

physical impairment. Both surgeries qualify as major operative procedures as defined by the AWRs¹. It is relevant that ovariectomy is being performed for the purpose of experimentation and not for routine veterinary care.

It is laudable that Benoit and Harding are considering the principles of the 3Rs and, more specifically, an approach that would ultimately reduce the animal numbers used by both projects. It appears, however, that Benoit's initial intent may be to reduce the overall cost of her research. The *Guide* explicitly precludes cost savings as a justification for multiple major survival surgeries and, in concert with the AWRs, requires that the surgical procedures be "essential components of a single research project or protocol"³. The key issue in the current scenario is that Benoit's and Harding's protocols are separate and unrelated.

If Benoit and Harding could combine their investigative efforts into one research project and protocol, the multiple surgeries involved may be justifiable. In that case, the IACUC could approve an exemption for multiple major survival procedures on the single protocol, whereas the IO would need to submit a request to the USDA/APHIS and receive approval to allow a regulated animal to undergo multiple major survival surgical procedures in separate unrelated research protocols². The regulations were designed to promote the well-being of research animals and prevent unnecessary pain and distress associated with multiple survival surgeries. However, this particular situation warrants special consideration in order to promote both animal welfare and the 3Rs principle of reduction. Researchers may find creative ways to work together to promote the 3Rs. That said, Benoit's amendment in its present form should not be approved by the IACUC given the current regulations and recommendations.

1. Animal Welfare Act Regulations. Code of Federal Regulations. Title 9, Chapter 1.
2. United States Department of Agriculture. Policy #14: Major Survival Surgery Dealers Selling Surgically-Altered Animals to Research. in Animal Care Policy Manual (USDA, Beltsville, MD, 2011).
3. 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

Collaborate to reduce

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The principles of the 3Rs in research form a fundamentally important and guiding concept for the IACUC. The proposed amendment to re-use Harding's ovariectomized rabbits in Benoit's research appears to fulfill the spirit of the 3Rs by reducing animal numbers. But the impact on the individual animals subjected to multiple studies, each involving major survival surgery, must be considered, as well as how the regulations pertain to utilizing the same animal on two different research protocols.

First, each of the proposed procedures, ovariectomy and induced bone fracture, satisfy the USDA definition of major surgery as each procedure "penetrates and exposes a body cavity, produces substantial impairment of physical or physiologic functions, or involves extensive tissue dissection or transection"¹.

Second, although Benoit's protocol has been reviewed and her scientific justification for requiring multiple survival surgeries has been accepted, use of animals from a previous, separate protocol was not included. The *Guide for the Care and Use of Laboratory Animals* states that "cost savings alone are not an adequate justification for performing multiple major survival surgical procedures."¹ Furthermore, USDA Policy 14 (ref. 2) states that in USDA-regulated species, "a major survival operative procedure must not be performed a second time on an animal in a separate proposal. In order to comply with the intent of the Animal Welfare Act (AWA), animals surviving a major operative procedure must be identified (written documentation) to prevent their use in a second major survival operative procedure." It is clear from this policy that using the same animals for subsequent unrelated proposals, which will require them to undergo additional major survival surgery or surgeries, is strongly discouraged.

The ARENA/OLAW *Institutional Animal Care and Use Committee Guidebook* states that exceptions to the single major survival surgery policy may be made if there is "scientific justification (e.g., related components of the same study) provided by the principal investigator in writing... or under other special circumstances which have been approved by the Administrator of APHIS"³. In this case, the two major survival procedures to be performed on the same animal are unrelated components of two different proposals; therefore, the IACUC and the Administrator of APHIS would have to approve this exception. If this exception were approved by the IACUC and the APHIS Administrator, then the exemption would require annual IACUC evaluation and inclusion in the annual report (APHIS form 7023)⁴.

The scientists and the IACUC must consider the potential effects of the administration of estrogen or other drugs and hormones to ovariectomized rabbits on the second study proposed by Benoit. Although Benoit's argument that she is working to reduce animal numbers has merit, the scientific validity of reusing these rabbits has not been fully explored. I feel that in this case, utilizing Harding's previously ovariectomized rabbits for Benoit's research protocol as it has been submitted in Benoit's amendment should not be approved by the IACUC. Instead, it would seem reasonable for Harding and Benoit to collaborate on a single research proposal that would satisfy both their research objectives, reduce the number of rabbits required to meet their scientific goals and remain compliant with all applicable regulations and policies.

1. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington, DC, 2011).
2. United States Department of Agriculture. Policy #14: Major Survival Surgery Dealers Selling Surgically-Altered Animals to Research. in Animal Care Policy Manual (USDA, Beltsville, MD, 2011).
3. ARENA/OLAW. *Institutional Animal Care and Use Committee Guidebook* 2nd edn. 146 (OLAW, Bethesda, MD, 2002).
4. Silverman, J., Suckow, M.A. & Murthy, S. *The IACUC Handbook* 2nd edn. (CRC Press, Boca Raton, FL, 2007).

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