed. The incident will be in the minutes and in the annual report, but it was quickly resolved, and the animals were well out of danger on a table and the potential danger to personnel eliminated.

This should, however, be a wake-up call for not only the veterinarian but also the IACUC. Careful consideration of each protocol or amendment should always be the rule regardless of standard operating procedures. Changes in housing, in circumstances such as this where environmental changes are required should be inspected for safe working conditions for both animals and

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personnel. Relocation of animals to anywhere other than regular housing, (such as cold rooms) should require notification to the vivarium manager or supervisor to ensure that the animals are taken care of properly. Notification may have made all parties aware that the relocation of the animals should be delayed until repairs to the cooling systems were completed, or accommodation could have been made by placing another table in the cooler. It is unclear who had been taking care of feeding, water needs, and cage changing, but the exposed wires should have been reported to the area supervisor for immediate attention.

1. National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126.
2. ARENA/OLAW. *Institutional Animal Care and Use Committee Guidebook* 2nd edn. (OLAW, Bethesda, MD, 2002).
3. U.S. Department of Health and Human Services. *Public Health Service Policy on Humane Care and Use of Laboratory Animals* (2015).

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RESPONSE

Collaborative decision making and navigating the red tape

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The ability to collaborate and come to a collective decision is key when reviewing the results of the semi-annual facility inspection results with the IACUC. In this case, the IACUC inspector, the vivarium director, and maintenance staff worked together seamlessly in identifying the problem of the exposed wiring and resolving the issue quickly without harm coming to animals and/or research staff that utilize the room. In reviewing ref. 1, considering that no animals or staff were harmed and that the exposed wires were quickly and safely replaced, it could be recommended that the IACUC classify this as a minor deficiency. It is always important to note that classifying deficiencies is not a one person decision, it is one that involves the IACUC and the IO cooperatively.

In response to a number of issues posed in this scenario, the Office of Laboratory Animal Welfare (OLAW) provides the following clarifications:

First, the PHS Policy IV.B.3.d., defines a significant deficiency as one that is a threat to the health and safety of animals.¹ In the scenario, the exposed electrical wires, while a hazard to personnel, do not pose a risk to the animals and therefore are considered a minor deficiency for reporting in the semiannual report to the Institutional Official (IO). The facility management must be promptly contacted and the wiring problem corrected.

Second, as mentioned by reviewers, the change in the protocol involves the addition of a procedure, i.e. housing mice in the school's cold room. Veterinary verification and consultation (VVC) may not be used to add a new procedure that was not previously approved on the protocol.² Existence of an SOP approved for other protocols does not justify the addition of a new procedure. In addition, exposing the mice to an environment outside of the recommended temperature range of the *Guide*, 68-79° F, is a change that has a negative impact on animal welfare and results in greater distress to the animals.^{2, 3} Such a change must be reviewed and approved by full committee review (FCR) or designated member review (DMR).²

Lastly, the IACUC office used VVC incorrectly. This error allowed "the conduct of animal-related activities without appropriate IACUC review and approval".⁴ Prompt reporting of this noncompliance is required.⁴

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986, revised 2015).
2. National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126 [online]. <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-126.html> (National Institutes of Health, Washington, DC, 26 August 2014).
3. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. pp. 43-44 (National Academies Press, Washington, DC, 2011).
4. National Institutes of Health. *Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals*. Notice NOT-OD-05-034 [online]. <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-034.html> (National Institutes of Health, Washington, DC, 24 February 2005).

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VVC continues to be one of the hot topics that many institutions are currently discussing. Based on the assumption that Blackmore is working at an AAALAC accredited facility, has an assurance on file with OLAW, and has an IACUC approved VVC Policy, it is my opinion that the IACUC office should have sent the modification to utilize the cold room for Blackmore's mice to DMR or FCR according to PHS Policy (IV.C.2)². The deciding factor surrounding this issue is that Blackmore's original IACUC approved protocol did not include the housing of mice in a cold room. It is my interpretation that the VVC process cannot be used to add new procedures to a previously approved protocol³ (even through the IACUC has an existing IACUC approved SOP for housing mice in the cold room) and

according to ref. 4, this modification would fall under 1. b. of the guidance (resulting in greater pain, distress, or degree of invasiveness) which would mandate that it be reviewed by DMR or FCR by the IACUC. Our institution utilizes cold rooms that as a stressor experiment for the animals and the IACUC classifies this housing procedure as a type of induced stress that has potential to cause greater pain or discomfort to the animal due to the altered macroenvironment which deviate from the standards set by the *Guide*⁵. If the IACUC decides that the VVC policy in this case was wrongly applied, then a report would need to be sent to OLAW underlining that an unapproved significant change was made and animal-related activities took place without appropriate IACUC review and approval.

1. National Institutes of Health. Guidance on Prompt Reporting to OLAW Under the PHS Policy on Humane Care and Use of Laboratory Animals. Notice NOT-OD-05-034.
2. U.S. Department of Health and Human Services. Public Health Service Policy on Humane Care and Use of Laboratory Animals (2015).
3. The IACUC Administrators Association. *Frequently Asked Questions on VVC*. <http://iacucaa.org/veterinary-verification-and-consultation-vvc>
4. National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126.
5. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington, DC, 2011).

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RESPONSE

Better safe than sorry

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The *Guide for the Care and Use of Laboratory Animals* 8th ed. views the safety of animals as well as humans as an important consideration in laboratory animal facilities¹.

It is unclear in this scenario whether the veterinarian was aware of the electrical hazard in the cold room prior to concurring with the requested room change. If the

attending veterinarian (AV) knew about the electrical hazard, the amendment should not have been approved through the veterinary verification and consultation (VVC) process because it should have been considered a significant change to a protocol². In that case the amendment should have gone to the IACUC for a full committee or designated member review. If the AV was unaware of the electrical hazard in the cold room, the change that was approved by VVC was merely a change in housing to an IACUC-approved site which would have been acceptable here. When there may be a question about whether the designated veterinarian has the authority to approve a change through VVC, the best practice should be to err on the side of letting the IACUC handle the review. Applying the VVC process incorrectly could constitute noncompliance resulting in a reportable situation to OLAW³. Regardless of the process, a hazard which represents a danger to animals or humans should be repaired as soon as possible and steps should be taken to prevent any injuries from occurring until the hazard no longer exists.

It is impossible to ascertain from the information given how long the bare wires had been there even though the words 'soon' and 'quickly' were used to describe the discovery and repair. Since there were already animals being housed in the cold room, the danger to personnel may have been present well before the inspection. To

prevent future hazardous situations, all personnel including the maintenance department should be asked to notify the vivarium director of any repairs and whether they may present a danger to personnel or animals. Also, at the time of such repairs, the maintenance department should designate potential hazards by clearly marking the area with cautionary materials.

No animals or humans were harmed because of this incident which is one criterion for a significant deficiency that should be reported to OLAW⁴. However, it is always best practice to check with OLAW by telephone or email when there is uncertainty as to whether to report⁵.

1. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington, DC, 2011).
2. National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126.
3. The IACUC Administrators Association. *Frequently Asked Questions on VVC*. <http://iacucaa.org/veterinary-verification-and-consultation-vvc>
4. U.S. Department of Health and Human Services. Public Health Service Policy on Humane Care and Use of Laboratory Animals (2015).
5. National Institutes of Health. Guidance on Prompt Reporting to OLAW Under the PHS Policy on Humane Care and Use of Laboratory Animals. Notice NOT-OD-05-034.

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