

CONTENTS

1.	SUMMARY AND EVALUATION, CONCLUSIONS AND RECOMMENDATIONS . . .	13
1.1	Summary and evaluation	13
1.1.1	Identity, properties, and analytical methods	13
1.1.2	Production and uses	13
1.1.3	Environmental transport, distribution, and transformation	13
1.1.4	Environmental levels and human exposure	14
1.1.5	Kinetics and metabolism	14
1.1.6	Effects on organisms in the environment	15
1.1.7	Effects on experimental animals and <i>in vitro</i> test systems	16
1.1.7.1	Reproduction	16
1.1.7.2	Mutagenicity	17
1.1.7.3	Carcinogenicity	18
1.1.7.4	Effects on different organs and systems	18
1.1.7.5	Primary mechanism of toxicity	19
1.1.8	Effects on humans	20
1.2	Conclusions	21
1.2.1	General population exposure	21
1.2.2	Subpopulations at high risk	21
1.2.3	Occupational exposure	21
1.2.4	Environmental effects	22
1.3	Recommendations	22

2.	IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS	23
2.1	Identity	23
2.2	Physical and chemical properties	24
2.3	Conversion factors	26
2.4	Analytical methods	27
3.	SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE	33
4.	ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION	34
4.1	Volatilization and air transportation	34
4.2	Water	34
4.2.1	Hydrolysis	34
4.2.2	Photolysis	37
4.2.3	Degradation by microorganisms	39
4.2.4	Persistence in surface water	42
4.2.5	Removal from water	46
4.2.6	Persistence in sea water	46
4.2.7	Bioaccumulation/biomagnification	48
4.3	Soil	50
4.3.1	Adsorption, desorption	50
4.3.2	Transformation	53
4.3.2.1	Photolysis in soil	53
4.3.3	Biotransformation in soil	54
4.3.4	Degradation by microorganisms	59
4.3.5	Persistence in soil	64
4.3.6	Interaction with other physical, chemical, or biological factors	68
4.3.7	Vegetation	68
4.3.7.1	Uptake and transformation in plants	68

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE	70
5.1 Environmental levels	70
5.1.1 Air	70
5.1.2 Water	70
5.1.3 Soil	73
5.1.4 Food and animal feed	76
5.1.4.1 Fruit, vegetables, and grain	76
5.1.4.2 Animal products	84
5.1.4.3 Animal feed crops	85
5.1.5 Other products	86
5.1.6 Terrestrial organisms	86
5.2 General population exposure	87
5.2.1 Exposure through the food	87
5.2.2 Exposure during insect control	89
5.3 Occupational exposure during manufacture, formulation, or use	89
6. KINETICS AND METABOLISM	94
6.1 Absorption	94
6.2 Distribution	96
6.3 Metabolism	102
6.3.1 <i>In vitro</i> studies on animal tissues	103
6.3.2 <i>In vivo</i> studies on animals	106
6.3.3 Metabolic transformation in plants	110
6.3.4 <i>In vitro</i> studies with human tissues	111
6.3.5 <i>In vivo</i> studies on humans	113
6.4 Elimination and excretion in expired air, faeces, urine, milk, and eggs	115
7. EFFECTS ON ORGANISMS IN THE ENVIRONMENT	121
7.1 Microorganisms	121
7.1.1 Soil microorganisms	121
7.1.2 Aquatic microorganisms	121
7.2.1 Aquatic invertebrates	122

7.2.2	Fish	133
7.2.2.1	Acute toxicity	133
7.2.2.2	Short-term and long-term toxicity	143
7.2.3	Amphibians	144
7.3	Terrestrial organisms	144
7.3.1	Worms	144
7.3.2	Insects	144
7.3.3	Birds	145
7.3.4	Mammals	147
7.4	Effects on the population and ecosystem	148
8.	EFFECTS ON EXPERIMENTAL ANIMALS AND <i>IN VITRO</i> TEST SYSTEMS	155
8.1	Single exposures	155
8.1.1	Oral toxicity	155
8.1.2	Acute inhalation toxicity	155
8.1.3	Dermal toxicity	160
8.1.4	Other routes of exposure	160
8.2	Skin and eye irritation, sensitization	160
8.2.1	Skin and eye irritation	160
8.2.2	Sensitization	161
8.3	Short- and long-term oral exposure	162
8.4	Short- and long-term inhalation toxicity	162
8.5	Reproduction and developmental toxicity	162
8.5.1	Mammalian reproductive toxicity studies	176
8.5.1.1	Mouse	176
8.5.1.2	Rat	176
8.5.1.3	Gerbil	177
8.5.2	Mammalian developmental toxicity studies	178
8.5.2.1	Mouse	178
8.5.2.2	Rat	178
8.5.2.3	Guinea-pig	179
8.5.2.4	Rabbit	179
8.5.2.5	Dog	179
8.5.2.6	Pig	179

8.5.2.7	Monkey	180
8.5.3	Reproductive and developmental toxicity studies in non-mammalian species	180
8.5.3.1	Fish	180
8.5.3.2	Amphibian	181
8.5.3.3	Birds	181
8.5.4	Appraisal	182
8.6	Mutagenicity of carbaryl and <i>N</i> -nitrosocarbaryl	182
8.6.1	Genotoxicity assays <i>in vitro</i>	183
8.6.1.1	Primary DNA damage	183
8.6.1.2	Gene mutation assay	190
8.6.1.3	Chromosomal aberration assays and sister chromatid exchange	194
8.6.2	Genotoxicity <i>in vivo</i>	196
8.6.2.1	Host-mediated assay	196
8.6.2.2	<i>Drosophila melanogaster</i> and other insects	196
8.6.2.3	Chromosomal aberrations and sister chromatid exchange	198
8.6.2.4	Dominant lethal assays in rodents	199
8.6.3	Other end-points	199
8.6.3.1	Cell transformation	199
8.6.3.2	Aneuploidy induction	200
8.6.4	Appraisal	202
8.7	Carcinogenicity	203
8.7.1	Carcinogenicity studies of carbaryl in rodents	203
8.7.1.1	Mouse	203
8.7.1.2	Rats	208
8.7.1.3	Overall appraisal of carbaryl carcinogenicity	209
8.7.2	Carcinogenicity studies of <i>N</i> -nitrosocarbaryl	209
8.7.2.1	Rats	210
8.7.2.2	Mice	213

	8.7.2.3	Overall evaluation of the carcinogenicity of N-nitrosocarbaryl	213
	8.7.3	Carcinogenicity of β -carbaryl	214
8.8		Special studies	215
	8.8.1	Neurotoxicity	219
	8.8.2	Effects on the immune system	219
		8.8.2.1 Appraisal on immunotoxicology	219
		8.8.2.2 <i>In vivo</i> studies	220
		8.8.2.3 <i>In vitro</i> studies	224
	8.8.3	Effects in blood	225
	8.8.4	Effects on the liver and other organs	228
	8.8.5	Effects on serum glucose	229
	8.8.6	Interactions with the drug metabolizing enzyme system	230
	8.8.7	Effects on the endocrine system	233
	8.8.8	Other studies	237
8.9		Factors modifying toxicity, toxicity of metabolites	237
	8.9.1	Factors modifying toxicity	237
	8.9.2	Toxicity of metabolites	240
	8.9.3	N-nitrosocarbaryl	241
8.10		Mechanism of toxicity - mode of action	242
	8.10.1	Inhibition of cholinesterase activity	242
9. EFFECTS ON HUMAN BEINGS			245
9.1		General population exposure	245
	9.1.1	Acute toxicity, poisoning incidents	245
	9.1.2	Controlled human studies	246
	9.1.3	Long-term exposure	247
9.2		Occupational exposure	248
	9.2.1	Epidemiological studies	248

10. PREVIOUS EVALUATION BY INTERNATIONAL BODIES	251
REFERENCES	253
APPENDIX	332
RESUME ET EVALUATION, CONCLUSIONS ET RECOMMANDATIONS	335
RESUMEN Y EVALUACION, CONCLUSIONES Y RECOMENDACIONES	347