Jerald Silverman, DVM, Column Coordinator

Using research animals as sentinels

Almost 20 years ago[1] and more recently in its Frequently Asked Questions[2], the NIH's Office of Laboratory Animal Welfare (NIH/OLAW) clarified that the use of sentinel animals in a laboratory animal disease recognition and prevention program should be covered by an IACUC-approved protocol. The Great Eastern University IACUC had always assumed that the school's IACUC-approved sentinel animal protocol met the intent of NIH/OLAW for helping to assure the well-being of animals and compliance with federal regulations. Furthermore, over the years, through many vivarium accreditation site visits and inspections by the veterinary medical officers of the USDA, no comments were ever made about Great Eastern's sentinel animal protocol.

Dr. Rhett Parks' guinea pigs arrived on a Monday, and after a few days of acclimatization to the vivarium, the assigned veterinary technician collected fresh feces and swabs of cells from the mucosal surface of the animals' cheeks. The samples were to be used to test for the presence of pathogen DNA by the polymerase chain reaction (PCR) method. The Great Eastern sentinel animal protocol specified that colony animals would be used for this testing because of the simplicity of the collection procedures and the greater likelihood of detecting pathogens from pooled samples taken directly from colony animals.

At the semiannual program review, the sentinel animal program was discussed, and one of the participants asked a simple question: if samples for PCR analysis are taken directly from a researcher's animal rather than from a sentinel animal, and if the animal must be handled in order to obtain the sample, should this activity be approved on the researcher's protocol or on the sentinel animal protocol? A simple question, perhaps, but is the answer simple? What is your opinion?

1. Potkay, S., Garnett, N.L., Miller, J.G., Pond, C.L. & Doyle, D.J. Frequently Asked Questions about the Public Health Service Policy on Humane Care and Use of Laboratory Animals. *Lab Anim. (NY)* **24**, 24–26 (1995).
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals—Frequently Asked Questions*. Protocol Review, Question No. D.16. (US Department of Health and Human Services, Washington, DC, 2006, revised 2013).

RESPONSE

Consider the purpose

Sridhar Samineni, DVM, MS, PhD, DACLAM & Richard W. Ermel, DVM, MPVM, PhD, DACLAM

Quarantine, animal biosecurity and disease surveillance are critical components of a comprehensive veterinary care program to detect and prevent the introduction of pathogens into animal research facilities, thereby enhancing the quality of research animals and minimizing the potential of confounding experimental variables. As part of the IACUC-approved sentinel animal protocol (animal health surveillance program), Great Eastern University's veterinary care staff collects feces and swab samples directly from research animals for diagnostic testing. However, a semiannual program review raised the question of whether these sample collection procedures should be listed and approved on the research protocol or on the sentinel animal protocol. To address this question, one should consider the purpose of the sample collection and the personnel who carry it out.

Both the Animal Welfare Act (AWA)[1] and the *Guide for the Care and Use of Laboratory Animals* (the *Guide*)[2] indicate that the attending veterinarian has responsibility for the health and well-being of all laboratory animals used at the institution and authority to ensure the provision of an appropriate veterinary care program. Specifically, the *Guide*[2] states that an adequate veterinary care program is an essential part of an institutional animal care and use program, which includes assessment of animal well-being and effective management of a preventive medicine program. Preventive medicine programs should consist of various combinations of policies, procedures and equipment related to quarantine, animal biosecurity and animal health surveillance. Similarly, for species covered by the AWA[1], adequate veterinary care must be provided and should include the use of appropriate methods to prevent, control, diagnose and treat diseases and injuries. Based on guidance from both the *Guide*[2] and the AWA[1], diagnostic sample collection activities on research animals for routine animal health surveillance and preventive medicine programs can be considered part of an adequate and comprehensive veterinary care program.

In addition, Great Eastern University veterinary technicians have the appropriate training and expertise to carry out the proposed activities (handling the research animals and collecting samples for the animal health surveillance program). Furthermore, these activities are not related to the research protocol, collected samples are not used in the research study, and animals are not handled by research staff for these procedures. Moreover, previous semiannual inspections and other regulatory authorities felt that the listing of these procedures in the IACUC-approved sentinel animal protocol was appropriate and justified. Therefore, Great Eastern University routine veterinary care

and preventive medicine practices should be listed in the veterinary care standard operating procedures or in the IACUC-approved sentinel animal protocol. In this regard, Great Eastern University is in compliance with the AWA and the *Guide* and is not mandated to list and approve such activities on a researcher protocol.

1. Animal Welfare Act and Regulations. Section 2.40, b, 2.
2. Institute of Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. 105–132 (National Academies Press, Washington, DC, 2011).

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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 guidance:

Though well intentioned, Great Eastern University's IACUC has incorrectly assumed that only a protocol is acceptable to OLAW to meet the oversight requirement described in the OLAW Frequently Asked Question (FAQ)[1]. The FAQ cited does not preclude the use of a standard operating procedure (SOP). Concerning animals used as sentinels, breeding stock, etc., the FAQ states "…the IACUC should review protocols and SOPs that involve animals for such purposes"[1]. The use of a sentinel protocol, a research protocol or an SOP is an institutional decision. It may be based on whether there is ongoing sentinel activity covering many different studies with the species. If only one study requires the species, then including the sentinel activity on the research protocol is an option with the principal investigator's concurrence. A third option is to describe the sentinel activity in an SOP reviewed and approved by the IACUC. Including research animals in the SOP should again have the investigator's concurrence. OLAW and USDA suggest that an institution inform investigators that their study animals may be used in this manner and provide a mechanism for them to decline participation with scientific justification.

The Animal Welfare Act Regulations (AWARs) §2.31 (d)(1) outlines the duties of the IACUC in regards to the review and approval of proposed and ongoing activities involving animals[2]. Under §2.31(e) of the AWARs, a proposal to make a significant change to an ongoing activity must contain the following information: (i) the identification of the species and the numbers of animals used; (ii) a rationale for involving animals and for the appropriateness and numbers of animals used; (iii) a complete description of the proposed use of the animals; (iv) a description of the methods used to assure that pain and distress will be limited to that which is unavoidable, along with the provisions for anesthetics, analgesics and tranquilizing agents where appropriate; and (v) a description of euthanasia methods[2].

In light of the AWARs, an amendment to the current sentinel monitoring protocol to incorporate the use of study animals or an amendment to the research protocol to reflect the sentinel use would be acceptable. Facilities may utilize an SOP instead of an IACUC-approved protocol for the sentinel monitoring program. Although the AWARs do not specifically address SOPs, USDA acknowledges their role in animal care and use programs and therefore deems the use of an SOP acceptable in this instance.

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals—Frequently Asked Questions.* Protocol Review, Question No. D.16. (US Department of Health and Human Services, Washington, DC, 2006, revised 2013).
2. Code of Federal Regulations. Title 9, Ch. 1, Part 2, Subpart C.

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RESPONSE

Approval required, methods may vary

Stephen J. Durkee, BS &
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Assessing the health status of animals is certainly part of the veterinary program. Many institutions use standard operating procedures to describe the procedures done by the veterinary staff during quarantine. The veterinary staff often carries out diagnostic work that may include monitoring and sample collection to ensure or to confirm the health status of new animals arriving at the facility. Veterinary diagnostic procedures do not typically require coverage under an IACUC-approved protocol, although the IACUC reviews the veterinary program, including these procedures, as part of the semiannual review.

In this case, the guinea pigs are being used as part of the sentinel program, rather than as part of quarantine procedures. The protocol covering the sentinel program should include a description of the veterinary technicians and other personnel who handle animals for this purpose. This protocol should include guinea pigs, along with any other species routinely monitored in the program. If guinea pigs are not included, the sentinel protocol should be amended to include the species, procedure descriptions and justification for the number of animals used in the guinea pig surveillance program. IACUC-approved procedures are protocol-specific and species-specific. Because samples are taken from live animals, which requires handling the animals, these procedures must be included in an IACUC-approved protocol. We see two options in this case: (i) the guinea pigs should be transferred to the already established institutional sentinel protocol for sample collection or (ii) the researcher's protocol should be amended to include the surveillance procedures, in a manner consistent with the institutional IACUC requirements.

The fact that site visitors and inspectors had never made comments about this topic in the past does not mean the institution handled it appropriately. It is unfortunate that it was not identified during the *de novo* review of the sentinel protocol. It sounds as

though this issue had gone undiscovered for quite some time. It is possible that the program did not include guinea pigs when the protocol was first approved and the protocol was not updated when guinea pigs were added to the program. It is also possible that guinea pigs were not present in the facility during the site visits. After all, Great Eastern did have a sentinel program in place with a sentinel protocol. The missing piece was the exclusion of this specific species because it was present as a non-colony animal. Accolades are due to the committee member who questioned this during the semiannual review.

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RESPONSE

Foster a team mentality

Maureen McCarthy, BS &
Karolynn B. Niven, LATg

This does seem to be a relatively simple question. Any manipulation of an animal, regardless of how simple it may be, must be covered under an animal use protocol[1]. Personnel carrying out such manipulations must also be listed on the same protocol. For the animals described in this scenario, both the research and the sentinel testing involve manipulations. Why complicate matters by having two, separate protocols for these animals?

This is an opportunity to foster a team mentality between research personnel and animal care personnel. The sentinel program is key to ensuring not only the health of the animals being tested but the health of all animals within a facility. Parks, the researcher in this scenario, no doubt realizes this, as do the animal care staff and presumably the IACUC. The least complicated path to ensuring that the animals are protected and the paperwork is in order would be to include on Parks' protocol those members of the animal care program who carry out the sentinel testing, as well as the veterinarian who heads the sentinel program. The sentinel sample collection procedures would also need to be included on Parks' protocol.

It seems that Parks has an existing protocol. We suggest that he should compose an amendment to this protocol stating that routine procedures for sentinel testing are being added, listing the swabbing and fecal collection and specifying animal care personnel who will carry out only these procedures, if that is what Parks is comfortable with. (A well-trained animal care person could be beneficial to other functions of the research too.) Research personnel can then be assigned to any and all techniques related to Parks' research[2]. Ideally, the research staff and the animal care staff should meet to familiarize everyone with the full scope of the protocol. In our experience, this type of meeting takes place far too infrequently, leading to questions from animal care staff about the science and questions from research personnel about animal care. This is where team-building can start. Including animal healthcare–related techniques and personnel on a research protocol is a perfect opportunity to marry up both groups into a successful research program.

It should be pointed out that this scenario does not involve multiple research-related procedures, circumstances under which concern for overuse or undue stress of a single animal comes into play[3]. This scenario addresses standard health screenings of a guinea pig colony being done on the colony individuals themselves instead of on additional animals used only for health testing. Apparently, at Great Eastern, this is the routine approach; we believe it to be commendable in that it reflects application of the principles of the 3Rs. If this is the routine approach, we believe that Parks and other researchers at Great Eastern would have presented this sentinel program structure to granting entities, thereby alleviating concern for research animals being used in non-programmatic or additional testing. In this situation, combining healthcare and research into a single protocol is absolutely a win-win situation for all persons and animals involved.

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals—Frequently Asked Questions*. Protocol Review, Question No. D.16. (US Department of Health and Human Services, Washington, DC, 2006, revised 2013).
2. Silverman, J. *et al.* One animal, two protocols – an appropriate application of the 3Rs? *Lab Anim. (NY)* **36**, 13–15 (2007).
3. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* Section IV.D.1 (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).

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