

## CONTENTS

1.	SUMMARY AND EVALUATION; CONCLUSIONS; RECOMMENDATIONS .....	13
1.1	Summary and evaluation .....	13
1.1.1	Exposure .....	13
1.1.2	Uptake, metabolism, and excretion .....	14
1.1.3	Effects on organisms in the environment .....	15
1.1.4	Effects on experimental animals and <i>in vitro</i> .....	15
1.1.5	Effects on human beings .....	17
1.2	Conclusions .....	18
1.3	Recommendations .....	18
2.	IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS .....	20
2.1	Identity .....	20
2.2	Physical and chemical properties .....	21
2.3	Conversion factors .....	22
2.4	Analytical methods .....	22
3.	SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE .....	30
3.1	Natural occurrence .....	30
3.2	Man-made sources .....	30
3.2.1	Production levels and processes, uses .....	30
3.2.1.1	World production figures .....	30
3.2.1.2	Manufacturing processes .....	31
4.	ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION .....	32
4.1	Transport and distribution between media .....	32
4.1.1	Air .....	32
4.1.2	Water .....	32

4.1.3	Soil .....	33
4.1.4	Soil-plants .....	34
4.2	Abiotic degradation .....	34
4.3	Biotransformation .....	36
4.3.1	Biodegradation .....	36
4.3.2	Bioaccumulation and biomagnification .....	36
5.	ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE .....	41
5.1	Environmental levels .....	41
5.1.1	Air .....	41
5.1.2	Soil, sediments, and sewage sludge .....	50
5.1.2.1	Soil .....	50
5.1.2.2	Sediments .....	50
5.1.2.3	Sewage sludge .....	68
5.1.3	Water .....	68
5.1.3.1	Surface water .....	68
5.1.3.2	Rain and snow .....	70
5.1.3.3	Drinking-water .....	70
5.1.3.4	Groundwater .....	71
5.1.4	Organisms in the environment .....	71
5.1.4.1	Birds .....	71
5.1.4.2	Fish and shellfish .....	73
5.1.4.3	Mixed species .....	75
5.1.5	Other food and feed .....	76
5.1.5.1	Cereals .....	76
5.1.5.2	Fruit and vegetables .....	76
5.1.5.3	Meat, poultry, and chicken eggs .....	77
5.1.5.4	Milk and milk products .....	78
5.1.5.5	Fat and oils .....	79
5.1.5.6	Animal feed .....	80
5.1.6	Miscellaneous products .....	80
5.2	Exposure of the general population .....	80
5.2.1	Total-diet studies .....	80
5.2.2	Levels in human tissues .....	82
5.2.2.1	Adipose tissue .....	82
5.2.2.2	Organs .....	83
5.2.2.3	Blood .....	83
5.2.2.4	Breast milk .....	83
5.2.2.5	Appraisal of exposure of the general population .....	84

5.3	Occupational exposure during manufacture, formulation, and use .....	84
5.3.1	Manufacture and formulation .....	84
5.3.2	Application .....	85
5.3.3	Appraisal of occupational exposure .....	87
6.	KINETICS AND METABOLISM .....	88
6.1	Absorption, distribution, and elimination .....	88
6.1.1	Laboratory animals .....	88
6.1.1.1	Oral administration .....	88
6.1.1.2	Intravenous administration .....	90
6.1.2	Domestic animals .....	91
6.1.3	Human beings .....	93
6.1.4	Systems <i>in vitro</i> .....	93
6.2	Biotransformation .....	93
6.2.1	Experimental animals .....	93
6.2.2	Human beings .....	96
6.2.3	Microorganisms .....	97
6.2.4	Plants .....	98
7.	EFFECTS ON ORGANISMS IN THE ENVIRONMENT .....	99
7.1	Microorganisms .....	99
7.2	Aquatic organisms .....	99
7.2.1	Invertebrates .....	99
7.2.2	Fish .....	106
7.2.2.1	Acute toxicity .....	106
7.2.2.2	Short-term toxicity .....	106
7.2.2.3	Studies of resistance .....	114
7.2.2.4	Interaction with other chemicals .....	115
7.2.2.5	Special studies .....	116
7.2.3	Amphibia .....	118
7.3	Terrestrial organisms .....	118
7.3.1	Honey bees .....	118
7.3.2	Birds .....	119
7.3.2.1	Acute toxicity .....	119
7.3.2.2	Short-term toxicity .....	119
7.3.2.3	Studies of reproduction .....	120
7.3.2.4	Interaction with other chemicals .....	121
7.3.2.5	Special studies .....	121
7.3.2.6	Behavioural studies .....	122

7.3.3	Mammals .....	122
7.3.3.1	Toxicity .....	122
7.3.3.2	Studies of resistance .....	123
7.4	Effects in the field .....	124
7.5	Appraisal of effects on organisms in the environment .....	126
8.	EFFECTS ON EXPERIMENTAL ANIMALS AND <i>IN VITRO</i> .....	127
8.1	Acute toxicity of technical-grade endrin .....	127
8.1.1	Oral administration .....	127
8.1.2	Dermal administration .....	127
8.1.3	Parenteral administration .....	127
8.1.4	Toxicity of metabolites and isomers .....	131
8.1.4.1	Mammalian metabolites .....	131
8.1.4.2	Isomers .....	132
8.1.5	Acute toxicity of formulated material .....	133
8.1.5.1	Oral and dermal administration .....	133
8.1.5.2	Inhalation .....	133
8.2	Short-term exposure .....	134
8.2.1	Oral administration .....	134
8.2.1.1	Mouse .....	134
8.2.1.2	Rat .....	134
8.2.1.3	Rabbit .....	135
8.2.1.4	Dog .....	135
8.2.1.5	Domestic animals .....	136
8.2.2	Inhalation .....	137
8.2.3	Dermal administration .....	137
8.3	Skin irritation .....	137
8.4	Reproduction, embryotoxicity, and teratogenicity .....	137
8.4.1	Reproduction .....	137
8.4.1.1	Mouse .....	137
8.4.1.2	Rat .....	138
8.4.2	Embryotoxicity and teratogenicity .....	138
8.4.2.1	Mouse .....	138
8.4.2.2	Rat .....	139
8.4.2.3	Hamster .....	140
8.4.2.4	Perinatal behavioural development .....	141
8.4.3	Appraisal of reproductive effects .....	142
8.5	Mutagenicity and related end-points .....	142
8.5.1	Effects on microorganisms .....	142
8.5.2	Point mutations in mammalian cells .....	144

8.5.3	Dominant lethal mutations .....	144
8.5.4	Chromosomal and cytogenetic effects .....	144
8.5.5	Host-mediated effects .....	145
8.5.6	Sister chromatid exchange .....	145
8.5.7	Effects in <i>Drosophila melanogaster</i> .....	145
8.5.8	Effects on DNA .....	146
8.5.9	Appraisal of mutagenicity and related end-points .....	146
8.6	Long-term exposure .....	147
8.7	Carcinogenicity .....	147
8.7.1	Oral administration .....	147
8.7.1.1	Mouse .....	147
8.7.1.2	Rat .....	148
8.7.1.3	Tumour promotion .....	150
8.7.2	Appraisal of carcinogenicity .....	150
8.8	Special studies .....	151
8.8.1	Nervous system .....	151
8.8.1.1	Electrophysiological studies .....	151
8.8.1.2	Histopathological studies .....	152
8.8.1.3	Neurotransmitter systems .....	152
8.8.1.4	Appraisal of effects on the nervous system .....	155
8.8.2	Cardiovascular system .....	155
8.8.3	Effects on liver enzymes .....	156
8.8.3.1	Mouse .....	156
8.8.3.2	Rat .....	157
8.8.3.3	Guinea-pig .....	158
8.8.3.4	In-vitro studies .....	158
8.8.4	Miscellaneous studies .....	159
8.8.5	Factors that influence toxicity .....	159
8.8.5.1	Nutrition .....	159
8.8.5.2	Potentiation .....	160
9.	EFFECTS ON HUMAN BEINGS .....	162
9.1	Exposure of the general population .....	162
9.1.1	Acute toxicity .....	162
9.1.2	Poisoning incidents .....	162
9.2	Occupational exposure .....	165
9.2.1	Factory workers .....	165
9.2.2	Dose-response relationships .....	167
9.2.3	Exposures to mixtures .....	168
9.2.4	Appraisal of effects of occupational exposures .....	170

10. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES ...	171
REFERENCES .....	173
ANNEX I Chemical names of endrin and its metabolites .....	218
ANNEX II Medical treatment of endrin poisoning.....	221
ANNEX III Management of major status epilepticus in adults .....	223
RESUME .....	226
RESUMEN .....	234