



IARC MONOGRAPHS

# TRICHLOROETHYLENE, TETRACHLOROETHYLENE, AND SOME OTHER CHLORINATED AGENTS

VOLUME 106

This publication represents the views and expert  
opinions of an IARC Working Group on the  
Evaluation of Carcinogenic Risks to Humans,  
which met in Lyon, 2-9 October 2012

LYON, FRANCE - 2014

IARC MONOGRAPHS  
ON THE EVALUATION  
OF CARCINOGENIC RISKS  
TO HUMANS

International Agency for Research on Cancer



# CONTENTS

---

NOTE TO THE READER.....	1
LIST OF PARTICIPANTS.....	3
<b>PREAMBLE.....</b>	<b>7</b>
A. GENERAL PRINCIPLES AND PROCEDURES .....	7
1. Background.....	7
2. Objective and scope.....	8
3. Selection of agents for review .....	9
4. Data for the <i>Monographs</i> .....	9
5. Meeting participants .....	10
6. Working procedures.....	11
B. SCIENTIFIC REVIEW AND EVALUATION .....	12
1. Exposure data.....	13
2. Studies of cancer in humans .....	14
3. Studies of cancer in experimental animals.....	18
4. Mechanistic and other relevant data.....	21
5. Summary .....	24
6. Evaluation and rationale.....	25
References.....	29
<b>GENERAL REMARKS .....</b>	<b>31</b>
<b>TRICHLOROETHYLENE.....</b>	<b>35</b>
1. Exposure Data .....	35
1.1 Identification of the agent .....	35
1.2 Production and use .....	37
1.3 Occurrence and exposure .....	40
1.4 Regulations and guidelines .....	48
2. Cancer in Humans .....	48
2.1 Introduction .....	48
2.2 Cohort studies .....	49
2.3 Case-control studies .....	72
2.4 Ecological studies .....	92
2.5 Meta-analyses and pooled analyses .....	95

3. Cancer in Experimental Animals .....	97
3.1 Mouse .....	98
3.2 Rat .....	112
3.3 Hamster .....	117
3.4 Administration with known carcinogens or other modifying factors .....	117
3.5 Effects of stabilizers .....	118
3.6 Carcinogenicity of metabolites .....	118
4. Mechanistic and Other Relevant Data .....	119
4.1 Toxicokinetic data .....	119
4.2 Genotoxicity and related effects .....	127
4.3 Non-genotoxic mechanisms of carcinogenesis .....	149
4.4 Susceptibility data .....	164
4.5 Other adverse effects .....	169
5. Summary of Data Reported .....	184
5.1 Exposure data .....	184
5.2 Human carcinogenicity data .....	184
5.3 Animal carcinogenicity data .....	186
5.4 Mechanistic and other relevant data .....	187
6. Evaluation .....	189
6.1 Cancer in humans .....	189
6.2 Cancer in experimental animals .....	189
6.3 Overall evaluation .....	189
6.4 Rationale .....	189
References .....	189
 <b>TETRACHLOROETHYLENE.....</b>	 <b>219</b>
1. Exposure Data .....	219
1.1 Identification of the agent .....	219
1.2 Production and use .....	220
1.3 Occurrence and exposure .....	222
1.4 Regulations and guidelines .....	234
2. Cancer in Humans .....	234
2.1 Cohort studies .....	238
2.2 Case-control studies .....	249
2.3 Ecological studies .....	271
2.4 Meta-analyses .....	272
3. Cancer in Experimental Animals .....	272
3.1 Mouse .....	272
3.2 Rat .....	277
3.3 Studies with mixtures of solvents .....	279
3.4 Initiation-promotion studies .....	279
3.5 Carcinogenicity of metabolites .....	279

---

4. Mechanistic and Other Relevant Data .....	280
4.1 Toxicokinetic data .....	280
4.2 Genotoxicity and related effects .....	292
4.3 Non-genotoxic effects and organ toxicity .....	301
4.4 Susceptibility .....	320
4.5 Mechanistic considerations .....	322
5. Summary of Data Reported .....	325
5.1 Exposure data .....	325
5.2 Human carcinogenicity data .....	326
5.3 Animal carcinogenicity data .....	327
5.4 Mechanistic and other relevant data .....	328
6. Evaluation .....	329
6.1 Cancer in humans .....	329
6.2 Cancer in experimental animals .....	329
6.3 Overall evaluation .....	329
References .....	329
<b>DICHLOROACETIC ACID.....</b>	<b>353</b>
1. Exposure Data .....	353
1.1 Identification of the agent .....	353
1.2 Production and use .....	355
1.3 Occurrence and exposure .....	355
1.4 Regulations and guidelines .....	357
2. Cancer in Humans .....	357
3. Cancer in Experimental Animals .....	357
3.1 Mouse .....	357
3.2 Rat .....	365
3.3 Co-administration with known carcinogens or other modifying factors .....	366
4. Mechanistic and Other Relevant Data .....	368
4.1 Absorption, distribution, metabolism, and excretion .....	368
4.2 Genotoxicity and related effects .....	368
4.3 Non-genotoxic mechanisms of carcinogenesis .....	375
4.4 Susceptibility data .....	381
4.5 Mechanistic considerations .....	383
5. Summary of Data Reported .....	385
5.1 Exposure data .....	385
5.2 Human carcinogenicity data .....	385
5.3 Animal carcinogenicity data .....	385
5.4 Mechanistic and other relevant data .....	385
6. Evaluation .....	386
6.1 Cancer in humans .....	386
6.2 Cancer in experimental animals .....	386
6.3 Overall evaluation .....	386
References .....	386

<b>TRICHLOROACETIC ACID .....</b>	<b>393</b>
1. Exposure Data .....	393
1.1 Chemical and physical data .....	393
1.2 Production and use .....	394
1.3 Occurrence .....	396
1.4 Regulations and guidelines .....	401
2. Cancer in Humans .....	401
3. Cancer in Experimental Animals .....	401
3.1 Mouse .....	402
3.2 Rat .....	406
3.3 Administration with known carcinogens or other modifying factors .....	406
4. Mechanistic and Other Relevant Data .....	407
4.1 Absorption, distribution, metabolism, and excretion .....	407
4.2 Genotoxicity and related effects .....	413
4.3 Nongenotoxic mechanisms of carcinogenesis .....	416
4.4 Susceptibility data .....	426
4.5 Mechanistic considerations .....	428
5. Summary of Data Reported .....	429
5.1 Exposure data .....	429
5.2 Human carcinogenicity data .....	429
5.3 Animal carcinogenicity data .....	429
5.4 Mechanistic and other relevant data .....	429
6. Evaluation .....	430
6.1 Cancer in humans .....	430
6.2 Cancer in experimental animals .....	430
6.3 Overall evaluation .....	430
References .....	430
<b>CHLORAL AND CHLORAL HYDRATE .....</b>	<b>439</b>
1. Exposure Data .....	439
1.1 Chemical and physical data .....	439
1.2 Production and use .....	441
1.3 Occurrence and exposure .....	442
1.4 Regulations and guidelines .....	443
2. Cancer in Humans .....	443
3. Cancer in Experimental Animals .....	444
3.1 Mouse .....	444
3.2 Rat .....	448
4. Mechanistic and Other Relevant Data .....	448
4.1 Toxicokinetic data .....	448
4.2 Genotoxicity and related effects .....	452
4.3 Non-genotoxic mechanisms of carcinogenesis .....	462

---

4.4 Susceptibility data .....	463
4.5 Toxic non-cancer effects .....	464
4.6 Synthesis of mechanistic considerations.....	465
5. Summary of Data Reported .....	466
5.1 Exposure data.....	466
5.2 Human carcinogenicity data.....	466
5.3 Animal carcinogenicity data.....	466
5.4 Mechanistic and other relevant data.....	467
6. Evaluation.....	467
6.1 Cancer in humans.....	467
6.2 Cancer in experimental animals.....	467
6.3 Overall evaluation .....	467
6.4 Rationale .....	468
References .....	468
<b>1,1,1,2-TETRACHLOROETHANE .....</b>	<b>475</b>
1. Exposure Data.....	475
1.1 Identification of the agent .....	475
1.2 Production and use .....	476
1.3 Occurrence and exposure.....	477
1.4 Regulations and guidelines .....	477
2. Cancer in Humans .....	477
3. Cancer in Experimental Animals .....	477
3.1 Mouse .....	479
3.2 Rat .....	479
4. Mechanistic and Other Relevant Data .....	479
4.1 Absorption, distribution, metabolism and excretion.....	479
4.2 Genotoxicity and related effects .....	482
4.3 Nongenotoxic mechanisms of carcinogenesis .....	485
4.4 Susceptibility .....	486
4.5 Synthesis of mechanistic considerations.....	486
5. Summary of Data Reported .....	486
5.1 Exposure data.....	486
5.2 Human carcinogenicity data.....	486
5.3 Animal carcinogenicity data.....	486
5.4 Mechanistic and other relevant data.....	487
6. Evaluation.....	487
6.1 Cancer in humans.....	487
6.2 Cancer in experimental animals.....	487
6.3 Overall evaluation .....	487
References .....	487

<b>1,1,2,2-TETRACHLOROETHANE .....</b>	<b>491</b>
1. Exposure Data .....	491
1.1 Identification of the agent .....	491
1.2 Production and use .....	492
1.3 Occurrence .....	493
1.4 Regulations and guidelines .....	495
2. Cancer in Humans .....	495
3. Cancer in Experimental Animals .....	495
3.1 Mouse .....	495
3.2 Rat .....	497
4. Mechanistic and Other Relevant Data .....	498
4.1 Absorption, distribution, metabolism and excretion .....	498
4.2 Genotoxicity and related effects .....	502
4.3 Nongenotoxic mechanisms of carcinogenesis .....	506
4.4 Other adverse effects .....	507
4.5 Mechanistic considerations .....	507
5. Summary of Data Reported .....	508
5.1 Exposure data .....	508
5.2 Human carcinogenicity data .....	508
5.3 Animal carcinogenicity data .....	508
5.4 Mechanistic and other relevant data .....	508
6. Evaluation .....	508
6.1 Cancer in humans .....	508
6.2 Cancer in experimental animals .....	509
6.3 Overall evaluation .....	509
References .....	509
<b>LIST OF ABBREVIATIONS .....</b>	<b>513</b>

## **NOTE TO THE READER**

---

The term ‘carcinogenic risk’ in the *IARC Monographs* series is taken to mean that an agent is capable of causing cancer. The *Monographs* evaluate cancer hazards, despite the historical presence of the word ‘risks’ in the title.

Inclusion of an agent in the *Monographs* does not imply that it is a carcinogen, only that the published data have been examined. Equally, the fact that an agent has not yet been evaluated in a *Monograph* does not mean that it is not carcinogenic. Similarly, identification of cancer sites with *sufficient evidence* or *limited evidence* in humans should not be viewed as precluding the possibility that an agent may cause cancer at other sites.

The evaluations of carcinogenic risk are made by international working groups of independent scientists and are qualitative in nature. No recommendation is given for regulation or legislation.

Anyone who is aware of published data that may alter the evaluation of the carcinogenic risk of an agent to humans is encouraged to make this information available to the Section of IARC Monographs, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France, in order that the agent may be considered for re-evaluation by a future Working Group.

Although every effort is made to prepare the *Monographs* as accurately as possible, mistakes may occur. Readers are requested to communicate any errors to the Section of IARC Monographs, so that corrections can be reported in future volumes.

