

RISK ASSESSMENT OF CHEMICALS

An Introduction

2nd edition

Edited by

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PREFACE

Chemicals are used to make virtually every man-made product and play an important role in the everyday life of people around the world. The chemical industry is the third largest industrial sector in the world and employs millions of people. Since 1930, global production of chemicals has risen from 1 million tonnes to over 400 million tonnes annually. In 2004 the global sales were estimated at € 1776 billion. The EU accounts for approximately 33% of global sales. This gradual increase in the production and widespread use of chemicals was not without “cost”. While chemicals play an important role in products for health and well-being, they may also pose risks to human health and the environment.

In 1992, at the United Nations Conference on Environment and Development (UNCED) in Rio de Janeiro, agreement was reached on an action plan for sustainable development in a number of policy areas. “Agenda 21” was born. The management of chemicals features prominently in Agenda 21, including the need to expand and accelerate the international assessment of chemical risks and strengthen national capacities for the management of chemicals. In the light of all of this, it is no coincidence that chemicals were again high on the agenda of the World Summit on Sustainable Development in Johannesburg in 2002. In South Africa our heads of state and governments undertook to minimize all adverse effects of chemicals within one generation, by the year 2020.

With the new legislative framework for industrial chemicals, i.e. REACH, Europe has moved from words to deeds in meeting the Johannesburg goal. REACH stands for Registration, Evaluation, Authorization and Restriction of CHemicals. The Regulation creates one system for the evaluation of all industrial chemicals with

regard to their production, formulation, use and disposal. It will provide a high level of protection of human health and the environment and, at the same time, enhance the competitiveness of the EU chemicals industry.

Successful implementation of REACH will be a challenge. It will involve 30,000 chemicals, 30,000 companies, a newly created European Chemicals Agency and many other stakeholders. REACH will also be a scientific challenge. It will boost further scientific research into sustainable chemistry. It will also make us aware of the scarce human resources currently available to meet these challenges. Therefore I hope that the scientific community will shoulder its responsibility for training students in chemistry, technology, biology, toxicology and other sciences related to the development, assessment and management of chemicals.

The present volume is the 2nd edition of a book published in 1995. It is an introduction to the risk assessment of chemicals and contains basic background information on sources, emissions, distribution and fate processes for the estimation of exposure of plant and animal species in the environment and humans exposed via the environment, consumer products and in the workplace. It includes chapters on environmental chemistry, toxicology and ecotoxicology, as well as information on estimation methods and intelligent testing strategies. It describes the basic principles and methods of risk assessment in their legislative frameworks (EU, USA, Japan and Canada). The book is intended to be used by students in technology, health and environmental sciences. It also provides background material for those who are currently involved in the risk assessment of chemicals. I hope that this book will contribute to meeting the challenges we are currently facing throughout the world.

Janez Potočnik
Commissioner for Science and Research
European Commission

EDITORS



Cornelis Johannes (Kees) Van Leeuwen (1955) studied biology at the University of Utrecht (UU), where he received his masters' degree in 1980 (*cum laude*) and obtained his PhD further to a thesis about the ecotoxicological effects of pesticides in 1986. He began his career in 1980 as a plant ecologist at the University

of Groningen and, shortly thereafter, became head of the Laboratory of Ecotoxicology at the Ministry of Transport and Public Works. He served in a research and advisory role in the implementation of the Netherlands' Pollution of Surface Waters Act. In 1987 he joined the Chemicals Division of the Ministry of Housing, Spatial Planning and Environment (VROM). In 1991 he became head of the Risk Assessment and Environmental Quality Division. He held a part-time professorship in biological toxicology at the Institute for Risk Assessment Sciences (IRAS) at the University of Utrecht. From 1997-2002 he was deputy director of the Centre for Substances and Risk assessment (CSR) at the National Institute for Public Health and the Environment (RIVM). He has been member of various policy and expert groups in the European Union, the International Rhine Committee, the Organization for Economic Co-operation and Development, the European and Mediterranean Plant Protection Organization and the Council of Europe. He was chairman of the OECD Hazard Assessment Advisory Body, vice-chairman of the OECD Joint Committee on Chemicals and member of the Scientific Committee on Toxicology, Ecotoxicology and the Environment (CSTEE) of the European Commission and external advisor to the Long-range Research Initiative (LRI) of CEFIC. In 2002 he became director of the Institute for Health and Consumer Protection of the Joint Research Centre of the European Commission. In this role he was responsible for the European Chemicals Bureau (ECB), the European Centre for the Validation of Alternative Methods (ECVAM), the Biotechnology and GMO unit, the Physical and Chemical Exposure unit and Biomedical Materials and Systems. In 2007 he retired from the European Commission and was appointed as principal scientist at TNO Quality of Life in the Netherlands.



Theodorus Gabriël (Theo) Vermeire (1953) studied chemistry and toxicology at the University of Utrecht. He received his MSc and teaching qualifications in 1978. After a 3-year teaching period as a volunteer in Zambia, he joined the Dutch Directorate-General of Environmental Protection

in 1982 and started his career in risk assessment as a toxicologist contributing to projects of the WHO International Programme on Chemical Safety (IPCS) and UNEP International Register of Potentially Toxic Chemicals (currently: UNEP Chemicals). In 1987, he joined the National Institute for Public Health and the Environment (RIVM) in Bilthoven, the Netherlands and has served in several scientific and managerial functions up to this day. As a project leader, he was involved in many projects in the area of toxicological standard setting, human and environmental exposure assessment, human toxicological dose-response assessment and the development of risk assessment methodologies and tools. Major projects include the development of the Netherlands' Uniform System for the Evaluation of Substances (industrial chemicals, plant protection products and biocides) and the European Union System for the Evaluation of Substances (industrial chemicals and biocides). His present position at RIVM is deputy head of the RIVM Expertise Centre for Substances. As an expert with a wide knowledge of toxicology and risk assessment, he has been involved in many expert groups developing risk assessment guidance for IPCS, the European Union and the Organization for Economic Co-operation and Development. Further to his interest in capacity building and teaching he has been involved in the organization of international risk assessment courses and EU twinning projects and taken part in them. He is a member of the Scientific Committee of the European Environment Agency and editor of the journal *Human and Ecological Risk Assessment*.

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The second edition of this book is the result of a joint effort between the National Institute for Public Health and the Environment (RIVM) in the Netherlands, the European Commission and many experts in the field of risk assessment and the management of chemicals throughout Europe, the USA, Japan and Canada. The aspects of the first edition that have made it useful as a reference to students, scientists and risk managers have been retained. The second edition has been further expanded to include an update on current testing procedures, data evaluation and interpretation, fate, effects, legislation and terminology. New authors have been added to broaden the input and provide expanded coverage of these fields.

The editors would like to thank the Commissioner, Janez Potočnik, and the Director-General of RIVM, Marc Sprenger, for their support and final approval of this project. The early contacts that were established with Reinout Woittiez and Jan Roels at RIVM were crucial in catalyzing and managing this process. Thanks!

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Tas, Martin Van Den Berg and Peter Van Der Zandt. We appreciate that you allowed us to update your previous contributions. We would also like to thank Christina Cowan, Mark Blainey and Ad Ragas for their contributions. In a period of particular change in the assessment and management of industrial chemicals we were very pleased that so many colleagues around the world volunteered to contribute to this book. We really appreciate your efforts on top of all the other obligations you face!

Special thanks are due to those who reviewed one or more chapters of this second edition. We would like to thank the members of the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) for their support. The involvement of industry experts in the drafting and review of the chapters has made it a real multi-stakeholder effort. We would like to thank Laura Bosatelli and Katrien Kouwenberg for their technical assistance and secretarial support. For the English correction we would like to thank Susan Hunt. Last, but not least, we would like to thank the Studio of RIVM (Wout Niezen, Jan de Bie and André Berends) for their creative inspiration. They turned our contributions (manuscripts, draft figures, tables and boxes) into camera-ready copy for the publisher.

CONTENTS OF THE BOOK

The contents of the book fall into 5 main sections.

- Part I deals with general issues in the risk management of industrial chemicals (Chapter 1).
- Part II is about exposure assessment. It starts with sources and emissions (Chapter 2), transport, accumulation and transformation processes (Chapter 3) and two chapters on exposure assessment, i.e., environmental and human exposure assessment (Chapters 4 and 5).
- Part III is related to human health and ecological effects assessment and risk characterization (Chapters 6 and 7).
- Part IV is about data and data estimation. It describes aspects of data needs, sources and quality evaluation (Chapter 8), the prediction of physicochemical properties and fate (Chapter 9), and the prediction of endpoints of toxicity and ecotoxicity (Chapter 10). Chapter 11 is devoted to so-called “Intelligent Testing Strategies”.
- Part V is about risk assessment and management of industrial chemicals in the EU (REACH), USA, Japan and Canada (Chapters 12-15), whereas the OECD chemicals programme to support international cooperation on the assessment and management of chemicals is presented in Chapter 16. Most chapters, where relevant, include a section on further reading and a list of references for those who want more information about data, methodologies or processes.
- In addition, the book contains a glossary of the major key issues and terminology. Risk terminology is difficult and may cause confusion as risk assessors may disagree on terminology. We have tried to be consistent with the risk terminology because without a common set of definitions, a meaningful discussion of this complex subject area is impossible.

The 16 chapters are summarized below.

Chapter 1. General introduction.

This chapter covers the general principles of risk assessment and risk management. It describes the role of risk assessment and other socio-economic and policy factors which contribute to the overall process of risk management of chemicals. Important definitions are given which are used in this field.

Chapter 2. Emissions of chemicals to the environment.

This chapter deals with the sources and emissions of chemicals into the environment, the life cycles of chemicals, point and diffuse sources of pollution and the classification of chemicals into main, industrial and use categories, as well as the development of “exposure scenarios”. This provides important information for estimating emissions.

Chapter 3. Transport, accumulation and transformation processes.

This chapter highlights the transport, transformation and accumulation processes, e.g. advection, dispersion, volatilization, sorption, sediment transport, wet and dry deposition, bioaccumulation and biomagnification. Biotic and abiotic transformation processes are also included.

Chapter 4. Environmental exposure assessment.

The central theme of this chapter is environmental exposure assessment, i.e. the determination of exposure concentrations. It reviews compartmental models for surface water, groundwater, soil and air, as well as multimedia approaches.

Chapter 5. Human exposure assessment.

The central theme of this chapter is (external) human exposure assessment, i.e. the determination of exposure concentrations as a result of (a) exposure through the environment. It also highlights (b) consumer exposure assessment and (c) occupational exposure.

Chapter 6. Toxicity testing for human health risk assessment.

The main theme of this chapter is the assessment of health effects in man. It describes short and long-term toxicity, reproductive toxicity, mutagenicity, carcinogenicity, sensitization and irritation. Extrapolation methodologies and assessment factors are given which are used for the determination of DNELs for man.

Chapter 7. Ecotoxicological effects.

This chapter deals with ecotoxicological effects assessment for the aquatic and terrestrial environments. It describes single-species tests with aquatic and terrestrial species as well as multi-species studies. Extrapolation methodologies and safety factors are given which can be used to derive PNECs for ecosystems. It also examines the issue of mixture toxicity and the assessment of PBT and vPvB chemicals.

Chapter 8. Data: needs, availability, sources and evaluation.

This chapter addresses the input of any risk assessment, i.e. the data related to releases of chemicals, fate, exposure and effects. The focus of this chapter is on effects data.

Chapter 9. Predicting fate-related physicochemical properties.

This chapter describes basic physicochemical properties such as water solubility, melting point, boiling point, Henry's law constant, vapour pressure (P_v), the octanol-water partition coefficient (K_{ow}). Structure-activity relationships (SARs) and quantitative structure-activity relationships (QSARs) are given for various physicochemical parameters, (bio)accumulation and (bio)degradation.

Chapter 10. Predicting toxicological and ecotoxicological endpoints.

This chapter is about SARs and QSARs for basic toxicological and ecotoxicological properties. The application of SARs and QSARs can help to overcome the problem of data gaps and reduce animal testing.

Chapter 11. Intelligent Testing Strategies.

This chapter brings together the previous chapters on exposure and effects assessment. It describes testing strategies combining use and exposure information and effects information obtained from QSARs, read-across methods, thresholds of toxicological concern (TTCs), and *in vitro* tests prior to *in vivo* testing, as this is a more rapid, efficient, and cost-effective way of performing a risk assessment of chemicals.

Chapter 12. The management of industrial chemicals in the EU.

This chapter is about REACH. It summarizes the main features and requirements of the REACH legislation.

Chapter 13. The management of industrial chemicals in the USA.

This chapter is about the Toxic Substances Control Act in the USA. It summarizes the main features and requirements of the legislation of industrial chemicals in the USA, including voluntary initiatives such as the Challenge Programme on High Production Volume Chemicals.

Chapter 14. The management of industrial chemicals in Japan.

This chapter is about chemicals management in Japan. It summarizes the main features and requirements of the legislation of industrial chemicals in Japan. It describes how risk assessment is applied in this regulatory context.

Chapter 15. The assessment and management of industrial chemicals in Canada.

This chapter summarizes the main features and requirements of the legislation of industrial chemicals in Canada, including the methodology of selecting priority chemicals. The relevant elements of how risk assessments are performed in Canada are included as well.

Chapter 16. The OECD chemicals programme.

This chapter describes the OECD activities relevant for the testing, assessment and management of industrial chemicals.

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