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## Multiple survival surgeries; multiple studies

There are times when applying the principles of the 3Rs (reduce, refine and replace) can lead to challenging problems for an IACUC. Drs. Sly Harding and Joan Benoit were both endocrinologists at Great Eastern University. Both carried out ovariectomies on rabbits as part of their research. Harding studied the impact of estrogen on certain behaviors, which were not considered by the IACUC to cause any pain or distress to the animals. Benoit studied the effects of various hormones, including estrogen, on the healing of induced bone fractures. The IACUC had always considered that Benoit's work consisted of two major operative procedures on the same animal and that appropriate

scientific justification to do this had been provided by Benoit.

During a lunchtime conversation, Harding and Benoit realized that the ovariectomized rabbits that were used in Harding's research could subsequently be used in Benoit's research after Harding's study ended. This would negate the need for Benoit to purchase and ovariectomize rabbits before inducing bone fractures. Benoit submitted a protocol amendment to the IACUC in which she explained that using Harding's rabbits in her studies would reduce the total number of rabbits purchased yet would still expose a single rabbit to the same number of major operative procedures that had been justified and approved in her

protocol. She considered this a win-win situation for herself and for the IACUC. Nevertheless, the IACUC had a difficult time deciding how to approach this request. There were two unrelated protocols, both of which required ovariectomized rabbits. Approving Benoit's amendment would obviously result in fewer animals being purchased, but Benoit was more interested in saving money than animals. Furthermore, although the scientific justification for multiple survival operative procedures was already approved for Benoit's protocol, use of animals from an unrelated protocol was not approved.

Do you think the IACUC should approve Benoit's amendment? Is approval from the USDA Animal Care division required?

### RESPONSE

#### Approve the amendment

Larry Carbone, DVM, PhD, DACLAM

Surgical ovariectomy penetrates the abdominal cavity and is a major operative procedure. Inducing bone fractures creates a physiological impairment, which may be permanent if healing fails, and is likewise a major operative procedure. The Great Eastern IACUC has already determined that Benoit must do both procedures on rabbit subjects to accomplish her studies. Harding and Benoit's studies are not parts of the same research protocol; will the IACUC approve individual rabbits to serve on both studies and undergo two major survival surgeries?

Yes, the IACUC should approve this modification. It may not require USDA/Animal Care approval, but it would be wise to seek the USDA's opinion.

The general prohibition against multiple major survival surgeries or operative procedures on individual animals dates back to the 1978 edition of the *Guide for the Care and Use of Laboratory Animals*<sup>1</sup> (the *Guide*)

and the 1991 Animal Welfare Regulations (AWRs)<sup>2</sup>. The prohibition is not absolute: the AWRs<sup>3</sup> and the *Guide*<sup>4</sup> agree that such multiple procedures on a single animal may be approved but must be part of a single study and cannot be justified by cost savings.

The gravity of this near-total prohibition is reflected in the facts that cost savings is explicitly disallowed as justification in the *Guide* only in the case of multiple major survival surgeries and that separate USDA approval is required beyond in-house IACUC approval in special circumstances where an investigator proposes to perform multiple major survival procedures on unrelated projects.

Neither the AWRs nor the *Guide* typically explain the ethical underpinnings of their rules and guidance; on this issue, however, they clearly favor a rights-based respect for fair treatment of the individual animal over a utilitarian calculus of the greatest good (or least harm) to the greatest number. Even if performing multiple major surgeries on some individuals has a lesser overall impact than dividing the procedures among a greater number of animals, the rights of the individual rabbit set limits. The ethical

principle involved is that it is an unfair violation to place the excessive burden on certain individuals.

The Harding-Benoit proposal will save animal and staffing costs; that is appropriate but not enough to justify approval. Had this been presented from the start as a single project on the behavioral and physiological effects of estrogen, in which intact and ovariectomized rabbits are first characterized behaviorally and then evaluated for bone healing, the IACUC would have approved it and never thought of contacting the USDA.

In this case, rabbit numbers (and costs) are lower in approving the rabbit-sharing proposal. No individual rabbit is subjected to greater potential pain or distress, and the IACUC should approve the amendment. But each case requires evaluation. Suppose Harding's project required removing the ovaries in two separate surgeries, whereas Benoit only cares that by the time of the fracture, both ovaries have been removed. Combining their work might mean that the rabbits would undergo two abdominal and one orthopedic surgery. In this case, individual rabbits' welfare costs are increased beyond that required for the science. The