ENVIRONMENTAL HEALTH CRITERIA FOR SELECTED NITRO- AND NITRO-OXY-POLYCYCLIC AROMATIC HYDROCARBONS

xiii

PREAMBLE

2.

ACRONYMS AND ABBREVIATIONS

SUMMARY

Identity, physical and chemical properties, and	
analytical methods	2
Sources of numan and environmental exposure	2
Environmental transport, distribution and	
transformation	4
1.3.1 Environmental transport and distribution	4
1.3.2 Biotransformation	4
1.3.3 Abiotic degradation	
Environmental levels and human exposure	6
1.4.1 Indoor air	
1.4.2 Food and beverages	
1.4.3 Other products	8
1.4.4 Occupational exposure	8
Kinetics and metabolism in laboratory animals	
and humans	9
Effects on laboratory mammals and in vitro	
test systems	10
Effects on humans	14
Effects on other organisms in the laboratory and	
field	4
NTITY, PHYSICAL AND CHEMICAL	
OPERTIES. AND ANALYTICAL METHODS	16
Identity	16
Physical and chemical properties	23
Conversion factors	23
Analytical methods	30
	Identity, physical and chemical properties, and analytical methods Sources of human and environmental exposure Environmental transport, distribution and transformation 1.3.1 Environmental transport and distribution 1.3.2 Biotransformation 1.3.3 Abiotic degradation Environmental levels and human exposure 1.4.1 Indoor air 1.4.2 Food and beverages 1.4.3 Other products 1.4.4 Occupational exposure Kinetics and metabolism in laboratory animals and humans Effects on laboratory mammals and <i>in vitro</i> test systems Effects on other organisms in the laboratory and field CNTITY, PHYSICAL AND CHEMICAL DPERTIES. AND ANALYTICAL METHODS Identity Physical and chemical properties Conversion factors Analytical methods

- 2.4.1 Sampling
- 2.4.2 Extraction
- 2.4.3 Cleanup
- 2.4.4 Analytical separation and detection
 - 2.4.4.1 Difficulties in analysis
 - 2.4.4.2 Complex mixtures
 - 2.4.4.3 Analysis of nitro-oxyPAHs
- 2.4.5 Use of bioassay (mutagenicity) fractionation and chemical analysis

SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

- 3.1 Industrially produced nitroPAHs
 - 3.1.1 Production levels and processes
 - 3.1.2 Uses of commercially produced nitroPAHs
- 3.2 Other sources of nitroPAHs
 - 3.2.1 Direct sources of nitroPAHs from combustion processes
 - 3.2.1.1 Diesel exhaust
 - 3.2.1.2 Diesel compared with gasoline exhaust
 - 3.2.1.3 Aeroplane emissions
 - 3.2.1.4 Emissions from combustion of heating oils
 - 3.2.1.5 Fumes from cooking oils
 - 3.2.1.6 Other combustion sources
 - 3.2.2 Atmospheric formation of nitroPAHs
 - 3.2.2.1 Reactions of gas-phase PAHs (and nitroPAHs) with the hydroxyl radical (daytime reactions)
 - 3.2.2.2 Reactions of gas-phase PAHs (and nitroPAHs) with the nitrate radical (nighttime reactions)
- 3.3 Oxygen-containing nitroPAHs

ENVIRONMENTAL TRANSPORT, DISTRIBUTION AND TRANSFORMATION

4. Transport and distribution between media 4.1.1 Distribution and transport in the atmosphere

	4.1.1.1 Distribution of nitroPAHs between	
	fine and coarse fractions of	
	inhalable atmospheric particulates	71
	4.1.2 Distribution and transport in the hydrospher	e 71
	4.1.3 Adsorption onto soils and sediments	71
	4.1.4 Bioaccumulation	72
	4.1.5 Biomagnification	72
4.2	Transformation	72
	4.2.1 Biotransformation	72
	4.2.1.1 Bacteria	72
	4.2.1.2 Fungi	75
	4.2.1.3 Plants	75
	4.2.1.4 Aquatic animals	76
	4.2.2 Abiotic degradation	76
	4.2.2.1 Direct photolysis	76
	4.2.2.2 Other atmospheric	
	transformations	85
ENV	/IRONMENTAL LEVELS AND HUMAN	
EXF	OSURE	87
51	Environmental levels	87
	5.1.1 Air	87
	5111 Ambient air	07
	5 1 1 2 Indoor air	107
	512 Water	107
	5.1.3 Soil sewage sludge sediment and	109
	incinerator ash	100
	514 Food and beverages	109
	5.1.4.1 Food	110
	5.1.4.2 Reverges	110
	5.1.5 Other sources	114
	5.1.5 Carbon black and tonors	110
	5.1.5.2 Cigarette smoke	110
52	General nonulation exposure	110
53	Occupational exposure	110
5.5	Occupational exposure	11/
KIN	ETICS AND METABOLISM IN LABORATORY	
ANI	MALS AND HUMANS	121
6.	Overview of the metabolism of nitroPAHs	121

6.

- 6.2 1-Nitropyrene metabolism in mammals
 - 6.2.1 Absorption
 - 6.2.2 Distribution
 - 6.2.3 Metabolism
 - 6.2.3.1 Introduction
 - 6.2.3.2 Identification of metabolites
 - 6.2.3.3 Cytochrome P450-mediated ring C-oxidative pathway
 - 6.2.3.4 Nitroreduction pathway
 - 6.2.3.5 Human and rodent intestinal microflora
 - 6.2.3.6 Suggested metabolic pathway
 - 6.2.4 Elimination and excretion
 - 6.2.4.1 Elimination
 - 6.2.4.2 Excretion
 - 6.2.4.3 Biliary excretion and enterohepatic circulation
 - 6.2.5 Reaction with body components
 - 6.2.5.1 Protein binding
 - 6.2.5.2 DNA adducts
 - 6.2.6 Biomonitoring studies
- 6.3 Mononitropyrenes (1-, 2- and 4-nitropyrene) a comparison
 - 6.3.1 Faecal and urinary excretion
 - 6.3.2 Metabolism
 - 6.3.3 DNA adducts
- 6.4 2-Nitrofluorene
 - 6.4.1 Absorption, distribution and elimination
 - 6.4.2 Metabolism/mechanism of action
 - 6.4.2.1 Metabolites
 - 6.4.2.2 DNA adducts
 - 6.4.2.3 Haemoglobin adducts
- 6.5 Dinitropyrenes (1,3-, 1,6- and 1,8-dinitropyrene)
- 6.6 Mononitrobenzo[a]pyrenes (1-, 3- and 6-nitrobenzo[a]pyrene)
- 6.7 The nitrofluoranthene family
- 6.8 2- and 9-nitroanthracene
- 6.9 6-Nitrochrysene
- 6.10 K- and H-*ras* mutations in tumours produced by nitroPAHs

	6.11	Human enzymes expected to be involved in nitroPAH metabolism	.71
7	EFFI IN V	ECTS ON LABORATORY MAMMALS AND <i>ITRO</i> TEST SYSTEMS	177
		A cute toxicity	172
		7 1 1 1-Nitronanbthalene	172
		7 1 2 2-Nitronaphthalene	173
		7.1.3 5-Nitroacenaphthene	173
		7.1.4 2-Nitrofluorene	173
		7.1.5 3.9-Dinitrofluoranthene	173
		7.1.6 1-Nitropyrene	173
	7.2	Short-term and long-term exposure (non-	
		neoplastic effects)	174
		7.2.1 1-Nitronaphthalene	174
		7.2.2 5-Nitroacenaphthene	174
		7.2.3 2-Nitrofluorene	219
		7.2.4 1-Nitropyrene	219
		7.2.5 1,3-Dinitropyrene	220
		7.2.6 1,6-Dinitropyrene	220
		7.2.7 1,8-Dinitropyrene	220
		7.2.8 6-Nitrochrysene	220
		7.2.9 1- and 3-nitrobenzo[a]pyrene	220
		7.2.10 1,6-Dinitrobenzo[a]pyrene	221
	7.3	Skin and eye irritation and sensitization	221
	7.4	Reproductive toxicity, embryotoxicity and	
		teratogenicity	221
	7.5	Mutagenicity and related end-points	221
		7.5.1 In vitro genotoxicity studies	237
		7.5.1.1 Salmonella typhimurium	
		microsome assay	237
		7.5.1.2 Comparison of the mutagenic	
		potency of nitroPAHs in the	202
		Salmonella microsome assay	293
		7.5.1.3 Studies into the pathways of	204
		micropial metabolism	294
		7.5.1.4 Kelationsnip between mutagenic	
		potency in S. rypnimurium and the	202
		chemical structure of hitroPAHs	203

- 7.5.1.5 Bacterial test systems other than the *Salmonella* microsome assay
- 7.5.1.6 Eukaryotic test systems
- 7.5.1.7 High potency in the Salmonella microsome assay in relation to gene mutation results from other *in vitro* assays
- 7.5.1.8 Assessment of data on genotoxicity in vitro
- 7.5.2 In vivo genotoxicity studies
 - 7.5.2.1 Comparison with in vitro results
- 7.5.3 Genotoxicity of oxygen-containing nitroPAHs
 - 7.5.3.1 3-Nitrobenzanthrone
 - 7.5.3.2 Nitrodibenzopyranones
 - 7.5.3.3 Nitropyrene lactones
 - 7.5.3.4 Comparison of mutation frequency at *hprt* versus *tk* locus in human Blymphoblastoid cell lines
- 7.5.4 Summary of the genotoxicity of nitroPAHs
- 7.5.5 Mutagenicity of complex mixtures
 - 7.5.5.1 Difficulties encountered when interpreting the mutagenicity of complex mixtures compared with individual compounds
 - 7.5.5.2 Mutagenicity of diesel engine exhaust
 - 7.5.5.3 Mutagenic effect of urban air samples
 - 7.5.5.4 Bioassay-directed chemical analysis of airborne particulate matter using a human cell mutagenicity assay
 - 7.5.5.5 DNA adducts
 - 7.5.5.6 Mutagenic contribution of selected nitroPAHs from their occurrence in air samples multiplied by the mutagenicity in the *Salmonella* mutagenicity test
 - 7.5.5.7 Municipal waste incinerator emissions
 - 7.5.5.8 Mutagenicity of soils exposed to automobile exhaust

	7.5.6 Effects of antimutagenic compounds on	
	nitroPAH mutagenicity	336
7.6	Carcinogenicity	337
	7.6.1 Route of administration	341
	7.6.2 Adequacy of data	342
	7.6.3 Type of induced tumours	343
	7.6.4 Ranking of carcinogenic potency in	
	comparative studies on nitroPAHs	349
	7.6.4.1 Comparison of the carcinogenicity	
	of nitroPAHs with parent PAHs	352
	7.6.4.2 Comparison of the dose	355
	7.6.5 Carcinogenicity of oxygen-containing	
	nitroPAHs	356
	7.6.6 Carcinogenicity of the metabolites	356
	7.6.7 Carcinogenic potency of nitroPAHs in	
	diesel exhaust	257
	7.6.8 Genotoxicity in vivo and in vitro versus	
	carcinogenicity	358
	7.6.9 Potency equivalency factors for nitroPAHs	359
	7.6.10 Mechanisms of carcinogenesis	360
7.7	Special studies: Target organ effects	360
	7.7.1 1-Nitronaphthalene	360
	7.7.2 2-Nitronaphthalene	361
	7.7.3 1-Nitropyrene	362
EFF	ECTS ON HUMANS	363
8.1	General population exposure	365
8.2	Occupational exposure	366
8.3	Indicators of exposure to nitroPAHs in diesel	
	exhaust	366
	8.3.1 Biomonitoring of exposure/effect	366
	8.3.1.1 DNA adducts	366
	8.3.1.2 Protein adducts	367
	8.3.1.3 1-Nitropyrene metabolites	368
	8.3.1.4 Immunochemical determination	369
	8.3.2 Biomarkers of susceptibility	369
	8.3.2.1 Cytochrome P450	369
	8.3.2.2 Influence of polymorphisms on	
	biomarkers	370

8.

9. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD

- 9 Laboratory experiments
 - 9.1.1 Aquatic species
 - 9.1.2 Biotransformation studies in aquatic species
 - 9.1.3 DNA damage in aquatic species
- 9.2 Field observations

10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT

- 10.1 Evaluation of human health risks
 - 10.1.1 Exposure levels
 - 10.1.1.1 NitroPAHs
 - 10.1.1.2 Nitroketones
 - 10.1.1.3 Nitrolactones
 - 10.1.2 Fate in the body
 - 10.1.2.1 NitroPAHs
 - 10.1.2.2 Nitroketones
 - 10.1.2.3 Nitrolactones
 - 10.1.3 Toxic effects
 - 10.1.3.1 Non-neoplastic effects
 - 10.1.3.2 Genotoxicity
 - 10.1.3.3 Neoplastic effects
 - 10.1.4 Evaluation of nitroPAHs, nitroketones and nitrolactones that seem to be of importance in the environment
- 10.2 Evaluation of effects on the environment
- 10.3 General considerations
- 10.4 Overall evaluation

RECOMMENDATIONS FOR PROTECTION OF HUMAN HEALTH AND THE ENVIRONMENT

RECOMMENDATIONS FOR FURTHER RESEARCH

PREVIOUS EVALUATIONS BY INTERNATIONAL RODIES

REFERENCES

RESUME

RESUMEN

465