

recommend that he consider carrying out a pilot study to allow him to evaluate the feasibility of this newer approach.

If Clark agrees to consider the veterinarian's suggestion to include a laparoscopic approach for the cholecystectomy, the institution and researcher should work together to implement this new technique and the institution should provide training to Clark's group.

1. Russell, W.M.S. & Burch, R.L. *The Principles of Humane Experimental Technique* (Methuen, London, 1959).
2. Tannenbaum, J. & Bennett, B.T. Russell and Burch's 3Rs then and now: the need for clarity in definition and purpose. *J. Am. Assoc. Lab. Anim. Sci.* **54**, 120–132 (2015).
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5. Animal Welfare Act regulations. 9 CFR. Chapter I, Subchapter A, Part 2, Subpart C.
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RESPONSE

A necessary consideration

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Assuming that the laboratory animal veterinarian's questions were diplomatic, Clark's reaction was unjustified. The veterinarian was acting as a representative of the IACUC, which has the duty to oversee and evaluate all aspects of the animal care and use program, including application of the '3Rs' for humane animal research¹. A laparoscopic cholecystectomy, which produces only one or two small incisions rather than one large incision, is a prime example of a technical refinement that can reduce the invasiveness of the surgical approach, thereby decreasing postoperative pain and recovery time for the patient. In a study of human patients with acute cholecystitis,

those that received laparoscopic cholecystectomies had shorter surgical times and hospital stays, as well as fewer postoperative complications, than those that received open cholecystectomies².

We expect that Clark did not adequately address the regulatory requirement to consider alternatives. During pre-review the veterinarian appropriately raised this issue of a potentially beneficial alternative, but the IACUC must ensure that there was a "reasonable and good faith effort... to determine the availability of alternatives" and to justify why this alternative was not used³. Great Eastern University might have procedures in place to address unresolved concerns that arise in the pre-review process; if not, the protocol should be called for a full committee review.

Clark's years of experience, surgical survival rate and publication record are not adequate reasons for refusing to consider alternatives that could refine his procedures. Clark may have perfected the open abdomen technique, but it remains unknown whether the monkeys in his studies experience fewer postoperative complications than they would with a laparoscopic approach. His reluctance is most likely due to a lack of familiarity and skill with the suggested technique. However, it is ultimately the responsibility of the institution, in conjunction with the IACUC and attending veterinarian, to ensure that research personnel are appropriately qualified and trained in the procedures used at that institution. This might require a consultant to be involved in pre-surgical planning and training^{4,5}. Although a laparoscopic cholecystectomy might be more technically demanding than the open approach, with training the technique might have substantial advantages over open cholecystectomy.

Clark doubts whether the refined approach will lead to better research. To examine potential benefits of the laparoscopic technique, the institution should support a pilot study to compare postoperative pain scores, time to recovery and histopathology results for the two surgical approaches. Additionally, the IACUC can ask to review past postoperative records to verify the well-being of Clark's monkeys, or seek consultation from surgeons who have utilized both techniques.

Positive relationships built on open dialogue between the IACUC and principal investigators allow for better science and research. If concerns arise, intolerance and aversion to change create unwanted tension between parties. Working with animals is a privilege not a right, therefore a deep respect for animal welfare is paramount to the future success of our field.

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RESPONSE

A mutual understanding can promote progress

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Refinement of the cholecystectomy technique in Dr. Clark's laboratory is appropriate, but the approach of the veterinarian and IACUC also needs refinement. Inquiries from the IACUC or veterinarians can often be received and permanently viewed as directives, regardless of assurances to the contrary. Initial misunderstandings greatly affect the success of efforts to implement the 3Rs.

From the IACUC's perspective this refinement is a simple matter of amending Clark's protocol, training his staff and purchasing new equipment. On the other hand, from the perspective of the principal investigator (PI), there are considerable costs associated with this refinement.