CHEMICAL MIXTURES





CHEMICAL MIXTURES





Chemical mixtures in source water and drinking-water

ISBN 978-92-4-151237-4

© World Health Organization 2017

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; https://creativecommons.org/licenses/by-nc-sa/3.0/igo).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization.

Suggested citation. Chemical mixtures in source water and drinking-water. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

Sales, rights and licensing. To purchase WHO publications, see http://apps.who.int/bookorders. To submit requests for commercial use and queries on rights and licensing, see http://www.who.int/about/licensing.

Third-party materials. If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

General disclaimers. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO be liable for damages arising from its use.

Design and layout by Paprika, Annecy, France.

Printed by the WHO Document Production Services, Geneva, Switzerland.

CONTENTS

GLOSSARY OF TERMINOLOGY, ACRONYMS AND ABBREVIATIONS	V
ACKNOWLEDGEMENTS	XIII
EXECUTIVE SUMMARY	XV
1. HUMAN EXPOSURE TO CHEMICAL MIXTURES IN SOURCE WATER AND DRINKING-WATER	1
1.1 INTRODUCTION	2
1.2 OCCURRENCE OF CHEMICALS IN SOURCE WATERS AND DRINKING-WATERS	3
1.3 CONCLUSIONS	4
2. APPROACHES FOR ASSESSING THE RISK OF CHEMICAL MIXTURES	5
2.1 INTRODUCTION	6
2.2 CHEMICAL INTERACTIONS AND THE ROLE OF MODES OF ACTION	6
2.2.1 Chemicals with similar modes of action	6
2.2.2 Chemicals with dissimilar modes of action	6
2.2.3 Interactive chemicals	7
2.3 THE WHO/IPCS RISK ASSESSMENT FRAMEWORK	7
2.3.1 Problem formulation	<u>C</u>
2.3.2 Framework tiered structure	11
2.3.3 Data-filling tools for use with the framework	12
2.3.4 Models for use with the framework	12
2.4 CONCLUSIONS	13
3. CONSIDERATIONS FOR THE APPLICATION OF THE WHO/IPCS RISK ASSESSMENT FRAMEWORK FOR CHEMICAL MIXTURES IN SOURCE WATER AND DRINKING-WATER	15
3.1 INTRODUCTION	16
3.2 TIER 0 RISK ASSESSMENT	16
3.2.1 Exposure assessment	16
3.2.2 Hazard assessment	17
3.2.3 Risk characterization	17
3.3 TIER 1 RISK ASSESSMENT	17
3.3.1 Exposure assessment	17
3.3.2 Hazard assessment	17

	3.3.3 Risk characterization	17
	3.4 TIER 2 RISK ASSESSMENT	18
	3.4.1 Exposure assessment	18
	3.4.2 Hazard assessment	18
	3.4.3 Risk characterization	18
	3.5 TIER 3 RISK ASSESSMENT	18
	3.5.1 Exposure assessment	18
	3.5.2 Hazard assessment	18
	3.5.3 Risk characterization	18
	3.6 CASE STUDIES ILLUSTRATING USE OF THE WHO/IPCS FRAMEWORK	19
	3.6.1 Assessment of risk to human health from exposure to pharmaceuticals in drinking-water	er19
	3.6.2 Assessment of risk to human health from exposure to microcystins in drinking-water	20
	3.6.3 Selecting pesticides for consideration in HIs on the basis of risk ranking and detection frequency	20
	3.6.4 Assessment of risk to human health from exposure to natural and synthetic oestrogens in drinking-water	
	3.6.5 Assessment of risk to human health from exposure N-methyl carbamate (NMC) insecticide residues in foods	21
	3.7 CONCLUSIONS	22
	WATER AND DRINKING-WATER (1 CONSIDERATIONS WHEN ASSESSING THE DISKS	23
	4.1 CONSIDERATIONS WHEN ASSESSING THE RISKS	24
	4.2 CONSIDERATIONS WHEN MANAGING THE RISKS	25
	4.3 KNOWLEDGE GAPS AND FUTURE RESEARCH NEEDS	26
	4.4 CONCLUSIONS	26
R	EFERENCES	29
A	PPENDIX 1: RATIONALES FOR CONSIDERING COMPOUNDS IN AN ASSESSMENT GROUP AND DATA-FILLING TOOLS	35
	A1.1 CATEGORY APPROACH	36
	A1.2 ANALOGUE APPROACH	36
	A1.3 DATA-FILLING TOOLS	37
	A1.3.1 Read-across	37
	A1.3.2 Trend analysis	37
	A1.3.3 QSARs	37
	A1.3.4 TTC approach	37

A1.3.5 Physiologically-based toxicokinetics (PBTK) and toxicodynamics (PBTD)	38
REFERENCES	38
APPENDIX 2: AVAILABLE TOOLS FOR USE WITH THE WHO/IPCS FRAMEWORK	41
A2.1 WHOLE-MIXTURE APPROACHES	42
A2.2 COMPONENT-BASED APPROACHES	42
A2.2.1 Models for chemicals with similar modes of action	42
A2.2.2 Models for chemicals with dissimilar modes of action	44
REFERENCES	48
APPENDIX 3: DETAILED CASE STUDY FOR THE USE OF THE WHO/IPCS FRAMEWORK TO ASSESS RISK TO HUMAN HEALTH FROM EXPOSURE TO PHARMACEUTICALS IN DRINKING-WATER APPENDIX 4: DETAILED CASE STUDY FOR THE USE OF THE WHO/IPCS FRAMEWORK TO ASSESS RISK TO HUMAN HEALTH FROM EXPOSURE TO MICROCYSTINS IN DRINKING-WATER	51
APPENDIX 5: DETAILED CASE STUDY FOR THE USE OF THE WHO/IPCS FRAMEWORK TO SELECT PESTICIDES FOR CONSIDERATION IN HAZARD INDICES ON THE BASIS OF RISK RANKING AND DETECTION FREQUENCY	63
APPENDIX 6: DETAILED CASE STUDY FOR THE USE OF THE WHO/IPCS FRAMEWORK TO ASSESS RISK TO HUMAN HEALTH FROM EXPOSURE TO NATURAL AND SYNTHETIC OESTROGENS IN DRINKING-WATER	67
APPENDIX 7: DETAILED CASE STUDY FOR THE USE OF THE WHO/IPCS FRAMEWORK TO ASSESS RISK TO HUMAN HEALTH FROM EXPOSURE TO N-METHYL CARBAMATE INSECTICIDES IN FOODS	73

GLOSSARY OF TERMINOLOGY, ACRONYMS AND ABBREVIATIONS

A lack of common terminology across governmental and industrial sectors is one of the recognised barriers currently impeding the harmonization of methods to assess and manage the risk associated with combined exposure to multiple chemicals. The World Health Organization – International Programme on Chemical Safety (WHO/IPCS) framework, described in detail in this document, adopts an explicit descriptive terminology as a means to increase understanding of relevant terms and to facilitate harmonization of multiple chemical risk assessment methodologies (WHO, 2009; Meek et al., 2011; Meek, 2013).

The following table summarises the descriptive terminology and associated definitions used throughout this document, and are those described or adapted from key documents from USEPA, 2000; ECETOC, 2002; EFSA, 2008; IGHRC, 2009; WHO, 2009; Meek et al., 2011; Meek, 2013; EFSA, 2013. These definitions may differ from definitions used in different jurisdictions (e.g. cumulative exposure). Of importance to note is that the framework described in this document addresses combined exposure to multiple chemicals (abbreviated to 'chemical mixtures' throughout).

GLOSSARY

Acceptable daily intake (ADI)

Additivity

Estimated maximum amount of an agent, expressed on a body mass basis, to which individuals in a (sub)population may be exposed, by all routes, daily over their lifetimes without appreciable health risk. The ADI is expressed in milligrams of the chemical per kilogram of body weight (the default assumption of bodyweight by WHO is 60 kg).

Dose additivity is applied in the case of chemicals in a mixture that act by the same mode of action and/or at the same target cell, tissue or organ and differ only in their potencies. Commonly used dose-additive methods include the hazard index (HI) approach (sum of the ratios of exposure of each component to a health endpoint – see HI method) and two index chemical approaches (sum of the doses of each mixture component that can induce the same response/effect, if appropriate scaled by their toxic potency relative to the index chemical; see relative potency factor - RPF and toxic equivalency factor - TEF methods).

Response additivity is applied in the case of chemicals that act via independent modes of action to elicit the same response. The toxic response (rate, incidence, risk or probability of effects) from the combination is equal to the conditional sum of component responses as defined by the formula for the sum of independent event probabilities.

预览已结束, 完整报告链接和二维码如下:

https://www.yunbaogao.cn/report/index/report?reportId=5 26371

