Jerald Silverman, DVM, Column Coordinator

Communication between collaborating IACUCs

Trying to be a good neighbor can, at times, be trying. New Antigen Inc. was a small biotechnology company located near Great Eastern University. The company leased animal facility space from the school, submitted protocols for review and approval by the school's IACUC and then carried out its research at the school. However, New Antigen also had its own IACUC because the company had a small business grant from the US Public Health Service (PHS) that required euthanizing animals at New Antigen, not at Great Eastern. For that grant, Great Eastern ordered the animals and housed them at the school. When New Antigen was ready for the animals, they would be transported to New Antigen by New Antigen employees, where they would be immediately euthanized for a tissue harvest. The transport process and euthanasia were approved by the Great Eastern and New Antigen IACUCs.

During a Great Eastern IACUC semiannual inspection, an inspector casually asked whether the IACUC had approval the transport of the mice he had just seen being taken to New Antigen. He was told that no, the New Antigen animals being used on the PHS grant were rats, not mice, and they were not being moved that day. The mice he had seen were part of a different New Antigen study and should never have left Great Eastern. A quick phone call to New Antigen revealed that the Great Eastern IACUC had approved the mouse study, that all of the work was to be done at Great Eastern and that the mice were being taken to New Antigen for euthanasia. "But you don't have authorization from the IACUC to move those animals," said Thai Morris, a Great Eastern animal facility supervisor. "Yes, we do," was the response from New Antigen. "The study is over. Moving the mice to New Antigen for euthanasia was approved by our IACUC after the study started."

We have a problem. The Great Eastern IACUC approved the entire study to be completed at the school. However, the New Antigen IACUC subsequently approved the transportation of the mice to its own premises where the animals would be euthanized. Both institutions and IACUCs were acting in good faith, but there was a breakdown in communications. Is the transportation and euthanasia of the mice at New Antigen a protocol violation? If it is, is it reportable to NIH/OLAW, and if so, which IACUC should make the report? How can future problems of this nature be prevented?

RESPONSE

Departure from approved procedures

David Cannon, AA, AAS, BA, CPIA

The Public Health Service *Policy on Humane Care and Use of Laboratory Animals* (PHS *Policy*; section IV.C)[1] requires the IACUC of any institution where animal activities are carried out to assure that the approved research projects will be done in accordance with the Animal Welfare Act and Regulations (section 2.31)[2]. The PHS *Policy* also requires research proposals to be consistent with the *Guide for the Care and Use of Laboratory Animals* (the *Guide*)[3] unless a departure is justified and approved by the IACUC. The IACUC should also determine whether the research projects conform to the institution's Assurance and meet various requirements, such as methods of euthanasia.

New Antigen Inc. has violated its agreement with Great Eastern University by not following the protocol approved by the Great Eastern IACUC, which indicated that the entire study would be done at Great Eastern University; this certainly would include disposition of the animals at the end of the study. New Antigen employees transported mice and used an external procedure location without the approval of the Great Eastern IACUC. Changing the disposition of animals at the protocol's conclusion constitutes a deviation from the approved protocol, regardless of any protocol approved by the New Antigen IACUC.

To determine whether this deviation is reportable to NIH/OLAW, I consulted the reporting requirements for OLAW under the PHS *Policy* (section IV.F.3.)[1]. The *Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals* (NOT-OD-05-034)[4] includes both conduct of animal-related activities without appropriate IACUC review and approval and failure to adhere to IACUC-approved protocols as reportable situations. Therefore, I believe this deviation is reportable, although the situation is understandable and can be corrected. Because the deviation involved the Great Eastern University protocol, it is the responsibility of Great Eastern University's Institutional Official to report it to OLAW.

Preventing these types of communication errors related to the approved protocol between collaborating institutions can be challenging but it is certainly achievable. Both parties should understand and agree that the approved procedures outlined in the protocol

must be strictly followed. Any changes to the protocol must receive approval from the IACUC of the institution where the study is being done. A useful way to maintain the lines of communication is to have a representative of each institution serve as a member on the other institution's IACUC (although there may be confidentiality issues to resolve). Both parties should establish safeguards to keep the communication clear and remain compliant.

1. Public Health Services. *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 Regulations. 9 CFR, Chapter 1, Subchapter A, Part 2.
3. Institute of Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington, DC, 2011).
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 21 February 2013). <http://grants.nih.gov/grants/guide/notice-files/not-od-05-034.html>

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RESPONSE

Too many cooks in the kitchen

Debra Hickman, DVM, MS, DACLAM, Chris Konz, BS, LATG & Randy Peper, DVM, PhD

Both institutions have acted in good faith, but there is clearly confusion regarding the responsibility and authority of each institution in this scenario. They would do well to consider the following statement from the *Guide for the Care and Use of Laboratory Animals* (the *Guide*)[1]:

"Interinstitutional collaboration has the potential to create ambiguities about responsibility for animal care and use. In cases of such collaboration involving animal use (beyond animal transport), the participating institutions should have a formal written understanding (e.g., a contract, memorandum of understanding, or agreement) that addresses the responsibility for offsite animal care and use, animal ownership, and IACUC review and oversight. In addition, IACUCs from the institutions may choose to review protocols for the work being conducted."

In our opinion, this situation does constitute noncompliance. As outlined in the scenario, the New Antigen IACUC approved rats to be housed at Great Eastern until transported to New Antigen for euthanasia. There is also a protocol approved by the Great Eastern IACUC for New Antigen mice to be housed at Great Eastern and for all procedures to be conducted there, with no provision for transport to New Antigen for euthanasia. The fact that New Antigen's IACUC subsequently approved its own protocol allowing mice to be transported to New Antigen for euthanasia does not alter the Great Eastern protocol. Therefore, it appears that transporting and euthanizing mice at New Antigen was not in accordance with the Great Eastern–approved protocol.

The criteria established for reporting incidents of noncompliance in the Public Health Service *Policy on Humane Care and Use of Laboratory Animals* (PHS *Policy*)[2] include any serious or continuing noncompliance with the PHS *Policy*, any serious deviation from the provisions of the *Guide* and any suspension of an activity by the IACUC. OLAW has also released examples of items that are considered reportable[3], and this list includes conduct of animal-related activities without appropriate IACUC review and approval and failure to adhere to IACUC-approved protocols. Although the situation does not meet the criteria outlined by the PHS *Policy*, we feel the institutions should plan to report the incident to OLAW.

In our opinion, the responsibility to report lies with Great Eastern University as it was there that the noncompliant procedures (transport of animals) were initiated. However, if Great Eastern's Assurance with OLAW states that only incidents associated with NIH-funded research will be reported, then the university will need to determine whether these mice were used on an NIH-funded study. If Great Eastern University is accredited by the Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC), International, then it should report the incident to this organization also. Because the incident involved mice, there is no need to report to the USDA.

To prevent future occurrences of miscommunication and noncompliance, we recommend that Great Eastern University and New Antigen Inc. develop a formal written understanding that addresses their relationship, including protocol review.

1. Institute of Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington, DC, 2011).
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 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 21 February 2013). <http://grants.nih.gov/grants/guide/notice-files/not-od-05-034.html>

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RESPONSE

It's all about communication

Amanda Underwood, BS, CPIA, Doug Powell, DVM, ACLAM & Ray Stricklin, PhD

The *Guide for the Care and Use of Laboratory Animals* (the *Guide*)[1] is right on when it says "interinstitutional collaboration has the potential to create ambiguities about responsibility for animal care and use; and participating institutions should have a formal written understanding that addresses responsibilities." Such

A word from OLAW and APHIS

In response to the questions posed in this scenario, the Office of Laboratory Animal Welfare (OLAW) and the Animal and Plant Health Inspection Service (APHIS) offer the following clarification and guidance, with two caveats: (i) the OLAW response presumes that the studies are funded by the Public Health Service; (ii) the APHIS response would apply if the species in question was a USDA-regulated species; at present, the species in the scenario (Mus musculus bred for research) is not.

This column presents the reader with the following questions: Is the transportation and euthanasia of the mice a protocol violation? If so, is it reportable to NIH/OLAW, and which IACUC should make the report? How can future problems of this nature be prevented?

In the scenario, two activities, transportation of the animals and change in location of the euthanasia procedure, were not approved by the IACUC with jurisdiction over the mice, the university's IACUC. The biotechnology company's IACUC acted outside of its oversight authority; therefore, the actions taken by its employees constitute a noncompliance. This is reportable to OLAW as a significant change implemented without IACUC approval[1]. In this particular circumstance, assuming the biotechnology company is the primary grantee, it bears the responsibility for compliance. Its IACUC would be expected to report the incident through the Institutional Official and to develop and implement corrective actions to prevent a repeat occurrence. OLAW will accept noncompliance reports from either the primary grantee or the performance site, depending on the nature of the noncompliance and which site is best able to take corrective action.

There is no federal requirement for dual review and approval of research activities. Therefore, review by both IACUCs is not indicated[2]. However, having a written agreement that clearly defines oversight of transportation between facilities and IACUC review of amendments that affect both institutions would provide a satisfactory resolution and preventive strategy. Such an agreement would meet the recommendations in the *Guide for the Care and Use of Laboratory Animals* and the requirements of the NIH Grants Policy Statement on written agreements[3,4]. At a minimum, the agreement must also address ways in which the Public Health Service *Policy on Humane Care and Use of Laboratory Animals* requirement for review and approval of proposed animal activities and semiannual facilities review by an IACUC will be met[5].

For a regulated species, section 2.31(e) (3) of the Animal Welfare Act Regulations (AWARs) requires a complete description of the proposed use of an animal to be written in the animal protocol[6]. This includes transportation to another facility for euthanasia and tissue harvest. An amendment can be added to the Great Eastern protocol to indicate that euthanasia will be performed at New Antigen, and transportation can begin after the IACUC has approved the amendment. Conditions during transportation must be in accordance with AWAR requirements for the species being used. Record-keeping requirements must be in accordance with AWAR section 2.35 where applicable[6].

1. 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 21 February 2013). <http://grants.nih.gov/grants/guide/notice-files/not-od-05-034.html>
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals—Frequently Asked Questions.* Protocol Review, Question No. D.8. (US Department of Health and Human Services, Washington, DC, 2006, revised 2013). <http://grants.nih.gov/grants/olaw/faqs.htm#d8>
3. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. 15 (National Academies Press, Washington, DC, 2011).
4. US National Institutes of Health. NIH Grants Policy Statement; Part II Terms and Conditions of NIH Grant Awards, Subpart B: Terms and Conditions for Specific Types of Grants, Grantees, and Activities, 15.2.1 Written Agreement. (US National Institutes of Health, Bethesda, MD, 2012). <http://grants.nih.gov/grants/policy/nihgps_2012/nihgps_ch15.htm#>
5. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
6. Code of Federal Regulations, Title 9, Ch. 1, Part 2, Subpart C, §2.31(e)(3) and §2.35.

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agreements are essentially formal written communications. In this case, sufficient lines of communication were not in place between Great Eastern and New Antigen, resulting in confusion.

In our opinion, this violation is minor because New Antigen and Great Eastern had approved protocols. Although the situation was not universally communicated, it was approved. The removal of animals without permission is concerning, but none of the procedures conducted caused undue harm to the animals or occurred without IACUC oversight. This scenario does not address whether New Antigen's veterinary staff approved the import of animals or whether there was an existing relationship between New Antigen and Great Eastern that negated the need for health histories or quarantine regarding the movement of animals.

Great Eastern's IACUC approved the entire study to be completed at the school, including the euthanasia of the animals. Since Great Eastern's IACUC had not approved movement of the animals to New Antigen, the transportation and euthanasia of the mice at New Antigen, in the eyes of Great Eastern, would be a protocol violation and would require reporting to OLAW. Since Great Eastern had taken responsibility for housing New Antigen's animals, Great Eastern should report the violation to OLAW. However, it should be reported as a

minor infraction and should address failure in communication as the primary programmatic issue.

The *Guide*[1] and the Public Health Service *Policy on Humane Care and Use of Laboratory Animals*[2] both address the importance of a memorandum of understanding (MOU), and this point is clarified in response to a frequently asked question[3]: "Institutions should have a formal understanding (e.g., MOU) that addresses responsibilities for animal care and use, ownership, and IACUC review and oversight." New Antigen and Great Eastern failed to establish a formal relationship, in writing, addressing ownership, IACUC oversight and potentially intellectual property rights as they pertained to the animal model. We believe that any protocol in which animals would inhabit both campuses should be maintained, and approved, at both campuses. In this case, we recommend that the location of primary research provide the primary protocol approval but that both institutions maintain copies of the original protocol and all amendments. How this information is shared between institutions should be clearly defined and laid out for all endeavors. Going forward in Great Eastern's animal care and use program, the MOU should be the first priority when establishing a relationship with an entity exterior to the institution.

1. Institute of Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington, DC, 2011).
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. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals–Frequently Asked Questions.* Protocol Review, Question No. D.8. (US Department of Health and Human Services, Washington, DC, 2006, revised 2013).

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