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# Preface

In 1959, Russell and Burch introduced the concepts of replacement, reduction and refinement (the Three Rs) as a starting point for the humane treatment of laboratory animals. They stated that scientists should continually examine their research for possibilities of replacing the use of higher animals by lower organisms or non-biological materials, to reduce the number of animals used, or to refine the scientific procedures so that any suffering, discomfort or pain endured by the animals was the minimum necessary for achieving the scientific objective. The importance of this approach is that there is a real possibility that by upholding these ethical principles there will be, at the same time, an improvement in the scientific quality of the research. Today, the 'Three Rs' are accepted concepts within the scientific community and they form the basis for existing legislation on animal experimentation.

Until relatively recently, the highest priority has been given to the R of replacement as being the most effective way to improve animal welfare. However, it is increasingly being recognized that replacement is also the most difficult R to achieve. Our knowledge of the fundamental physiological and pathophysiological processes needed for the development of *in vitro* methods is still very limited. Even when there appears to be a successful replacement *in vitro* method, acceptance of it is often hampered by a lack of sound validation data and, therefore, it can be expected that large numbers of animals will continue to be used. This emphasizes the need to concentrate on the R of refinement.

Many sorts of animal procedures may cause severe pain and discomfort to the animals. In 1997, according to Dutch statistics, they formed about 19% of all experiments; and in the UK about 2% of project licences were banded as substantial (the difference between the UK and The Netherlands may well represent a difference in the categorization of certain scientific procedures). The severity is often related to the endpoint being used, and endpoints such as lethality in safety testing (e.g. tests of vaccine potency and acute toxicity) as well as in the research and development of new medicines (e.g. models of infection and cancer) are not uncommon. If refinement is taken seriously by the scientific community, then it should start with these types of experiments.

From 23–25 November 1998, a conference was held in Zeist (The Netherlands) to discuss the possibilities and opportunities for the implementation of humane endpoints. It was attended by about 100 delegates from industry, regulatory bodies, animal welfare organizations and academia. The purpose of the conference was to bring together those with expertise in various areas of biomedical research to present their latest research results with an emphasis on practical implications. Each paper has been peer reviewed before publication in this volume. During the conference, important issues relating to the recognition and assessment of adverse effects in animals, and the determination, validation, implementation and acceptance of humane endpoints were addressed. Papers were presented on new techni-

ques, new approaches and new strategies using non-invasive methods, as well as on the training of observers and the use of recently developed remote sensing devices.

One of the outcomes of the conference was that it showed that humane endpoints could only be evaluated on a study-by-study basis. Input is required from the scientist commissioning the work and processing the data, and also from others involved, such as laboratory animal scientists, animal welfare officers, veterinarians, regulators, and especially the animal care and technical staff involved in the day-to-day care of the animals. Humane endpoints are part of a dynamic process, influenced by scientific developments as well as by animal welfare concerns as they evolve with time. It is very likely, therefore, that what we consider to be 'humane' today will not be in the future, and so we need to strive constantly to develop less-inhumane endpoints, and to continually re-assess and re-evaluate the endpoints in animal experiments. For that reason we hope that this conference will be the first of many.

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**Organizing Committee of the International Conference on Humane  
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