



Editorial

Animal Research and Publication Ethics

The Veterinary Journal, as an international journal of veterinary research, publishes original articles in which animals may have been employed in controlled clinical trials or laboratory experiments. Animals are used in biomedical research when there are no alternative means of studying the pathogenesis, treatment or prevention of disease, or in the safety or efficacy testing of veterinary or human medicines. Scientists working with animals must appreciate the sensitivity of the ethical debate that surrounds animal experimentation and be aware of the need to operate to the highest possible standards in caring for the animals and causing them the very minimum of distress. This awareness is a basic humane and moral necessity, but it is also of scientific importance as the inclusion of a suffering or distressed animal can markedly affect its physiology and therefore the validity of a study.

Guidelines for scientific research journals publishing papers involving the use of animals have been recommended by the Fund for the Replacement of Animals in Medical Experiments (FRAME) as part of the acceptance criteria for submitted manuscripts (www.frame.org.uk/guidelines.htm). This *Journal* supports FRAME's ideals and has established its own ground rules, clearly set out in our Instructions to Authors, which state that any paper will be rejected where there is reason to believe that experimental animals may have been subjected to unnecessary (or avoidable) pain or distress. The purpose of this editorial is to provide advice to our authors and to explain how *The Veterinary Journal* implements its policy.

Over 40 years' ago, Russell and Burch (1959) proposed the three Rs of animal research – replacement, reduction and refinement; a concept that has survived the test of time. The *replacement* of animals is the hardest challenge of all. Certainly progress has been made, particularly with the use of multimedia material to replace animal experiments in teaching programmes, for example in physiology and pharmacology. There has also been

considerable success in research and testing. But although tissue culture and cellular models provide valuable means of assessing specific effects at the cell or molecular level, they cannot totally replace whole animals. There are two main reasons for this. Firstly, a model must be as compelling and statistically sound as existing validation systems; this is particularly important when considering toxicity and safety studies for human medicines and for veterinary drugs used in animals destined for human consumption. The thalidomide catastrophes of the 1960s show how seriously a lack of sufficient rigour in safety testing can impact on human health. Secondly, the living animal is highly complex and the whole is not simply a sum of its parts, which limits the value of *in vitro* alternatives. Sophisticated mathematical models are being developed for particular diseases or conditions, and the arrival of virtual controls and placebos offer interesting possibilities (Higgins, 2001). However, as animals are likely to be used in medical and veterinary research for the foreseeable future, work must continue to find ways to replace them where possible. The US Department of Agriculture Animal Welfare Information Center has published a directory of resources on alternatives and animal use (Larson *et al.*, 1998), and there is a regularly updated website which provides comprehensive sources of information for improved animal care and use in research, teaching and testing (www.nal.usda.gov/awic).

Reduction of animal use should be increasingly achievable with better study design and statistical input to ensure the minimum number of animals is used to reach a valid conclusion. But improved design can lead to the need for additional studies in order to pursue further lines of investigation, so the absolute number of animals used in experiments may not decrease markedly, at least in the short term. There has also been a dramatic increase in the use of transgenic animals and this trend is set to continue. *The Veterinary Journal* will continue to ask its referees to comment on the

statistical methods employed, and if these suggest poor experimental planning or the use of unnecessary animals, specialist reviewers will be consulted before the paper is accepted.

Refinement means making improvements in the conditions of experimental animals from birth to death, including, *inter alia*, the development and implementation of better housing, management, breeding, veterinary care, anaesthetic use and methods of euthanasia (Jennings *et al.*, 1998; Morton *et al.*, 1993). The refinement of animal procedures to make them more humane should be an integral part of all scientific research and this *Journal* requires and expects its contributors to have an awareness of the need for refinement in animal husbandry and to work within a system that demands close monitoring and the routine implementation of changes for the better care of animals.

For many years, *TVJ* has adopted as its working reference standard, the British Government's Animals (Scientific Procedures) Act 1986, which is generally recognized to be one of the most thorough and tightly regulated pieces of legislation on animal research anywhere in the world. The Executive Board's consensus view has been that work should not normally be published in the *Journal* if it would not be permitted under the 1986 Act (Higgins, 1993). The Act regulates for the UK all experimental and other scientific procedures applied to protected animals, which may have the effect of causing pain, suffering, distress or lasting harm. For further details, see www.homeoffice.gov.uk/animact/aspag1.htm. At the heart of the 1986 Act is *balance* – the need to weigh any harm to an animal (in terms of potential pain, suffering, distress and lasting damage or death) against the likely benefits of the research.

A cost-benefit (or cost-harms) analysis will continue to form part of this *Journal's* decision-making process in assessing whether a paper reporting animal work should be published. Authors should provide the necessary justification routinely within the text of their paper, but where this is not clearly stated or where there is doubt or concern, the article will be reassessed in terms of the *Journal's* policy on animal use. Specifically, the Introduction should explain clearly and in enough detail why the work was necessary, what questions the authors were seeking to answer and how the report contributes to advances in veterinary and/or scientific knowledge. The Materials and Methods section must contain sufficient information about the statistical approaches used in selecting the number of

animals, the appropriateness of the species, the procedures employed and how pain was alleviated and discomfort kept to a minimum. The Results and Discussion should show how the outcome of the research justified the use of the animals. Authors must also state that the work was approved in advance by an ethical review system within the authors' institute or by some other appropriate authority. Where the stringency of an institute's system or the national legislation governing animal use is unknown or does not approach the rigours of the UK requirements referred to above, an editorial judgment will be made, often following receipt of further advice from one or more referees specializing in experimental animal welfare.

The issue of animal experimentation will remain contentious and some people will always oppose the use of animals on moral or principled grounds. Scientists need to be aware of these views and to consider carefully the ethics of causing animals pain, suffering or death in order to understand and alleviate the suffering of other animals or humans. Likewise, the veterinary profession has a duty to lead the way in ensuring the principles of humane science are incorporated into animal research. This *Journal* takes the view that providing a critical cost-benefit/harms analysis has been undertaken, that there has been a thoughtful application of the three Rs, and that stringent controls (including ethical review) are in place and enforced, it can be unethical *not* to employ animals if their use is manifestly expected to lead to improved health of the wider animal or human community.

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