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EDITORIAL

The Three Rs and Biomedical Research

In 1959, British scientists William M. S. Russell and Rex L. Burch wrote that scientific excellence and humane use of laboratory animals are inextricably linked. In *The Principles of Humane Experimental Technique*,* they described the "three Rs"—reduction, refinement, and replacement—of animal use in the life sciences, concepts now known as "alternatives." Legislation mandating the incorporation of the three Rs into animal research and testing has been passed in the United States and Europe. Because some scientists view discussion of alternatives as driven exclusively by political and social forces rather than by scientific considerations, an international group of scientists prominent in the alternatives field met at a May 1995 workshop to reaffirm the scientific basis of the three Rs and to discuss how these concepts can best be disseminated to the scientific community.†

Published surveys of the scientific literature have found inefficient use of animals due to poor experimental design or inappropriate statistical analysis of results or both. Reduction alternatives allow comparable amounts of data to be obtained from fewer animals or more information to be obtained from a given number of animals. The number of animals used should be the minimum necessary to test the experimental hypothesis and give statistically usable results.

Refinement alternatives are methods that eliminate or minimize pain and distress or enhance animal well-being. Assessments of animal pain and distress are currently based on subjective evaluation of abnormal behavior and appearance. Because proper evaluation of pain relies largely on the ability to understand the behavior and needs of each species of laboratory animal, it is best for investigators to assume that a procedure that inflicts pain and distress on humans will inflict pain and distress on animals. Much pain and distress can be diminished or eliminated with the proper use of anesthetics and analgesics. Researchers can enhance animals' well-being by using environmental enrichment techniques, such as proper handling, appropriately sized cages, and group housing of social species.

Replacement alternatives are methods that use organisms with limited sentience or that do not use whole animals. They include improved information exchange to avoid unnecessary repetition of animal experiments; physicochemical techniques and structure-activity relations; mathematical and computer models; use of invertebrates, plants, and microorganisms; in vitro methods; and human studies, including the use of human volunteers, postmarketing surveys, and epidemiology. In the biomedical sciences, in vitro methods are increasingly being used, not because they provide precisely the same information as do animal studies but because they offer the best scientific approach. Such methods often use results from past animal studies as a basis for cellular and molecular investigations.

Successful implementation of the three Rs requires that scientists and technicians be formally trained to scientifically and ethically evaluate the use of laboratory animals and to perform animal experiments that meet the highest scientific and animal welfare standards. Coursework should be included in graduate training programs and should focus on strengthening the principles of experimental design and teaching competence in animal handling, how to make ethical decisions about using animals in experiments, and how to find alternative methods. As the participants at the workshop concluded, present and future scientists should be encouraged to view the three Rs as an intellectual challenge and an opportunity to enhance the scientific, economic, and ethical value of their research.

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*W. M. S. Russell and R. L. Burch, *The Principles of Humane Experimental Technique* (Methuen, London, 1959; reprinted by Universities Federation for Animal Welfare, Potters Bar, UK, 1992). †This workshop was sponsored by the European Centre for the Validation of Alternative Methods (ECVAM) and CAAT. ECVAM was established by the European Commission in 1991 to promote the scientific and regulatory acceptance of alternative methods. CAAT was founded in 1981 to foster the development of scientifically acceptable in vitro and other alternatives for use in the development and safety evaluation of commercial and therapeutic products. Proceedings of the workshop were recently published [M. Balls *et al.*, *Altern. Lab. Anim.* **23**, 838 (1995)].