

- 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

Gotcha!

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Following the letter of the law and considering the information provided in this scenario, Great Eastern should not appeal the citation and should further train their PIs and IACUC members to avoid future citations. Common sense plays very little role when it comes to legal matters and the current verbiage of AWA regulations makes no exceptions for terminal procedures (§2.31,d, ii; ref.1). Further, clarification on the requirements regarding a search for alternatives to painful procedures are provided in the Animal Care Policy Manual². As with the AWA regulations, no exceptions are mentioned for terminal procedures.

I can understand the IACUC chair's logic regarding the level of pain in this case. Assuming the animal(s) were under deep anesthesia, there would be no conscious perception of pain, only a physiologic response at best. Furthermore, postoperative pain and/or morbidity are completely out of the picture. Perhaps the best argument—other than legal—for providing evidence of this search is in the rare case where anesthetic depth might not be as deep as was intended. While there is no published data suggesting how often inadequate anesthesia is a problem for animals, a small amount of human data is available. In humans, the incidence of intra-operative awareness is approximately 0.13% in the United States with similar rates in other countries³.

A PI can easily search for alternative procedures and with that information potentially make an argument for their chosen method/approach should they need further justification. Perhaps more importantly, a good faith effort to search for alternatives should be performed in deference to the animal's well-being.

1. Animal Welfare Act Regulations, 9 CFR, Chapter I, Part 2, Subpart C.

- United States Department of Agriculture, Animal and Plant Health Inspection Service. *Animal Care Policy Manual.* Policy #12.
- Sebel, P. et al. The incidence of awareness during anesthesia: a multicenter United States study. *Anesth. Analg.* **99**, 833–839 (2004).

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RESPONSE

The spirit of the law

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Much to his chagrin, IACUC Director Bailey believed that Dr. Mann was “reading between the lines” in issuing her citation. After all, this was a terminal procedure during which the animal was euthanized while under anesthesia and there was no expectation of pain or distress. While a literal reading of the Animal Welfare Regulations (AWR) seems to support Bailey's position, what is missed is the “spirit” of the law and regulations, namely the “perceived intent” that potentially painful or distressful procedures be refined or replaced whenever possible¹.

There is often an assumption that non-survival procedures do not have the same requirements, including the literature search for alternative methods, as survival procedures. However, a careful reading of the law, regulations and guidance documents prove this assumption false. The Animal Welfare Act requires the “principal investigator to consider alternatives to any procedure likely to produce pain or distress in an experimental animal” and the research facility to assure that said alternatives were considered (§2143; ref. 2). The AWR define a painful procedure as one which would “reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied” (§1.1; ref. 2). In this regard, the definition makes no distinction between survival and non-survival procedures. Furthermore, the AWR specifically address the search for alternatives to painful procedures and do not distinguish between survival or terminal procedures (§2.31,d,1,ii; ref. 2). Reading on in this section, only

subsection (ix) seemingly lessens the requirements for non-survival surgery, and even then, only the conditions under which such procedures can be performed.

To further clarify the basis for Mann's citation, guidance can be found in the USDA Animal Care Policies and Animal Care Inspection Guide. Animal Care Policy states that surgery, both survival and terminal, are considered to be painful procedures and holds the IACUC responsible for assuring that the principal investigator has considered alternative methods³. It further stipulates that a database search is the recognized method for assuring compliance with the requirement for consideration of alternatives⁴. Additionally, Chapter 7 of the Inspection Guide details the expectations of the IACUC in its review of animal use protocols⁵. This section lists surgery, both survival and terminal as a painful or distressful procedure and states that protocols with such procedures must consider “refinement alternatives that may further minimize or avoid pain and/or distress.”

The Animal Care Policy Manual and the Animal Care Inspection Guide are publicly available. To understand the “spirit of the law,” IACUC professionals and attending veterinarians should be familiar with the specifics of these two documents. We do not believe that Great Eastern University has a basis for appealing this citation. The IACUC should clarify to researchers that a literature search is required for both survival and non-survival painful or distressful procedures following the guidelines provided in Animal Care Policy⁴.

- Garcia, S.M., Chen, P., Gordon, M.T. The letter versus the spirit of the law: a lay perspective on culpability. *Judgement and Decision Making* **9**, 479–490 (2014).
- U.S. Department of Agriculture. *Animal Welfare Act Regulations* (2013).
- United States Department of Agriculture, Animal and Plant Health Inspection Service. *Animal Care Policy Manual.* Policy #11.
- United States Department of Agriculture, Animal and Plant Health Inspection Service. *Animal Care Policy Manual.* Policy #12.
- United States Department of Agriculture. *Animal Welfare Inspection Guide* (US Department of Agriculture, Riverdale, MD, 2015).

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