



**SOME NITROBENZENES
AND OTHER INDUSTRIAL
CHEMICALS**

VOLUME 123

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, 9–16 October 2018

LYON, FRANCE - 2020

**IARC MONOGRAPHS
ON THE EVALUATION
OF CARCINOGENIC RISKS
TO HUMANS**

CONTENTS

NOTE TO THE READER	1
LIST OF PARTICIPANTS	3
PREAMBLE	7
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>	10
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
GENERAL REMARKS	31
2-CHLORONITROBENZENE	35
1. Exposure Data.....	35
1.1 Identification of the agent.....	35
1.2 Production and use.....	35
1.3 Methods of measurement and analysis.....	36
1.4 Occurrence and exposure.....	37
1.5 Regulations and guidelines.....	39
2. Cancer in Humans.....	39

3. Cancer in Experimental Animals	39
3.1 Mouse	39
3.2 Rat	45
4. Mechanistic and Other Relevant Data	46
4.1 Absorption, distribution, metabolism, and excretion	46
4.2 Mechanisms of carcinogenesis	48
4.3 Other adverse effects	54
4.4 Data relevant to comparisons across agents and end-points	55
5. Summary of Data Reported	61
5.1 Exposure data	61
5.2 Cancer in humans	62
5.3 Cancer in experimental animals	62
5.4 Mechanistic and other relevant data	62
6. Evaluation	63
6.1 Cancer in humans	63
6.2 Cancer in experimental animals	63
6.3 Overall evaluation	63
References	63
4-CHLORONITROBENZENE	67
1. Exposure Data	67
1.1 Identification of the agent	67
1.2 Production and use	67
1.3 Methods of measurement and analysis	69
1.4 Occurrence and exposure	70
1.5 Regulations and guidelines	72
2. Cancer in Humans	73
3. Cancer in Experimental Animals	73
3.1 Mouse	78
3.2 Rat	79
4. Mechanistic and Other Relevant Data	80
4.1 Absorption, distribution, metabolism, and excretion	80
4.2 Mechanisms of carcinogenesis	83
4.3 Other adverse effects	90
4.4 Data relevant to comparisons across agents and end-points	91
5. Summary of Data Reported	91
5.1 Exposure data	91
5.2 Cancer in humans	91
5.3 Cancer in experimental animals	91
5.4 Mechanistic and other relevant data	92
6. Evaluation	92
6.1 Cancer in humans	92
6.2 Cancer in experimental animals	93
6.3 Overall evaluation	93
References	93

1,4-DICHLORO-2-NITROBENZENE	99
1. Exposure Data	99
1.1 Identification of the agent	99
1.2 Production and use	100
1.3 Methods of measurement and analysis	100
1.4 Occurrence and exposure	101
1.5 Regulations and guidelines	102
2. Cancer in Humans	102
3. Cancer in Experimental Animals	102
3.1 Mouse	102
3.2 Rat	105
4. Mechanistic and Other Relevant Data	106
4.1 Absorption, distribution, metabolism, and excretion	106
4.2 Mechanisms of carcinogenesis	107
4.3 Other adverse effects	109
4.4 Data related to comparisons across agents and end-points	110
5. Summary of Data Reported	110
5.1 Exposure data	110
5.2 Cancer in humans	110
5.3 Cancer in experimental animals	110
5.4 Mechanistic and other relevant data	111
6. Evaluation	111
6.1 Cancer in humans	111
6.2 Cancer in experimental animals	111
6.3 Overall evaluation	111
References	111
2,4-DICHLORO-1-NITROBENZENE	113
1. Exposure Data	113
1.1 Identification of the agent	113
1.2 Production and use	114
1.3 Methods of measurement and analysis	114
1.4 Occurrence and exposure	114
1.5 Regulations and guidelines	116
2. Cancer in Humans	116
3. Cancer in Experimental Animals	116
3.1 Mouse	116
3.2 Rat	119
4. Mechanistic and Other Relevant Data	120
4.1 Absorption, distribution, metabolism, and excretion	120
4.2 Mechanisms of carcinogenesis	121
4.3 Other adverse effects	122
4.4 Data related to comparisons across agents and end-points	123
5. Summary of Data Reported	123

5.1	Exposure data	123
5.2	Cancer in humans	123
5.3	Cancer in experimental animals	123
5.4	Mechanistic and other relevant data	124
6.	Evaluation	124
6.1	Cancer in humans	124
6.2	Cancer in experimental animals	124
6.3	Overall evaluation	124
	References	124
2-AMINO-4-CHLOROPHENOL		127
1.	Exposure Data	127
1.1	Identification of the agent	127
1.2	Production and use	128
1.3	Methods of measurement and analysis	128
1.4	Occurrence and exposure	129
1.5	Regulations and guidelines	129
2.	Cancer in Humans	130
3.	Cancer in Experimental Animals	130
3.1	Mouse	130
3.2	Rat	130
4.	Mechanistic and Other Relevant Data	133
4.1	Absorption, distribution, metabolism, and excretion	133
4.2	Mechanisms of carcinogenesis	134
4.3	Other adverse effects	135
4.4	Data relevant to comparisons across agents and end-points	135
5.	Summary of Data Reported	135
5.1	Exposure data	135
5.2	Cancer in humans	135
5.3	Cancer in experimental animals	135
5.4	Mechanistic and other relevant data	136
6.	Evaluation	136
6.1	Cancer in humans	136
6.2	Cancer in experimental animals	136
6.3	Overall evaluation	136
	References	137
ORTHO-PHENYLENEDIAMINE AND ORTHO-PHENYLENEDIAMINE DIHYDROCHLORIDE		139
1.	Exposure Data	139
1.1	<i>ortho</i> -Phenylenediamine	139
1.2	<i>ortho</i> -Phenylenediamine dihydrochloride	143
2.	Cancer in Humans	144
3.	Cancer in Experimental Animals	144
3.1	Mouse	144
3.2	Rat	151

4. Mechanistic and Other Relevant Data	152
4.1 Absorption, distribution, metabolism, and excretion	152
4.2 Mechanisms of carcinogenesis.....	153
4.3 Other adverse effects	153
4.4 Data relevant to comparisons across agents and end-points	157
5. Summary of Data Reported	157
5.1 Exposure data.....	157
5.2 Cancer in humans.....	158
5.3 Cancer in experimental animals.....	158
5.4 Mechanistic and other relevant data.....	158
6. Evaluation and Rationale.....	159
6.1 Cancer in humans.....	159
6.2 Cancer in experimental animals.....	159
6.3 Overall evaluation	159
6.4 Rationale	159
References.....	160
<i>PARA-NITROANISOLE</i>	163
1. Exposure Data.....	163
1.1 Identification of the agent	163
1.2 Production and use.....	163
1.3 Methods of measurement and analysis	164
1.4 Occurrence and exposure.....	164
1.5 Regulations and guidelines	165
2. Cancer in Humans	165
3. Cancer in Experimental Animals	165
3.1 Mouse.....	165
3.2 Rat	170
4. Mechanistic and Other Relevant Data	170
4.1 Absorption, distribution, metabolism, and excretion	170
4.2 Mechanisms of carcinogenesis.....	172
4.3 Other adverse effects	175
4.4 Data relevant to comparisons across agents and end-points	175
5. Summary of Data Reported	175
5.1 Exposure data.....	175
5.2 Cancer in humans.....	176
5.3 Cancer in experimental animals.....	176
5.4 Mechanistic and other relevant data.....	176
6. Evaluation.....	176
6.1 Cancer in humans.....	176
6.2 Cancer in experimental animals.....	177
6.3 Overall evaluation	177
References.....	177

<i>N,N</i>-DIMETHYLACETAMIDE	181
1. Exposure Data.....	181
1.1 Identification of the agent.....	181
1.2 Production and use.....	182
1.3 Methods of measurement and analysis.....	182
1.4 Occurrence and exposure.....	183
1.5 Regulations and guidelines.....	187
1.6 Critical review of exposure assessment in key epidemiological studies.....	187
2. Cancer in Humans.....	187
2.1 Cohort studies.....	187
2.2 Case-control studies.....	189
3. Cancer in Experimental Animals.....	189
3.1 Mouse.....	189
3.2 Rat.....	197
3.3 Hamster.....	198
4. Mechanistic and Other Relevant Data.....	199
4.1 Absorption, distribution, metabolism, and excretion.....	199
4.2 Mechanisms of carcinogenesis.....	200
4.3 Other adverse effects.....	201
4.4 Data relevant to comparisons across agents and end-points.....	203
5. Summary of Data Reported.....	203
5.1 Exposure data.....	203
5.2 Cancer in humans.....	204
5.3 Cancer in experimental animals.....	204
5.4 Mechanistic and other relevant data.....	205
6. Evaluation.....	205
6.1 Cancer in humans.....	205
6.2 Cancer in experimental animals.....	205
6.3 Overall evaluation.....	205
References.....	206
LIST OF ABBREVIATIONS	211
ANNEX 1. SUPPLEMENTARY MATERIAL FOR TOXCAST/TOX21	213