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Best Two Out of Three?

Let's face it—replacement is the most alluring of Russell and Burch's three Rs. Unfortunately, it also seems to be the least attainable. Indeed, since 1958 when Russell and Burch laid down the framework for the now legally mandated search for alternatives, just a few non-animal alternative tests have been developed and approved.

Is this because not enough people are looking for non-animal alternatives? Because there's not enough funding to inspire the search? Or is it because it's just not feasible, in most cases, to extract the same information from a petri dish full of cells or a computer simulation as one could obtain from a whole animal? The answer is certainly debatable—and certainly oft debated—but one thing's for sure: the other two—albeit less sexy—Rs are being attained all around us and may ultimately do more to improve laboratory animal welfare than the simple pursuit of replacement alternatives. The pages of this issue contain four current examples of reduction and refinement alternatives at work.

When it comes to reducing the number of animals used in research, the importance of proper experimental design cannot be underestimated. While the use of too many animals in a particular experiment cannot be justified, the use of too few animals may fail to produce statistically significant results. Authors van Wilgenburg, van Schaick Zillesen, and Krulichova (p. 39) describe two computer programs that are meant to guide researchers-in-training on how to properly design an experiment, including how to determine the optimal number of animals. These programs—ExpDesign and Sample Power—are available free-of-charge from the authors.

Another group has applied the principles of reduction to toxicity testing. International Organization for Standardization (ISO) guidelines demand that all medical devices undergo testing for cytotoxicity, sensitization, and irritation. The standard test for irritation has traditionally involved injecting three rabbits with a test solution to determine whether chemicals released from device materials may produce skin irritation, as characterized by redness and swelling. Authors Upman, Anderson, and Tasse (p. 26) took a retrospective look at the results of a random sample of 100 dermal toxicity tests and determined that in the vast majority of cases, the same results will be obtained with two rabbits as with three.

The concept of refinement is nicely exemplified by the ongoing efforts of the research community to employ environmental enrichment systems to encourage animals' natural behaviors. While the Animal Welfare Act mandates that nonhuman primates be provided with environmental enrichment devices, relatively little is known about what characteristics make for good choices. After all, what good are such devices if the animals don't use them or if they actually contribute to an increase in negative behaviors, such as fighting between cage mates? Authors Majolo, Buchanan-Smith, and Bell explore this issue with marmosets, and report their results on p. 32.

The move from injectable to inhalation anesthesia represents another success in the field of refinement alternatives, since the latter is generally considered safer and more efficient. It is easy to adjust the anesthetic depth, and because the anesthetics are eliminated from the blood by exhalation, with less reliance on drug metabolism to remove the drug from the body, there is less chance for drug-induced toxicity. The use of inhalation agents requires specialized equipment for delivery, and so author Diven (p. 44) provides an overview of commonly used agents and equipment.

Tanja Schub, Editor

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