## Foreword

While SCOPE is primarily an organization devoted to scientific inquiry, it is, of course, highly sensitive to societal priorities and, hence, also has a keen interest in mechanisms that quickly deliver scientific results to decision-makers and organizations in a position to apply these results in practice.

One such mechanism is provided by the Scientific Group on Methodologies for the Safety Evaluation of Chemicals (SGOMSEC). This group was set up in 1978 and is supported by SCOPE as well as the World Health Organization (WHO), the United Nations Environment Programme (UNEP) and the International Labour Organization (ILO) with the framework of the International Programme on Chemical Safety (IPCS).

The present study is the fourth book produced by this successful group and deals with an important, practical and very specific topic within its wide mandate: reliable *in vitro* tests for toxicity which are a cornerstone in the development of environmentally acceptable chemicals as they have a direct impact on the costs of R & D for new chemicals. In this sense SGOMSEC has been working in this study, as it should, at the cutting edge between science and society.

J.W.W. LARIVIERE President, SCOPE (1984)

## Foreword

Toxicity testing of chemicals in experimental animals to detect potential hazards to human health and the environment for decades has been the cornerstone of national and international programmes on chemical safety. Over the last several years, major advances in the biological and medical sciences have led to the development of new short-term tests for non-genotoxic end-points. Although many of these tests hold great promise for improving the risk assessment process, as well as for decreasing the use of experimental animals in toxicology, the relevance to the intact animal of the scientific data obtained from such short-term tests have yet to be evaluated. The fourth workshop of the Scientific Group on Methodologies for the Safety Evaluation of Chemicals (SGOMSEC) was organized to address such important scientific issues, providing assistance to the scientific community to develop new and improved methods for assessing risks from chemical exposures.

It is hoped that the personal views and opinions expressed by the individual experts in their Contributed Papers will lead to in-depth scientific discussions followed by the research needed to develop new short-term tests well supported by scientific data, perhaps, even more relevant to the intact animal than that obtained from those tests presently available. The Joint Workshop Report, in turn, should provide scientists and decision makers with a summary of the potential uses of presently available methodologies and the research needed to validate these short-term tests, leading to their more widespread use.

Both of these results will be of great assistance to the IPCS as we attempt to promote the development, improvement, validation, and use of methods (laboratory, epidemiological and ecological) suitable for the evaluation of health and environmental risks and hazards from chemicals in an effort to provide scientific guidance to national chemical safety programmes.

> MICHEL J. MERCIER Manager International Programme on Chemical Safety



## Preface

This study was undertaken by the Scientific Group on Methodologies for the Safety Evaluation of Chemicals (SGOMSEC), an international group which examines difficult issues relating to safety evaluation. In doing so, it attempts to identify those methods that may be adequate and useful at this time, those which need improvement, and to suggest research that may improve them.

SGOMSEC operates under the sponsorship of the International Programme on Chemical Safety (IPCS) within the World Health Organization (WHO), which has the joint input of the United Nations Environment Program (UNEP) and the International Labour Organization (ILO). A second sponsor is the Scientific Committee on Problems of the Environment (SCOPE), which operates under the International Council of Scientific Unions (ICSU).

This project was held in Ottawa, Canada, 13–16 August 1984. It was undertaken with the view that something less than full scale *in vivo* studies may have useful predictive value in characterizing the toxicity of chemicals of public health and ecological importance. It was not anticipated that this exploratory study would necessarily reveal techniques ready at this time to serve as substitutes for classical toxicological and environmental assessments. However, in some instances, it has been possible to identify experimental approaches to the resolution of specific questions relating to the adverse effects of chemicals and thus supplement classical *in vivo* approaches. Not surprisingly, in some cases, there were substantial limitations in the information that could be secured in simplified systems.

The issue was dealt with through a series of inquiries: cell cultures involving primarily undifferentiated cells; a systematic examination of short-term tests of the functional ability of organs or components thereof; and a series of systems— haematopoietic, immunologic, reproductive, and so forth—were also examined.

In each such instance, experts in the respective fields undertook the preparation of background papers exploring the presently available information. At the Workshop, these contributors, together with other experts, prepared a Joint Report by collectively examining each of the various topics.

The Joint Report is published together with the contributed papers; we thus have in this volume an examination of the ability of short-term tests to provide useful supplementary information for the evaluation of the effects of chemicals in mammalian systems and in non-human biota.

This is the fourth volume in the SGOMSEC series. This activity was guided by the co-chairpersons, Dr Emmanuel Somers of the Department of National Health and Welfare, Canada, and Dr Philippe Bourdeau, Director of Environmental Research, Commission of the European Communities. The participants who contributed papers and who participated in the preparation of the Joint Report are included in the list of *Participants of the Workshop*.

The entire volume has been edited by and prepared under the supervision of Mr J.R. Hickman of the Department of National Health and Welfare, Canada, to whom we owe much for his skill and discernment.

It is hoped that this survey will provide a useful starting point for further exploration in an endeavour to improve the efficiency of safety evaluation of chemicals and thus aid in providing needed information more quickly and more economically. Obviously, much additional work in nearly every area will be required before major gains can be secured in these objectives.

SGOMSEC is indebted for encouragement or financial support to a number of sponsors, including the Scientific Committee on Problems of the Environment, the International Programme on Chemical Safety, the Canadian Department of National Health and Welfare, the National Research Council of Canada, the Commission of European Communities, the US National Institute of Environmental Health Sciences, the US Environmental Protection Agency, and to many other organizations and individuals.

Co-operation in Ottawa included many services and facilities, which are most gratefully acknowledged. This came from the National Research Council of Canada, where the Workshop was held, and the Environmental Health Directorate of the Canadian Department of National Health and Welfare. We owe much to the secretarial services of Ms Anita Redfern (Mr Hickman's secretary), and Mrs Jane Calvin of New York University, who was of indispensable aid to the Chairman of SGOMSEC in the guiding and control of the manuscripts as they were completed.

> NORTON NELSON Chairman Scientific Group on Methodologies for the Safety Evaluation of Chemicals

xxvi