

## Preface

The Fourth World Congress on Alternatives and Animal Use in the Life Sciences was held in New Orleans, Louisiana, USA, on 11–15 August 2002. Over 500 participants from more than 30 countries attended, including scientists, veterinarians, regulators, educators and animal protectionists. The publication of the Congress proceedings coincides with the 45th anniversary of the publication of Russell and Burch's landmark book, *The Principles of Humane Experimental Technique*, and this new volume is a fitting tribute to William Russell and Rex Burch and their legacy. It reflects the progress that has been made in implementing the concept of the Three Rs of *reduction*, *refinement* and *replacement* in animal research, education and testing.

Within the span of 45 years, the Three Rs approach has become codified into laws, policies, and guidelines throughout the world; has become the focus of several government and academic centres; has become a guiding principle in the work of thousands of scientists and laboratory personnel and of numerous animal protection organisations; has been responsible, in part, for the dramatic reductions in animal use that occurred during the last quarter of the 20th century; and has led to significant changes in the techniques of research, testing, and education, to the benefit of science, public health, and education, as well as animals. These trends are evident in the pages of this volume. Some of the more dramatic advances in recent years have been in the areas of skin corrosivity, phototoxicity, and monoclonal antibody production. Less well-known, but important, advances have been made in the assessment of biologicals, in methods of medical and veterinary school instruction, and in the housing and handling of animals. An important milestone in the history of the Three Rs and animal testing was the December 2002 de-listing of the LD50 test from international guidelines governing chemicals testing.

In many ways, however, much of the practical potential of the Three Rs approach has yet to be realised. This state of affairs serves as a source of both frustration and discouragement, on the one hand, and motivation and hope on the other. Just a few examples should suffice to illustrate how far we still need to go.

The Three Rs approach has not penetrated as deeply into the culture of academia and biomedical science as it has into industrial and toxicological science. Governments still devote little funding explicitly for Three Rs work. Attention to *reduction* lags far behind that given to *refinement* and *replacement*. Information about advances in *refinement* is slow to diffuse among institutions and across

national boundaries, given limited opportunities for publication and other factors. National and international profiles of current animal usage are still inadequate to rationally set priorities for research and development on the Three Rs. Finally, the science of validation has matured only in recent years, and now stands ready for increased application in toxicology and elsewhere.

Not only do some old challenges remain, but new ones have emerged. Large-scale chemical testing programmes are being developed (e.g. the European Union [EU] Registration, Evaluation and Authorisation of Chemicals [REACH] programme) or are already under way (e.g. endocrine disruptor testing in the USA, EU, and elsewhere), and threaten to vastly increase animal usage. The genetic engineering of mice has halted the downward trend in global animal use and has begun to reverse it. And more ominously, the threat of global terrorism is expanding animal use in bioterrorism research in the United States and elsewhere, with its attendant animal suffering.

In the face of these and other challenges, it seems fitting to view the emergence of the 21st century and the new millennium as a time for reassessment, adjustment, and renewed determination on the Three Rs. In an era of increasing globalisation, with its advantages and disadvantages, we should strive to both increase the global reach of the alternatives approach and increase cooperation among existing centres of Three Rs activity. We should capitalise on the calls for large-scale chemical testing by harnessing the potential of non-animal methods and tiered-testing strategies to minimise animal use. Techniques such as (quantitative) structure–activity relationship analysis seem ideally suited for high volume chemical screening. Similarly, the emerging fields of genomics, proteomics, and metabolomics have been viewed as vaguely offering tremendous promise to limit animal usage, but what role should the Three Rs community play in exploring and advancing these technologies? And finally, how can we better harness the power of the Internet and other technologies to make information about alternatives more widely available, especially in the area of *refinement*, so that those outside the Three Rs community can have greater access to the latest developments?

For those especially interested in *refinement*, two inter-related developments were evident at the Fourth World Congress. One was the small but expanded participation of animal welfare scientists in the programme. Second, while it is now axiomatic that good animal welfare is a prerequisite for good science, animal welfare scientists are

uncovering dramatic illustrations of the adverse impacts of keeping animals in barren laboratory conditions. These studies go beyond documenting acute effects or heightened data variability, and instead illustrate chronic effects on behaviour, physiology, and even microanatomy, that can cast fresh doubt on the relevance of the experimental models to their analogous human conditions. These studies offer a new round of examples of how animal welfare and the Three Rs go hand in hand with good science.

The co-organisers of the Fourth World Congress on Alternatives wish to offer a special thank you to the meeting participants who gave talks or presented posters, and whose presentations are collected in this volume. We hope the proceedings not only document the content of the meeting, but will also serve to inspire, provoke, and influence.

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