

Information Resources in

Toxicology

Edited by
PHILIP WEXLER
Steven G. Gilbert | Asish Mohapatra
Sol Bobst | Antoinette Hayes
Sara T. Humes

VOLUME TWO:
THE GLOBAL ARENA



INFORMATION RESOURCES IN TOXICOLOGY

FIFTH EDITION

INFORMATION RESOURCES IN TOXICOLOGY

Volume 2: The Global Arena

FIFTH EDITION

Editor-in-Chief

PHILIP WEXLER

Associate Editors

STEVEN G. GILBERT ASISH MOHAPATRA SOL BOBST ANTOINETTE HAYES SARA T. HUMES



Academic Press is an imprint of Elsevier 125 London Wall, London EC2Y 5AS, United Kingdom 525 B Street, Suite 1650, San Diego, CA 92101, United States 50 Hampshire Street, 5th Floor, Cambridge, MA 02139, United States The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, United Kingdom

Copyright © 2020 Elsevier Inc. All rights reserved.

Exception to the above (Chapters 11, 30, and 37): Copyright © 2009 Elsevier Inc. All rights reserved.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system, without permission in writing from the publisher. Details on how to seek permission, further information about the Publisher's permissions policies and our arrangements with organizations such as the Copyright Clearance Center and the Copyright Licensing Agency, can be found at our website: www.elsevier.com/permissions.

This book and the individual contributions contained in it are protected under copyright by the Publisher (other than as may be noted herein).

Notices

Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

Note about the National Library of Medicine's (NLM) Toxicology Information Resources

For decades, the U.S. National Library of Medicine has played a prominent role in offering free publicly available information resources in toxicology. These have been built variously by NLM and other organizations and made accessible via its Toxicology and Environmental Health Information Program (TEHIP), a unit within the Division of Specialized Information Services (SIS). In June of 2019, SIS was merged into the Division of Library Operations (LO) and the Office of Computer & Communications Systems (OCCS). NLM has reviewed and evaluated services and offerings formerly offered by SIS, including TEHIP, identifying which products support the NLM Strategic Plan and represent unique offerings from NLM. NLM has been intent on integrating SIS offerings into more current and standard technology and migrated TOXNET information, a large part of which has been retained, to PubChem, PubMed, and Bookshelf, in late 2019 and early 2020.

The authors and editors have tried to assure that individual chapter information related to NLM resources, as well as those originating elsewhere, is current as we were going to press. Inevitably there is a gap in time between seeing proofs and actual hard copy monograph publication. In short, this note is intended as a caveat for readers to dig further if, for example, a particular resource seems to be no longer available or a URL may not work.

For more information on NLM resources - custserv@nlm.nih.gov or 1-888-346-3656; also consider consulting https://support.nlm.nih.gov and https://www.nlm.nih.gov/toxnet/index.html.

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data

A catalog record for this book is available from the Library of Congress

ISBN: 978-0-12-821611-8

For Information on all Academic Press publications visit our website at https://www.elsevier.com/books-and-journals

Publisher: Andre Gerhard Wolff Acquisitions Editor: Kattie Washington Editorial Project Manager: Megan Ashdown Production Project Manager: Punithavathy Govindaradjane

Cover Designer: Christian Bilbow

Typeset by MPS Limited, Chennai, India



DEDICATIONS, WITH LOVE

Philip Wexler

To my wife, Nancy; mom, Yetty; dad, Will (in memory of); son, Jake; and spaniel mix, Gigi

Steven G. Gilbert

To knowledge, may it lead to truth.

Asish Mohapatra

To my wife Sarah, daughter Maya, my Mom (Kanak), and Dad (Mahendra)

Sol Bobst

I dedicate this edition to Jessica Culley, for her love and support of my projects and business, and for being gracious with me and my idiosyncrasies.

Antoinette Hayes

To my husband and fellow scientist Martin, my son Tauer, and my daughter Gigi

Sara T. Humes

To my husband Richard and my parents Ed and Maria

As Well As

To the many casualties of the 2020 global COVID-19 pandemic and the brave, caring, and generous people helping us get through it and return to normalcy.

and

With appreciation to the scientists and other good people working to reverse the ravages of pollution and global climate change and take us to a habitable, clean, healthy, and sustainable environment.

Contents

List of Contributors		References	
Foreword to Fourth (previous) Edition	xv xix	Other sources of information consulted (Spanish only)	
Foreword to Fifth Edition			
Preface	xxi xxiii	4. Australia	
	AAIII	PAUL F.A. WRIGHT	
			2.5
1. Overview of international activities		Introduction Performance	35 37
JENS KÜLLMER AND ULRICH SCHLOTTMANN		References Resources	38
Introduction	1		
International activities	1	5. Brazil	
Intergovernmental organizations	8	CRISTIANA L. CORREA, GIULIANA F.R. SELMI AND FLAVIO A.D.	
Main features of European Community chemicals legislation	8	ZAMBRONE	
References	9		
List of important abbreviations	10	Introduction	57
List of important URLs	10	Resources	58
2. European Union		6. Canada	
JAN VAN DER KOLK		KANNAN KRISHNAN, PAMELA PRUD'HOMME AND JOSEPH ZAYED	
Introduction	11	Introduction	71
Registration	11	Resources	71
Data requirements and test methods	11	Legislation and regulation of chemicals in Canada	78
Animal testing	12	Federal government departments	81
Consortia for registration by different manufacturers or		Provincial agencies	84
importers	12	Toxicology education in Canada: schools and programs	86
European Chemicals Agency and Member States, substances			
of high concern	12	7. Chile	
Authorization	12		
Decision-making	12	JUAN CARLOS RIOS, LORENA SILVA AND SANDRA SOLARI	
Scientific committees	12	Introduction	93
Compliance, enforcement, and inspection	13	Resources	93
Related EU bodies and initiatives	13	resources	,,,
Access to information on chemicals	13		
International collaboration Current discussions	13 13	8. China	
Other groups of chemicals	13	XINSHENG GU	
Conclusion	14		
Websites	14	Background narrative	99
Websites	1 1	Core documents	100
		Organizations—government	113
3. Argentina		Organizations—nongovernment	118
SUSANA I. GARCÍA, EDDA C. VILLAAMIL LEPORI AND		Universities	120
ADRIANA I. HAAS		Professional societies	123
		Poison control centers	124
Introduction	15	Legislation	125
Resources	17	Miscellaneous resources	126

viii	Cor	atents	
9. The Czech Republic		15. Greece	
M. HORNYCHOVÁ, J. VESELÁ AND M. VYSLOUŽILOVÁ		P. APALAKI, E. VAKONAKI AND A.M. TSATSAKIS	
Introduction	127	Introduction	205
References	129	Books	205
Books	129	Journals	206
Reports, bulletins	132	Databases	206
Journals	132	Organizations	206
Databases	133	Nongovernmental organizations	206
Organizations—government	133	Universities	207
Organizations nongovernment	138	Professional societies	208
Universities	138	1 foressional societies	200
Professional societies	141		
Poison control center	141	16. India	
Legislation	142	SURESH K. NAGUMALLI	
		Introduction	211
10 D 1		Resources	211
10. Denmark		Disclaimer	246
LISBETH E. KNUDSEN		Discialmer	240
Introduction	143	17. Iran	
Resources	148	MOHAMMAD ABDOLLAHI, SHEKOUFEH NIKFAR, YASNA BEHMANE: AND SHABNAM KHARABAF	SH
11. Ecuador			2.45
HOMERO C. HARARI, RAUL E. HARARI AND RAMIRO I. LOPEZ		History of Modern Toxicology in Iran	247
		Poisoning in Iran	247
Introduction	155	Teaching of toxicology	248
Resources	156	Drug and poison information services	248
Technical reports and other documents	157	Poison treatment centers in Iran	248
Databases	158	Toxicology laboratories	248
Organizations (government)	158	National committee on chemical safety	248
Organizations (nongovernment)	159	The Iranian Society of Toxicology	249
Universities	160	Government agencies	249
Professional societies	160	Nongovernment organizations	250
Poison control centers	160	Universities with toxicology program of study (in alphabetic	
Legislation	161	order)	250
Ecgiolation	101	Professional societies and institutes with toxicology-related	
		activities	251
12. Finland		Drug and poison information centers	251
JAANA RYSÄ AND MATTI VILUKSELA		Books in toxicology and related subjects written or edited by Iranian scientists	252
Introduction	163	Core References	256
Resources	164		
		18. Israel	
13. France		YEDIDIA BENTUR	
MAGALI OLIVA-LABADIE, JEAN-CHRISTOPHE GALLART, EMMANUEI PUSKARCZYK AND VINCENT DANEL	L	Background narrative	257
T 1 .	100	Books	257
Introduction	177	Journal titles	257
Resources	178	Databases	258
		Organizations—government	258
14. Germany		Nongovernment organizations	262
•		Universities	262
HERBERT DESEL AND NINA GLASER		Professional societies	263

187 188

About Israel

Introduction

Resources

National poison information center Miscellaneous resources

264 264 264

	•
Contents	17
Contents	12

	Cont	ents	IX
19. Italy	OD O	24. The Netherlands	
MARINA MARINOVICH, MAURELLA DELLA SETA, CARLO ALESSANI LOCATELLI, LEONELLO ATTIAS, MARISTELLA RUBBIANI AND IDA MARCELLO	JKO	Short history of toxicology in the Netherlands	357
Introduction Resources Databases Organizations—government Poison control centers	265 265 269 271 275	Resources 25. New Zealand DIANA MONTENEGRO	358
Other national institutions Organizations—nongovernment Education	276 278 279	References Journals Databases Government Agencies	370 371 371 371
20. Japan		Non-Government Organizations	372
TAKESHI MORITA, YOSHIYUKI SHIGETA AND TOSHIME IGARASHI		Universities Victoria University of Wellington	372 373
Introduction Resources	289 289	Professional Societies Poison Control Centers	373 373
21. Kenya		26. Norway	
HARRIET KAMENDI		BIRGITTE LINDEMAN	
Introduction History of toxicology Education Development partners Resources Data capture and reporting Toxicology research areas References Further reading 22. Malaysia KOK MENG CHAN, CHOO TA GOH, JAHANGIR KAMALDIN, MAZRUI SAHANI, NOOR AMALINA RAMLE, ASNIDA ARIFIN AND SALMAAN HUSSAIN INAYAT-HUSSAIN Introduction Malaysian Society of Toxicology Resources	315 315 315 316 316 316 317 317	Background narrative Core documents Reviews and other key papers Organizations—government Organizations—nongovernment Universities Professional societies Poison control centers Legislation Online databases and tools Miscellaneous resources 27. Peru MONICA G. ARANA-PUSE AND FANNY L. CASADO Introduction Resources	375 376 376 376 380 380 381 381 381 382 382
23. Mexico maria e. gonsebatt and luz maría del razo		28. Poland MAREK BANASIK, TODD STEDEFORD AND MAREK MURIAS Introduction	393
Introduction Books Journals Organizations Poison control centers Legislation and regulations Education/schools	341 342 350 353 354 355 356	Resources 29. Portugal FERNANDO REMIÃO, JORGE SOARES AND FÉLIX CARVALHO Overview	394 413
Acknowledgements	356	Organizations (Government)	413
Further reading	356	Miscellaneous Resources	417

x	Con	tents	
30. Russia		Resources	462
B.A. KURLYANDSKIY, KH. KH. KHAMIDULINA AND K.K. SIDOROV		Technical reports and other documents Technical reports	467 467
History and current state of toxicology in Russia	419	Governmental strategies, guidelines, action plans, and	101
State Registration of chemical and biological substances	117	reports	468
in the Russian Federation	420	Databases	468
Resources	420	Organizations—government	469
		Organizations—nongovernment	470
31. Saudi Arabia		25 V D 11: (
K.M. ALHARTHY, H.N. ALTHURWI AND F.F. ALBAQAMI		35. Korea, Republic of	
		JONGWOON KIM, HYUN KIL SHIN, JANG-SIK CHOI,	
Introduction	435	SEOKJOO YOON AND TAE HYUN YOON	
Resources	436	Introduction	487
The National Drug and Poison Information Center	436	Toxicology in Korea	488
Hospitals' Drug and Poisons Information Centers Poison Control Centers	436 437	Resources	489
Poison control committees	438		
The General Authority of Meteorology and Environmental	130	26 Sanata	
Protection	438	36. Spain	
Toxicology education of Saudi Arabia	438	GUILLERMO REPETTO, ANA DEL PESO, RAQUEL ROJAS,	
Scientific journals	439	SARA MAISANABA AND MANUEL REPETTO	
Books	439	Introduction	505
References	440	Further reading	506
Samples of toxicological publications related to		Resources	506
Saudi Arabia	440	Acknowledgements	523
Acknowledgment	443		
		37. Sweden	
32. Serbia, Republic of		LARS WIKLUND	
VESNA MATOVIĆ, DANIJELĄ UKIĆ-ĆOSIĆ, ALEKSANDRA BUHA OR	.EVIĆ	and water	
AND STEFAN MANDIĆ-RAJČEVIĆ		Introduction	525
The history of toxicology in Serbia	447	Historical notes in Swedish toxicology	525
Toxicological education in Serbia	447	Toxicology becomes organized	526
Modern toxicology education	448		
Universities and faculties teaching toxicology in Serbia	449	38. Switzerland	
Resources	450		
Relevant national legislation	451	IRENE M. BASKERVILLE-ABRAHAM, TODD STEDEFORD AND CAROLE HIRN	
Governmental agencies	452	THIS CAROLL THRIV	
Nongovernmental organizations and professional societies	452	Introduction	543
Databases	452	Societies	543
Centers	453	Toxicological registries	544
Institutes	453	Toxicological information sources	544
Acute poisonings	453		
		39. Taiwan	
33. Singapore		JUNG-DER WANG, TSUN-JEN CHENG AND CHEN-CHANG YANG	
R. PONAMPALAM			T 4 T
Introduction	455	Introduction Resources	545 545
References	456	resources	J † J
Resources	456		
	120	40. Turkey	
34. South Africa		ERDEM COSKUN AND EREN OZCAGLI	
MARY GULUMIAN, TARRYN LEE BOTHA AND VICTOR WEPENER		History of toxicology in Turkey	557
January Land Section West Control West Events		References	558
Introduction	461	Resources	559
References	462	Organizations	561

Contents			xi
Universities	562	43. Venezuela	
Professional societies	563	ARISLEIDA J. RODRÍGUEZ, MAYLIN E. VELÁSQUEZ,	
Poison control centers	564	AND MARITZA ROJAS	
Legislation and regulation	564		
Acknowledgement	565	Introduction	601
		Resources	604
41 11 1 121 1		Government institutions related to Toxicology	607
41. United Kingdom		Other Organizations	608
LISA HOFFMAN AND ASISH MOHAPATRA		Other services	608
		Examples of nongovernmental organizations	609
Introduction	567	Postgraduate studies (postgrados)	612
Resources	568	• •	
42 11		Appendix 1: Glossary of Terms Used in	
42. Uruguay		Toxicology, 2 nd Edition: (IUPAC	
CAROLINA JUANENA, ALBA NEGRIN AND AMALIA LABORDE		Recommendations 2007)	613
Introduction	595	Appendix II: Toxicology Quotes	697
Toxicology at the Health Sector	595	Index	703
Journal articles	598	Huca	103

xii

Contents

Volume I Contents

Part I Introduction

1. Toxicology: a primer

A. WALLACE HAYES

2. History of toxicology

KENNETH R. STILL, KATHERINE D. WATSON AND PHILIP WEXLER

3. Development of toxicoinformatics

DEVIN HUNT, MEGAN BRANSON, ELIZABETH PUTNAM AND MARK PERSHOUSE

4. Toxicoinformatics today

DEVIN HUNT, MEGAN BRANSON, ELIZABETH PUTNAM AND MARK PERSHOUSE

5. Starting points for finding toxicology resources stephanie holmgren, stacey mantooth and eleanor weston

Part II Subject categorization: books and more

6. General texts

STACEY HERRIAGE AND CAREY POPE

7. Analytical toxicology

SHAYNE GAD

8. Animals in research

SHAYNE GAD

9. Biomarkers

KENNETH J. OLIVIER, JR., CECILE M. KREJSA AND JEREMY A. FREEMAN

10. Biotechnology

GRACE A. CHAPPELL

11. Biotoxins

KENNETH R. STILL AND ASISH MOHAPATRA

12. Cancer

KAREN TILMANT AND JAMES E. KLAUNIG

13. Chemical compendia

ANTOINETTE HAYES

14. Chemicals: cosmetics and other consumer products

ESTHER M. HAUGABROOKS

15. Pediatric environmental health: exposures and interactions

IRIS AN AND RUTH A. ETZEL

16. Climate change toxicology resources

ASISH MOHAPATRA

17. Drugs

WILLIAM IRWIN

18. Chemicals: dusts and fibers

JOSEPH A. CICHOCKI AND GREGORY J. SMITH

19. Metal toxicology

STEVEN G. GILBERT

20. Chemicals: pesticides

ALLAN S. FELSOT

21. Chemicals: solvents

MARIE BOURGEOIS, KEVIN GUTH AND RAYMOND D. HARBISON

22. Chemicals: selected chemicals

ANTOINETTE HAYES

23. Clinical toxicology and clinical analytical toxicology

DEXTER W. SULLIVAN, JR. AND SHAYNE GAD

24. Developmental and reproductive toxicology

REBEKAH PETROFF

25. Disaster preparedness and management

CHARLES C. BARTON, EDWARD P. LOCKE AND ASISH MOHAPATRA

26. Environmental toxicology: aquatic

SAMANTHA J. JONES AND MEREDITH G. LASSITER

27. Environmental toxicology: air

DIETRICH (DIETER) SCHWELA

28. Environmental toxicology: hazardous waste

CHARLES C. BARTON AND MARTINS O. AINERUA

29. Environmental toxicology: terrestrial

ALICIA A. TAYLOR AND CHARLES C. BARTON

30. Environmental toxicology: wildlife

CHARLES C. BARTON AND MARTINS O. AINERUA

31. Epidemiology

AMANDA S. PERSAD AND AISHA S. DICKERSON

Contents Xiii

32. Ethical considerations

STEVEN G. GILBERT

33. Exposure science

M. ELIZABETH MARDER

34. Food and nutrient toxicology

CLARK CARRINGTON

35. Forensic toxicology

SOL BOBST

36. Genetic toxicology

ROBERT R. YOUNG

37. Chemical mixtures: toxicologic interactions and risk assessment

JOHANNA E. SCHAAPER, RICHARD C. HERTZBERG, JANE ELLEN SIMMONS, M. MOIZ MUMTAZ AND GLENN E. RICE

38. Molecular, cellular, and biochemical toxicology

DEVIN HUNT, MEGAN BRANSON, ELIZABETH PUTNAM AND MARK PERSHOUSE

39. Nanotechnology

SARA T. HUMES AND TARA SABO-ATTWOOD

40. Noise and Noise-Induced Hearing Loss (NIHL)

GUANG-DI CHEN

41. Occupational health

ANDREW MAIER, DEBRA CHERRY AND ELIZABETH FRIEDMAN

42. Omics resources

DEVIN HUNT, MEGAN BRANSON, VICTORIA GIFFORD, ELIZABETH PUTNAM AND MARK PERSHOUSE

43. Pathology

BRENDA CARITO

44. Toxicokinetics, pharmacokinetics, and absorption, distribution, metabolism, and excretion

ANSHUL GUPTA

45. Precautionary principle

STEVEN G. GILBERT

46. Radiation information and resources online BRUCE BUSBY

47. Regulatory toxicology

AMANDA S. PERSAD

48. Risk assessment

AMANDA S. PERSAD AND SOL BOBST

49. Substances of abuse

GREET B.A. TEUNS

50. Target sites: general

WILLIAM IRWIN

51. Target sites: cardiovascular

LOUIS ANTHONY COX JR.

52. Endocrine toxicology

KAREN CHOU

53. Gastrointestinal tract

SOL BOBST

54. Target sites: hematopoietic

LOUIS ANTHONY COX JR.

55. Target sites: immune

MEGAN BRANSON, DEVIN HUNT, ELIZABETH PUTNAM AND MARK PERSHOUSE

56. Target sites: kidney

GARY O. RANKIN AND MONICA A. VALENTOVIC

57. Target sites: liver

JOSEPH A. CICHOCKI

58. Target sites: nervous system

VIRGINIA MOSER AND ABBY A. LI

59. Target sites: respiratory

GREGORY J. SMITH AND JOSEPH A. CICHOCKI

60. Target sites: sensory

CYNTHIA SANTOS AND LEWIS S. NELSON

61. Target sites: skin

HEATHER N. LYNCH AND JULIE E. GOODMAN

62. Terrorism and warfare (chemical, biological, and radioactive and nuclear)

BARBARA B. SAUNDERS-PRICE

xiv Contents

63. Testing methods and toxicity assessment (including alternatives)

MARYAM ZARE JEDDI, YURI BRUINEN DE BRUIN AND SANDER VAN DER

64. Veterinary toxicology

DAVID C. DORMAN

Part III Other resources

65. Organizations

JOHN P. WISE JR., JAMES T.F. WISE, CATHERINE F. WISE, JAMIE L. YOUNG AND JOHN PIERCE WISE SR.

66. Journals and blogs

FREDERICK W. STOSS

67. General interest, popular, and trade works: informing the citizenry FREDERICK W. STOSS

68. Government information and documents and technical reports

FREDERICK W. STOSS

69. Audio visual, nonprint, graphic, and other visualized resources

FREDERICK W. STOSS

Part IV The online environment and data science

70. The internet: recent trends

ASISH MOHAPATRA

71. Web-based databases

NINA CHING Y. WANG

72. Software tools for toxicology and risk assessment ASISH MOHAPATRA

Part V Special topics

73. Laws and regulations

ESTHER M. HAUGABROOKS AND TAMARA HOUSE-KNIGHT

74. Resources for chemical hazard communication compliance

MICHELE R. SULLIVAN

75. Careers and professional education in toxicology STEVEN G. GILBERT AND KATIE FREVERT

76. K-12 and public education

STEVEN G. GILBERT AND KATIE FREVERT

77. Grants, scholarships, and funding

FREDERICK W. STOSS

78. Poison control centers

AXEL HAHN

79. Patents

WILLIAM IRWIN

List of Contributors

- Mohammad Abdollahi Department of Toxicology and Pharmacology, Faculty of Pharmacy, and Toxicology and Diseases Group, Pharmaceutical Sciences Research Center (PSRC), The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences (TUMS), Tehran, Iran
- F.F. Albaqami Pharmacology and Toxicology Department, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-kharj, Saudi Arabia
- K.M. Alharthy Pharmacology and Toxicology Department, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-khari, Saudi Arabia
- H.N. Althurwi Pharmacology and Toxicology Department, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al-kharj, Saudi Arabia
- P. Apalaki Department of Immunology, Genetics and Pathology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden
- Monica G. Arana-Puse Institute of Omics and Applied Biotechnology (ICOBA), Pontificia Universidad Catolica del Peru, San Miguel, Peru
- Asnida Arifin Center for Toxicology and Health Risk Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, Kuala Lumpur, Federal Territory, Malaysia
- Leonello Attias Centro Nazionale Sostanze Chimiche, Prodotti Cosmetici e Protezione del Consumatore, Istituto Superiore di Sanità, Viale Regina Elena, Rome, Italy
- Marek Banasik Institute of Public Health and Environmental Protection (IPHEP), Warsaw, Poland
- **Irene M. Baskerville-Abraham** JT International SA, Geneva, Switzerland
- **Yasna Behmanesh** Drug and Poison Information Center, Iranian Food and Drug Administration, Tehran, Iran
- Yedidia Bentur Israel Poison Information Center, Rambam Health Care Campus, Haifa, Israel; The Ruth & Bruce Rappaport Faculty of Medicine, Haifa, Israel; Technion-Israel Institute of Technology, Haifa, Israel
- Tarryn Lee Botha Water Research Group, Unit for Environmental Management, North-West University, Potchefstroom, South Africa
- Aleksandra Buha Đorðević Department of Toxicology "Akademik Danilo Soldatović," Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia
- **Félix Carvalho** UCIBIO, REQUIMTE, Laboratory of Toxicology, Department of Biological Sciences, Faculty of Pharmacy, University of Porto, Porto, Portugal

- Fanny L. Casado Department of Engineering and Institute of Omics and Applied Biotechnology (ICOBA), Pontificia Universidad Catolica del Peru, San Miguel, Peru
- Kok Meng Chan Center for Toxicology and Health Risk Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, Kuala Lumpur, Federal Territory, Malaysia
- **Tsun-Jen Cheng** Institute of Occupational Medicine and Industrial Hygiene, College of Public Health, National Taiwan University, Taipei, Taiwan
- Jang-Sik Choi Institute of Next Generation Material Design, Hanyang University, Seoul, Republic of Korea
- **Cristiana L. Correa** Planitox, São Paulo, Brazil; IBTox, São Paulo, Brazil
- Erdem Coskun Biomolecular Measurement Division, National Institute of Standards and Technology, Gaithersburg, MD, United States; Institute for Bioscience and Biotechnology Research, Rockville, MD, United States
- Vincent Danel Université Grenoble Alpes, Grenoble, France
- Yuri Bruinen de Bruin European Commission Joint Research Centre, Knowledge for Security & Migration, Ispra, Italy
- Maurella Della Seta Istituto Superiore di Sanità, Viale Regina Elena, Rome, Italy
- **Ana del Peso** National Institute of Toxicology and Forensic Sciences, Sevilla, Spain
- **Luz María Del Razo** Department of Toxicology, Cente for Research and Advanced Studies from the National Polytecnic Institute (CINVESTAV), Mexico City, Mexico
- **Herbert Desel** German Federal Institute for Risk Assessment (BfR), Max-Dohrn-Straße, Berlin, Germany
- **John H. Duffus** The Edinburgh Centre for Toxicology, Edinburgh, Scotland, United Kingdom
- **Danijela Đukić-Ćosić** Department of Toxicology "Akademik Danilo Soldatović," Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia
- **Jean-Christophe Gallart** Centre antipoison de Toulouse, Toulouse, France
- **Susana I. García** Faculty of Medicine, University of Buenos Aires, Buenos Aires city, Argentina
- **Nina Glaser** German Federal Institute for Risk Assessment (BfR), Max-Dohrn-Straße, Berlin, Germany
- Choo Ta Goh Institute for Environment and Development (LESTARI), Universiti Kebangsaan Malaysia, Selangor, Malaysia

XVi List of Contributors

Maria E. Gonsebatt Department of Medical Genomics and Environmental Toxicology, Biomedical Research Institute, National Autonomous University of Mexico, Ciudad Universitaria, Mexico City, Mexico

- Xinsheng Gu Department of Pharmacology, Hubei University of Medicine, Shiyan, P.R. China; Department of Preventive Medicine, Hubei University of Medicine, Shiyan, P.R. China
- Mary Gulumian National Institute for Occupational Health and Haematology and Molecular Medicine Department, University of the Witwatersrand, Johannesburg, South Africa
- Adriana I. Haas National Poison Center, National Hospital "Posadas", Buenos Aires city, Argentina; Ministry of Health of the Nation, Buenos Aires, Argentina
- **Homero C. Harari** Institute for Development of Production and Work Environment, Quito, Ecuador
- **Raul E. Harari** Institute for Development of Production and Work Environment, Quito, Ecuador
- Carole Hirn JT International SA, Geneva, Switzerland
- **Lisa Hoffman** Manager of Toxicology, Global Product Safety and Regulatory Operations, Avon Products Inc. Suffern, NY, United States
- M. Hornychová National Institute of Public Health, Prague, Czechia
- **Toshime Igarashi** Division of Cellular & Molecular Toxicology, National Institute of Health Sciences, Kawasaki, Japan
- Salmaan Hussain Inayat-Hussain Group Health, Safety, Security and Environment, Petroliam Nasional Berhad (PETRONAS), Persiaran KLCC, Kuala Lumpur City Center (KLCC), Kuala Lumpur, Federal Territory, Malaysia
- **Maryam Zare Jeddi** Wageningen University and Research, Division of Toxicology, Wageningen, The Netherlands
- Carolina Juanena Toxicology Department, Faculty of Medicine, University of the Republic, Montevideo, Uruguay
- Jahangir Kamaldin Advanced Medical and Dental Institute, Universiti Sains Malaysia, Pulau Pinang, Malaysia
- Harriet Kamendi Kandih Group, LLC, Silver Spring, MD, United States
- Kh. Kh. Khamidulina Russian Register of Potentially Hazardous Chemical and Biological Substances, Moscow, Russia
- Shabnam Kharabaf Library and Public Affairs, Pharmaceutical Sciences Research Center (PSRC), The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences (TUMS), Tehran, Iran
- Jongwoon Kim Chemical Safety Research Center, Korea Research Institute of Chemical Technology (KRICT), Daejeon, Republic of Korea
- Lisbeth E. Knudsen Department of Public Health, University of Copenhagen, Copenhagen, Denmark and on behalf of Danish Society of Toxicology and Pharmacology, Aarhus, Denmark

- Kannan Krishnan Robert Sauvé Occupational Health and Safety Research Institute (IRSST), Montreal, QC, Canada
- **Jens Küllmer** Federal Ministry for the Environment, Nature Conservation and Nuclear Safety, Bonn, Germany
- B.A. Kurlyandskiy Russian Register of Potentially Hazardous Chemical and Biological Substances, Moscow, Russia
- Amalia Laborde Toxicology Department, Faculty of Medicine, University of the Republic, Montevideo, Uruguay
- **Birgitte Lindeman** Department of Toxicology and Risk Assessment, Norwegian Institute of Public Health, Oslo, Norway
- Carlo Alessandro Locatelli Istituti Clinici Scientifici Maugeri SpA SB IRCCS Pavia, Via Salvatore Maugeri, Pavia, Italy
- Ramiro I. Lopez Ministry of Public Health of Ecuador and Biomedicine Center, Central University, Quito, Ecuador
- **Sara Maisanaba** Area of Toxicology, University Pablo de Olavide, Sevilla, Spain
- **Stefan Mandić-Rajčević** School of Public Health and Health Management, Institute of Social Medicine, Faculty of Medicine, University of Belgrade, Belgrade, Serbia
- Ida Marcello Centro Nazionale Sostanze Chimiche, Prodotti Cosmetici e Protezione del Consumatore, Istituto Superiore di Sanità, Viale Regina Elena, Rome, Italy
- Marina Marinovich Università degli Studi di Milano, Via Balzaretti, Milan, Italy
- Vesna Matović Department of Toxicology "Akademik Danilo Soldatović," Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia
- **Asish Mohapatra** Contaminated Sites, Environmental Health Program, Health Canada, Calgary, AB, Canada
- **Diana Montenegro** The School of Biological Sciences, The University of Auckland, Auckland, New Zealand
- **Takeshi Morita** Chemical Management Center, National Institute of Technology and Evaluation, Tokyo, Japan
- Marek Murias Department of Toxicology, Poznan University of Medical Sciences, Poznan, Poland
- Suresh K. Nagumalli Division of Biochemical Toxicology, National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, AR, United States
- **Alba Negrin** Toxicology Department, Faculty of Medicine, University of the Republic, Montevideo, Uruguay
- Shekoufeh Nikfar Department of Pharmacoeconomics and Pharmaceutical Administration, Faculty of Pharmacy, Pharmaceutical Sciences Research Center (PSRC), The Institute of Pharmaceutical Sciences (TIPS), Tehran University of Medical Sciences (TUMS), Tehran, Iran
- **Monica Nordberg** Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
- **Magali Oliva-Labadie** Centre antipoison de Bordeaux, Bordeaux, France
- **Eren Ozcagli** Department of Pharmaceutical Toxicology, Faculty of Pharmacy, Istanbul University, Istanbul, Turkey

List of Contributors XVII

- **R. Ponampalam** Department of Emergency Medicine, Singapore General Hospital, Singapore
- Pamela Prud'homme Robert Sauvé Occupational Health and Safety Research Institute (IRSST), Montreal, QC, Canada
- Emmanuel Puskarczyk Centre antipoison de Nancy, Nancy, France
- Noor Amalina Ramle Center for Toxicology and Health Risk Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, Kuala Lumpur, Federal Territory, Malaysia
- **Fernando Remião** UCIBIO, REQUIMTE, Laboratory of Toxicology, Department of Biological Sciences, Faculty of Pharmacy, University of Porto, Porto, Portugal
- **Guillermo Repetto** Area of Toxicology, University Pablo de Olavide, Sevilla, Spain
- Manuel Repetto Colegio Oficial de Químicos, Sevilla, Spain
- Juan Carlos Rios Centro Información Toxicológica, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile; Departamento de Laboratorios Clínicos, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile; Programa de Farmacología y Toxicología, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile
- **Arisleida J. Rodríguez** Center for Toxicological Investigations of the University of Carabobo (CITUC), Valencia, Estado Carabobo, Venezuela
- Maritza Rojas Center for Toxicological Investigations of the University of Carabobo (CITUC), Valencia, Estado Carabobo, Venezuela
- **Raquel Rojas** Area of Toxicology, University Pablo de Olavide, Sevilla, Spain
- Maristella Rubbiani Istituto Superiore di Sanità, Viale Regina Elena, Rome, Italy
- **Jaana Rysä** School of Pharmacy, University of Eastern Finland, Kuopio, Finland
- Mazrura Sahani Center for Toxicology and Health Risk Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, Kuala Lumpur, Federal Territory, Malaysia
- **Ulrich Schlottmann** Federal Ministry for the Environment, Nature Conservation and Nuclear Safety, Bonn, Germany
- **Giuliana F.R. Selmi** Planitox, São Paulo, Brazil; IBTox, São Paulo, Brazil
- **Yoshiyuki Shigeta** Division of Risk Assessment, National Institute of Health Sciences, Kawasaki, Japan
- **Hyun Kil Shin** Toxicoinformatics Group, Department of Predictive Toxicology, Korea Institute of Toxicology, Daejeon, Republic of Korea
- **K.K. Sidorov** Russian Register of Potentially Hazardous Chemical and Biological Substances, Moscow, Russia
- **Lorena Silva** Centro Información Toxicológica, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

Jorge Soares UCIBIO, REQUIMTE, Laboratory of Toxicology, Department of Biological Sciences, Faculty of Pharmacy, University of Porto, Porto, Portugal

- Sandra Solari Centro Información Toxicológica, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile; Departamento de Laboratorios Clínicos, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile; Programa de Farmacología y Toxicología, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile
- **Todd Stedeford** Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Washington, D.C., United States
- **Douglas M. Templeton** Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada
- **A.M. Tsatsakis** Laboratory of Toxicology Science and Research, Medical School, University of Crete, Crete, Greece
- E. Vakonaki Laboratory of Toxicology Science and Research, Medical School, University of Crete, Crete, Greece
- Jan van der Kolk Ecoconseil, Voorburg, The Netherlands
- Maylin E. Velásquez Center for Toxicological Investigations of the University of Carabobo (CITUC), Valencia, Estado Carabobo, Venezuela
- J. Veselá National Institute of Public Health, Prague, Czechia
- **Edda C. Villaamil Lepori** Faculty of Pharmacy and Biochemistry, University of Buenos Aires, Buenos Aires city, Argentina
- Matti Viluksela School of Pharmacy, University of Eastern Finland, Kuopio, Finland; Environmental Health Unit, Finnish Institute for Health and Welfare, Kuopio, Finland
- M. Vysloužilová National Institute of Public Health, Prague, Czechia
- **Jung-Der Wang** National Cheng-Kung University College of Medicine and Hospital, Tainan, Taiwan
- Victor Wepener Water Research Group, Unit for Environmental Management, North-West University, Potchefstroom, South Africa
- Philip Wexler National Library of Medicine, Bethesda, MD, United States (Retired)
- **Lars Wiklund** RegSafe-Regulatory Safety Sciences, Stocksund, Sweden
- Paul F.A. Wright School of Health and Biomedical Sciences, RMIT-University, Melbourne, VIC, Australia; Australasian College of Toxicology and Risk Assessment (ACTRA), Fitzroy, VIC, Australia
- **Chen-Chang Yang** Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan
- **Seokjoo Yoon** Molecular Toxicology Research Group, Department of Predictive Toxicology, Korea Institute of Toxicology, Daejeon, Republic of Korea

XVIII List of Contributors

Tae Hyun Yoon Institute of Next Generation Material Design, Hanyang University, Seoul, Republic of Korea; Department of Chemistry, School of Natural Sciences, Hanyang University, Seoul, Republic of Korea

Flavio A.D. Zambrone Planitox, São Paulo, Brazil; IBTox, São Paulo, Brazil

Joseph Zayed Robert Sauvé Occupational Health and Safety Research Institute (IRSST), Montreal, QC, Canada

Foreword to Fourth (previous) Edition

Toxicology, like other sciences, has developed in phases. Toxicologists, however, claim that the initial phase of our discipline preceded that of most other biological sciences since it involved recognition by primitive man of the safe and dangerous agents in his environment. The next phase (antiquity and the Middle Ages) was characterized by the use of this information for good (therapeutics) and evil (poisoning). It was during the Renaissance that Paracelsus recognized the importance of the dose-response paradigm, and this marked the beginning of modern toxicology. Today toxicology is focused on molecular mechanisms, and using the Internet to store and exchange this and other information is becoming a key part in the evolution of toxicology. A major problem with using the Internet in toxicology is that the amount of information is overwhelming and that it varies greatly in quality. Information Resources in Toxicology addresses this problem by providing a roadmap for today's online enthusiast, and an annotated bibliography for other information sources in toxicology. This book is a gold mine for those of us who make lists of our favorite toxicology and regulatory websites, and will be invaluable to everyone who wants to know where to find general and specific information in all areas of toxicology and risk assessment in the United States and around the world.

The fourth edition of Information Resources in Toxicology reflects the exponential growth of our discipline. Despite the book's increased size, it is easier to navigate because its many chapters have been logically clustered into relatively few sections. Each chapter in the global arena and subject categorization sections has been written by a well-recognized expert to insure that it is both authoritative and current. Similarly, the chapters on the Internet and Digital Tools and Special Topics (legal, education, funding, etc.) provide a pragmatic hands-on approach that will be of immense value to scientific researchers not well versed in such ancillary concerns. The section on Other Resources offers chapters on print media (journals, newsletters, bibliographies and similar collections, agency and organization documents and reports, etc.), as well as a delightful chapter on General Interest and Popular Works which nicely supplements the chapters on Scientific Principles and History in the introductory section.

John Doull

University of Kansas Medical Center, Kansas City, KS, United States

Foreword to Fifth Edition

Toxicology is a paradoxical science; it has been used to kill and to cure. Like a living system, toxicology has a dynamic that reflects the almost daily changes in our understanding of biology and the interests, capabilities, and needs of toxicologists, regulators, and the public. Toxicologists must be involved in the decision-making processes, recognizing the need for scientific understanding, including translation of scientific findings into understandable terms that are suitable for decision-making and ensuring consistent prediction of hazards and risks before the actual exposure has occurred and to permit benefit—risk assessments of the consequences for such exposure.

Remember the scares about artificial sweeteners, pesticide residues in foods, genetically modified organisms, fluoride in toothpaste and drinking water, plasticizers, and flame-retardant chemicals? The problem generally comes from a narrow focus on an effect in isolation without giving equal weight to the biology of the system or species and the exposure. There often has been a lack of caution in extrapolating toxicity to other species and circumstances. How often do we have to relearn Paracelsus' fundamental concept about the primacy of the dose?

The 5th edition of Information Resources in Toxicology helps with many of these misconceptions by guiding the toxicologist, the regulator, and the public health official to the numerous resources on the internet as well as providing a bibliography for an array of other information resources. This guidance directs the reader to both general and specific information in toxicology and risk assessment in the broadest global sense.

This new 5th edition somehow manages to contain the explosive growth of toxicology and risk assessment and the ever-increasing big data explosion in a mere two volumes. They are organized in a logical manner with chapters clustered appropriately, making for an easy read and for readily finding information, especially in exploring online sources. Part III (Other Resources) is unique, and may be the most useful, section of Volume I. Arranged by various resource formats, it complements the other specialized topical chapters. Volume II (The Global Arena) highlights resources available across the globe. The book is well indexed for quick and easy referencing. Chapter authors represent an array of experts, well recognized in the areas for which they have been asked to write. This is a tome that should be on your bookshelf.

A. Wallace Hayes

University of South Florida, College of Public Health, Tampa, FL, United States; Institute for Integrative Toxicology, Michigan State University, East Lansing, MI, United States

Preface

The 1st edition of this work, *Information Resources in Toxicology* (IRT), was published in 1982, almost ancient times by scientific reckoning. Toxicology, back then, although not quite a fledgling science, had yet to achieve maturity. The evolution of its experimental and theoretical underpinnings was gradual and continues to be refined, although its standing as a peer of other scientific disciplines has for some time now been assured.

The societal impact of toxicology lends it a layer of practical relevance that not every science can claim. Given that we cannot avoid interacting with xenobiotics on a daily basis, toxicology is, in a sense, integral to our lives. News reports of toxicological incidents continue to fascinate and alarm. The media regularly reminds us of old and ongoing, or new and emerging, concerns to broad segments of the population, be it the exposure of inner-city residents, particularly children, to lead exposure, the scourge of tobacco and smoking (and now new potential dangers of vaping), human and animal food poisoning, the health effects of pesticides on homeowners, applicators, and their families, or the bourgeoning opioid crisis. Individual incidents whether high profile cases cloaked in intrigue such as the nerve agent poisonings of four people in Britain, victims of a suspected Russian assassination attempt, or the average (perhaps not quite average) Virginia man who pleaded guilty to attempting to kill his 95-year-old mother-in-law by spiking her coffee with methamphetamine, easily grab world and local headlines.

On the scale of the wider environment, chemicals are ubiquitous and adamant in their refusal to respect geographic boundaries. Developing countries with bourgeoning economies are fueling much of this pollution, compromising the health of their citizens and people at a distance. And yet asking the developing world to eschew rapid economic progress in favor of a paced and sustainable approach for the benefit of the Earth and future generations, requires discussion, diplomacy, compromise, and patience. While piecemeal efforts are being made around the globe to limit greenhouse gas emissions and otherwise rein in chemical releases, there is no international coordinated approach available, although the United Nations' Paris Agreement, ratified by 185 Parties as of April, 2019 is a

start. Much work remains to be done. Those who ignore the reality of global climate change do so at the peril of the Earth and civilization.

The current 5th edition's (IRT-5) overall structure and goals adhere closely to those established in the previous four editions. The intent remains to provide an extensive annotated bibliography and sourcebook to information in toxicology, a compilation of references to key documents, organizations, and other resources. The extent to which digital versions of these resources, either complementing or replacing traditional paper formats, has expanded, is considerable. It becomes an ever greater challenge to encompass the diversity and multiple nodes of toxicology within a single publication such as this one. However, the editors felt that despite the pervasiveness of information on the Internet, its search capabilities, and free availability, there were still significant advantages to a structured compendium, avoiding much of the extraneous information widely scattered on the Web, and focusing on the relevant, regardless of format. For some, hard copy books, remain the reference tool of choice, even today. But IRT-5's availability on Science Direct gives readers Elsevier's comfortable with the digital environment, the option of also navigating and searching the book's content in an online environment.

IRT-5 also benefits from being a highly curated work. The resources have been selected by six editors and well over 100 authors, prominent leaders in toxicology with expertise in the various topical and geographical areas represented in the chapters. Readers can feel confident that the resources here have not been indiscriminately thrown together but selected for quality and organized to facilitate efficient retrieval.

The dual stream of advances in the science of toxicology itself and in the information technology to assist in its research and deliver its results has resulted in an array of new tools for generating, capturing, organizing, and disseminating data. These Web tools and resources have been extensively covered in this new edition.

Toxicology's forward scientific advance has resulted in the blossoming of a host of new areas ripe for **XXIV** Preface

further investigation. Emerging subjects, such as "-omics" (including transcriptomics), nanotechnology, high-throughput screening, predictive modeling, alternative test systems, utilizing new biochemical reactivity assays, humans on a chip, etc., are joined with new perspectives on issues rooted in the past (e.g., chemical and biological warfare, animal welfare, effects of mixtures, risk assessment, ethical concerns). The Tox21 initiative (Toxicology in the 21st Century), for example, is a US federal research collaboration aimed at developing methods to rapidly and efficiently evaluate the safety of commercial chemicals, pesticides, food additives and contaminants, and medical products. The US Environmental Protection Agency, the National Toxicology Program, the National Center for Advancing Translational Sciences, and the Food and Drug Administration constitute the consortium which formed Tox 21.

And who can tell what the implications will be of other cutting edge and still to come technologies such as robotics. To what extent, for example, will drones help us monitor and perhaps neutralize carbon emissions and other sources of pollution. Or, for that matter, the recent creation of the world's first 3D printed heart using human tissue may offer a new approach to noninvasively testing toxic agents on human organs.

Although the focus of toxicology has always been on chemicals, the scope of each edition of IRT, including this one, has included biological and physical agents, particularly radiation, since their potentially hazardous effects are widespread and part and parcel of the science.

The online Web environment is now an inevitable part of the professional and personal lives of most of us in the developed world, and remote and economically deprived regions are catching up

quickly. Google, Wikipedia, blogs, online social networking, virtual environments, and 5G networks, have entered our daily vocabulary and lives, and offer ever more novel approaches to make sense of raw, sprawling information, offering ways to make it find just what we are looking for whenever, wherever. Toxicology has benefited from these technologies.

IRT-5 also continues the tradition of being as globally encompassing as practicable. We have included virtually all the countries from the 4th edition plus added over a dozen more, highlighting their most significant toxicological information resources. A separate chapter looks at multilateral activities, including international conventions and initiatives relevant to the science.

Thanks are due, foremost, to my five Associate Editors, Sol Bobst, Steve Gilbert, Toni Hayes, Sara Humes, and Asish Mohapatra. Their unparalleled knowledge of the science and significance of toxicology and its information infrastructure proved invaluable. Our overlapping networks of well-informed colleagues from whose ranks we drew chapter contributors, and our ability to work well together, made the creation of this book a smooth and enjoyable process. And, of course, our many contributors, among whom the above editors are also included, form both the backbone of the book and the cement which holds it together.

Additional acknowledgment and praise is due to Kattie Washington, Megan Ashdown, and Punithavathy Govindaradjane, our Acquisitions, Developmental, and Production Editors respectively, and other staff on down the Elsevier line, for recognizing the value of a 5th edition, nudging it through its amorphous beginning and helping it solidify into a well-designed whole.

Editor-in-Chief **Philip Wexler**

1

Overview of international activities

Jens Küllmer and Ulrich Schlottmann

Federal Ministry for the Environment, Nature Conservation and Nuclear Safety, Bonn, Germany

The risks connected with chemical substances have been assessed in a number of conventions that have aimed to apply restrictions on the use of dangerous chemicals, and control of their worldwide trade. The developments in chemicals policy at the European and world level are discussed, with an insight into the interlaced structure of international cooperation that exists at both the political and the technical level.

Introduction

The industrialization that the world has achieved in the past 200 years is inextricably connected with the production and use of chemicals. According to OECD estimates, sales are twice as high as in the telecommunications sector. Chemical products have undoubtedly contributed to a substantial improvement in the quality of life. Plastics, surfactants, and a large number of basic chemicals are improving the medical and hygienic situation worldwide. However, numerous toxic substances present risks and hazards that occur during the entire life cycle of a substance: during production, during transport and trade, and during storage, use, and disposal. Awareness of environmental and health risks has grown over the last 20 years. Today this is making itself felt in an increasingly complex set of international regulations on chemical safety. The focus is increasingly shifting toward the developing countries and their populations, as people there are less aware of the risks and hazards than those in the industrialized countries. Today the worldwide spread of persistent, bioaccumulating, and toxic chemicals by air or water, their occurrence in places where they are not used, and the destruction of the ozone layer are making it clear to everyone that chemical safety is an international challenge and not just an empty phrase. But it should not be necessary for risks arising from chemicals to assume international dimensions before action is taken. That is why national or European regulations provide an appropriate framework for a large number of chemicals. Moreover, national laws and European Community (EC) legislation are enforceable law. Compliance with this law is monitored, while noncompliance is prosecuted and punished.

International activities

Protocols and conventions

The Montreal Protocol

The gaps in the ozone layer over the polar region present a threat to humans, animals, and plants, because of the increase in UV-B radiation reaching the surface of the earth.

This natural protective shield has been damaged by the worldwide use of ozone-depleting substances (ODS), such as chlorofluorocarbons (CFCs) and halons, which are used for fire protection materials. The Montreal Protocol (MP) is the international contractual basis for the United Nations worldwide program for discontinuing the use of ODS. The year 2017 marks an important milestone for the MP: it is the 30th anniversary of the treaty's signature. It is thus an opportune time to reflect on why the MP is well on its way to achieving its goals.

Thirty years ago, 46 countries undertook to stop producing and using substances that were damaging to the ozone layer. In the meantime 191 countries have signed this protocol. The signatory states are responsible for a total of over 90% of the consumption of these substances. The original target (from 1987) of halving

the consumption of CFCs by the year 2000 has since been raised considerably on a number of occasions in light of the alarming reports on the status of the ozone layer. For example, the production of CFCs in the industrialized countries was discontinued at the beginning of 1996. The amendment to the MP that was passed in Peking in 1999 states that from 2002 onward the production and use of the substance bromochloromethane, which can be used as a solvent and fire extinguisher, is to be totally banned in the signatory states. This amendment and the treaty modifications adopted at the same meeting were transposed into European law by decree of the EC Council. It follows from the reasons given for this decision that additional steps must be taken to monitor trade in ODS, especially partially halogenated CFCs and new substances. Methyl bromide remained unnoticed by the public for a very long time; this is despite the fact that one atom of bromine destroys 80 times more ozone than a chlorine atom (Zellner, 2001). Thus the bromine content of a compound such as methyl bromide is more reactive and has a greater impact on stratospheric ozone than the chlorine content of CFCs. This pesticide has nevertheless been in use for decades as a preferred means of treating arable land. In Germany its use in the agricultural sector was banned in 1982 owing to its harmful effects on the groundwater. Since then most of the industrialized countries have banned the use of methyl bromide. Under the MP, the United States agreed a ban on methyl bromide in 2005 and the developing countries by 2015.

The MP is closely linked to the Convention on Climate Change (Kyoto Protocol, into force since February 2005). The climate protection already achieved by the MP is far larger than the reduction target of the first commitment period of the Kyoto Protocol (Velders et al., 2007). Additional climate benefits that are significant compared with the Kyoto Protocol reduction target could be achieved by actions under the MP, by managing the emissions of substitute fluorocarbon gases and/or implementing alternative gases with lower global warming potentials (http://www.uneptie.org/ozonaction).

The Stockholm Convention (POPs)

The POPs Convention implements international prohibition and restriction measures with regard to certain persistent organic pollutants (POPs). The core of the Convention is that 12 particularly dangerous POPs for the environment are to be prohibited or reduced until they are totally eliminated. The dynamic design of the rules of the Convention allows the original POPs substances to be joined by further substances that meet the four criteria of persistency,

bioaccumulation, long-range transport potential, and harmful properties. The POPs Convention prohibits the following chemicals: aldrin, dieldrin, endrin, chlordane, mirex, toxaphene, heptachlor, hexachlorobenzene, di(para-chlorophenyl), trichloroethane (DDT), polychlorinated biphenyls (PCBs), polychlorinateddibenzodioxins, and polychlorinated dibenzofurans. With the exception of DDT, which may still be produced and used on a country-specific basis for combating malaria, and of unwanted by-products, all other substances are listed in the Appendix (Appendix A) to the Convention, which regulates the phasing out of the production and use of these substances. The production and use of DDT for vector control will remain necessary until inexpensive alternatives become available. The relevant countries must inform the United Nations Environment Program (UNEP) on Chemicals and the World Health Organization (WHO) about the use of DDT. The Secretariat, in cooperation with WHO, holds reviews periodically to gather information about the amounts of DDT used by Parties, the conditions of such use and its relevance to that Party disease management strategy. The use of DDT as a pesticide in the agricultural sector is however prohibited.

In May 2001 the signatory conference for the POPs Convention took place in Stockholm. The Convention entered into force once it had been ratified by 50 countries. This was the case on May 17, 2004. Up to November 2018 there had been 182 ratifications. April 2004 saw the introduction of Regulation (EC) No. 850/2004 of the European Parliament and the Council on POPs (http://www.pops.int).

The Rotterdam Convention (PIC)

According to estimates by the World Health Organization (WHO), about one million accidents each year are caused worldwide through poisoning from pesticides. The worldwide trade in dangerous chemicals is merely the beginning of the life cycle of a chemical; it is followed by storage, use, and the disposal of residual stocks. That is why steps should be taken as early as the trade stage to ensure that dangerous chemicals do not adversely affect man and the environapplies particularly to developing ment. countries, most of which are today suffering from the effects of incorrect usage. For this reason, a meeting of the International Community of States in Rotterdam in 1998 decided to adopt a convention defining binding rules for the trade in dangerous chemicals (PIC Convention). In accordance with the precautionary principle, this convention allows states to impose a ban on imports before a chemical is imported. This does not prohibit trade in chemicals, but makes International activities 3

it subject to very stringent rules, namely the "PIC procedure," where PIC stands for "prior informed consent." In the context of imports, this means that the potential importing country must be informed about the chemical and take a decision before the chemical is actually imported.

The Convention covers pesticides and industrial chemicals that have been banned or severely restricted for health or environmental reasons by Parties and which have been notified by Parties for inclusion in the PIC procedure. One notification from each of two specified regions triggers consideration of addition of a chemical to Annex III of the Convention. Severely hazardous pesticide formulations that present a hazard under conditions of use in developing countries or countries with economies in transition may also be nominated for inclusion in Annex III. There are 39 chemicals listed in Annex III of the Convention and subject to the PIC procedure, including 24 pesticides, four severely hazardous pesticide formulations, and 11 industrial chemicals. Many more chemicals are expected to be added in the future. The Conference of the Parties decides on the inclusion of new chemicals. Once a chemical is included in Annex III, a "decision guidance document" containing information concerning the chemical and the regulatory decisions to ban or severely restrict the chemical for health or environmental reasons is circulated to all Parties. Parties have 9 months to prepare a response concerning the future import of the chemical. The response can consist of either a final decision (to allow import of the chemical, not to allow import, or to allow import subject to specified conditions) or an interim response. Decisions by an importing country must be trade neutral (i.e., apply equally to domestic production for domestic use as well as to imports from any source). The import decisions are circulated and exporting country Parties are obligated under the Convention to take appropriate measure to ensure that exporters within its jurisdiction comply with the decisions.

The Convention promotes the exchange of information on a very broad range of chemicals, through:

- requirement for a Party to inform other Parties of each national ban or severe restriction of a chemical;
- possibility for Party which is a developing country or a country in transition to inform other Parties that it is experiencing problems caused by a severely hazardous pesticide formulation under conditions of use in its territory;
- requirement for a Party that plans to export a chemical that is banned or severely restricted for use within its territory to inform the importing

Party that such export will take place, before the first shipment and annually thereafter;

- requirement for an exporting Party, when exporting chemicals that are to be used for occupational purposes, to ensure that an up-to-date safety data sheet is sent to the importer; and
- labeling requirements for exports of chemicals included in the PIC procedure, as well as for other chemicals that are banned or severely restricted in the exporting country.

The text of the Convention was adopted on September 10, 1998, by a Conference of Plenipotentiaries in Rotterdam, the Netherlands. The Convention entered into force on February 24, 2004, once it had been ratified by 50 countries. Up to date (November 2018) there are 160 ratifications.

Spring 2003 saw the introduction of Regulation (EC) No. 304/2003 of the European Parliament and the Council on the Export and Import of Dangerous Chemicals. This superseded the existing Council Regulation (EEC) No. 2455/92 (July 1992) concerning the Export and Import of Certain Dangerous Chemicals. No reductions were to be made in the level of environmental and health protection in the importing countries. In order to achieve this goal, some of the provisions go beyond those of the PIC Convention. This conforms with Article 15, Paragraph 4 of the PIC Convention, which states that the contracting parties may take measures that provide more stringent protection for human health and the environment than laid down in the Convention, provided these measures are compatible with the Convention and with international law. The EC also considered it advantageous in terms of practicability that there should be a single agency responsible for contact between the EC, the PIC Secretariat, other contracting parties, and other countries. The Commission has assumed the function of the point of contact for this purpose. Exports of dangerous chemicals that are prohibited in the Community or subject to strict restrictions continue to be subject to a joint export notification procedure. In the case of imports, the EC must take decisions before the importation of chemicals that are subject to the international PIC procedure is allowed. The fact that exporters and importers are obliged to furnish information on the quantities of chemicals in international trade that are covered by this Regulation makes for better monitoring and assessment of the impacts and effectiveness of this Regulation (http://www.pic.int).

The Basel Convention

The cross-border transport of hazardous wastes seized the public's attention in the 1980s after

misadventures of "toxic ships" sailing from port to port trying to offload the poisonous cargoes.

The Basel Convention regulates the transboundary movements of hazardous and other wastes, applying the "Prior Informed Consent" procedure. Shipments to and from non-Parties are illegal unless there is a special agreement. Each Party is required to introduce appropriate national or domestic legislation to prevent and punish illegal traffic in hazardous and other wastes. The Convention obliges its Parties to ensure that hazardous and other wastes are managed and disposed of in an environmentally sound manner. Therefore Parties are expected to minimize the quantities that are moved across borders, to treat and dispose of wastes as close as possible to their place of generation, and to prevent or minimize the generation of wastes at source. Strong controls have to be applied from the movement of generation of hazardous waste to its storage, transport, treatment, reuse, recycling, recovery, and final disposal. Recently the Basel Conventions handled issues like electronic and electrical wastes (e-waste), mercury and asbestos wastes, and illegal dumping of hazardous wastes. The Convention entered into force May 5, 1992. Up to November 2018 there had been 186 ratifications. For more information: https://www.basel.int.

The Aarhus Convention

The United Nations Economic Commission for (UNECE) Convention on Access Information, Public Participation in Decision-Making and Access to Justice in Environmental Matters was adopted on June 25, 1998, in the Danish city of Aarhus at the Fourth Ministerial Conference as part of the "Environment for Europe" process. It entered into force on October 30, 2001. The Convention establishes a number of rights of the public (individuals and their associations) with regard to the environment. It provides for the right of everyone to receive environmental information that is held by public authorities, to participate in environmental decision-making, and the right to review procedures to challenge public decisions that have been made.

Autumn 2006 saw the introduction of Regulation (EC) No. 1367/2006 of the European Parliament and the Council on the application of the provisions of the Aarhus Convention in Environmental Matters to Community institutions and bodies. Bodies, offices or agencies established by, or on the basis of the EC Treaty, had to adapt their internal procedures and practices to the provisions of the Regulation until June 28, 2007. For more information: https://www.unece.org/env/pp/introduction.html.

The Minamata Convention on Mercury

The Minamata Convention provides that it shall enter into force on the 90th day after the date of deposit of the 50th instrument of ratification, acceptance, approval, or accession. That milestone was reached on May 18, 2017, allowing the Convention to enter into force on August 16, 2017, once it had been ratified by 50 countries. Up to November 2018 there had been 101 ratifications.

For more information: http://www.mercuryconvention.org.

Intergovernmental forums and activities

The Stockholm Conference

The Stockholm Conference, held June 5–16, 1972, in Stockholm, environmental was an watershed (Engfeldt, 2002). The Conference adopted recommendations for action at the international level. As a result of the Conference, environment ministries and agencies were established in more than 100 countries, a key requirement for carrying forth the results of the Conference. It also marked the beginning of the explosive increase in nongovernmental and intergovernmental organizations dedicated to environmental preservation. The United Nations Environment Program (UNEP) was established.

The Declaration and the Action Plan of Stockholm have been particularly instrumental in the rapid development of international environmental law.

The United Nations Conference on Environment and Development

The first Conference on Environment and Development (UNCED) was held in Rio de Janeiro in 1992, in which the positive experiences of the MP were maintained. Numerous heads of state and heads of government approved Chapter 19 of Agenda 21, which sets out details of the principles for internationally effective chemical safety. This chapter contains objectives for environmentally sound handling and use of chemicals, including measures to prevent illegal international trade in toxic and dangerous products. An important point is the intensification of international cooperation and the coordination of ongoing international and regional activities (www.un.org/geninfo/bp/enviro.html).

The World Summit on Sustainable Development

Ten years after the conference in Rio de Janeiro (UNCED), the World Summit for Sustainable Development (WSSD) in Johannesburg ended with the approval of the declaration tabled by South