

ARSENIC, METALS, FIBRES, AND DUSTS

VOLUME 100 C
A REVIEW OF HUMAN CARCINOGENS

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, 17-24 March 2009

LYON, FRANCE - 2012

IARC MONOGRAPHS
ON THE EVALUATION
OF CARCINOGENIC RISKS
TO HUMANS

CONTENTS

NOTE TO THE READER	1
LIST OF PARTICIPANTS	3
PREAMBLE	11
A. GENERAL PRINCIPLES AND PROCEDURES	11
1. Background.....	11
2. Objective and scope.....	12
3. Selection of agents for review	13
4. Data for the <i>Monographs</i>	13
5. Meeting participants.....	14
6. Working procedures.....	15
B. SCIENTIFIC REVIEW AND EVALUATION.....	16
1. Exposure data	17
2. Studies of cancer in humans	18
3. Studies of cancer in experimental animals.....	22
4. Mechanistic and other relevant data.....	25
5. Summary.....	28
6. Evaluation and rationale.....	29
References	33
GENERAL REMARKS.....	35
ARSENIC AND ARSENIC COMPOUNDS.....	41
1. Exposure Data	41
1.1 Identification of the agents.....	41
1.2 Chemical and physical properties of the agents	41
1.3 Use of the agents	41
1.4 Environmental occurrence	43
1.5 Human exposure	45
2. Cancer in Humans.....	46
2.1 Types of human exposure circumstances studied	46
2.2 Cancer of the lung	48
2.3 Cancer of the urinary bladder and of the kidney.....	49
2.4 Cancer of the skin.....	50

2.5	Cancer of the liver	51
2.6	Cancer of the prostate	52
2.7	Synthesis.....	52
3.	Cancer in Experimental Animals	53
3.1	Oral administration.....	53
3.2	Intratracheal administration	54
3.3	Intravenous administration	58
3.4	Transplacental and perinatal exposures.....	58
3.5	Studies in which arsenic modifies the effects of other agents.....	60
3.6	Gallium arsenide	76
3.7	Synthesis.....	79
4.	Other Relevant Data	79
4.1	Absorption, distribution, metabolism, and excretion.....	79
4.2	Genetic and related effects.....	81
4.3	Co-carcinogenic and <i>in utero</i> carcinogenic effects.....	83
4.4	Synthesis.....	84
5.	Evaluation	85
	References	85

	BERYLLIUM AND BERYLLIUM COMPOUNDS.....	95
1.	Exposure Data	95
1.1	Identification of the agents.....	95
1.2	Chemical and physical properties of the agents	95
1.3	Use of the agents	96
1.4	Environmental occurrence	98
1.5	Human exposure	99
2.	Cancer in Humans.....	104
2.1	Cohort studies and nested case–control studies.....	105
2.2	Synthesis.....	107
3.	Cancer in Experimental Animals	107
3.1	Inhalation exposure	107
3.2	Intratracheal administration	107
3.3	Intravenous administration	114
3.4	Other routes of exposure	114
3.5	Synthesis.....	114
4.	Other Relevant Data	114
4.1	Absorption, distribution, metabolism, and excretion.....	114
4.2	Genetic and related effects.....	115
4.3	Synthesis.....	116
5.	Evaluation	116
	References	116

CADMIUM AND CADMIUM COMPOUNDS.....	121
1. Exposure Data	121
1.1 Identification of the agents.....	121
1.2 Chemical and physical properties of the agents	121
1.3 Use of the agents	121
1.4 Environmental occurrence	123
1.5 Human exposure	124
2. Cancer in Humans.....	128
2.1 Cancer of the lung	128
2.2 Cancer of the prostate	129
2.3 Other cancers	130
2.4 Synthesis.....	131
3. Cancer in Experimental Animals	131
3.1 Oral administration	131
3.2 Inhalation and intratracheal administration	133
3.3 Subcutaneous administration	133
3.4 Administration with known carcinogens or other agents.....	133
3.5 Synthesis.....	138
4. Other Relevant Data	138
4.1 Absorption, distribution, metabolism, and excretion.....	138
4.2 Genetic and related effects.....	138
4.3 Synthesis.....	140
5. Evaluation	141
References	141
CHROMIUM (VI) COMPOUNDS	147
1. Exposure Data	147
1.1 Identification of the agents.....	147
1.2 Chemical and physical properties of the agents	147
1.3 Use of the agents	150
1.4 Environmental occurrence	150
1.5 Human exposure	151
2. Cancer in Humans.....	153
2.1 Introduction.....	153
2.2 Cancer of the lung.....	154
2.3 Cancer of the nose and nasal sinus.....	155
2.4 Cancer of the stomach.....	155
2.5 Synthesis.....	156
3. Cancer in Experimental Animals	156
3.1 Studies published since the previous <i>IARC Monograph</i>	157
3.2 Synthesis.....	157
4. Other Relevant Data	161
4.1 Absorption, distribution, metabolism, and excretion.....	161
4.2 Genetic and related effects.....	161
4.3 Synthesis.....	163
5. Evaluation	164
References	164

NICKEL AND NICKEL COMPOUNDS	169
1. Exposure Data	169
1.1 Identification of the agents.....	169
1.2 Chemical and physical properties of the agents	169
1.3 Use of the agents	169
1.4 Environmental occurrence	174
1.5 Human exposure	176
2. Cancer in Humans.....	183
2.1 Cohort studies and nested case–control studies.....	183
2.2 Synthesis.....	190
3. Cancer in Experimental Animals	190
3.1 Oral administration.....	190
3.2 Inhalation exposure	191
3.3 Parenteral administration.....	192
3.4 Transplacental exposure.....	207
3.5 Synthesis.....	207
4. Other Relevant Data	207
4.1 Absorption, distribution, metabolism, and excretion.....	207
4.2 Genetic and related effects.....	208
4.3 Synthesis.....	210
5. Evaluation	210
References	211
ASBESTOS	
(CHRYSOTILE, AMOSITE, CROCIDOLITE, TREMOLITE, ACTINOLITE, AND ANTHOPHYLLITE)	219
1. Exposure Data	219
1.1 Identification of the agent.....	219
1.2 Chemical and physical properties of the agent.....	219
1.3 Use of the agent	221
1.4 Environmental occurrence	222
1.5 Human exposure	225
1.6 Talc containing asbestos-form fibres.....	230
2. Cancer in Humans.....	233
2.1 Introduction.....	233
2.2 Cancer of the lung.....	235
2.3 Mesothelioma.....	238
2.4 Other cancer sites.....	241
2.5 Synthesis.....	256
3. Cancer in Experimental Animals	259
3.1 Introduction.....	259
3.2 Inhalation exposure	259
3.3 Intrapleural and intraperitoneal administration.....	272
3.4 Intratracheal administration	272
3.5 Oral administration.....	272
3.6 Intragastric administration	273
3.7 Studies in companion animals.....	273
3.8 Synthesis.....	279

4. Other Relevant Data	279
4.1 Toxicokinetics, deposition, clearance, and translocation in humans	279
4.2 Molecular pathogenesis of human cancers related to mineral dust exposure	281
4.3 Mechanisms of carcinogenesis	283
4.4 Susceptible populations.....	291
4.5 Synthesis.....	294
5. Evaluation	294
References	294
ERIONITE	311
1. Exposure Data	311
1.1 Identification of the agent.....	311
1.2 Chemical and physical properties of the agent.....	311
1.3 Use of the agent	311
1.4 Environmental occurrence	312
1.5 Human exposure	312
2. Cancer in Humans.....	313
2.1 Pleural and peritoneal mesothelioma	313
2.2 Other cancers	315
2.3 Synthesis.....	315
3. Cancer in Experimental Animals	315
4. Other Relevant Data	315
5. Evaluation	315
References	315
LEATHER DUST	317
1. Exposure Data	317
1.1 Identification of the agent.....	317
1.2 Chemical and physical properties of the agent.....	317
1.3 Use of the agent	318
1.4 Occupational exposure	318
2. Cancer in Humans.....	321
2.1 Sinonasal cancer	322
2.2 Other respiratory cancers.....	348
2.3 Leukaemia.....	348
2.4 Cancer of the bladder.....	349
2.5 Other cancers	349
2.6 Synthesis.....	349
3. Cancer in Experimental Animals	350
4. Other Relevant Data	350
5. Evaluation	350
References	350

SILICA DUST, CRYSTALLINE, IN THE FORM OF QUARTZ OR CRISTOBALITE	355
1. Exposure Data	355
1.1 Identification of the agent.....	355
1.2 Chemical and physical properties of the agent.....	355
1.3 Use of the agent	355
1.4 Environmental occurrence	357
1.5 Human exposure	357
2. Cancer in Humans.....	370
2.1 Cancer of the lung.....	370
2.2 Other cancers	377
2.3 Synthesis.....	378
3. Cancer in Experimental Animals	379
3.1 Inhalation exposure	379
3.2 Intranasal administration.....	381
3.3 Intratracheal administration	381
3.4 Intrapleural and intrathoracic administration	385
3.5 Intraperitoneal administration.....	386
3.6 Subcutaneous administration	386
3.7 Intravenous administration	387
3.8 Administration with known carcinogens.....	387
3.9 Synthesis.....	388
4. Other Relevant Data	389
4.1 Deposition and biopersistence	389
4.2 Mechanisms of carcinogenicity.....	390
4.3 Molecular pathogenesis of cancer of the lung.....	394
4.4 Species differences and susceptible populations	396
4.5 Synthesis.....	396
5. Evaluation	396
References	397
WOOD DUST	407
1. Exposure Data	407
1.1 Identification, chemical, and physical properties of the agent.....	407
1.2 Occupational exposure	407
2. Cancer in Humans.....	414
2.1 Sinonasal cancer.....	415
2.2 Cancer of the nasopharynx.....	431
2.3 Cancer of the pharynx	431
2.4 Cancer of the larynx	436
2.5 Cancer of the lung.....	440
2.6 Other cancer sites.....	443
2.7 Furniture and cabinet-making industry	443
2.8 Synthesis.....	443
3. Cancer in Experimental Animals	449
3.1 Inhalation.....	449
3.2 Intraperitoneal injection.....	450

3.3 Administration with known carcinogens or other modifying factors	450
3.4 Exposure to wood dust extracts	451
3.5 Exposure to wood shavings	451
3.6 Synthesis.....	451
4. Other Relevant Data	453
4.1 Deposition and clearance of particulates in the nasal region	453
4.2 Molecular pathogenesis	453
4.3 Mechanisms of toxicity and carcinogenicity.....	455
4.4 Other risk factors for sinonasal and nasopharyngeal cancers	458
4.5 Synthesis.....	459
5. Evaluation	459
References	459
LIST OF ABBREVIATIONS	467
CUMULATIVE CROSS INDEX TO IARC MONOGRAPHS	469

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.

