



March 31, 2015

Dear Investigator,

MSU's IACUC would like to clarify expectations about the section of animal protocols dealing with database searches and identifying alternatives (i.e., General Section, Question 3e). Some PIs do not provide explanations when they have answered 'No' on finding alternatives to their proposed procedures that would allow reduction, replacement, or refinement. However, protocols that do provide information under 'Explain' better address the concerns of the IACUC and thereby reduce the need for revisions by the PIs. The IACUC is, therefore, now asking that all PIs provide these explanations in their new protocols.

The following excerpt from the National Research Council of the National Academies Guide for the Care and Use of Laboratory Animals, 8th edition, explains the Three Rs: reduction, replacement, and refinement.

"The Three Rs represent a practical method for implementation of animal care and use principles. In 1959, W. M. S. Russell and R. L. Burch published a practical strategy of replacement, refinement, and reduction—referred to as the Three Rs—for researchers to apply when considering experimental design in laboratory animal research (Russell and Burch 1959). Over the years, the Three Rs have become an internationally accepted approach for researchers to apply when deciding to use animals in research and in designing humane animal research studies.

- Reduction involves strategies for obtaining comparable levels of information from the use of fewer animals or for maximizing the information obtained from a given number of animals (without increasing pain or distress) so that in the long run fewer animals are needed to acquire the same scientific information. This approach relies on an analysis of experimental design, applications of newer technologies, the use of appropriate statistical methods, and control of environmentally related variability in animal housing and study areas.
- Replacement refers to methods that avoid using animals. The term includes absolute replacements (i.e., replacing animals with inanimate systems such as computer programs) as well as relative replacements (i.e., replacing animals such as vertebrates with animals that are lower on the phylogenetic scale).
- Refinement refers to modifications of husbandry or experimental procedures to enhance animal well-being and minimize or eliminate pain and distress. Whereas institutions and investigators should take all reasonable measures to eliminate pain and distress through refinement, IACUCs should understand that with some types of studies there may be either unforeseen or intended experimental outcomes that produce pain.

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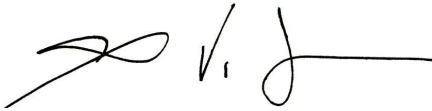
These outcomes may or may not be eliminated based on the goals of the study.”

Addressing refinement in the database search and alternatives section of the protocol is especially important because it gives the PI an opportunity to explain, based on the literature, why the proposed techniques are the best for accomplishing study objectives while also minimizing pain and distress. Although replacement is rarely possible because of the species-specific nature of our research and the efficacy of our model species, it should be considered when examining general questions, such as ecological principles, that apply across taxa. Reduction is usually addressed explicitly in the “Justification of Animal Numbers” section of the protocol, but including an explanation of search findings in the general section ensures that the relevant literature has been considered.

For additional information, please view the webinar on the OLAW Educational Resources website entitled “Meeting Requirements for Alternatives Searches” (http://grants.nih.gov/grants/olaw/educational_resources.htm).

Thanks very much for complying with this request. It should help make the IACUC protocol process more efficient for all of us.

Sincerely,

A handwritten signature in black ink, appearing to read 'Alexander V. Zale', with a stylized flourish at the end.

Alexander V. Zale
IACUC Chair

Russell, W. M. S., and R. L. Burch. 1959. The principles of humane experimental technique. Methuen, London.