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Concise International Chemical Assessment Document 34

CHLORINATED NAPHTHALENES

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The **International Programme on Chemical Safety (IPCS)**, established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organization (ILO), and the World Health Organization (WHO). The overall objectives of the IPCS are to establish the scientific basis for assessment of the risk to human health and the environment from exposure to chemicals, through international peer review processes, as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the sound management of chemicals.

The **Inter-Organization Programme for the Sound Management of Chemicals (IOMC)** was established in 1995 by UNEP, ILO, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization, the United Nations Institute for Training and Research, and the Organisation for Economic Co-operation and Development (Participating Organizations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen cooperation and increase coordination in the field of chemical safety. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

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FOREWORD

Concise International Chemical Assessment Documents (CICADs) are the latest in a family of publications from the International Programme on Chemical Safety (IPCS) — a cooperative programme of the World Health Organization (WHO), the International Labour Organization (ILO), and the United Nations Environment Programme (UNEP). CICADs join the Environmental Health Criteria documents (EHCs) as authoritative documents on the risk assessment of chemicals.

International Chemical Safety Cards on the relevant chemical(s) are attached at the end of the CICAD, to provide the reader with concise information on the protection of human health and on emergency action. They are produced in a separate peer-reviewed procedure at IPCS. They may be complemented by information from IPCS Poison Information Monographs (PIM), similarly produced separately from the CICAD process.

CICADs are concise documents that provide summaries of the relevant scientific information concerning the potential effects of chemicals upon human health and/or the environment. They are based on selected national or regional evaluation documents or on existing EHCs. Before acceptance for publication as CICADs by IPCS, these documents undergo extensive peer review by internationally selected experts to ensure their completeness, accuracy in the way in which the original data are represented, and the validity of the conclusions drawn.

The primary objective of CICADs is characterization of hazard and dose–response from exposure to a chemical. CICADs are not a summary of all available data on a particular chemical; rather, they include only that information considered critical for characterization of the risk posed by the chemical. The critical studies are, however, presented in sufficient detail to support the conclusions drawn. For additional information, the reader should consult the identified source documents upon which the CICAD has been based.

Risks to human health and the environment will vary considerably depending upon the type and extent of exposure. Responsible authorities are strongly encouraged to characterize risk on the basis of locally measured or predicted exposure scenarios. To assist the reader, examples of exposure estimation and risk characterization are provided in CICADs, whenever possible. These examples cannot be considered as representing all possible exposure situations, but are

provided as guidance only. The reader is referred to EHC 170.¹

While every effort is made to ensure that CICADs represent the current status of knowledge, new information is being developed constantly. Unless otherwise stated, CICADs are based on a search of the scientific literature to the date shown in the executive summary. In the event that a reader becomes aware of new information that would change the conclusions drawn in a CICAD, the reader is requested to contact IPCS to inform it of the new information.

Procedures

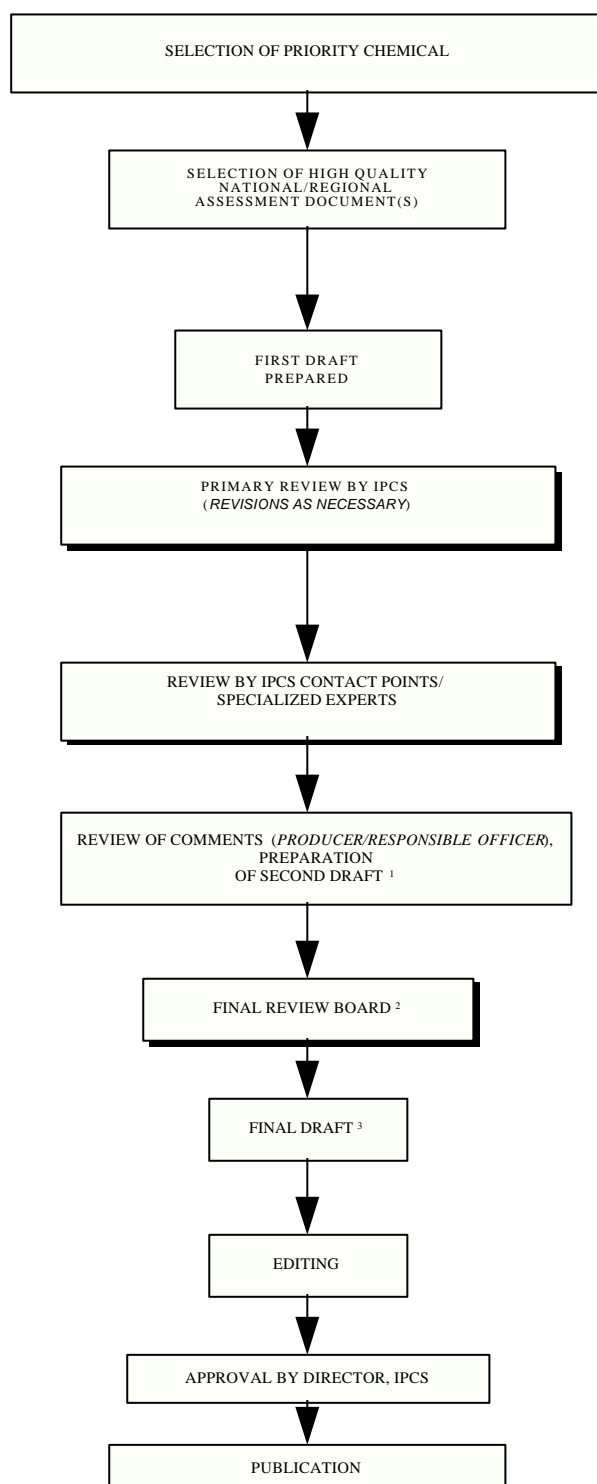
The flow chart on page 2 shows the procedures followed to produce a CICAD. These procedures are designed to take advantage of the expertise that exists around the world — expertise that is required to produce the high-quality evaluations of toxicological, exposure, and other data that are necessary for assessing risks to human health and/or the environment. The IPCS Risk Assessment Steering Group advises the Co-ordinator, IPCS, on the selection of chemicals for an IPCS risk assessment, the appropriate form of the document (i.e., EHC or CICAD), and which institution bears the responsibility of the document production, as well as on the type and extent of the international peer review.

The first draft is based on an existing national, regional, or international review. Authors of the first draft are usually, but not necessarily, from the institution that developed the original review. A standard outline has been developed to encourage consistency in form. The first draft undergoes primary review by IPCS to ensure that it meets the specified criteria for CICADs.

The second stage involves international peer review by scientists known for their particular expertise and by scientists selected from an international roster compiled by IPCS through recommendations from IPCS national Contact Points and from IPCS Participating Institutions. Adequate time is allowed for the selected experts to undertake a thorough review. Authors are required to take reviewers' comments into account and revise their draft, if necessary. The resulting second draft is submitted to a Final Review Board together with the reviewers' comments. At any stage in the international review process, a consultative group may be necessary to address specific areas of the science.

¹ International Programme on Chemical Safety (1994) *Assessing human health risks of chemicals: derivation of guidance values for health-based exposure limits*. Geneva, World Health Organization (Environmental Health Criteria 170).

CICAD PREPARATION FLOW CHART



¹ Taking into account the comments from reviewers.

² The second draft of documents is submitted to the Final Review Board together with the reviewers' comments.

³ Includes any revisions requested by the Final Review Board.

The CICAD Final Review Board has several important functions:

- to ensure that each CICAD has been subjected to an appropriate and thorough peer review;
- to verify that the peer reviewers' comments have been addressed appropriately;
- to provide guidance to those responsible for the preparation of CICADs on how to resolve any remaining issues if, in the opinion of the Board, the author has not adequately addressed all comments of the reviewers; and
- to approve CICADs as international assessments.

Board members serve in their personal capacity, not as representatives of any organization, government, or industry. They are selected because of their expertise in human and environmental toxicology or because of their experience in the regulation of chemicals. Boards are chosen according to the range of expertise required for a meeting and the need for balanced geographic representation.

Board members, authors, reviewers, consultants, and advisers who participate in the preparation of a CICAD are required to declare any real or potential conflict of interest in relation to the subjects under discussion at any stage of the process. Representatives of nongovernmental organizations may be invited to observe the proceedings of the Final Review Board. Observers may participate in Board discussions only at the invitation of the Chairperson, and they may not participate in the final decision-making process.

1. EXECUTIVE SUMMARY

This CICAD on chlorinated naphthalenes was prepared by the Centre for Ecology & Hydrology, Monks Wood, United Kingdom, and the Fraunhofer Institute for Toxicology and Aerosol Research, Hanover, Germany. It is based on the United Kingdom's *Environmental hazard assessment: Halogenated naphthalenes* (Crookes & Howe, 1993) and the work of the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (Greim, 1997), supplemented by a literature search (June 2000). Information on the nature of the peer review and availability of the source documents is presented in Appendix 1. Information on the peer review of this CICAD is presented in Appendix 2. This CICAD was approved as an international assessment at a meeting of the Final Review Board, held in Geneva, Switzerland, on 8–12 January 2001. Participants at the Final Review Board meeting are listed in Appendix 3. The International Chemical Safety Cards for trichloronaphthalene (ICSC 0962), tetrachloronaphthalene (ICSC 1387), pentachloronaphthalene (ICSC 0935), hexachloronaphthalene (ICSC 0997), and octachloronaphthalene (ICSC 1059), produced by the International Programme on Chemical Safety (IPCS, 1993a,b,c, 1999a,b), have also been reproduced in this document.

There are 75 possible congeners of chlorinated naphthalenes. Commercial products are generally mixtures of several congeners and range from thin liquids to hard waxes to high melting point solids. Their main uses have been in cable insulation, wood preservation, engine oil additives, electroplating masking compounds, capacitors, and refractive index testing oils and as a feedstock for dye production.

The major sources of release of chlorinated naphthalenes into the environment are likely to be from waste incineration and disposal of items containing chlorinated naphthalenes to landfill.

Chlorinated naphthalenes are expected to adsorb onto soil and sediments to a large extent. Predicted soil organic carbon/water partition coefficients show an increase as the degree of chlorination in the chlorinated naphthalene increases. Thus, the lower chlorinated congeners are likely to show a moderate sorption tendency, and the higher chlorinated congeners are likely to show a strong sorption tendency.

Chlorinated naphthalenes have been shown to be highly bioaccumulative in fish, but less so in shrimp and algae. The amount of bioaccumulation observed increases with the degree of chlorination of the chlorinated naphthalenes, but the most highly

chlorinated naphthalenes (e.g., octachloronaphthalene) do not appear to bioaccumulate due to their very limited absorption.

Monochloronaphthalenes appear to be readily degradable by soil and water microorganisms under aerobic conditions. No information was found on the biodegradation of higher chlorinated congeners by microorganisms.

One report gave an atmospheric half-life of 2.7 days for 1,4-dichloronaphthalene. No other information was found regarding the atmospheric fate of other chlorinated naphthalenes. As all chlorinated naphthalenes absorb light at environmentally relevant wavelengths, direct photolysis reactions may occur in water, in air, or on soil.

In the past, chlorinated naphthalene concentrations of up to 14.5 mg/m³ have been measured in the workplace, while levels of 25–2900 ng/m³ have been recorded in outdoor air in the vicinity of manufacturing sites. More recently, monitoring studies have revealed chlorinated naphthalene concentrations of up to 150 pg/m³ at “semirural” sites and 1–40 pg/m³ at remote sites. Predominant congeners in outdoor air were tri- and tetrachloronaphthalenes. In the 1970s, surface water concentrations of up to 5.5 µg/litre were measured near chlorinated naphthalene manufacturing plants, with higher levels recorded in groundwater. Recent studies have found surface water levels in the low ng/litre range. A single study on chlorinated tap water revealed chlorinated naphthalene concentrations of up to 0.15 ng dichloronaphthalene/litre and up to 0.44 ng monochloronaphthalene/litre. Sediment levels of up to 100 mg/kg have been recorded in the past; however, recent results show levels of 0.2 µg/kg at unpolluted sites and 250 µg/kg at polluted sites. Similarly, soil levels of up to 1300 mg/kg were measured at contaminated sites in the early 1980s compared with a more recent value for a former chlor-alkali plant of 18 mg/kg dry weight. Chlorinated naphthalene concentrations in fish range up to a maximum of around 300 µg/kg lipid weight. Tetra- and pentachloronaphthalene congeners tend to predominate in biota. Monitoring studies with seabird eggs have revealed a decrease in chlorinated naphthalene levels between 1974 and 1987.

Chlorinated naphthalenes, especially dioxin-like congeners, have been detected in adipose tissue, liver, blood, and breast milk samples of the general population at concentrations in the ng/kg lipid range. The chlorinated naphthalene congener/isomer pattern found in human specimens was significantly different from that in commercial chlorinated naphthalene mixtures. The dominating congeners in almost all human specimens

examined were two penta- and two hexa- isomers, namely 1,2,3,5,7/1,2,4,6,7-pentachloronaphthalene and 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene, and to a lesser extent some tetra- isomers.

Chlorinated naphthalenes can be absorbed via oral, inhalative, and dermal routes, with absorption and distribution over the whole body after oral administration. The main target organs are liver and fat tissue (besides kidney and lung), both showing a high retention, especially for higher chlorinated congeners such as 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene. Half-lives of 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene were calculated to be 41 days in adipose tissue and 26 days in the liver of rats. Calculations with monitoring data from human blood samples suggested half-lives of 1.5–2.4 years for these hexa- isomers in humans. Hydroxy metabolites have been identified mostly for the lower chlorinated naphthalenes (mono- to tetra-) in experimental animals. There are also preliminary indications for the occurrence of methylthio- or methyl sulfoxide chloronaphthalene metabolites in faeces of rats. Elimination of parent compounds and/or metabolites occurs via faeces and urine. There was also a transfer of 1,2,3,4,6,7-hexachloronaphthalene to offspring of rats via placental and lactational routes.

LD₅₀ values of some chlorinated naphthalenes ranged from >3 (2,3,6,7-tetrachloronaphthalene) to 1540(1-monochloronaphthalene) mg/kg body weight. Short-term exposure to higher chlorinated naphthalenes resulted in mortality, liver damage, degeneration of kidneys, etc., in rats, rabbits, and cattle. Cattle developed severe systemic disease (bovine hyperkeratosis) during a 5- to 10-day oral exposure to 1.7–2.4 mg/kg body weight per day of penta-, hexa-, hepta-, or octachlorinated naphthalenes. Similar symptoms (death, severe weight loss, and liver damage) have also been observed during medium-term oral or inhalative exposures of laboratory and domestic animals. The higher chlorinated congeners appeared to be more toxic than the lower chlorinated ones. Inhalation of 1.4 mg/m³ (8 h/day) of a penta/hexachlorinated naphthalene mixture for 143 days resulted in slight to moderate histological liver damage in rats.

Long-term and carcinogenicity studies with chlorinated naphthalenes have not been performed.

The few chlorinated naphthalenes tested for mutagenicity — 1-monochloronaphthalene and 1,2,3,4-tetrachloronaphthalene — have proved to be not mutagenic in the *Salmonella* Ames test.

1,2,3,4,6,7-Hexachloronaphthalene has been found to accelerate the onset of spermatogenesis in male

offspring of rats when given to dams at 1 µg/kg body weight per day on days 14–16 of gestation.

Like related compounds, chlorinated naphthalenes have been demonstrated to be inducers of the cytochrome P-450 (CYP)–dependent microsomal enzymes. Two very persistent (and frequently identified in human and environmental samples) hexachlorinated naphthalene isomers (i.e., 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene) caused induction of CYP1A1 — typical for dioxin-like compounds — in several *in vitro* and *in vivo* test systems. Chlorinated naphthalenes were also found to change lipid peroxidation and antioxidant enzyme activities in rats in a manner indicative of increased oxidative stress. At least some of the biological and toxic responses of chlorinated naphthalenes are believed to be mediated via the cytosolic Ah receptor, resembling those of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and related compounds.

All chlorinated naphthalenes tested caused skin irritations, and the penta- and hexachlorinated naphthalenes showed hyperkeratotic activity in the rabbit ear test and in hairless mice, consistent with findings in cattle (bovine hyperkeratosis or X-disease) and humans (chloracne).

Severe skin reactions (chloracne) and liver disease have both been reported after occupational exposure to chlorinated naphthalenes. Chloracne was common among workers handling chlorinated naphthalenes in the 1930s and 1940s.

Other symptoms described in workers exposed to chlorinated naphthalenes included irritation of the eyes, fatigue, headache, anaemia, haematuria, impotentia, anorexia, nausea, vomiting, and occasionally severe abdominal pain. At least 10 deaths were reported from acute atrophy of the liver. Systemic effects resulting in liver disease have been reported only from the inhalation of chloronaphthalenes.

After dermal application of various Halowax samples to adult subjects, only Halowax 1014, containing penta- and hexachloronaphthalenes, produced chloracne; Halowaxes containing mono-, di-, tri-, tetra-, hepta-, and/or octachloronaphthalenes did not.

A cohort mortality study on workers exposed to chlorinated naphthalenes at a cable manufacturing plant found an excess of deaths from cirrhosis of the liver. However, individuals who had shown symptoms of chloracne did not show a higher mortality due to liver cirrhosis compared with other workers. The mortality from all cancers was slightly but significantly elevated among all exposed men (standardized mortality ratio =

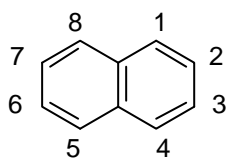
1.18) but was not more elevated in the subcohort with chloracne. This subcohort showed statistically significant excess mortality from cancer of the oesophagus and from “benign and unspecified neoplasms.”

There are only a few miscellaneous reports on the effects of incidental exposure to chlorinated naphthalenes on the general population. With one exception, they involve ingestion of oil contaminated with other chemicals as well as chlorinated naphthalenes, resulting in general systemic symptoms followed by chloracne.

Chlorinated naphthalenes appear to be of moderate to high acute toxicity to aquatic organisms.

2. IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

Chlorinated naphthalenes are a group of compounds based on the naphthalene ring system, but where one or more hydrogen atoms have been replaced by chlorine. The generic molecular formula is $C_{10}H_{8-1-n}Cl_n$, where $n = 1-8$. There are 75 possible chlorinated naphthalenes, and they are usually identified using the numbering system shown below:



Chlorinated naphthalenes are often called polychlorinated naphthalenes, or PCNs.

Most of the industrially produced PCNs are not pure materials, but are usually a mixture of several congeners. The commercial products range from thin liquids to hard waxes to high melting point solids, with melting points ranging from ! 40 to 180 °C. Liquid PCNs are soluble in most organic solvents, whereas the waxy or solid PCNs are soluble in chlorinated solvents, aromatic solvents, and petroleum naphthas and can be mixed with petroleum waxes, chlorinated paraffins, polyisobutylates, and plasticizers. PCNs have low flammability and are of medium to low volatility, volatility decreasing with increasing chlorination.

Some relevant physical and chemical properties of PCNs and commercial PCNs are listed in Tables 1 and 2, respectively. Additional physical/chemical properties are presented in the International Chemical Safety Cards reproduced in this document.

3. ANALYTICAL METHODS

Highly sensitive and specific analytical techniques are necessary for the measurement of PCNs because of their complexity. Another analytical complication is the co-occurrence of bulk quantities of polychlorinated biphenyls (PCBs) or organochlorine pesticides in environmental matrices when typical gas chromatography–electron capture detector methods are used (Falandysz, 1998).

Various methods have been used to overcome this difficulty, typically to perchlorinate the PCNs and PCBs to give octachloronaphthalene and decachlorobiphenyl, respectively, or to hydrodechlorinate the PCNs and PCBs to give naphthalene and biphenyl, respectively. The products from these reactions can be more easily quantified by gas chromatographic techniques, but the methods suffer from interference from naphthalene already present in the samples; also, a lot of information about the individual PCNs originally present in the samples is lost. Recent advances in the analysis of PCNs include the use of mass spectrometric detection, which allows individual compounds in complex analyses to be identified and quantified, but this is possible only if authentic standard material is available for all the possible PCNs (Crookes & Howe, 1993).

All 75 PCN congeners have been synthesized, although sometimes only in mixtures (Nikiforov et al., 1992, 1993; Auger et al., 1993; Imagawa et al., 1993; Imagawa & Yamashita, 1994, 1997; Takasuga et al., 1994). Quantification of all PCN congeners with gas chromatography–mass spectrometry using the molar response of electron impact ionization and based on one or two reference compounds is possible (Falandysz, 1998).

For congener-specific determination of PCNs in environmental matrices, a contaminant enrichment procedure using an activated carbon column is required, coupled with final separation and quantification using high-resolution capillary gas chromatography and electron capture negative ionization mass spectrometry (Järnberg et al., 1993, 1997; Haglund et al., 1995; Schlabach et al., 1995; Falandysz & Rappe, 1996, 1997; Falandysz et al., 1996b).

Falandysz (1998) states that a further problem in the analysis of samples for PCNs is the co-elution of some PCN congeners when using a single column in capillary gas chromatographic separation. However, advances in the analytical separation of PCN congeners are being identified. For example, Helm et al. (1999)

Table 1: Physical/chemical properties of chlorinated naphthalene congeners.^a

Chlorinated naphthalene	CAS No.	Relative molecular mass	Boiling point (°C)	Melting point (°C)	Vapour pressure (kPa)	Aqueous solubility (µg/litre)	Henry's law constant (Pa·m ³ /mol)	Log octanol/water partition coefficient
Monochloro-naphthalene	25586-43-0							
1-chloro	90-13-1	162.61	260	12.3	2.1×10^{-3} ^a ; 3.9×10^{-3} ^b	2870	36 ^c	3.9
2-chloro	91-58-7	162.61	259	59.5–60	1.1×10^{-3} ^d	924		3.98; 4.19
Dichloro-naphthalene								
1,2-dichloro	2050-69-3	197	295–298	37		137		4.42
1,3-dichloro	2198-75-6	197	291	61.5–62				
1,4-dichloro	1825-31-6	197	287	71–72	1.7×10^{-4} ^a	314; 309		4.66; 4.88; 6.93 ^e
1,5-dichloro	1825-30-5	197		107		396		4.67
1,6-dichloro	2050-72-8	197		48.5–49				
1,7-dichloro	2050-73-9	197		63.5		235		4.56
1,8-dichloro	2050-74-0	197		89–89.5		590; 309		4.19; 4.41
2,3-dichloro	2050-75-1	197		120		862; 85		4.51; 4.71
2,6-dichloro	2065-70-5	197	285	137–138				
2,7-dichloro	2198-77-8	197		115–116		240		4.81
Trichloro-naphthalene	1321-65-9	231.5						
1,2,3-trichloro	50402-52-3	231.5		84				
1,2,4-trichloro	50402-51-2	231.5		92				7.27 ^e
1,2,5-trichloro	55720-33-7	231.5		79				
1,2,6-trichloro	51570-44-6	231.5		92.5				
1,2,7-trichloro	55720-34-8	231.5		88				
1,2,8-trichloro	55720-35-9	231.5		83				
1,3,5-trichloro	51570-43-5	231.5		103				7.32 ^e
1,3,6-trichloro	55720-36-0	231.5		81				
1,3,7-trichloro	55720-37-1	231.5	274 ^a	113	1.3×10^{-4} ^a	64.4; 65		5.35; 5.59
1,3,8-trichloro	55720-38-2	231.5		85				
1,4,5-trichloro	2437-55-0	231.5		133				7.56 ^e
1,4,6-trichloro	2737-54-9	231.5		68				7.27 ^e
1,6,7-trichloro	55720-39-3	231.5		109				
2,3,6-trichloro	55720-40-6	231.5		91		16.7		5.12
Tetrachloro-naphthalene	1335-88-2	266						
1,2,3,4-tetrachloro	20020-02-4	266		198		4.2		5.75; 5.50
1,2,3,5-tetrachloro	53555-63-8	266		141		3.7		5.77
1,2,3,6-tetrachloro								
1,2,3,7-tetrachloro	55720-41-7	266		115				

Table 1 (contd).

Chlorinated naphthalene	CAS No.	Relative molecular mass	Boiling point (°C)	Melting point (°C)	Vapour pressure (kPa)	Aqueous solubility (µg/litre)	Henry's law constant (Pa·m ³ /mol)	Log octanol/water partition coefficient
1,2,3,8-tetrachloro								
1,2,4,5-tetrachloro		266						8.58 ^e
1,2,4,6-tetrachloro	51570-45-7	266		111				8.08 ^e
1,2,4,7-tetrachloro	67922-21-8	266		144				8.08 ^e
1,2,4,8-tetrachloro		266						8.41 ^e
1,2,5,6-tetrachloro	67922-22-9	266		164				
1,2,5,7-tetrachloro	67922-23-0	266		114				8.08 ^e
1,2,5,8-tetrachloro		266						8.4 ^e
1,2,6,7-tetrachloro								
1,2,6,8-tetrachloro	67922-24-1	266		125–127				
1,2,7,8-tetrachloro								
1,3,5,7-tetrachloro	53555-64-9	266		179		4.0; 4.3		6.19; 6.38
1,3,5,8-tetrachloro	31604-28-1	266		131		8.2; 8.3		5.76; 5.96
1,3,6,7-tetrachloro	55720-42-8	266		120				
1,3,6,8-tetrachloro								
1,4,5,8-tetrachloro	3432-57-3	266		183				8.45 ^e
1,4,6,7-tetrachloro	55720-43-9	266		139		8.1		5.81; 8.13 ^e
2,3,6,7-tetrachloro								
Pentachloro-naphthalene	1321-64-8	300.4					11.9	
1,2,3,4,5-pentachloro	67922-25-2	300.4		168.5				
1,2,3,4,6-pentachloro	67922-26-3	300.4		147				8.91 ^e
1,2,3,5,6-pentachloro								
1,2,3,5,7-pentachloro	53555-65-0	300.4	313*	171	4.2 × 10 ⁻⁶ *	7.3		6.87*; 8.73 ^e
1,2,3,5,8-pentachloro		300.4						9.13 ^e
1,2,3,6,7-pentachloro								

Table 1 (contd).

Chlorinated naphthalene	CAS No.	Relative molecular mass	Boiling point (°C)	Melting point (°C)	Vapour pressure (kPa)	Aqueous solubility (µg/litre)	Henry's law constant (Pa·m ³ /mol)	Log octanol/water partition coefficient
1,2,3,6,8-pentachloro								
1,2,3,7,8-pentachloro								
1,2,4,5,6-pentachloro		300.4						
1,2,4,5,7-pentachloro		300.4						8.86 ^e
1,2,4,5,8-pentachloro		300.4						9.18 ^e
1,2,4,6,7-pentachloro		300.4						8.73 ^e
1,2,4,6,8-pentachloro		300.4						8.78 ^e
1,2,4,7,8-pentachloro		300.4						9.06 ^e
Hexachloro-naphthalene	1335-87-1	335			3 × 10 ⁻⁸ *		8.8 *	
1,2,3,4,5,6-hexachloro		335						10.11 ^e
1,2,3,4,5,7-hexachloro	67927-27-4	335	331*	194	9.5 × 10 ⁻⁷ *	0.11*		7.58*; 9.8 ^e
1,2,3,4,5,8-hexachloro		335						10.37 ^e
1,2,3,4,6,7-hexachloro		335						9.7 ^e
1,2,3,5,6,7-hexachloro		335						9.7 ^e
1,2,3,5,6,8-hexachloro		335						9.8 ^e
1,2,3,5,7,8-hexachloro		335						9.83 ^e
1,2,3,6,7,8-hexachloro								
1,2,4,5,6,8-hexachloro		335						6.98 ^f ; 9.89 ^e
1,2,4,5,7,8-hexachloro		335						9.89 ^e
Heptachloro-naphthalene	32241-8-0	369.5						
1,2,3,4,5,6,7-heptachloro		369.5						7.69 ^f
1,2,3,4,5,6,8-heptachloro	58863-15-3	369.5	348*	194	3.7 × 10 ⁻⁷ *	0.04*		8.3*
Octachloro-naphthalene	2234-13-1	404	365*	198	1.3 × 10 ⁻⁷ *	0.08	4.8 *	6.42; 8.4 ^g

^a * indicates estimated value.; ^b Schoene et al. (1984); ^c Mackay et al. (1982).

^d Budavari et al. (1996).; ^e Harner & Bidleman (1998); ^f Burreau et al. (1997).

^g Opperhuizen et al. (1985).

Table 2: Physical/chemical properties of commercial chlorinated naphthalenes.

Chlorinated naphthalene	CAS No.	Chlorine content (%)	Chlorinated naphthalene composition (% weight)	Boiling point (°C)	Melting point (°C)	Vapour pressure (kPa)	Aqueous solubility	Henry's law constant (Pa·m ³ /mol)
Halowaxes								
Halowax 1031	25586-43-0	22	95% mono-, 5% di-	250 ^a	! 25	1.9 × 10 ⁻³	Insoluble ^a	31.9
Halowax 1000	58718-66-4	26	60% mono-, 40% di-	250 ^a	! 33		Insoluble ^a	
Halowax 1001	58718-67-5	50	10% di-, 40% tri-, 40% tetra-, 10% penta-	308 ^a	98		Insoluble ^a	
Halowax 1099	39450-05-0	52	10% di-, 40% tri-, 40% tetra-, 10% penta-	315 ^a	102		Insoluble ^a	
Halowax 1013	12616-35-2	56	10% tri-, 50% tetra-, 40% penta-	328 ^a	120		Insoluble ^a	
Halowax 1014	12616-36-3	62	20% tetra-, 40% penta-, 40% hexa-	344 ^a	137		Insoluble ^a	
Halowax 1051		70	10% hepta-, 90% octa-		185			
Nibren waxes								
D88					90			
D116N					113			
D130					135			
Seekay waxes^c								
68 (R Grade)		46.5						
93 (R Grade)		50						
123 (R Grade)		56.5						
700 (R Grade)		43						
93 (RC Grade)		50						
123 (RC Grade)		56.5						
Clonacire waxes								
90					90			
115					115			
130					130			

^a Brinkman & De Kok (1980).^b Estimated value.^c R Grade = refined or white wax; RC Grade = electrical grade.

reported the complete resolution of all 14 pentachloro-naphthalenes and all 10 hexachloronaphthalenes. No individual published method reports the ability to discriminate all individual congeners; for this reason, comparison between results from different research groups is difficult (see later sections).

Detection limits of 0.1 ng/g for fly ash, 1 ng/g dry weight for sediment, 0.2 pg/g wet weight for biota, and 0.01 ng/g fat for adipose tissue have been reported (Wiedmann & Ballschmiter, 1993; Williams et al., 1993; Kannan et al., 2000a,b).

4. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

No information was found relating to possible natural sources of PCNs.

Past sources of release such as PCN manufacturing sites (US EPA, 1977; Erickson et al., 1978a,b) and sites using PCN pesticides (Kauppinen, 1986) have been identified.

Major current sources of release of PCNs are likely to be emissions from both municipal and special waste incinerators (Ross & Whitmore, 1984; Tong et al., 1984; Rubey et al., 1985; Oehme et al., 1987; Janssens & Schepens, 1988; Alarie et al., 1989; Benfenati et al., 1991; Schneider et al., 1998; Abad et al., 1999) and disposal of items containing PCNs to landfill (De Kok et al., 1983; Weistrand et al., 1992; Espadaler et al., 1997; Martí & Ventura, 1997).

PCNs have been detected in water and sediments receiving both industrial and municipal sewage discharges (Kuehl et al., 1984b; Vogelgesang, 1986; Furlong et al., 1988) or via leaching from hazardous waste sites (Elder et al., 1981; Kaminsky et al., 1983; Jaffe & Hites, 1984). A characteristic profile of PCNs in soil, sediment, and biota samples collected near a chlor-alkali plant suggests the formation of PCN congeners during the chlor-alkali process (Järnberg et al., 1997; Kannan et al., 1998).

PCNs have been shown to be formed following the use of chlorine to treat drinking-water supplies (Lin et al., 1984; Shiraishi et al., 1985).

It has been estimated that a world total of about 9000 tonnes of PCNs was produced annually in the 1920s. Between the 1930s and 1950s, PCNs were used extensively in the manufacture of electrical insulation; in 1956, it was estimated that approximately 3200 tonnes of PCNs were produced in the USA. By 1978, production in the USA had fallen to about 320 tonnes/year due to the replacement of PCNs by a variety of substitutes. Production of PCNs by Koppers Company, Inc. (manufacturers of Halowaxes) ceased in the USA in 1977 (Kirk-Othmer, 1980), and the last US producer of PCNs (Chemisphere) had stopped manufacture by 1980. Small amounts of PCNs were still being imported into the USA in 1981, around 15 tonnes/year, mainly for use in refractive index testing oils and capacitor dielectrics (US EPA, 1983).

There are no known commercial uses for purified individual isomers of di-, tri-, tetra-, penta-, hexa-, or heptachloronaphthalene. Monochloronaphthalenes and mixtures of mono- and dichloronaphthalenes have been used for chemical-resistant gauge fluids and instrument seals, as heat exchange fluids, as high boiling speciality solvents, for colour dispersions, as engine crankcase additives, and as ingredients in motor tune-up compounds. Monochloronaphthalenes have also been used as a raw material for dyes and as a wood preservative with fungicidal and insecticidal properties (Crookes & Howe, 1993).

The tri- and higher chlorinated naphthalene products have been used as impregnants for condensers and capacitors and dipping encapsulating compounds in electronic and automotive applications, as temporary binders in the manufacture of ceramic components in paper coating and impregnation, in precision casting of alloys, in electroplating stop-off compounds, as additives in gear oils and cutting compounds, in flame-proofing and insulation of electrical cable and conductors, as moisture-proof sealants, as separators in batteries, in refractive index testing oils, as masking compounds in electroplating, and in grinding wheel lubricants (Kirk-Othmer, 1980; US EPA, 1983).

The most important uses, in terms of volume, have been in cable insulation, wood preservation, engine oil additives, electroplating masking compounds, feedstocks for dye production, dye carriers, capacitors, and refractive index testing oils (US EPA, 1983). The use of PCNs as wood preservatives was popular in the 1940s and 1950s, but they are no longer used for this purpose in the USA (US EPA, 1975).

The US Environmental Protection Agency stated that in the USA, only very small amounts of PCNs (about 15 tonnes/year in 1981) were still being used, mainly as refractive index testing oils and as capacitor dielectrics. It did note that the most likely possible new uses for PCNs would be as intermediates for polymers and as flame retardants in plastics (US EPA, 1983).

Popp et al. (1997) reported that PCNs were used in a German plant producing models and tools for car manufacturing and mining until 1989. The production of waxes containing PCNs ceased in the mid-1980s.

5. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

Most of the possible sources of PCN release to the environment are likely to result in emissions to air (possibly adsorbed onto particulate matter), water, and soil. There is some evidence that the emissions of PCNs from incineration processes are associated with particulate matter. This means that there is the possibility that PCNs adsorbed to particulate matter may be removed from the atmosphere by rain. PCNs have moderate to low vapour pressures. The vapour pressure is estimated to decrease as the degree of chlorination increases. This means that volatilization of the more highly chlorinated naphthalenes from water and soil is likely to be small, but volatilization may be important for the less highly chlorinated

congeners (Crookes & Howe, 1993). Atmospheric PCN concentrations are controlled by air-surface exchange and advection even during periods of stable conditions and high temperatures, suggesting that there are ongoing emissions affecting ambient concentrations (Lee et al., 2000). There is evidence for the long-range transport and atmospheric stability of PCNs based on the fact that they have been reported in remote areas such as the Arctic (Harner et al., 1998).

PCN fluxes were measured in a dated core from freshwater sediment in the United Kingdom. The vertical profile showed that flux remained fairly constant at 0.4–0.6 $\mu\text{g}/\text{m}^2$ per year until the early 1940s, rising sharply to a subsurface maximum of around 12 $\mu\text{g}/\text{m}^2$ per year in the late 1950s to mid-1960s followed by a 4-fold decrease to the sediment-water interface. There was no significant difference in homologue profiles with time (Gevao et al., 2000).

The high octanol/water partition coefficients measured for PCNs indicate that adsorption onto soil or sediment may be significant. Soil organic carbon/water partition coefficients have been estimated for several PCNs using molecular connectivity regression equations ranging from 2.97 for monochloronaphthalene to 5.38 for octachloronaphthalene (Koch & Nagel, 1988). The estimated partition coefficients increase as the degree of chlorination increases, indicating that the lower chlorinated naphthalenes are likely to show moderate sorption tendency from water onto soil and sediments and that the higher chlorinated naphthalenes are likely to show a high sorption tendency from water onto soil and sediment.

Photolysis of PCNs has been carried out in methanol solution at 30 °C in the presence of atmospheric amounts of oxygen. A light source with peak energy output at 300 nm and an ultraviolet cut-off at 285 nm was used. Dechlorination and dimerization were the major reaction pathways observed, with traces of methoxylated naphthalenes being formed by reaction with the solvent. PCNs with vicinal or peri-substituted chlorine atoms gave mostly dechlorinated products, while the more unhindered PCNs gave mostly dimer products. The reaction was found to be slower for the more highly chlorinated naphthalenes due to increased stabilization of the radical intermediate with increased chlorination (Ruzo et al., 1975a). Similar reactions may occur in the environment, although the intensity of natural light is likely to be lower than that used in this experiment. More recently, in experiments to test the feasibility of using solar photons for the destruction of waste, photothermal oxidative destruction of chloronaphthalene was demonstrated using ultraviolet photons (Nimlos et al., 1994). Järnberg et al. (1999) found a general shift towards lower chlorinated congeners during exposure of Halowax 1014 in methanol to sunlight.

The reaction of 1,4-dichloronaphthalene with hydroxyl radicals has been studied in smog chamber experiments. At 300 °K, the rate constant for the reaction was found to be 6×10^{-12} $\text{cm}^3/\text{molecule per second}$, using nitrous acid photolysis as a source of hydroxyl radicals. Assuming a typical atmospheric hydroxyl radical concentration of 5×10^5 molecules/ cm^3 , this corresponds to an atmospheric half-life of 2.7 days (Klöppfer et al., 1988).

Little information appears to be available concerning the biodegradation of PCNs. Walker & Wiltshire (1955) found that two species of bacteria isolated from soil were capable of using 1-chloronaphthalene as the sole carbon source. Morris & Barnsley (1982) showed that both 1- and 2-chloronaphthalene were metabolized by pseudomonads grown on naphthalene as the sole source of carbon and energy. Using a sewage sludge inoculum grown on naphthalene, it was shown that 1- and 2-chloronaphthalene were both degraded on incubation with the inoculum (Okey & Bogan, 1965). Bacteria of the genera *Pseudomonas*, *Alcaligenes*, and *Moraxella* from the River Rhine have been shown to metabolize 2-chloronaphthalene in the presence of 1,2-dichlorobenzene or 4-chlorophenol. Two metabolites were identified, a hydroxy compound and 1-oxy-3-carboxymethyl-5(6)-chloro-isocoumarin (Springer & Rast, 1988). Half-lives for degradation of 2-chloronaphthalene by soil microorganisms of 38 days in waste sludge, 59 days in slop oil sludge, and 70–104 days in wood preserving sludge were obtained (Kincannon & Lin, 1985). Järnberg et al. (1999) did not find any measurable change in the congener composition of tetra- to hexachlorinated naphthalenes (Halowax 1014) in a 28-day aerobic degradation experiment. They stated that lower chlorinated congeners (mono- to trichloronaphthalenes) may have been affected but were not determined.

No information appears to be available on the degradation of PCNs under anaerobic conditions.

The large octanol/water partition coefficients measured for PCNs (see Table 1) indicate that bioaccumulation may be significant. The general trend among the PCNs is for the bioconcentration factor (BCF) to increase as the degree of chlorination increases. This follows closely the trend observed in the octanol/water partition coefficients of PCNs (Table 1). BCFs have been measured in fish for a range of PCNs and are shown in Table 3. The measured BCFs in fish indicate that bioaccumulation is likely to occur to a large extent with PCNs up to and including the hexachlorinated naphthalenes, but is not likely to occur for the hepta- or octachlorinated naphthalenes. However, it should be noted that heptachloronaphthalene residues have been measured in some fish species (see section 6). The

Table 3: Bioconcentration factors for chlorinated naphthalenes in fish.

Chlorinated naphthalene	Species	Exposure concentration (µg/litre)	BCF	Reference
Monochloronaphthalene	<i>Cyprinus carpio</i>		191	Matsuo (1981)
2-Chloronaphthalene	<i>Poecilia reticulata</i>	100–1000 ^a	4 266	Opperhuizen et al. (1985)
1,4-Dichloronaphthalene	<i>Poecilia reticulata</i>	10–1000 ^a	2 291	Opperhuizen et al. (1985)
1,4-Dichloronaphthalene	<i>Oncorhynchus mykiss</i>	1.7×10^{-3}	5 600	Oliver & Niimi (1984)
1,8-Dichloronaphthalene	<i>Poecilia reticulata</i>	10–100 ^a	6 166	Opperhuizen et al. (1985)
2,3-Dichloronaphthalene	<i>Poecilia reticulata</i>	10–100 ^a	10 965	Opperhuizen et al. (1985)
2,7-Dichloronaphthalene	<i>Poecilia reticulata</i>	10–100 ^a	10 965	Opperhuizen et al. (1985)
Trichloronaphthalene	<i>Cyprinus carpio</i>		4 677	Matsuo (1981)
1,3,7-Trichloronaphthalene	<i>Poecilia reticulata</i>	1–100 ^a	26 915	Opperhuizen et al. (1985)
Tetrachloronaphthalene	<i>Cyprinus carpio</i>		8 710	Matsuo (1981)
1,2,3,4-Tetrachloronaphthalene	<i>Poecilia reticulata</i>	0.1–10 ^a	33 113 ^b	Opperhuizen et al. (1985)
1,2,3,4-Tetrachloronaphthalene	<i>Oncorhynchus mykiss</i>	5.6×10^{-3}	5 100	Oliver & Niimi (1985)
1,3,5,7-Tetrachloronaphthalene	<i>Poecilia reticulata</i>	0.1–1 ^a	33 884 ^b	Opperhuizen et al. (1985)
1,3,5,8-Tetrachloronaphthalene	<i>Poecilia reticulata</i>	1–10 ^a	25 119 ^b	Opperhuizen et al. (1985)
Pentachloronaphthalene	<i>Cyprinus carpio</i>		10 000	Matsuo (1981)
Heptachloronaphthalene	<i>Poecilia reticulata</i>		0	Opperhuizen et al. (1985)
Octachloronaphthalene	<i>Poecilia reticulata</i>		0	Opperhuizen et al. (1985)
Octachloronaphthalene	<i>Oncorhynchus mykiss</i>	1.3×10^{-2}	330	Oliver & Niimi (1985)

^a Exposure concentrations are estimated ranges from a graphical presentation of results.

^b Equilibrium was not reached within the duration of the experiment.

increase in log BCF occurs up to a maximum of about 4.5 in the experiments with the guppy (*Poecilia reticulata*), whereas no uptake and hence no accumulation occurred with heptachloronaphthalenes or octachloronaphthalene (Opperhuizen et al., 1985; Opperhuizen, 1986). This has been explained by the fact that loss of membrane permeation occurs for large molecules, so the chemical cannot pass from water into the cell. The cross-sectional size of the molecule for which this phenomenon occurs has been estimated at around 1 nm (Opperhuizen et al., 1985; Opperhuizen, 1986; Anliker et al., 1988).

Slight to moderate accumulation occurred in algae (*Chlorococcum* sp.) after exposure to Halowax (1000, 1013, and 1014) for 24 h, with BCFs ranging from 25 to 140. Accumulation increased as the chlorine content of the Halowax increased (Walsh et al., 1977). BCFs of 257 for Halowax 1099, 187 for Halowax 1013, and 63 for Halowax 1000 were measured in grass shrimp (*Palaemonetes pugio*) exposed to 40 µg/litre for 15 days (Green & Neff, 1977). A BCF of 21 000 was found for worms (*Tubifex tubifex* and *Limnodrilus hoffmeisteri*) maintained in spiked sediment (1300 ng 1,2,3,4-tetrachloronaphtha-

lene/g) for up to 79 days, and a depuration half-life of 30 days was measured (Oliver, 1987).

BCFs ranging from 0.73 to 2.5 were reported for tetra-, penta-, hexa-, and heptachloronaphthalenes fed to salmon (*Salmo salar*) in their diet (0.1–10 µg Halowax 1001, 1014, and 1051/g food) for up to 41 weeks (Tysklind et al., 1998; Åkerblom et al., 2000).

6. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

6.1 Environmental levels

Crookes & Howe (1993) stated that relatively few environmental levels of PCNs had been reported by the early 1990s. The authors found this surprising, since their uses and environmental releases were similar to those of PCBs, for which numerous reports of contamination of the environment existed. One reason for this may have been due to the analytical methodology used in determining PCN residues. It was reported that in many analytical techniques, particularly gas chromatography

with electron capture detection, PCNs and PCBs interfered with each other, and so determination of one class of compound in the presence of the other was extremely difficult (Cooke et al., 1980; Kennedy et al., 1982).

During recent years, substantial progress has been made in both the synthesis and analysis of PCNs, enabling the identification of individual congeners in wildlife and abiotic environmental matrices (Falandysz, 1998). For example, such studies have shown a similarity in the pattern of tetra- to heptachlorinated naphthalenes in such abiotic environmental matrices as gas-phase air and fresh water collected in Sweden (Järnberg et al., 1997), riverine sediments in Poland, and subsurface marine plankton (Falandysz & Rappe, 1996; Falandysz et al., 1996a). However, apart from very well defined local situations, it can be very difficult or impossible to relate the pattern of PCNs found in abiotic and biological matrices to any particular source of environmental pollution (Falandysz, 1998). In the following sections, it has been indicated, wherever possible, which of the congeners have been identified. Care should be taken in interpreting the data, particularly those quoted as levels of total PCNs, as it is not always clear if all possible congeners were looked for in the original samples. Data have, in some cases, been summarized into classes of PCNs; this reflects the volume of data if all individual congeners were to be reported and also the differences in resolution between congeners in specific methodologies from different laboratories.

Mean atmospheric PCN concentrations at an urban site (Chicago, USA) and a semiurban site (Toronto, Canada) were 68 and 17 pg/m³, respectively. For urban air, approximately 40% was identified as 1,4,6-trichloronaphthalene (Harner & Bidleman, 1997). Similarly, Dorr et al. (1996) reported PCN concentrations of 60 pg/m³ for urban air (Augsburg, Germany) and 24 pg/m³ for a rural area. Concentrations in urban air ranging up to 98 pg/m³ were reported by Helm et al. (2000), whereas concentrations at the Great Lakes (Canada/USA) ranged from 3 to 27 pg/m³. More than 85% of the PCNs in the air samples were tri- and tetra- isomers. Lee et al. (2000) reported a mean PCN concentration of 152 pg/m³ for a semirural site at Lancaster, United Kingdom. They found that tri- and tetrachloronaphthalenes contributed >95% of the total. Tri- and tetrachloronaphthalenes also formed >90% of the mean PCN concentrations in Arctic air. Mean concentrations were 40 pg/m³ for the Barents Sea, 11.6 pg/m³ for the eastern Arctic Ocean, 7.1 pg/m³ for the Norwegian Sea, 3.5 pg/m³ for Ellesmere Island, Canada, and 0.84 pg/m³ for Dunai Island, Siberia (Harner et al., 1998).

PCNs have been detected at levels of 0.08 µg/m³ (*n* = 2) and 3.4 µg/m³ (*n* = 1) in the ambient air of household basements in Niagara Falls, New York, USA. Highly

elevated levels of a wide range of organic chemicals were found in the basement, with the higher PCN levels suggesting major contamination. The authors stated that there were several known toxic waste dumps in the area (Pellizzari, 1982).

Levels of PCNs in air have been measured at various manufacturing sites in the USA where PCN use was suspected (US EPA, 1977; Erickson et al., 1978a,b). PCN levels of between 25 and 2900 ng/m³ (*n* = 7) were measured near a PCN manufacturing site, the congeners detected being mainly mono- (27%), di- (31%), and trichloronaphthalenes (37%), but other congeners were also detected. PCN levels of not detected to 33 ng/m³ (3 of 16 samples were below the detection limit of 0.3 ng/m³) were measured near two capacitor manufacturing plants, and levels of not detected to 3.1 ng/m³ were measured near a paper manufacturing plant.

2-Chloronaphthalene has been detected in fly ash from municipal incinerators in the USA at levels up to 3 µg/kg (Alarie et al., 1989). A concentration of up to 19.6 µg 2-chloronaphthalene/m³ was detected at the scrubber inlet during incineration of sewage sludge (corresponding to an emission of 0.0011 kg/h), but no 2-chloronaphthalene was detected in the scrubber outlet gases (Gerstle, 1988). 2-Chloronaphthalene and 1,2,3,4-tetrachloronaphthalene have been detected in the emissions from the incineration of hexachlorobenzene (Ross & Whitmore, 1984). Similarly, tri- and tetrachloronaphthalenes have been shown to be formed in the high-temperature degradation of 2,3,4,4',5-pentachlorobiphenyl (Rubey et al., 1985). Levels of 0.10 µg monochloronaphthalene/m³, 2 µg dichloronaphthalene/m³, and 0.10 µg trichloronaphthalene/m³ have been measured in flue gas samples from a municipal incinerator (Eklund & Strömberg, 1983).

PCNs have been detected at 19 Finnish plywood plants. The source of the PCNs was the pesticide Basilum SP-70, which contains approximately 80% PCNs (mainly mono- and dichlorinated isomers) and 4% tributyltin oxide. The pesticide was mixed into the glues used to make the plywood, and monochloronaphthalene and dichloronaphthalene concentrations of 0.2–8 mg/m³ were detected in the glueing department (Kauppinen, 1986).

A laboratory investigation was initiated in order to investigate the possible individual exposure levels at the workplace for those using Beranit® for casting moulds (Popp et al., 1997). After a 1-h emission, assuming a working room volume of 100 m³ and no ventilation, mean air concentrations of halogenated compounds were 14.5 mg/m³ for total PCNs, 4.9 mg/m³ for trichloronaphthalene, 1.0 mg/m³ for pentachloronaphthalene, 0.025 mg/m³ for PCBs, and 2.2 pg international toxicity equivalency factor (I-TEF)/m³ for polychlorinated dibenzo-*p*-dioxins (PCDDs)

and polychlorinated dibenzofurans (PCDFs) (NATO/CCMS, 1988).

Levels of PCNs in water have been measured at various manufacturing sites in the USA where PCN use was suspected (US EPA, 1977; Erickson et al., 1978b). PCN levels of 0.6 and 1.4 µg/litre were measured in two water samples near a PCN manufacturing plant. Levels of not detected to 5.5 µg/litre (four of seven samples were below the detection limit of 0.2 µg/litre) were measured in water near two capacitor manufacturing sites, and PCNs were generally not detected near a paper manufacturing plant.

Monochloronaphthalene at levels of 650–750 ng/litre and dichloronaphthalene at levels of 150–260 ng/litre have been detected in the River Besòs and River Llobregat, Barcelona, Spain. Both rivers receive a wide spectrum of waste discharges, including domestic, industrial, and agricultural wastes (Gomez-Belinchon et al., 1991). In groundwater, total PCNs (expressed as Halowax 1099 equivalents) ranged from <0.5 ng/litre to 79.1 µg/litre for the Llobregat aquifer, with tri- and tetrachloronaphthalenes the major groups of congeners identified. The authors reported that the higher levels probably originated from the poor disposal of illegal landfills closed during the 1970s (Espadaler et al., 1997; Martí & Ventura, 1997). Total PCN concentrations of 0.89 and 2.6 ng/litre were reported for a PCB-polluted river and percolating water at a city dump site (Stockholm, Sweden), respectively (Järnberg et al., 1997).

Levels of chloronaphthalene and dichloronaphthalene have been measured in two samples of Tsukuba (Japan) tap water after chlorination. The detection limit in the experiment was 0.003 ng/litre, and the levels of both chloronaphthalene and dichloronaphthalene were below the detection limit in the raw water before chlorination. After chlorination, levels of 0.03–0.44 ng/litre for chloronaphthalene and levels of not detected to 0.15 ng/litre for dichloronaphthalene were measured (Shiraishi et al., 1985).

Octachloronaphthalene was detected in sediments from Bayou d'Inde (Louisiana, USA), near an industrial outfall. Octachloronaphthalene levels expressed in terms of organic carbon were 12 mg/kg in bottom sediments and 0.8 mg/kg in suspended sediments. No octachloronaphthalene was detected in water from the same area (Pereira et al., 1988). PCN concentrations of up to 23 mg/kg dry weight were found in sediments collected in an area contaminated by disposal of wastes from the chlor-alkali process. Hexa- and heptachloronaphthalenes were the most abundant congeners, accounting for >70% of the total; a characteristic profile of PCNs suggested the formation of congeners during the chlor-alkali process

(Kannan et al., 1998). Octachloronaphthalene has been detected in estuarine sediment samples from the USA at levels of 104 mg/kg dry weight (Rostad & Pereira, 1989).

Levels of 1-chloronaphthalene ranging up to 100 µg/kg dry weight have been measured in marine sediments of Cortiou Creek in the sewage outfall area of Marseilles, France (Milano et al., 1985; Milano & Vernet, 1988). Surface sediment samples from Venice and Orbetello lagoons, Italy, collected during 1995 contained total PCN levels ranging from 0.03 to 1.51 µg/kg dry weight. Tetra- and pentachlorinated naphthalenes were the predominant congeners (Eljarrat et al., 1999). Falandysz et al. (1996a) reported that >80% of the total PCNs found in surface sediment (Gdansk Basin, Baltic Sea) at a concentration of 6.7 µg/kg dry weight was tetrachloronaphthalene, with the congeners 1,2,4,6-, 1,2,4,7-, 1,2,5,7-, 1,2,5,8-, and 1,2,6,8- being the most predominant. Similarly, Ishaq et al. (2000) found that tetrachloronaphthalenes (65%) were the predominant congeners in Baltic sediment, followed by pentachloronaphthalene (27%).

Pentachloronaphthalenes have been detected at levels of 1.3 µg/kg wet weight in sediments from Lake Järnsjön on the River Emån, Sweden. Hexachloro- and heptachloronaphthalenes were not detected in the same samples (Asplund et al., 1990a). Similarly, Järnberg et al. (1997) found a total PCN level of 0.23 µg/kg dry weight (tetra- to hepta- congeners) in an unpolluted Swedish river, compared with concentrations of up to 260–270 µg/kg near chlor-alkali plants and in PCB-polluted rivers. Kannan et al. (2000a) found total PCN levels ranging from 0.08 to 187 µg/kg dry weight for surface sediments from the Detroit and Rouge rivers, Michigan, USA, with penta- and hexachloronaphthalenes the predominant congeners.

Levels of 20 mg chloronaphthalene/kg, 8 mg dichloronaphthalene/kg, and 6 mg trichloronaphthalene/kg have been measured in sediments from the Niagara River, New York, USA, near a dump site (Elder et al., 1981). Another report on the same area gave sediment levels (dry weight) of 5 mg chloronaphthalene/kg, 10 mg dichloronaphthalene/kg, and 4.4 mg trichloronaphthalene/kg. These levels were found at the surface of the sediment. The levels were found to decrease markedly with depth. Lower levels were measured at other sites in the area, and the source of contamination was thought to be a storm sewer outfall from a toxic dump site (Jaffe & Hites, 1984). Levels of PCNs in 33 sediment samples from the Trenton Channel of the Detroit River, Michigan, USA, have been measured. The channel receives waste discharges from several chemical manufacturers. PCNs with 2–8 chlorine atoms were identified,

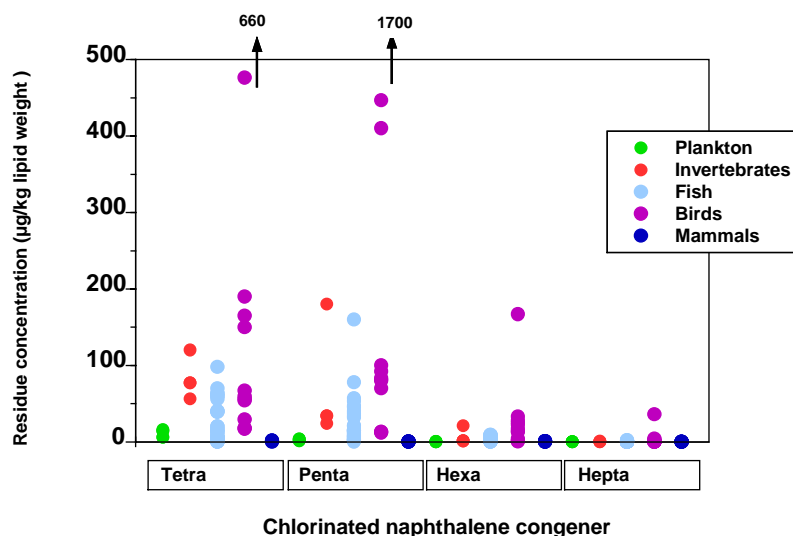


Figure 1: Residues of chlorinated naphthalene congeners in biota from the Baltic.

Data from Tarhanen et al. (1989), Asplund et al. (1990a,b), Järnberg et al. (1993), Falandysz & Rappe (1996), Falandysz et al. (1996a,b, 1997a,b), Falandysz (1998). For birds, the data are residues in liver, for mammals, residues in blubber. Both birds and mammals represented are fish-eating species. For all other organisms, data are whole-body residues. All residues are expressed in terms of lipid weight. For some residue values, original data have been transformed in terms of lipid weight.

and total PCN levels between not detected and 61 mg/kg dry weight were reported (Furlong et al., 1988).

Levels of PCNs have been measured in soils near various manufacturing plants in the USA where PCNs are thought to have been used (US EPA, 1977; Erickson et al., 1978b). Near a PCN manufacturing plant, levels of 130–2300 ng/kg were measured, made up of mainly tri-, tetra-, and pentachloronaphthalenes. PCN levels of between not detected and 21 µg/kg and between not detected and 470 µg/kg were measured near two capacitor manufacturing facilities, and levels ranging from not detected to 34 µg/kg were measured near a paper manufacturing plant (detection limit 0.05 µg/kg).

PCNs have been detected in contaminated soil samples from areas in the Netherlands that have been used for municipal waste disposal. The distribution of congeners was the same as that for Halowax 1013, suggesting that this was the source of contamination and that the composition of the PCNs had not changed, despite being buried in the landfill for 10–15 years. PCN levels of 31–38 mg/kg dry soil and 1180–1290 mg/kg dry soil were measured in two soils; a third soil contained no PCNs (De Kok et al., 1983). Kannan et al. (1998) found PCN concentrations of 17.9 mg/kg dry weight in soil near a former chlor-alkali plant; hexa- and heptachloronaphthalene congeners accounted for >70% of the total concentration. Harner et al. (2000) analysed rural soils in

the United Kingdom dating back to the 1940s. They found a peak level of 12 µg/kg dry weight in the 1960s, falling to 0.5–1 µg/kg in 1990. More detailed analysis revealed that tetra- and pentachloronaphthalenes reached a peak in the 1950s, whereas peak values for trichlorinated isomers were recorded during the 1970s.

During 1968, commercial rice oil was found to be contaminated with PCBs containing total PCN concentrations of 2.6 µg/g. Penta-, hexa-, and heptachloronaphthalenes were the principal isomers (Haglund et al., 1995).

Residues of PCN congeners in biota from the Baltic are summarized in Figure 1. Tetra- and pentachloronaphthalenes predominate at all trophic levels. Because residues in lower organisms (plankton, invertebrates, and fish) are expressed as whole body and residues in higher organisms (birds and mammals) are expressed in specific tissues, it is not possible to directly compare trophic levels. When moving upwards in the food-chain, the homologue distribution does become richer in the higher chlorinated homologues. Ishaq et al. (2000) found that the predominant congeners in isopods were pentachloronaphthalenes (53%), whereas in fourhorned sculpins (*Myoxocephalus quadricornis*), which feed on isopods and amphipods, hexachloronaphthalenes comprised 42% of the total. Furthermore, it was found that polychlorinated congeners that lack two unsubstituted

carbon atoms adjacent to each other bioaccumulate to a greater extent than other congeners.

Levels of 2-chloronaphthalene have been measured in oysters (*Crassostrea virginica*) and clams (*Rangia cuneata*) from Lake Pontchartrain, USA. The levels were 34 µg/kg wet weight in oysters and 140 and 970 µg/kg wet weight in clams (McFall et al., 1985). PCN levels of 39 µg/kg in fish have been measured near a PCN manufacturer in the USA (US EPA, 1977; Erickson et al., 1978b). Levels of tetra- to hexachlorinated naphthalenes in one species of crab and two species of estuarine fish ranged from non-detectable to 0.3 µg/kg wet weight in the vicinity of a coastal former chlor-alkali plant (Kannan et al., 1998).

Congeners of PCNs have been detected in fish from 16 out of 18 watersheds sampled in the Great Lakes. It was concluded that PCNs were widely distributed in the fish samples, although not all congeners were found in all 16 samples (Kuehl et al., 1984a). Freshwater fish sampled in the Great Lakes and their US catchments (1996–1997) showed total PCN levels ranging from 0.04 to 31.4 µg/kg wet weight (Kannan et al., 2000b).

PCNs have been reported to be present at levels of <1 µg/kg in marine fish from Japan; however, some samples taken at a river mouth contained several hundred µg/kg (Takeshita & Yoshida, 1979a). Total PCN concentrations ranging from 6.3 to 260 µg/kg lipid weight have been recorded for fish in the Baltic Sea (Falandysz et al., 1996a). Sinkkonen & Paasivirta (2000) found PCN concentrations in Arctic cod (*Cadus callarias*) liver ranging from 0.078 to 0.78 µg/kg lipid weight for the penta- congeners and from 0.05 to 0.48 µg/kg for the hexa- congeners during the period 1987–1998.

PCNs have been detected in the livers of gulls from the Mediterranean at levels of up to 62.5 mg/kg wet weight (Vannucchi et al., 1978). Guillemot (*Uria aalge*) eggs sampled from the same site on the Baltic coast of Sweden between 1974 and 1987 showed decreasing trends in tetra-, penta-, and hexachloronaphthalene residues (Järnberg et al., 1993).

Total PCNs have been detected in British birds of prey (Eurasian kestrel *Falco tinnunculus*, sparrowhawk *Accipiter nisus*, and common barn-owl *Tyto alba*) at concentrations ranging from 10 to 180 µg/kg wet weight for liver tissue, from 13 to 120 µg/kg for muscle, and from 120 to 340 µg/kg for kidney (Cooke et al., 1980).

Jansson et al. (1984) found PCN levels of 13 and 15 µg/kg in seal blubber and oil, respectively, from the Baltic area in archived material from the 1940s.

6.2 Human exposure

PCNs have been detected in human adipose tissue (Takeshita & Yoshida, 1979b; Williams et al., 1993; Haglund et al., 1995; Westrand & Noren, 1998; Witt & Niessen, 2000), liver (Westrand & Noren, 1998), blood (Ryan & Masuda, 1994; Westrand et al., 1997), and breast milk (Hayward et al., 1989; Lunden & Noren, 1998; Noren & Meironyte, 2000) at concentrations in the ng/kg lipid range (Table 4). Maximum concentrations for total PCNs (tetra- to hexa-) as high as 26 113 and 17 000 ng/kg lipid, respectively, have been found in liver (Westrand & Noren, 1998) and adipose tissue samples (Takeshita & Yoshida, 1979b) of the general population. Analyses of breast milk from several hundred mothers collected from 1972 to 1992 in Sweden showed a decline in average concentrations of total PCNs from 3081 to 483 ng/kg lipid (Lunden & Noren, 1998). For comparison, the corresponding values for the sum of PCDFs determined in the same breast milk samples were 132 and 30 ng/kg lipid, respectively (Lunden & Noren, 1998).

The only (pilot) study available for a possible occupational exposure (cable incineration and installation and repair of electronic equipment) did not find significant differences in PCN blood plasma levels between exposed workers and controls, but the number of participants ($n = 5$) was very small (Westrand et al., 1997).

Persons who had ingested contaminated rice oil (Yu-cheng incident) had blood levels of up to 30 400 ng 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene/kg lipid (Ryan & Masuda, 1994).

Significant associations ($P < 0.05$) between estimated fish intake and blood plasma levels have been found for 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene, but not for several other PCNs, including 1,3,5,7-tetrachloronaphthalene, in samples from 37 males selected according to varying intake of fish from the Baltic Sea; occupational exposure to PCNs was not known, but was possible in some cases. The blood plasma concentrations of 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene were found to be 2400 (no fish consumption, $n = 9$), 3800 (moderate fish consumption, $n = 14$), and 9400 (high fish consumption, $n = 14$) ng/kg wet weight (Asplund et al., 1994b).

The PCN congener/isomer pattern found in human samples was significantly different from that in the commercial PCN mixtures. The dominating congeners in almost all human specimens examined were two penta- and two hexa- isomers, namely 1,2,3,5,7/1,2,4,6,7-pentachloronaphthalene and 1,2,3,4,6,7/1,2,3,5,6,7-

Table 4: Polychlorinated naphthalene concentrations detected in human tissues and fluids.^a

Sample	Country (sampling date)	Subjects and further details	PCN concentration		Reference
			Measure ^b	ng/kg lipid	
Adipose tissue	Japan (n. sp.)	subjects (<i>n</i> = 10)	range (<i>n</i> = 10): sum of PCNs (tri- to hexa-)	3100–16 900	Takeshita & Yoshida, 1979b
Adipose tissue (from autopsies)	Canada (n. sp.)	persons from 7 municipalities (total <i>n</i> = 30, 16 m, 14 f, 41–88 years)	range of overall means (<i>n</i> = 7): 1,2,3,4,6,7/1,2,3,5,6,7-hexaCN unknown hexaCN unknown pentaCN	430–1040 20–480 560–4890	Williams et al., 1993
Adipose tissue (from autopsy)	Japan (1977)	victim from Yusho rice oil poisoning incident in 1968 (<i>n</i> = 1, m, 59 years)	1,2,5,7/1,2,4,6/1,2,4,7-tetraCN 1,2,3,5/1,3,5,8-tetraCN 1,2,4,8-tetraCN 1,2,5,8/1,2,6,8-tetraCN 1,4,5,8-tetraCN 1,2,3,5,7/1,2,4,6,7-pentaCN 1,2,3,4,6,7/1,2,3,5,6,7-hexaCN sum of PCNs	75 99 64 296 97 165 605 1401	Haglund et al., 1995
Adipose tissue (from autopsies)	Sweden (n. sp.)	persons (<i>n</i> = 7, 5 m, 2 f, 47–80 years)	range (<i>n</i> = 7): 1,3,5,7-tetraCN 1,2,5,7/1,2,4,6/1,2,4,7-tetraCN 1,4,6,7-tetraCN 1,2,3,5/1,3,5,8-tetraCN 1,2,4,8-tetraCN 1,2,5,8/1,2,6,8-tetraCN 1,4,5,8-tetraCN 1,2,3,5,7/1,2,4,6,7-pentaCN 1,2,4,6,8-pentaCN 1,2,4,5,6-pentaCN 1,2,4,7,8-pentaCN 1,2,3,5,8/1,2,3,6,8-pentaCN 1,2,4,5,8-pentaCN 1,2,3,4,6,7/1,2,3,5,6,7-hexaCN 1,2,3,5,6,8-hexaCN sum of PCNs	23–128 39–419 6–93 22–215 15–170 27–332 28–173 191–1219 14–53 <5–36 18–98 <5–22 15–44 389–1094 12–137 999–3909	Weistrand & Noren, 1998
Adipose tissue (from surgery)		children (median age 6–10 years)	sum of PCNs (tetra- to hexa-)		Witt & Niessen, 2000
	Germany (Mannheim)	(<i>n</i> = 10)	mean median	12 000 6800	
	Germany (Rheda-Wiedenbrück)	(<i>n</i> = 10)	mean median	4600 4200	
	Germany (Stralsund)	(<i>n</i> = 10)	mean median	2100 1700	
	Russia (Saratov)	(<i>n</i> = 9)	mean median	8800 8500	
	Kazakhstan (Almaty)	(<i>n</i> = 9)	mean median	7700 6700	
Liver (from autopsies)	Sweden (n. sp.)	persons (<i>n</i> = 7, 5 m, 2 f, 47–80 years)	range (<i>n</i> = 7): 1,3,5,7-tetraCN 1,2,5,7/1,2,4,6/1,2,4,7-tetraCN 1,4,6,7-tetraCN 1,2,3,5/1,3,5,8-tetraCN 1,2,4,8-tetraCN 1,2,5,8/1,2,6,8-tetraCN 1,4,5,8-tetraCN 1,2,3,5,7/1,2,4,6,7-pentaCN 1,2,4,6,8-pentaCN 1,2,4,5,6-pentaCN 1,2,4,7,8-pentaCN 1,2,3,5,8/1,2,3,6,8-pentaCN 1,2,4,5,8-pentaCN 1,2,3,4,6,7/1,2,3,5,6,7-hexaCN 1,2,3,5,6,8-hexaCN sum of PCNs	25–101 106–446 15–72 22–173 19–145 30–314 37–174 169–2635 22–74 <5–113 38–335 <5 17–59 438–21 490 <5–225 1375–26 113	Weistrand & Noren, 1998

Table 4, continued

Sample	Country (sampling date)	Subjects and further details	PCN concentration		Reference			
			Measure ^b	ng/kg lipid				
Blood (whole)	Taiwan (1980–1989)	3 persons from Yu-cheng poisoning incident; days after first sampling:	1,2,3,4,6,7/1,2,3,5,6,7-hexaCN:		Ryan & Masuda, 1994			
		0	range (<i>n</i> = 3)	8590–14 100				
		171	range (<i>n</i> = 3)	14 000–30 400				
		425	range (<i>n</i> = 2)	10 500–11 200				
		1049	range (<i>n</i> = 3)	1640–4950				
		2025	range (<i>n</i> = 2)	1410–1470				
		3502	range (<i>n</i> = 1)	1150				
Blood plasma	Sweden (n. sp.)	men with (<i>n</i> = 28) and without (<i>n</i> = 9) fish consumption	range (<i>n</i> = 37): 1,2,3,5,7-pentaCN 1,2,3,4,6,7/1,2,3,5,6,7-hexaCN	300–32 000 400–4100	Asplund et al., 1994b			
		Blood plasma	Sweden (n. sp.)	workers ^c potentially exposed to organochlorine compounds (<i>n</i> = 5, m, 29–61 years)		range (<i>n</i> = 5): 1,2,3,5,7-pentaCN 1,2,3,4,6,7/1,2,3,5,6,7-hexaCN 1,2,4,5,6,8-hexaCN ^d 1,2,3,4,5,6,7-heptaCN octaCN	54–423 98–261 <14–22 <(3–4) ^e <(3–4) ^e	Weistrand et al., 1997
				control workers ^d with no known high exposure to organochlorine compounds (<i>n</i> = 6, m, 31–53 years)		range (<i>n</i> = 6): 1,2,3,5,7-pentaCN 1,2,3,4,6,7/1,2,3,5,6,7-hexaCN 1,2,4,5,6,8-hexaCN ^d 1,2,3,4,5,6,7-heptaCN octaCN	121–293 134–361 <(11–20) ^e <(2–4) ^e <(2–4) ^e	
Breast milk	USA (Los Angeles, California) (n. sp.)			pooled samples from 7 or 10 mothers, split according to fish consumption:	PCNs (sum of gas chromatographic responses corresponding to Halowax 1013 standard)	Hayward et al., 1989		
				no	mean (<i>n</i> ^g = 2)		1710	
				medium	mean (<i>n</i> ^g = 2)		3020	
high	mean (<i>n</i> ^g = 2)			1730				
Breast milk	Sweden (Stockholm)			pooled samples from:	sum of PCNs:		Lunden & Noren, 1998	
		1972	75 mothers	mean (<i>n</i> ^g = 1)	3081			
		1976	78 mothers	mean (<i>n</i> ^g = 1)	1732			
		1980	116 mothers	mean (<i>n</i> ^g = 1)	1230			
		1984–85	102 mothers	mean (<i>n</i> ^g = 2)	886			
		1990	60 mothers	mean (<i>n</i> ^g = 3)	711			
		1991	60 mothers	mean (<i>n</i> ^g = 3)	501			
		1992	40 mothers	mean (<i>n</i> ^g = 2)	483			
		1992	40 mothers (average age: 29 years)	individual PCNs: range (<i>n</i> ^g = 2): tetraCN tetraCN 1,2,5,6-tetraCN 1,2,3,5,7-pentaCN 1,2,3,4,6,7/1,2,3,5,6,7-hexaCN 1,2,4,5,6,8/1,2,4,5,7,8-hexaCN 1,2,3,4,5,6-hexaCN	24–50 21–133 n.d. 112–409 63–142 0–10 n.d.			

^a f = female; m = male; n.d. = not detected; n. sp. = not specified; CN = chloronaphthalene.

^b Sum of PCNs means sum of tetra- to hexachloronaphthalenes, if not otherwise specified.

^c Three workers occupied in cable incineration for a few months, 1 year, and 10 years, respectively, and two workers occupied in installation and reparation of electronic equipment for 20 and 30 years, respectively.

^d Separation from 1,2,4,5,7,8-hexachloronaphthalene not confirmed.

^e More than one detection limit reported.

^f Three office employees, one construction engineer, one salesman, one chemical laboratory technician.

^g Number of pooled samples.

hexachloronaphthalene, and to a lesser extent some tetra-isomers (see Table 4). At least the predominance of the hexa- isomers is strongly consistent with findings in animals (see sections 6.1 and 7). However, tetrachloronaphthalenes prevailed in adipose tissue samples from children in Germany, Russia, and Kazakhstan, their median concentrations ranging from 900 ng/kg lipid (Stralsund, Germany) to 7000 ng/kg lipid (Saratov, Kazakhstan) (Witt & Niessen, 2000).

7. COMPARATIVE KINETICS AND METABOLISM IN LABORATORY ANIMALS AND HUMANS

Although experimental data are limited, the kinetic behaviour of PCNs resembles that of related polyhalogenated aromatic compounds (e.g., PCDFs/PCDDs, PCBs), which can be absorbed via oral, dermal, and inhalative routes. As with these classes of substances, the lower chlorinated PCNs are less persistent in the body than the more highly chlorinated ones. Accordingly, metabolism and the main route of elimination (via faeces or urine) seem to be influenced by the degree of chlorination.

From studies on the metabolism of PCNs (see below), it can be concluded that mono- and dichloronaphthalenes (>80–90%) and tetrachloronaphthalenes (>45%) are well absorbed by the gastrointestinal tract. Higher chlorinated PCNs are less well absorbed, presumably very poorly absorbed, but no quantification is possible, as data on metabolites in faeces are missing. Dermal and inhalation absorption of PCNs can be concluded from systemic effects in animals and humans. A quantification is not possible.

Investigations with individual lower chlorinated PCNs (mono- and di-) in rats (Chu et al., 1976, 1977a,b), rabbits (Chu et al., 1976), and pigs (Ruzo et al., 1975b, 1976a) indicated metabolism with excretion of the administered dose within days. For example, radioactively labelled 1,2-dichloronaphthalene was absorbed after oral administration, with the highest level of radioactivity at 1 h in the blood of rats. After 24 and 48 h, the highest tissue levels of radioactivity were found in liver, kidneys, intestine, bladder, and adipose tissue. After 7 days, virtually no radioactivity could be detected in these tissues except for adipose tissue (0.04% of total dose) and skin (0.01% of total dose). Elimination occurred via faeces (42% of total dose, within 7 days, as unchanged parent compound) and urine (35% in 7 days, as hydroxylated metabolite). After intravenous application of 1,2-dichloronaphthalene, reabsorption from the intestine

(30% of the dose excreted into faeces) was found in bile duct cannulated rats (Chu et al., 1977a). A similar tissue distribution pattern as mentioned above in rats has been found 1 day after intraperitoneal injection of 1,8- and 2,7-dichloronaphthalene in mice (Oishi & Oishi, 1983); in pigs, 6 h after retrocarotid administration of 1- or 2-monochloronaphthalene, concentrations were the highest in brain and kidneys (Ruzo et al., 1976a).

An early study compared PCNs with low and high degree of chlorination (Cornish & Block, 1958). After oral administration of mono-, di-, tetra-, penta-, hexa-, hepta-, and octachloronaphthalenes to rabbits, phenolic and conjugated urinary metabolites were measured (by means of titration and precipitation procedures; no structure determination). Results suggested a 70–90% excretion for mono- and dichloronaphthalenes and a 45% excretion for tetrachloronaphthalenes in 4 days, whereas no urinary metabolites were detected for penta-, hexa-, hepta-, or octachloronaphthalene. 1,2-Dichloronaphthalene and 1,2,3,4-tetrachloronaphthalene administered retrocarotidally to pigs gave urinary phenolic metabolites, but 1,2,3,4,5,6-hexachloronaphthalene was not metabolized (Ruzo et al., 1976b). Consistently, another study comparing di- and octachloronaphthalenes found higher half-lives for octachloronaphthalene (3.72 days) than for 1,8-dichloronaphthalene (0.27 days) or 2,7-dichloronaphthalene (0.80 days) in adipose tissue of mice, if calculated from tissue levels at various time points up to 28 days (Oishi & Oishi, 1983). Nevertheless, the half-life observed for octachloronaphthalene is unexpectedly short for such a highly chlorinated, lipophilic compound.

Elimination and distribution of a ^{14}C -PCN mixture containing three tetrachloronaphthalene (45%), six pentachloronaphthalene (30%), and four hexachloronaphthalene (10%) isomers have been studied in female Sprague-Dawley rats ($n = 3$). Five days after oral dosing with the ^{14}C -PCN mixture (0.58 mmol/kg body weight, in peanut oil), about 94% of the totally recovered radioactivity (from absorbed and unabsorbed material) was found in faeces. The total urinary excretion was 4.3%. Within tissues, the highest concentrations of radioactivity were observed in liver and abdominal fat (about 10 pmol/mg fresh weight each), followed by the kidney (about 3 pmol/mg fresh weight) and lungs, blood plasma, and adipose tissue (about 1.5 pmol/mg fresh weight each) (Jakobsson et al., 1994).

Most of the metabolites identified in urine and/or faeces of rats, pigs, and frogs after treatment with mono- and dichloronaphthalenes were hydroxylated PCNs (phenolic and conjugated forms), with evidence for metabolism via arene oxide (Ruzo et al., 1975b, 1976a,b;

Sundström et al., 1975; Chu et al., 1976, 1977a,b; Safe et al., 1976). There were also preliminary indications for the presence of methylthio-PCNs and methyl sulfoxide-PCNs as additional PCN metabolites in faeces of rats dosed with a mixture of tetra- to hexachloronaphthalenes (Klasson-Wehler et al., 1996). A whole-body autoradiography study (intraperitoneal administration) and quantitative measurements of extractable and irreversible radioactivity (oral administration) have been performed with ^{14}C -labelled PCNs (composition as noted above) in rats. Most of the ^{14}C in liver, kidney, and lung was non-extractable and therefore considered to be covalently bound as metabolites to macromolecules (Jakobsson et al., 1994; Klasson-Wehler et al., 1996).

Detailed data are available for environmentally relevant (ubiquitous) hexa- congeners. Asplund and co-workers (Asplund et al., 1986, 1994a) examined the retention in liver and adipose tissue of two hexa- isomers, which are minor components of the commercial PCN product Halowax 1014. Rats (Sprague-Dawley, female; $n = 12$) were given single oral doses of Halowax 1014 (20 mg/kg body weight) or of a mixture (0.053 mg/kg body weight) of hexachloronaphthalenes (consisting of equal amounts of 1,2,3,5,6,7-hexachloronaphthalene, 1,2,3,4,6,7-hexachloronaphthalene, and a third unidentified hexachloronaphthalene). The hepatic and adipose residue levels were measured 1, 10, 30, and 120 days after dosing. One day after exposure, the PCN pattern in the adipose tissue of the animals administered Halowax 1014 was similar to that of the technical product, but the relative levels of hepta- and octachloronaphthalenes were lower, possibly due to a less effective absorption of these compounds. However, within 10 days, the two hexa-isomers (co-eluting in gas chromatography) were dominant; after 120 days, they were the only congeners detected, their concentrations being still about 50% of that measured after 1 day. In liver samples, this selective retention was seen after only 1 day. Rats dosed with the hexachloronaphthalene mixture also showed a strong, similar retention of the 1,2,3,5,6,7- and 1,2,3,4,6,7-hexachloronaphthalene (the other unidentified hexachloronaphthalene could not be detected). The concentration ratios (based on the total concentrations of the two hexa- isomers) for liver/adipose tissue were found to be remarkably high: 7.3, 1.1, 0.8, and 0.63 at 24 h and 10, 35, and 120 days, respectively, based on the fresh weights, or 140, 23, 17, and 13, based on the lipid weights. The half-lives were calculated to be 41 days in the adipose tissue and 26 days in the liver. This order of magnitude is comparable to that reported for slowly eliminated PCDF congeners in experimental animals (Ahlborg et al., 1990).

The transfer of 1,2,3,4,6,7-hexachloronaphthalene from dam to offspring has been studied in Wistar rats

orally (gavage) dosed with 1 μg 1,2,3,4,6,7-hexachloronaphthalene/kg body weight per day (in corn oil) on gestation days 14–16. Concentrations of 1,2,3,4,6,7-hexachloronaphthalene in fat of female offspring were $22.18 \pm 6.59 \mu\text{g/kg}$ (corresponding to 1.5–1.6 ng/pup) at birth (postnatal day 0) and $9.78 \pm 2.86 \mu\text{g/kg}$ (corresponding to 13–26 ng/pup) at weaning (postnatal day 21), and concentrations in fat of dams were $5.75 \pm 2.81 \mu\text{g/kg}$ at weaning; 1,2,3,4,6,7-hexachloronaphthalene was not detected in the control samples (Omura et al., 2000). Such a transfer pattern via placental and (to a greater extent) lactational routes appears to be similar to that observed with TCDD and related compounds (e.g., Nagayama et al., 1980; Nau et al., 1986).

Analyses of human tissues and fluids confirmed the high retention potency of the 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene isomers (see section 6.2). Paired samples (Weistrand & Noren, 1998) of liver and adipose tissue from seven subjects showed concentration ratios (on a lipid weight basis) from 0.5 to 20 for these hexa-isomers. The ratio of the sum of PCNs in liver to that in adipose tissue ranged from 0.7 to 10 (median 1.2).

Human blood samples from three individuals exposed to PCN-contaminated rice oil in 1979 in Taiwan were monitored for the 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalenes over a period of about 10 years (see also Table 4). The measured concentrations resulted in calculated half-lives of 1.5–2.4 years (Ryan & Masuda, 1994). Again, these long half-lives in humans are similar to those reported for selected PCDFs (Ryan et al., 1993).

Studies on the induction of drug-metabolizing enzymes are addressed in section 8.7.1.

8. EFFECTS ON LABORATORY MAMMALS AND *IN VITRO* TEST SYSTEMS

8.1 Single exposure

Mortality due to single oral exposure of rats, mice, guinea-pigs, or rabbits to PCNs occurred at concentrations ranging from >3 to 1540 mg/kg body weight (Table 5). The lowest value was the 30-day LD_{50} of 2,3,6,7-tetrachloronaphthalene from the guinea-pig. This was nearly the only experiment taking into account the prolonged time to death, which is typical for dioxin-like compounds. According to McConnell (1989), the mean time to death for such substances is 2–3 weeks after a single exposure for most small laboratory animals and even longer for larger domestic animals, dogs, and non-human primates. Compared on a molar basis, 2,3,6,7-

Table 5: Mortality observed after single oral exposure of rats, mice, and rabbits to polychlorinated naphthalenes.

Congeners	Species	Dose (mg/kg body weight)	Observation period (days)	Mortality	Reference
1-Monochloronaphthalene	Rat	1540		LD ₅₀	Nikunen et al., 1990
	Mouse	1091		LD ₅₀	Nikunen et al., 1990
Mono-, di-, or tetrachloronaphthalene ^a	Rabbit	500	7	No mortality (0/3)	Cornish & Block, 1958
2,3,6,7-Tetrachloronaphthalene	Guinea-pig	>3	30	LD ₅₀	McKinney & McConnell, 1982
Pentachloronaphthalene ^a	Rabbit	500	7	60	Cornish & Block, 1958
Heptachloronaphthalene ^a	Rabbit	500	7	62	Cornish & Block 1958
Octachloronaphthalene ^a	Rabbit	500	7	62	Cornish & Block, 1958

^a Ninety-eight percent purity with respect to chlorine content (several isomers).

tetrachloronaphthalene was less toxic than its brominated counterpart 2,3,6,7-tetrabromonaphthalene and TCDD, which have 30-day LD₅₀ values of >11.3, 0.547, and 0.006 µmol/kg body weight, respectively, in the guinea-pig, corresponding to >3000, 242, and 2 µg/kg body weight (McConnell, 1989).

Studies using routes other than oral exposure are not available.

8.2 Short-term exposure

There are two short-term studies on laboratory rodents, both using only a single dose level. No dermal irritation has been found in mice orally administered trichloronaphthalene at 2.5 mg/day per mouse for 20 days (Shakhnovskaya, 1953). Rats fed a mixture of penta/hexachloronaphthalenes (125 mg/rat per alternate day) for 26 days showed moderate liver changes (swollen and vacuolated liver cells, as well as necrosis and degeneration of scattered cells). All other organs (no specification) were found to be normal after microscopic examination (Bennett et al., 1938).

After daily subcutaneous administration of two PCN mixtures consisting mainly of tetra/pentachloronaphthalenes and of penta/hexachloronaphthalenes at doses of 30 mg (in paraffin oil) per day per rabbit, all rabbits died (5/5 per group) by days 12–26. At autopsy, the livers had many yellow areas and a wide zone of necrosis. None of the rabbits (*n* = 5) receiving a mixture containing mainly tri/tetrachloronaphthalenes died (Flinn & Jarvik, 1936).

Cattle developed severe hyperkeratosis during 5–10 days of exposure to 1.7–2.4 mg/kg body weight per day of purified penta-, hexa-, hepta-, or octachloronaphthalene congeners (containing mainly several isomers of equal degree of chlorination) (Bell, 1953; see also section 8.7.3).

Oral exposure of pigs to hexachloronaphthalene at 19–22 mg/kg body weight per day for up to 10 days caused degeneration of liver and kidneys and mortality (Link et al., 1958; Huber & Link, 1962). However, a total hexachloronaphthalene dose of 198 mg/kg body weight given orally over a period of 9 days was fatal.

8.3 Medium-term exposure

Some medium-term experiments, which have been reviewed earlier (US EPA, 1980; Crookes & Howe, 1993; Hayward, 1998), have been performed with technical mixtures of PCNs in rats and guinea-pigs. The main features reported are weight loss, liver damage (mainly enlarged liver cells with increased granularity and vacuolization), and death after oral, dietary, and inhalative exposures (Table 6). The higher chlorinated mixtures appear to be more toxic than the lower chlorinated ones.

Daily oral administration of 2.5–10 mg/kg body weight of technical PCN (mainly pentachloronaphthalene) resulted in death of guinea-pigs within 22–48 days, connected with severe weight loss (33–44%) and fatty degeneration of the liver (Bentz & Herdmann, 1956; see also Table 6).

Technical PCN mixtures given in feed led to slight histological liver changes (tri/tetrachloronaphthalenes) or to deaths (tetra/pentachloronaphthalenes; penta/hexachloronaphthalenes) (Drinker et al., 1937; Bennett et al., 1938; see also Table 6).

Whereas inhalation of about 11 mg/m³ of a mixture consisting mainly of tri- and tetrachloronaphthalenes (16 h/day) caused only moderate histological liver damage in rats, all rats inhaling about 9 mg/m³ of a penta/hexachloronaphthalene mixture died within 52 days. Inhalation of 1.4 mg/m³ of penta/hexachloronaphthalenes

Table 6: Effects observed after medium-term exposure of rats and guinea-pigs to polychlorinated naphthalenes.

Route	Species	PCN congeners (technical mixtures)	Concentration	Duration of exposure	Effects	Reference
Oral	Guinea-pig	Pentachloro	2.5, 5, 10 mg/kg body weight per day	48, 46, 22 days	All dead ($n = 3$), severe weight loss and liver damage (fatty degeneration)	Bentz & Herdmann, 1956
In feed ^a	Rat	Tri/tetrachloro	300 mg/rat per day	9–136 days	Slight liver damage ^b	Drinker et al., 1937; Bennett et al., 1938
In feed	Rat	Tetra/pentachloro	50 mg/rat per day	63 days	All moribund or dead ($n = 10$)	Drinker et al., 1937; Bennett et al., 1938
In feed	Rat	Penta/hexachloro	100 mg/rat per day	55 days	All moribund or dead ($n = 10$)	Drinker et al., 1937; Bennett et al., 1938
In feed	Rat	Penta/hexachloro	300 mg/rat per day	33 days	All dead ($n = 10$)	Drinker et al., 1937; Bennett et al., 1938
In feed	Rat	Hexachloro	0.3, 0.9, 2.3 mg/rat per day ^c	56–84 days	Dose-dependent increases in relative liver weights	Weil & Goldberg, 1962
Inhalation ^d	Rat	Tri/tetrachloro	1.31 mg/m ³	16 h/day, 134 days	Very slight liver damage ^b	Drinker et al., 1937; Bennett et al., 1938
Inhalation	Rat	Tri/tetrachloro	10.97 mg/m ³	16 h/day, 102 days	Moderate liver damage ^b	Drinker et al., 1937; Bennett et al., 1938
Inhalation	Rat	Penta/hexachloro	1.44 mg/m ³	8 h/day, 143 days	Slight to moderate liver damage ^b	Drinker et al., 1937; Bennett et al., 1938
Inhalation	Rat	Penta/hexachloro	1.16 mg/m ³	16 h/day, 134 days	Slight to moderate liver damage ^b	Drinker et al., 1937; Bennett et al., 1938
Inhalation	Rat	Penta/hexachloro	8.88 mg/m ³	16 h/day, 52 days	All moribund or dead ($n = 55$)	Drinker et al., 1937; Bennett et al., 1938

^a The actual dose from feeding is difficult to ascertain because one of the effects of PCNs is irregular feeding; no details on food consumption given in the study by Drinker et al. (1937).

^b Histological changes included enlargement of liver cells, fatty vacuolization, enhanced granulation, and presence of rare mitotic figures (more or less pronounced); dead/moribund animals showed fatty degeneration of the liver; numbers of rats for histological examinations not accurately specified (mostly in the range of 3–15); no significant histological changes in any other organs (no specification) from representative animals (numbers not specified).

^c Dose calculated according to mean food consumption given by the authors (11.5, 14.5, 15.6 g/rat per day for 0.02%, 0.0063%, and 0.002% hexachloronaphthalene in food, respectively). Numbers of rats per group = 15–25.

^d All inhalation experiments with analytical control of exposure concentration.

(8 h/day; analytical control of exposure concentration) for 143 days resulted in slight to moderate histological liver damage in rats. Gross or histological changes in other organs (no specification) were not reported (Drinker et al., 1937; Bennett et al., 1938; see also Table 6). Histological changes induced in liver cells by inhalation of the penta/hexachloronaphthalene mixture persisted for at least 2 months after treatment (Drinker et al., 1937).

Additionally, a synergistic effect between PCNs (inhaled) and carbon tetrachloride (orally administered, 0.75 ml/kg body weight) could be demonstrated (Drinker et al., 1937). For example, no deaths occurred in rats exposed solely to a technical mixture of penta/hexachloronaphthalenes (about 1 mg/m³, 16 h/day for 144 days) or to carbon tetrachloride (single dose of 0.75 ml/kg body weight in ethyl alcohol). However, 9 of 10 rats pre-exposed to the penta/hexachloronaphthalene mixture (in

the above manner) died within 6 days after administration of the carbon tetrachloride preparation.

Medium-term tests applying single individual PCN congeners have not been performed with laboratory animals.

Generally, domestic animals (see also section 8.7.3) appear to react more sensitively to PCNs than the classical laboratory animals. Severe liver damage and mortality were reported at 1.1 mg/kg body weight per day of a tetra/penta/hexachloronaphthalene mixture in sheep given gelatin capsules for 90–135 days (Brock et al., 1957).

Altogether, the few studies available show trends, but do not allow a no-observed-adverse-effect level (NOAEL) or lowest-observed-adverse-effect level (LOAEL) to be defined.

8.4 Long-term exposure and carcinogenicity

No long-term toxicity or carcinogenicity studies with PCNs have been identified.

8.5 Genotoxicity and related end-points

1,2,3,4-Tetrachloronaphthalene was not mutagenic in the Ames test with or without metabolic (S-9) activation in *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 at concentrations of 100–10 000 µg/plate; toxic effects were not reported (Haworth et al., 1983). There was also no mutagenic activity of 1-monochloronaphthalene in the Ames test with or without metabolic (S-9) activation in *Salmonella typhimurium* strains TA98 and TA100 at concentrations ranging from 0.1 to 100 µg/plate. 1-Monochloronaphthalene exerted a toxic effect in strain TA100 at a concentration of 100 µg/plate and in both strains tested at a concentration of 1000 µg/plate (Löfroth et al., 1985).

There are no data available for any other PCNs or from any other *in vitro* or *in vivo* test system on genotoxicity or related end-points.

8.6 Reproductive toxicity

8.6.1 Effects on fertility

Effects on spermatogenesis in male offspring of rats have been observed after gestational administration of 1 µg 1,2,3,4,6,7-hexachloronaphthalene/kg body weight per day (see section 8.6.3).

Several reproductive abnormalities have been observed in cattle, pigs, and sheep exposed to PCNs — for example, squamous metaplasia of seminal vesicles and epididymides, testicular degeneration, and decreased sperm production (in bulls), as well as squamous metaplasia of vaginal wall, uterine congestion and haemorrhage, abortion (in cows and ewes), and decreased milk production (in cattle suffering from bovine hyperkeratosis) (Bell, 1953; Vlahos et al., 1955; Brock et al., 1957; Link et al., 1958; Huber & Link, 1962; Beck et al., 1972, reviewed with more details by EHD, 1982). Applied doses were mostly in the mg/kg body weight per day range (over days or weeks). However, dose–response relationships or NOAELs cannot be derived from the available data.

8.6.2 Developmental toxicity

No embryotoxicity or apparent gross malformations have been observed in male or female offspring of Wistar rats given orally (gavage) 1 µg 1,2,3,4,6,7-hexachloronaphthalene/kg body weight per day (in corn oil) on days

14, 15, and 16 of gestation (Omura et al., 2000).

8.6.3 Endocrine disruption

Gestational administration of 1,2,3,4,6,7-hexachloronaphthalene (1 µg/kg body weight per day in corn oil by gavage) to pregnant rats (Wistar) has been found to accelerate the onset of spermatogenesis in male offspring (Omura et al., 2000). In this study, dams ($n = 7$) were treated on days 14, 15, and 16 of gestation. All of their offspring were examined at the day of birth (postnatal day 0) and during lactation; the males (one male from each litter) were tested further at various phases of sexual maturation on postnatal days 31, 48, 62, and 89. Mothers and all offspring showed no significant differences in size of litters, body weights, survival, and day of eye opening between 1,2,3,4,6,7-hexachloronaphthalene-treated and control groups. Changes within the male offspring on postnatal day 31 included an increase in testis weight (compared with controls; but not significant) and an increase in postmeiotic tubules to approximately 190% of the control value. Concomitantly, serum concentrations of luteinizing hormone and follicle-stimulating hormone had already reached the maximum level on postnatal day 31 (compared with postnatal day 48 in the control group). On day 48, there was (compared with controls) a non-significant increase in testis weight and a significant increase in the seminal vesicle weight, and the homogenization-resistant (advanced) testicular spermatids increased to approximately 160% of the control value. The sperm counts increased in the cauda epididymis to approximately 180% of the control value on postnatal day 62, accompanied by a non-significant increase in the epididymis weight (relative to control). However, on day 89, the age of sexual maturity, the sperm count was not significantly different from the control. These changes, which suggested an accelerated onset of spermatogenesis, occurred at relatively low doses of 1,2,3,4,6,7-hexachloronaphthalene and were associated with a body burden of 5.75 ± 2.81 µg/kg in fat of the dams at weaning.

Another study of endocrine disruption testing the specific binding to bovine calf uterine estrogen receptor was negative for 2-monochloronaphthalene and 1,2,3,4-tetrachloronaphthalene. The maximum concentrations tested were 50 and 2.8 µmol/litre (corresponding to 8 and 0.7 mg/litre), respectively (Kramer & Giesy, 1999).

8.7 Other toxicity/mode of action

8.7.1 Induction of microsomal enzymes and related effects

PCNs are able to induce the cytochrome P-450-dependent microsomal monooxygenases, as shown in

studies with rats *in vivo* (Wagstaff, 1973; Ahotupa & Aitio, 1980; Campbell et al., 1981, 1983; Cockerline et al., 1981; Safe et al., 1981; Mäntylä & Ahotupa, 1993) and *in vitro* (rat hepatoma cells; Hanberg et al., 1990, 1991), with chick embryos *in ovo* (Engwall et al., 1993, 1994) and *in vitro* (Brunström et al., 1995), with eider duck embryos *in ovo* (Engwall et al., 1993, 1994), and with fish *in vivo* (Holm et al., 1993, 1994; Norrgren et al., 1993).

The commercial mixtures Halowax 1013, 1014, and 1051 (containing highly chlorinated congeners) produced a mixed phenobarbital (PB) and 3-methylcholanthrene (MC)-type induction in rat liver, whereas the lower chlorinated mixtures (Halowax 1000, 1001, 1099) were PB-type inducers (with a slight MC-type induction possible at high doses) (Cockerline et al., 1981; Safe et al., 1981). Maximum doses administered (intraperitoneally, in corn oil) were 600 µmol (about 131–235 mg)/kg body weight (Safe et al., 1981). MC-type induction (Ah receptor-dependent induction of CYP1A1, mostly measured as ethoxresorufin-*O*-deethylase [EROD] and/or arylhydrocarbon hydroxylase [AHH] activity) is typical for TCDD-like compounds.

The induction of EROD activity by PCNs was found to be long-lasting. Three months after a single intraperitoneal dose of Halowax 1014 (20 mg/kg body weight) to male Sprague-Dawley rats, this activity was still elevated (Mäntylä & Ahotupa, 1993).

8.7.2 Effects on lipid peroxidation and antioxidant enzyme activities

Several parameters of increased oxidative stress have been examined in adult male Sprague-Dawley rats given a single intraperitoneal dose of Halowax 1014 (20 mg/kg body weight) and followed for 1, 3, 7, 14, or 90 days post-exposure. In rat liver, there was an increase in lipid peroxidation level (conjugated dienes) as well as a decrease in activities of the reactive oxygen detoxifying enzymes, superoxide dismutase and catalase, evident up to 3–14 days after dosing (Mäntylä & Ahotupa, 1993). The activities of these enzymes were also reduced in the testes of the rats. Additionally, 3 months after dosing, the testicular activities of glutathione peroxidase and glutathione transferase were decreased. The only significant change in lipid peroxidation measurement in the testes was a decrease in thiobarbituric acid-reactive species 1 day after administration (Peltola et al., 1994). Consistently, in another study, the thiobarbituric acid value in liver of rats had increased 1 h and 24 h after intraperitoneal doses (7 g/kg body weight) of a PCN mixture (tetra- to hepta-) (Ohguma, 1979).

8.7.3 Skin irritation, dermal lesions, and acne (including bovine hyperkeratosis)

A common feature of toxicity of dioxin-like compounds is their hyperkeratotic activity in humans and some animal species (IPCS, 1989, 1993d, 1994, 1998).

Only few results are available from rabbit ear tests, a commonly used method for detecting acnegenic activity. The commercial mixture Halowax 1014 and the more or less purified congeners mono-, di-, and hexachloronaphthalenes (dissolved in acetone) have been topically applied to the ear canal skin of rabbits (1 ml of each solution, daily for 5 days). Both the Halowax mixture and the hexachloronaphthalene preparation showed hyperkeratotic activity at the applied concentration of 30 mg/g acetone (corresponding to 23.7 mg/day per ear), but the mono- and dichloronaphthalenes did not at concentrations of up to 590 and 290 mg/g acetone, respectively. The monochloronaphthalene (at 90 mg/g acetone) and dichloronaphthalene (at 45 mg/g acetone) congeners produced only very slight erythema without follicular accentuation and, histologically, a minimal inflammation. At the higher concentrations (590 and 290 mg/g acetone, respectively), severe primary irritant dermatitis resulted within 24 h following a single application; histologically, severe inflammation was seen without sebaceous gland decrease, lysis, and necrosis (Hambrick, 1957). There are no rabbit ear studies providing information on minimum dose levels for induction of hyperkeratosis. (For comparison, minimum TCDD dose levels for induction of hyperkeratosis are 1–160 µg/ear after a single administration, depending on vehicle.)

Guinea-pigs ($n = 5$) dermally exposed to a PCN-containing string (technical mixture, composition and concentration unknown) developed strong dermal irritations within a few days, whereas the control animals ($n = 3$) showed no reactions (Bentz & Herdmann, 1956).

In experiments with hairless mice, another animal model for chloracne, Halowax 1014 and Halowax N-34 (dissolved in acetone, 29 mg, applied 3 times/week, and 20 mg, applied 5 times/week, respectively, for 2 weeks) induced hyperkeratotic changes within 14 days of topical treatment. Octachloronaphthalene (20 mg, 5 times/week for 2 weeks) did not induce gross or histological changes in skin of hairless mice (Puhvel et al., 1982).

Much of the past concern over PCNs has been centred on the poisoning of cows, causing a disease called bovine hyperkeratosis or X-disease (Olson, 1969; Panciera et al., 1993). The disease was of major economic concern in the USA in the 1940s and 1950s and was associated with the accidental ingestion by cows of PCNs from lubricants used in machinery making pelletized feed,

from wood preservatives, from wax used for binding twine, and from rubber mats contaminated with PCNs. The toxicity of the PCNs to cows was found to increase with increasing degree of chlorination, the tetrachlorinated and lower chlorinated congeners having little or no effect. The main effects of the higher chlorinated PCNs in cows appear to be interference with the biotransformation of carotene to vitamin A. As the disease progresses, vitamin A deficiency is followed by inflammation of oral mucosa, lacrimation, excessive salivation, and irregular food consumption. Gross physical effects include thickening of the skin and loss of hair, and the horns may show signs of degeneration or irregular growth. On continued exposure to the higher chlorinated PCNs, anaemia, dehydration, loss of weight, fever, severe liver damage, and death occur. Panciera et al. (1993) reported a case of bovine hyperkeratosis as recently as the early 1990s.

Experimental studies on cattle have revealed severe systemic disease (bovine hyperkeratosis) at PCN concentrations of 1.7, 1.1, 0.69, and 2.4 mg/kg body weight per day for the congeners penta-, hexa-, hepta-, and octachloronaphthalene, respectively, during 5- to 10-day exposure periods (Bell, 1953). Further experiments have also been carried out on other domesticated animals. Pentachloronaphthalene has been shown to cause mild hyperkeratosis when applied to the skin of a pig at a concentration of 60 mg/litre, 3 litres/day, 6 days/week, for 6 weeks (i.e., 180 mg/day for a total dose of 6.5 g) (Link et al., 1958). They found no evidence of systemic disease after spraying pigs with a total dose of 6710–8250 mg hexachloronaphthalene/kg body weight in oil over a period of 28 days.

8.7.4 Toxic equivalency factor (TEF) and relative potency (REP) concept

At least some of the biochemical (e.g., drug-metabolizing enzyme induction, hormonal changes) and toxic (e.g., skin disorders, weight loss, hepatotoxicity, reproductive toxicity) responses of PCNs are believed to be mediated via the cytosolic Ah receptor, comparable to related halogenated hydrocarbons (Goldstein & Safe, 1989), which has been intensively studied for the model compound TCDD (reviewed by IPCS, 1998). For PCNs, binding affinities for the Ah receptor have not yet been determined.

Due to the lack of sufficient experimental data up to now, PCNs are not included in an internationally agreed toxic equivalency factor (TEF) system, which estimates the overall dioxin-like toxicity of the compound relative to TCDD (Van den Berg et al., 1998). However, some congeners, in particular those with a planar structure (four lateral chlorines at 2,3,6,7, i.e., congeners 2,3,6,7-tetrachloronaphthalene, 1,2,3,6,7-pentachloronaphthalene,

1,2,3,4,6,7-hexachloronaphthalene, 1,2,3,5,6,7-hexachloronaphthalene, 1,2,3,6,7,8-hexachloronaphthalene, 1,2,3,4,5,6,7-heptachloronaphthalene, and 1,2,3,4,5,6,7,8-octachloronaphthalene) similar to TCDD, may exert a toxicity comparable to the more toxic PCBs.

Because of some confusion in the literature on the term TEF, it should be noted that, according to the definition of WHO, the TEF value is based on the results of several *in vivo* and *in vitro* studies. Relative potency (REP) values, however, are derived from a single *in vivo* or *in vitro* study (Van den Berg et al., 1998).

As observed for other halogenated aryl hydrocarbons, the relative induction potencies of PCNs appear to depend on the degree and position of chlorine substitution of the naphthalene ring (see text above). In several different test systems, the most potent EROD and AHH inducers include 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene, 1,2,3,4,5,6,7-heptachloronaphthalene, and some unidentified congeners present in Halowax 1014 (Campbell et al., 1983; Hanberg et al., 1990, 1991; Engwall et al., 1993, 1994; Norrgren et al., 1993; Brunström et al., 1995). Octachloronaphthalene was also found to cause a dose-dependent AHH increase in microsomes of rats (Campbell et al., 1981). Halowax 1014 and the two hexa- isomers maximally induced EROD to a level of about 15–20% of the maximal activity induced by TCDD in cultured chick embryo liver (Brunström et al., 1995). REPs (compared with TCDD) determined for EROD induction in rat hepatoma H4IIE cells *in vitro* were given as 0.002 for the 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene and two other hexa- isomers and as 0.003 for a hepta- congener (Hanberg et al., 1990, 1991). The lowest observed effective dose for EROD induction in chick embryos by the 1,2,3,4,6,7/1,2,3,5,6,7-hexachloronaphthalene mixture administered via the air sac was 0.1 mg/kg egg (Engwall et al., 1993, 1994). ED₅₀ values for EROD induction in chick embryos by this hexa-mix and Halowax 1014 were estimated to be 0.06 mg/kg egg and 0.2 mg/kg egg, respectively (Engwall et al., 1993, 1994).

Another test for dioxin-like activity, the rat hepatoma H4IIE-luc cell (luciferase) bioassay (measuring Ah receptor-dependent reporter gene activation by using rat hepatoma cells stably transfected with an Ah receptor-controlled luciferase reporter gene construct), confirmed that the more highly chlorinated Halowax mixtures 1013, 1014, and 1051 (composed of mostly tetra- through octachloronaphthalenes) are active in contrast to the lower chlorinated Halowax mixtures 1000, 1001, and 1099 (composed of mostly mono-, di-, tri-, and tetrachloronaphthalenes), which were found to be inactive. Similarly, of the individual PCN congeners tested, penta-, hexa-, and

heptachloronaphthalenes gave full dose–response curves, whereas most of the lower chlorinated congeners as well as octachloronaphthalene were inactive in this assay (maximum of at least six concentrations tested varied for each congener and ranged from 1.9 to 1250 ng/well; the duration of exposure was 72 h). The most potent congener was 1,2,3,4,6,7-hexachloronaphthalene, showing an REP value (compared with TCDD) of approximately 0.003 (Blankenship et al., 1999). Similar results have been obtained by another study (Villeneuve et al., 2000) testing individual PCN congeners using the luciferase (and the EROD) assay with recombinant H4IIE rat hepatoma cells. Again, hexa- and heptachloronaphthalenes tested were the most potent congeners, exhibiting REPs around 10^{-3} to 10^{-4} (relative to TCDD). Penta-chlorinated congeners typically had REP values around 10^{-4} to 10^{-7} . Tetra, tri-, di-, and monochloronaphthalenes were found to be less active. There was also a rank order of potency within the penta- and hexachloronaphthalene isomers, in a manner suggesting that the presence of meta-substituted chlorines is linked to decreased potency. For example, for hexachloronaphthalenes, an approximate ranking order was given as 1,2,3,6,7,8 > 1,2,3,4,6,7 > 1,2,3,5,6,7 > 1,2,3,5,6,8.

9. EFFECTS ON HUMANS

9.1 Occupational exposure

Severe skin reactions and liver disease have both been reported after occupational exposure to PCNs. The clinical and toxicological symptoms of PCNs are very similar to those caused by PCBs, PCDDs, and PCDFs (Kimbrough & Jensen, 1989).

The skin reactions caused by PCNs are referred to variously as chloracne (Herxheimer, 1899), perna disease (Teleky, 1927), Halowax acne, or cable rash (Schwartz, 1943) and can result both from skin contact via the fumes (sublimate) and, in rare cases, with the solid itself and through inhalation (Crow, 1970; EHD, 1982). Chloracne was common among workers handling PCNs in such operations as the sealing of electrical cables and components, the patching of sealed cables, the chromium plating industry, and the manufacturing of PCNs (EHD, 1982). It is linked with poor personal and occupational hygienic measures (Kleinfeld et al., 1972). Most cases of chloracne associated with PCN exposure are from the 1930s and 1940s (e.g., Mayers & Silverberg, 1938; Good & Pensky, 1943; Schwartz, 1943) and 1950s (Grimmer, 1955), but more recent outbreaks have been reported (Kleinfeld et al., 1972). In this study of 59 workers, the average

duration of exposure to PCNs was 8.3 months, with a range of 4–9 months. The average time from exposure to the onset of dermatitis was 3.6 months and ranged from 1 to 7 months (Kleinfeld et al., 1972).

The effect of dermal application of a range of commercial products containing PCNs was studied in 31 male adults (Shelley & Kligman, 1957). A 50% mineral oil suspension of Halowax 1000, 1001, 1014, 1052, and 1051, respectively (for composition, see Table 2), was applied daily to the pinna of the ear for 30 days. Only Halowax 1014, containing penta- and hexachloronaphthalenes, produced chloracne; Halowaxes containing mono-, di-, tri-, tetra-, hepta-, and octachloronaphthalenes did not. Further experiments with this mixture showed that chloracne can be produced all over the body, even far from the site of application, through “passive transfer.” Follicular hyperkeratinization was observed within 1–3 weeks, and eventually the entire follicular appendage was transformed into a sac of keratin (comedones). Additionally, sebaceous glands were greatly diminished or disappeared altogether (see also section 8.7.3).

Whether the penta/hexa mixture is the sole cause of chloracne under industrial conditions is disputed. Crow (1970) suggested that the presence of pitch together with tri- and tetrachloronaphthalenes might be responsible for the reported symptoms of vesicular dermatitis on the face and photosensitivity, which have been reported together with chloracne from use as a paper capacitor impregnant (Mayers & Silverberg, 1938).

Apart from chloracne, other systemic effects, in particular liver disease, have been reported after occupational exposure to PCNs. There is not necessarily an association between chloracne and liver disease. Liver toxicity as a result of exposure to PCNs has been reported without occurrence of chloracne; the symptoms of chloracne have often been reported without mention of liver toxicity (Ward et al., 1996; Popp et al., 1997).

Other symptoms described in workers (e.g., cable insulation) exposed to PCNs included irritation of the eyes, fatigue, headache, anaemia, haematuria, impotencia, anorexia, nausea, vomiting, and occasionally severe abdominal pain (Greenburg et al., 1939; Mayers & Smith, 1942; von Wedel et al., 1943). There was a possible exposure to other chemicals, but PCNs are thought to have been implicated.

Systemic effects resulting in liver disease have been reported only from the inhalation of PCNs, as fumes arising from hot PCN wax processing operations (EHD, 1982). At least 10 cases of mortality were reported in the

1930s and 1940s in workers exposed to PCNs who had acute atrophy of the liver (Flinn & Jarvik, 1936; Greenburg et al., 1939; Collier, 1943; Strauss, 1944; Ward et al., 1996). In many case reports, chloracne was not recorded; in some instances, it was definitively given as not present.

Concentrations of mixed penta- and hexachloronaphthalene between 1 and 2 mg/m³ were measured in the air of industrial plants where fatal cases of yellow atrophy of the liver occurred (Elinks, 1959). A non-fatal case of toxic hepatitis was reported to have been induced by occupational Halowax exposure of about 3.4 mg/m³ (trichloronaphthalene) (Mayers & Smith, 1942), but tetrachloronaphthalene was probably also present (ACGIH, 1992).

Many case histories report extensive liver damage and death to be a latent response, occurring weeks to months after removal from the source of PCN poisoning. This may be attributable to a continued release into the circulation of PCNs from storage in fatty tissues (EHD, 1982). Recovery from PCN poisoning, whether the manifestations were chloracne or systemic effects, generally ranged from several months to over a year (EHD, 1982).

No derangements of liver function (serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase) or total bilirubin determinations were found in the case of five workers whose dermatoses were especially severe after exposure to tetra- and pentachloronaphthalenes in the application of wax insulation to wire coils at an electric plant (Kleinfeld et al., 1972).

The cases of 16 former employees from a German plant producing models and tools for car manufacturing and mining who had been exposed to fumes of waxes (Beranit®; used for casting moulds) containing 90% PCNs (and asbestos) from 1958 to 1989, when the plant closed, were investigated (Popp et al., 1993, 1997). Some waxes contained only 5% pentachloronaphthalene; others consisted of 40% pentachloronaphthalene and 35% hexachloronaphthalene. Concentrations were estimated at 14.5 mg/m³ for total PCNs, 4.9 mg/m³ for trichloronaphthalene, 1.0 mg/m³ for pentachloronaphthalene, 0.025 mg/m³ for PCBs, and 2.2 pg I-TEF/m³ for PCDDs and PCDFs (see section 6.1). The wax was usually heated to about 130–150 °C and afterwards cast into moulds. There was no protection for the workers. In the group of 16 workers, no chloracne had occurred, but elevated liver enzyme values (especially gamma-glutamyl transpeptidase) were noted in 6 of these workers (and maybe more, but not all could be contacted). Fatty livers were detected histologically in two workers. The liver function

disturbances of three workers were accepted as occupational diseases. Alcohol abuse was ruled out. Analysis of the fumes in a laboratory investigation of some of the remaining wax (see section 6.2) showed that PCNs were the most relevant emissions and that exposure to them was the main reason for the liver dysfunction found in the exposed workers (Popp et al., 1997).

A cohort study on acute and chronic liver toxicity (Ward et al., 1996) and a cancer mortality study (Ward et al., 1994) were conducted on workers (*n* = 9028) employed at a cable manufacturing plant from 1940 to 1944 who were exposed to PCNs (but also, to a lesser extent, chloroform and PCBs). Vital status was followed to the end of 1985. Historical records document that PCNs were melted in open vats through which wires coated with asbestos were drawn to saturate them. Exposure to PCNs was widespread in the plant, and 460 cases of chloracne were recognized (Ward et al., 1996).

In the study on the acute and chronic liver toxicity from this cohort (Ward et al., 1996), eight deaths from “acute yellow atrophy of the liver” were reported in the company records and/or death certificates. A further 10 workers were reported as having abnormal liver function tests and/or symptoms of liver dysfunction. An excess of deaths from cirrhosis of the liver was observed (observed [OBS] = 150; standardized mortality ratio [SMR] = 1.84; 95% confidence interval [CI] = 1.56–2.16). In the 460 individuals (431 men, 29 women) who had shown symptoms of chloracne, cirrhosis deaths were elevated to a similar degree (OBS = 8; SMR = 1.51; CI = 0.65–2.98). Liver cirrhosis is also associated with alcohol consumption, but there was no evidence for increased alcoholism in this cohort based on other alcohol-related causes of death (SMR for oesophageal cancer = 1.01; SMR for deaths from alcoholism = 0.99). The SMR for “non-alcoholic cirrhosis (no mention of alcoholism)” (OBS = 83; SMR = 1.67; CI = 1.33–2.07) was similar to that for “alcoholic cirrhosis (with mention of alcoholism)” (OBS = 59; SMR = 1.96; CI = 1.49–2.53). The study concluded that the excess mortality from cirrhosis of the liver observed in this cohort is due to the chronic effect of PCNs (Ward et al., 1996).

In the cancer mortality study on this cohort (Ward et al., 1994), SMRs for all cancers were 1.03 in women (OBS = 238; CI = 0.90–1.17) and 1.18 in men (OBS = 814; CI = 1.10–1.26). There were no significant elevations in malignant neoplasms of connective tissue, liver, and lymphatic and haematopoietic organs that could have been hypothesized as being associated with PCNs, although an excess of malignancies of the connective tissue was suggested for workers with over 1 year of exposure and 25 years of latency (SMR = 3.54; CI =

0.97–9.07). Cancer mortality among the 460 individuals with chloracne was similar to that of the entire cohort, although the chloracne subcohort showed significant excesses in two rare causes of death (malignant neoplasms of oesophagus, OBS = 5; SMR = 3.26; CI = 1.05–7.61; “benign and unspecified neoplasms,” OBS = 4; SMR = 4.93; CI = 1.34–12.6).

In another mortality study of this cohort (10 240 workers) exposed to PCNs, 12 subjects were identified with deaths due to soft tissue sarcoma (Suruda et al., 1993). In addition, four of the seven deaths coded under “malignant neoplasms of the peritoneum and retroperitoneum” (SMR = 1.95; CI = 0.78–4.02) for men were identified as soft tissue sarcomas on the death certificates. In the general population, these tumours are rare, accounting for less than 1% of all fatal cancers. (Soft tissue sarcomas have been associated with exposure to products contaminated with TCDD but also with exposure to various phenoxy acid herbicides and chlorophenols, some of which did not contain TCDD.)

9.2 General population exposure

There are only a few miscellaneous reports on the effects of incidental exposure to PCNs on the general population. A child whose father sealed his mattress with PCNs showed symptoms of chloracne (Höfs, 1957). Six people showed general systemic symptoms followed by severe chloracne after eating food fried in an oil possibly containing hexachloronaphthalene (Herzberg, 1947). Incidents of consumption of contaminated rice oil in two populations in Taiwan (called Yusho or oil disease) and China (Yu-Cheng) with symptoms similar to those described for PCN exposure have been extensively studied. The contaminants have been identified as PCBs, PCDFs, polychlorinated quaterphenyls (PCQs), and PCDDs (Kuratsune, 1989). Recently, PCN (635 µg/g) was also identified in samples of the rice oil (Haglund et al., 1995). Further, PCNs have also been reported in blood (from Yusho) and adipose tissue (Yu-cheng) specimens (Ryan & Masuda, 1994; see section 6.2).

There are no reports of reproductive abnormalities or developmental toxicity in humans.

10. EFFECTS ON OTHER ORGANISMS IN THE LABORATORY AND FIELD

10.1 Aquatic environment

Selected data demonstrating effect concentrations are shown in Table 7.

In a 7-day test, Halowax 1000 significantly reduced the growth of the marine alga *Dunaliella tertiolecta* at 0.1 mg/litre, and Halowax 1013 reduced the growth of *Nitzschia* sp. at 0.5 mg/litre. Halowax 1014 had no significant effect on the growth of any of the marine algal species tested at up to 1.0 mg/litre (Walsh et al., 1977).

Neff & Giam (1977) exposed juvenile horseshoe crabs (*Limulus polyphemus*) to Halowax 1099. For late T₁ crabs (first-tailed stage) exposed to 80 µg/litre, an LT₅₀ of 27 days was found. Significant effects on moulting were observed at 20, 40 and 80 µg/litre. Halowax 1099 (20 µg/litre) caused a significant increase in respiration rate of juvenile mud crabs (*Rhithropanopeus harrisi*) in 5-day tests at a salinity of 15‰ (Laughlin & Neff, 1979).

10.2 Terrestrial environment

Ingestion studies have been carried out with broad-breasted poult (turkeys) and New Hampshire chickens. Birds were fed a diet containing Halowax 1014 for 40 days. A dose of 20 mg/kg feed had little effect on the chickens; however, 50% of the turkeys died, and an average decrease in weight of 51% was noted in those surviving. At 5 mg/kg feed, the PCNs caused 6.5% turkey mortality, and weight gain was reduced by 33%. At a dose of 100 mg/kg feed, all the turkeys died within 33 days, while weight gain was reduced by 8% in chickens. On gross histological examination of the turkeys, enlarged and darkened livers were noted. Octachloronaphthalene at a dose of 125 mg/kg feed caused no significant effects on the turkeys (Pudelkiewicz et al., 1958, 1959).

11. EFFECTS EVALUATION

11.1 Evaluation of health effects

11.1.1 Hazard identification and dose–response assessment

Due to the lack of appropriate long-term studies, the toxicological profile of PCNs is experimentally not very well characterized. Nevertheless, the data available show some significant trends.

PCNs are thought to interact with the Ah receptor. Therefore, it is expected that exposure to PCNs could result in a pattern of biochemical and toxic responses typical for dioxin-like compounds. This has been confirmed in part.

Table 7: Aquatic toxicity of chlorinated naphthalenes.

Species	Chlorinated naphthalene	End-point (effect)	Concentration ^a (mg/litre)	Reference
<i>Tetrahymena pyriformis</i>	1-Chloro	60-h EC ₅₀ (growth inhibition)	25	Schultz et al., 1983
Invertebrates				
Water flea (<i>Daphnia magna</i>)	1-Chloro	48-h LC ₅₀	1.6 n	LeBlanc, 1980
	1-Chloro	No observed effect (48-h)	<0.17 n	LeBlanc, 1980
	Octachloro	48-h LC ₅₀	>530 n	LeBlanc, 1980
	Octachloro	No observed effect (48-h)	530 n	LeBlanc, 1980
Brine shrimp (<i>Artemia salina</i>)	1-Chloro	48-h LC ₅₀	0.82 n	Abernethy et al., 1986
	2-Chloro	48-h LC ₅₀	1.99 n	Abernethy et al., 1986
	1-Chloro	24-h LC ₅₀	1.84 n	Abernethy et al., 1986
	2-Chloro	24-h LC ₅₀	2.82 n	Abernethy et al., 1986
Mysid shrimp (<i>Mysidopsis bahia</i>)	1-Chloro	24-h LC ₅₀	0.91 m	Foster & Tullis, 1984
	1-Chloro	96-h LC ₅₀	0.37 n	US EPA, 1980
Brown shrimp (<i>Penaeus aztecus</i>)	Octachloro	96-h LC ₅₀	>500 n	US EPA, 1980
	Halowax 1014	96-h LC ₅₀	0.0075 m	US EPA, 1980
Grass shrimp (<i>Palaemonetes pugio</i>)	Halowax 1000	96-h LC ₅₀	0.44 m	Green & Neff, 1977
	Halowax 1000	96-h LC ₅₀	0.325 m	Green & Neff, 1977
	Halowax 1013	96-h LC ₅₀	0.074 m	Green & Neff, 1977
	Halowax 1099	96-h LC ₅₀	0.069 m	Green & Neff, 1977
	Halowax 1099	96-h LC ₅₀	0.09 m	Green & Neff, 1977
	Halowax 1014	96-h LC ₅₀	0.248 m	US EPA, 1980
Vertebrates				
Bluegill (<i>Lepomis macrochirus</i>)	1-Chloro	96-h LC ₅₀	2.3 n	Buccafusco et al., 1981
Sheepshead minnow (<i>Cyprinodon variegatus</i>)	1-Chloro	96-h LC ₅₀	2.4 n	Heitmuller et al., 1981
	1-Chloro	No observed effect (96-h)	1.2 n	Heitmuller et al., 1981
	Octachloro	96-h LC ₅₀	>560 n	Heitmuller et al., 1981
	Octachloro	No observed effect (96-h)	560 n	Heitmuller et al., 1981
	1-Chloro	96-h LC ₅₀	0.690 m	Ward et al., 1981
	Halowax 1014	96-h LC ₅₀	>0.343	US EPA, 1980
	1-Chloro	No observed effect (embryo-larval test)	<0.39 m	Ward et al., 1981
Striped mullet (<i>Mugil cephalus</i>)	Halowax 1014	96-h LC ₅₀	>0.263	US EPA, 1980

^a n = based on nominal concentrations; m = based on measured concentrations.

Some PCNs have enzyme-inducing properties (AHH, EROD, luciferase) comparable to PCDDs, PCDFs, and PCBs. For the most active and persistent PCN congeners, REP values of about 0.002 or 0.003 (compared with TCDD) have been found. REPs for some of the active PCN congeners were similar to those of some PCBs. Therefore, PCNs should be included in the development of TEFs.

Some PCN congeners or mixtures caused a relatively high acute toxicity in animals, connected with weight loss and delayed time to death, but were less acutely toxic than TCDD. For example, the 30-day LD₅₀ values were >11.3 µmol/kg body weight for 2,3,6,7-tetrachloronaphthalene and 0.006 µmol/kg body weight for TCDD.

Dermal lesions have been observed in humans (chloracne) and domestic animals (X-disease). The hyperkeratotic activity of certain PCNs has been proven in animal model studies (rabbit ear test, hairless mice test). Hyperkeratotic changes and severe systemic disease in cattle have been observed at concentrations as low as 0.69–2.4 mg/kg body weight per day for penta- through octachloronaphthalene congeners. A NOAEL was not established.

Hepatotoxicity is another obvious effect of PCN exposure in experimental animals and humans. The lowest dose that induced slight histological liver damage has been demonstrated in rats after inhalative (8-h) exposure to penta/hexachloronaphthalenes and was 1.44 mg/m³. In humans, acute yellow atrophy of the liver and chronic liver cirrhosis can be attributed to PCN exposure. In the one epidemiological study, excess mortality for cirrhosis of the liver in humans (SMR = 1.84) was reported after exposure to PCNs. Dose–response relationships for histological liver damage have not been established.

Studies in humans and animals have shown that toxicity is dependent on the congener/isomer. There is agreement in all studies that the penta- and hexa- isomers are the most toxic. In a human study, only Halowax 1014, containing mainly penta- and hexachloronaphthalenes, produced chloracne in humans, not tri-, tetra-, hepta-, or octachloronaphthalene. In studies on bovine hyperkeratosis, penta-, hexa-, and heptachloronaphthalenes were the most toxic congeners. Octachloronaphthalene given in solution, but not in suspension, produced symptoms.

Mutagenicity has been tested only with 1,2,3,4-tetrachloronaphthalene and 1-monochloronaphthalene, which were not mutagenic in the Ames test with or without metabolic activation.

With respect to carcinogenicity, no animal experiments are available. No conclusion can be drawn from an epidemiological study due to the many limitations.

No valid experiments on the reproductive toxicity of PCNs have been performed with laboratory rodents. However, a recent study demonstrated that very low doses of 1,2,3,4,6,7-hexachloronaphthalene (1 µg/kg body weight per day) given to pregnant rats could result in endocrine disruption in male offspring, leading to an accelerated onset of spermatogenesis.

There is also a lack of studies on possible immunotoxicity and neurotoxicity, which may be expected in analogy to dioxin-like compounds.

Because some of the PCNs, in particular penta- and hexachloronaphthalenes, were found to be strongly bioaccumulating and persistent (having half-lives of

several years in humans), the possible long-term effects mentioned above are of most concern.

Up to now, PCNs have been detected in human blood, liver, adipose tissue, and breast milk samples of the general population, indicative of a real (existing) exposure of the general population.

11.1.2 Criteria for setting tolerable intakes/ concentrations or guidance values for chlorinated naphthalenes

Due to the lack of appropriate (long-term) studies establishing clear dose–response relationships, a confident risk characterization cannot be performed.

In general, exposure to PCNs should be minimized as much as possible, because, for example, effects on endocrine functions have been shown to occur at very low doses.

11.1.3 Sample risk characterization

As seen by the limited human monitoring data, the general population is exposed to PCNs. The levels found in Swedish breast milk samples were only 1 order of magnitude lower than those of PCDFs.

Possible routes of exposure of the general population to PCNs include food, mainly fish (more recent measurements, which will be mainly tetra- and pentachloronaphthalenes, have shown a maximum concentration around 300 µg/kg lipid weight), drinking-water (a single study of the production of PCNs by chlorination showed up to 0.15 ng dichloronaphthalene/litre and up to 0.44 ng monochloronaphthalene/litre), and air (recent maxima at 150 pg/m³ in outdoor air; up to 3000 ng/m³ near manufacturing plants in former years). Levels in soil close to a former chlor-alkali plant are currently 18 mg/kg dry weight. Increased exposure may be expected near present or former sites of special industries or near sites of (municipal) waste incineration.

Due to the presence of PCNs in breast milk, breast-fed babies are a special group at risk. However, it appears that levels of PCNs in breast milk are decreasing (e.g., in Sweden, from 3081 ng/kg lipid in 1972 to 483 ng/kg lipid in 1992).

For the occupational environment, liver toxicity and chloracne were recorded at estimated workplace air concentrations of 1–>10 mg/m³. Inhalative LOAELs (for histological liver damage) reported in a rat study were

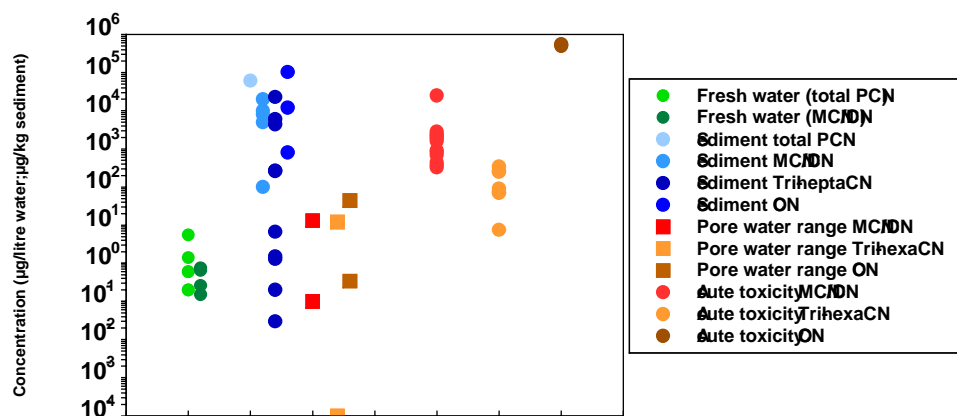


Figure 2: Plot of reported acute toxicity values for chlorinated naphthalenes and measured concentrations in environmental media.

PCN - polychlorinated naphthalene; MCN - monochlorinated naphthalene; DCN - dichlorinated naphthalene; OCN - octachlorinated naphthalene. Pore water values are calculated from the plotted sediment values; top and bottom of the range are plotted.

1.16 mg/m³ (penta/hexachloronaphthalenes) or 1.31 mg/m³ (tri/tetrachloronaphthalenes).

As it seems that PCNs are no longer produced in the USA or Western Europe, occupational exposure to these chemicals is no longer thought to be a hazard in those countries. There are no data on whether PCNs are produced in other countries.

11.2 Evaluation of environmental effects

Manufacture of PCNs has ceased in the USA and Western Europe; in these areas, environmental contamination will come largely from leakage of old landfill sites and poor disposal of major electrical equipment containing PCNs. There will also be input from incineration of waste. Existing residues in the environment will also be redistributed.

Atmospheric PCNs may degrade by photolysis; an atmospheric half-life has been estimated at 2.7 days for 1,4-dichloronaphthalene.

Biotic degradation has been reported under aerobic conditions for monochloronaphthalenes but not for higher chlorinated congeners.

The estimated partition coefficients increase as the degree of chlorination increases, indicating that the lower chlorinated PCNs are likely to show moderate sorption tendency from water onto soil and sediments and that the higher chlorinated PCNs are likely to show a high

sorption tendency from water onto soil and sediment.

PCNs bioaccumulate in organisms with increasing uptake as level of chlorination increases, up to heptachloronaphthalene. Octachloronaphthalene does not appear to be taken up by organisms. There is greater accumulation in fish than in lower organisms. No experimental studies have been conducted on accumulation in birds or mammals; however, residues (mainly tetra- and pentachloronaphthalenes) have been found in piscivorous birds and mammals in the field.

Toxicity studies on organisms relevant to the environment are all acute and limited with respect to PCN congeners. Most studies have been conducted with mono- and octachloronaphthalene or with commercial mixtures (Halowax). The range of results in these tests has been plotted in Figure 2 for three ranges of PCNs: mono- and di-, tri- to hexa-, and octachlorinated naphthalenes. Results for the Halowaxes have been allocated according to the predominant PCNs in the mixture. The tri- to hexachlorinated range shows the highest toxicity, with octachlorinated naphthalene significantly less toxic than the other ranges (presumably reflecting poor uptake of octachloronaphthalene by organisms).

There are no data on the chronic toxicity of PCNs, a major deficiency in the database, since these compounds bioaccumulate, and chronic tissue exposure would be expected. There are also no test results on sediment-dwelling organisms, although these would be the most exposed.

Data on measured concentrations in environmental media are also plotted in Figure 2. These data range in

time from the 1970s, when manufacture was still continuing, to the present day, and from locally polluted sites to more remote ones. The data are too few to separate out these categories. Similarly, marine and freshwater sediment values have been pooled. In addition, pore water concentrations have been calculated against the sediment levels; here, the upper and lower ends of the ranges are plotted in the figure.

Concentrations in surface water scarcely overlap toxicity values, even with the higher concentrations reported in the past. Current water concentrations would suggest low risk to the most sensitive invertebrates in the water body and negligible risk to fish (which are substantially less sensitive). Pore water concentrations in heavily polluted sediments from the past are sufficiently high to have caused acute toxicity, assuming that sediment-dwelling organisms are equally sensitive to those tested. However, more recently measured sediment concentrations are unlikely to cause acute effects. There is a large margin of safety between concentrations of octachloronaphthalene and its toxic concentration at any time over the last 30 years, despite the fact that it has been measured at very high concentrations in the past.

Lack of data prevents further risk estimation for chronic effects or for higher organisms.

11.3 Uncertainties in the evaluation

The data on short-term exposure to experimental animals are scarce. It was not possible to derive NOAELs/LOAELs. In accidental and early laboratory exposure studies, no congener-specific analysis was possible.

There are no data on long-term exposure to PCNs or carcinogenicity studies. There are scarce data on genotoxicity.

There is one study in rats with 1,2,3,4,6,7-hexachloronaphthalene (1 µg/kg body weight per day) showing indications of endocrine disruption. This finding needs to be confirmed by further studies.

Although there are data gaps, due to the strong relationship to TCDD, PCNs should be treated analogously concerning their toxicity.

In human occupational studies, qualitative and quantitative details of exposure and effects were lacking. Although PCNs were thought to be the cause of the symptoms reported, in all cases other chemicals could have been implicated.

Few toxicity studies were available for specific PCN congeners in environmentally relevant organisms. However, the persistence and bioaccumulation of the

compounds demonstrate high hazard for PCNs and the need to prevent further environmental contamination.

As the chemicals no longer seem to be produced or in use and as exposure comes only from possible contact with waste materials containing PCNs or from PCNs in the environment, data gaps in both the health and environmental aspects are unlikely to be filled. PCNs fulfil the criteria for persistent organic pollutants (persistence, bioaccumulation, toxicity, volatility, measurements of the chemical in remote regions, bioavailability) (WWF, 1999; UNEP, 2001). International risk management measures for PCBs, for prevention of further environmental contamination by, for example, disposal of large-scale electrical equipment, would also be appropriate for PCNs.

12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

No previous evaluations by international bodies were available.

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APPENDIX 1 — SOURCE DOCUMENTS

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Environmental hazard assessment: Halogenated naphthalenes was drafted by the Building Research Establishment (United Kingdom Department of the Environment) and the Institute of Terrestrial Ecology (United Kingdom Natural Environment Research Council), with M.J. Crookes and P.D. Howe as the authors. The draft document was peer reviewed both within the United Kingdom and internationally. Comments and additional material were received from H. Börndal (Swedish Environmental Protection Agency), E.F. Bryan (Exposure Evaluation Division, US Environmental Protection Agency), J.A. Cotruvo (Health and Environmental Review Division, US Environmental Protection Agency), A.F. Dearsley (Environment Policy and Planning Manager, Thames Water Utilities, United Kingdom), J. Duffus (The Edinburgh Centre for Toxicology, Heriot-Watt University, United Kingdom), M. Gem (Food Science Division, Ministry of Agriculture, Fisheries and Food, United Kingdom), B. Jansson (Institute of Applied Environmental Research, Stockholm University, Sweden), D. Keating (Environmental Risk Assessment Section, Health and Safety Executive, United Kingdom), P. Koundakjian (Technology and Health Services Division, Health and Safety Executive, United Kingdom), B. Lefèvre (Commission of the European Communities), A. Lundgren (Swedish National Chemicals Inspectorate [KEMI], Sweden), P. Matthiessen (Biological Effects Group, Ministry of Agriculture, Fisheries and Food, United Kingdom), T. Sheils (Water Resources and Marine Division, Department of the Environment, United Kingdom), and M.E. Weber (Economics and Technology Division, US Environmental Protection Agency) and were incorporated into the final document. The document was published in 1993 and covers published and unpublished material up to 1992.

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The scientific documents of the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK) are based on critical evaluations of the available toxicological and occupational medical data from extensive literature searches and from well documented industrial data. The evaluation documents involve a critical examination of the quality of the database indicating inadequacy or doubtful validity of data and identification of data gaps. This critical evaluation and the classification of substances are the result of an extensive discussion process by the members of the Commission proceeding from a draft documentation prepared by members of the Commission, by ad hoc experts, or by the Scientific Secretariat of the Commission. Scientific expertise is guaranteed by the members of the Commission, consisting of experts from the scientific community, industry, and employer associations.

APPENDIX 2 — CICAD PEER REVIEW

The draft CICAD on chlorinated naphthalenes was sent for review to institutions and organizations identified by IPCS after contact with IPCS national contact points and Participating Institutions, as well as to identified experts. Comments were received from:

A. Aitio, International Programme on Chemical Safety, World Health Organization, Switzerland

M. Baril, Institut de Recherche en Santé et en Sécurité du Travail, Canada

R. Benson, Drinking Water Program, US Environmental Protection Agency, USA

L. Birnbaum, US Environmental Protection Agency, USA

R. Cary, Health and Safety Executive, United Kingdom

M. Feeley, Bureau of Chemical Safety, Health Canada

H. Gibb, National Center for Environmental Assessment, US Environmental Protection Agency, USA

R. Hertel, Federal Institute for Health Protection of Consumers and Veterinary Medicine, Germany

U. Järnberg, Stockholm University, Sweden

N. Roney, Agency for Toxic Substances and Disease Registry, USA

L. Schuda, US Environmental Protection Agency, USA

K. Ziegler-Skylakakis, GDCh Advisory Committee on Existing Chemicals of Environmental Relevance (BUA), Germany

Dr O.M. Faroon, Division of Toxicology, Agency for Toxic Substances and Disease Registry, Atlanta, GA, USA

Dr H. Gibb, National Center for Environmental Assessment, US Environmental Protection Agency, Washington, DC, USA

Dr R.F. Hertel, Federal Institute for Health Protection of Consumers and Veterinary Medicine, Berlin, Germany

Dr A. Hirose, Division of Risk Assessment, National Institute of Health Sciences, Tokyo, Japan

Dr P.D. Howe, Centre for Ecology and Hydrology, Cambridgeshire, United Kingdom (*Rapporteur*)

Dr D. Lison, Industrial Toxicology and Occupational Medicine Unit, Université Catholique de Louvain, Brussels, Belgium

Dr R. Liteplo, Existing Substances Division, Bureau of Chemical Hazards, Health Canada, Ottawa, Ontario, Canada

Dr I. Mangelsdorf, Chemical Risk Assessment, Fraunhofer Institute for Toxicology and Aerosol Research, Hanover, Germany

Ms M.E. Meek, Existing Substances Division, Safe Environments Program, Health Canada, Ottawa, Ontario, Canada (*Vice-Chairperson*)

Dr S. Osterman-Golkar, Department of Molecular Genome Research, Stockholm University, Stockholm, Sweden

Dr J. Sekizawa, Division of Chem-Bio Informatics, National Institute of Health Sciences, Tokyo, Japan

Dr S. Soliman, Department of Pesticide Chemistry, Faculty of Agriculture, Alexandria University, El-Shatby, Alexandria, Egypt

Dr M. Sweeney, Education and Information Division, National Institute for Occupational Safety and Health, Cincinnati, OH, USA

Professor M. van den Berg, Environmental Sciences and Toxicology, Institute for Risk Assessment Sciences, University of Utrecht, Utrecht, The Netherlands

APPENDIX 3 — CICAD FINAL REVIEW BOARD

Geneva, Switzerland, 8–12 January 2001

Members

Dr A.E. Ahmed, Molecular Toxicology Laboratory, Department of Pathology, University of Texas Medical Branch, Galveston, TX, USA

Mr R. Cary, Health and Safety Executive, Merseyside, United Kingdom (*Chairperson*)

Dr R.S. Chhabra, General Toxicology Group, National Institute of Environmental Health Sciences, National Institutes of Health, NC, USA

Dr S. Czerczak, Department of Scientific Information, Nofer Institute of Occupational Medicine, Lodz, Poland

Dr S. Dobson, Centre for Ecology and Hydrology, Cambridgeshire, United Kingdom

Observers

Dr W.F. ten Berge, DSM Corporate Safety and Environment, JH Heerlen, The Netherlands

Dr K. Ziegler-Skylakakis, Commission of the European Communities, Luxembourg

Secretariat

Dr A. Aitio, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Dr Y. Hayashi, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Dr P.G. Jenkins, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

Dr M. Younes, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland

TRICHLORONAPHTHALENE

0962

March 2001

CAS No: 1321-65-9
RTECS No: QK4025000

$C_{10}H_5Cl_3$
Molecular mass: 231.5

TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/SYMPTOMS	PREVENTION	FIRST AID/FIRE FIGHTING
FIRE	Combustible. Gives off irritating or toxic fumes (or gases) in a fire.	NO open flames.	Water spray, foam, powder, carbon dioxide.
EXPLOSION			

EXPOSURE		PREVENT DISPERSION OF DUST!	
Inhalation		Local exhaust or breathing protection.	Fresh air, rest.
Skin	Redness.	Protective gloves. Protective clothing.	Remove contaminated clothes. Rinse and then wash skin with water and soap.
Eyes	Redness. Pain.	Safety spectacles.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
Ingestion	Nausea. Vomiting.	Do not eat, drink, or smoke during work.	

SPILLAGE DISPOSAL	PACKAGING & LABELLING
Sweep spilled substance into containers; if appropriate, moisten first to prevent dusting. Carefully collect remainder, then remove to safe place. Do NOT let this chemical enter the environment. (Extra personal protection: P2 filter respirator for harmful particles).	

EMERGENCY RESPONSE	STORAGE
	Separated from strong oxidants, food and feedstuffs.

IMPORTANT DATA

Physical State; Appearance

COLOURLESS TO YELLOW SOLID IN VARIOUS FORMS, WITH CHARACTERISTIC ODOUR.

Chemical dangers

The substance decomposes on burning producing toxic and corrosive fumes including hydrogen chloride. Reacts with oxidants, causing fire hazard.

Occupational exposure limits

TLV: 5 mg/m³ (as TWA) (skin) (ACGIH 2000).
MAK: 5 mg/m³ (skin) (MAK 1995).

Routes of exposure

The substance can be absorbed into the body by inhalation of its fumes and through the skin.

Inhalation risk

A harmful contamination of the air will not or will only very slowly be reached on evaporation of this substance at 20°C; on spraying or dispersing, however, much faster.

Effects of short-term exposure

The substance is mildly irritating to the eyes and the skin.

Effects of long-term or repeated exposure

The substance may have effects on the liver, resulting in liver impairment.

PHYSICAL PROPERTIES

Boiling point: 304-354°C
Melting point: 93°C
Density: 1.58 g/cm³
Solubility in water: none

Vapour pressure, Pa at 20°C: <0.1
Relative vapour density (air = 1): 8
Flash point: 200°C o.c.
Octanol/water partition coefficient as log Pow: 5.12-7.56

ENVIRONMENTAL DATA

This substance may be hazardous to the environment; special attention should be given to crustacea. In the food chain important to humans, bioaccumulation takes place, specifically in fish. It is strongly advised not to let the chemical enter into the environment because it persists in the environment. The substance may cause long-term effects in the aquatic environment.

NOTES

Halowax is a trade name for chlorinated naphthalenes. The health effects may vary with the proportion of the different isomers present.

ADDITIONAL INFORMATION

LEGAL NOTICE

Neither the EC nor the IPCS nor any person acting on behalf of the EC or the IPCS is responsible for the use which might be made of this information

TETRACHLORONAPHTHALENE

1387

March 2001

CAS No: 1335-88-2
RTECS No: QK3700000

C₁₀H₄Cl₄
Molecular mass: 265.9

TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/SYMPTOMS	PREVENTION	FIRST AID/FIRE FIGHTING
FIRE	Combustible. Gives off irritating or toxic fumes (or gases) in a fire.	NO open flames.	Water spray, foam, powder, carbon dioxide.
EXPLOSION			

EXPOSURE		PREVENT DISPERSION OF DUST!	
Inhalation		Local exhaust or breathing protection.	Fresh air, rest.
Skin	Redness.	Protective gloves. Protective clothing.	Remove contaminated clothes. Rinse and then wash skin with water and soap.
Eyes	Redness. Pain.	Safety spectacles.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
Ingestion	Abdominal pain. Headache. Nausea. Vomiting.	Do not eat, drink, or smoke during work.	Rinse mouth. Rest. Refer for medical attention.

SPILLAGE DISPOSAL	PACKAGING & LABELLING
Sweep spilled substance into sealable containers; if appropriate, moisten first to prevent dusting. Carefully collect remainder. Do NOT let this chemical enter the environment. (Extra personal protection: P2 filter respirator for harmful particles.)	

EMERGENCY RESPONSE	STORAGE
Transport Emergency Card: TEC (R)-61G12b	Separated from strong oxidants, food and feedstuffs. Keep in a well-ventilated room.

IMPORTANT DATA

Physical State; Appearance

COLOURLESS TO PALE YELLOW CRYSTALS, WITH CHARACTERISTIC ODOUR.

Chemical dangers

The substance decomposes on burning producing toxic gases (hydrogen chloride, phosgene). Reacts with strong oxidants causing fire and explosion hazard.

Occupational exposure limits

TLV: 2 mg/m³ (ACGIH 2000).

MAK: 5 mg/m³; (2000)

Routes of exposure

The substance can be absorbed into the body by inhalation of its fumes and through the skin.

Inhalation risk

A harmful contamination of the air will not or will only very slowly be reached on evaporation of this substance at 20°C; on spraying or dispersing, however, much faster.

Effects of short-term exposure

The substance is mildly irritating to the eyes and the skin.

Effects of long-term or repeated exposure

The substance may have effects on the liver, resulting in liver impairment.

PHYSICAL PROPERTIES

Boiling point: 312-360°C

Melting point: 182°C

Density: 1.6 g/cm³

Solubility in water: none

Vapour pressure, Pa at 25°C: 0.1

Relative vapour density (air = 1): 9.2

Flash point: 210°C o.c.

Octanol/water partition coefficient as log Pow: 5.75-6.19

ENVIRONMENTAL DATA

In the food chain important to humans, bioaccumulation takes place, specifically in fish. It is strongly advised not to let the chemical enter into the environment because it persists in the environment. The substance may cause long-term effects in the aquatic environment.

NOTES

Halowax is a trade name for chlorinated naphthalenes. The health effects may vary with the proportion of the different isomers present.

ADDITIONAL INFORMATION

LEGAL NOTICE

Neither the EC nor the IPCS nor any person acting on behalf of the EC or the IPCS is responsible for the use which might be made of this information

PENTACHLORONAPHTHALENE**0935**

March 2001

CAS No: 1321-64-8
RTECS No: QK0300000
EC No: 602-041-00-5

$C_{10}H_3Cl_5$
Molecular mass: 300.4

TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/SYMPTOMS	PREVENTION	FIRST AID/FIRE FIGHTING
FIRE	Not combustible. Gives off irritating or toxic fumes (or gases) in a fire.		Water spray, foam, powder, carbon dioxide.
EXPLOSION			

EXPOSURE		PREVENT DISPERSION OF DUST! STRICT HYGIENE!	IN ALL CASES CONSULT A DOCTOR!
Inhalation		Local exhaust or breathing protection.	Fresh air, rest.
Skin	MAY BE ABSORBED! Redness. Pain.	Protective gloves. Protective clothing.	Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention.
Eyes	Redness. Pain.	Face shield, or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
Ingestion		Do not eat, drink, or smoke during work.	Rinse mouth. Refer for medical attention.

SPILLAGE DISPOSAL	PACKAGING & LABELLING
Sweep spilled substance into sealable containers; if appropriate, moisten first to prevent dusting. Carefully collect remainder, then remove to safe place. Do NOT let this chemical enter the environment. Chemical protection suit. (Extra personal protection: P2 filter respirator for harmful particles).	Xn Symbol N Symbol R: 21/22-36/38-50/53 S: (2-)35-60-61 Note: C

EMERGENCY RESPONSE	STORAGE
	Separated from strong oxidants, food and feedstuffs.

IMPORTANT DATA

Physical State; Appearance

PALE YELLOW OR WHITE SOLID, WITH CHARACTERISTIC ODOUR.

Chemical dangers

The substance decomposes on heating producing toxic fumes of hydrogen chloride. Reacts with strong oxidants.

Occupational exposure limits

TLV (as TWA): 0.5 mg/m³ (skin) (ACGIH 2000).

Routes of exposure

The substance can be absorbed into the body by inhalation of fumes and through the skin.

Inhalation risk

Evaporation at 20°C is negligible; a harmful concentration of airborne particles can, however, be reached quickly.

Effects of short-term exposure

The substance is irritating to the eyes and the skin.

Effects of long-term or repeated exposure

Repeated or prolonged contact with skin may cause dermatitis (chloracne). The substance may have effects on the liver, resulting in liver impairment.

PHYSICAL PROPERTIES

Boiling point: 327-371°C

Melting point: 120°C

Density: 1.7 g/cm³

Solubility in water: none

Vapour pressure, Pa at 20°C: 0.1

Relative vapour density (air = 1): 10.4

Octanol/water partition coefficient as log Pow: 8.73-9.13

ENVIRONMENTAL DATA

In the food chain important to humans, bioaccumulation takes place, specifically in fish. It is strongly advised not to let the chemical enter into the environment because it persists in the environment. The substance may cause long-term effects in the aquatic environment.

NOTES

Halowax is a trade name for chlorinated naphthalenes.

ADDITIONAL INFORMATION

LEGAL NOTICE

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HEXACHLORONAPHTHALENE

0997

March 2001

CAS No: 1335-87-1
RTECS No: QJ7350000

$C_{10}H_2Cl_6$
Molecular mass: 334.7

TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/SYMPTOMS	PREVENTION	FIRST AID/FIRE FIGHTING
FIRE	Not combustible. Gives off irritating or toxic fumes (or gases) in a fire.		Water spray, foam, powder, carbon dioxide.
EXPLOSION			

EXPOSURE		PREVENT DISPERSION OF DUST! STRICT HYGIENE!	IN ALL CASES CONSULT A DOCTOR!
Inhalation		Local exhaust or breathing protection.	Fresh air, rest.
Skin	MAY BE ABSORBED! Redness. Pain.	Protective gloves. Protective clothing.	Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention.
Eyes	Redness. Pain.	Face shield, or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
Ingestion		Do not eat, drink, or smoke during work.	Rinse mouth. Refer for medical attention.

SPILLAGE DISPOSAL	PACKAGING & LABELLING
Sweep spilled substance into sealable containers; if appropriate, moisten first to prevent dusting. Carefully collect remainder, then remove to safe place. Do NOT let this chemical enter the environment. Chemical protection suit. (Extra personal protection: P2 filter respirator for harmful particles).	

EMERGENCY RESPONSE	STORAGE
	Separated from strong oxidants, food and feedstuffs.

IMPORTANT DATA

Physical State; Appearance

WHITE SOLID IN VARIOUS FORMS, WITH CHARACTERISTIC ODOUR.

Chemical dangers

The substance decomposes on burning producing toxic gases including hydrogen chloride and phosgene. Reacts with strong oxidants.

Occupational exposure limits

TLV: (as TWA) 0.2 mg/m³ skin (ACGIH 2000).

Routes of exposure

The substance can be absorbed into the body by inhalation of its fumes and through the skin.

Inhalation risk

Evaporation at 20°C is negligible; a harmful concentration of airborne particles can, however, be reached quickly.

Effects of short-term exposure

The substance is irritating to the eyes and the skin.

Effects of long-term or repeated exposure

Repeated or prolonged contact with skin may cause dermatitis (chloracne). The substance may have effects on the liver, resulting in liver impairment.

PHYSICAL PROPERTIES

Boiling point: 344-388°C

Melting point: 137°C

Density: 1.78 g/cm³

Solubility in water: none

Vapour pressure, Pa at °C: 0.01

Relative vapour density (air = 1): 11.6

Octanol/water partition coefficient as log Pow: 7.59

ENVIRONMENTAL DATA

In the food chain important to humans, bioaccumulation takes place, specifically in fish. It is strongly advised not to let the chemical enter into the environment because it persists in the environment. The substance may cause long-term effects in the aquatic environment.

NOTES

Halowax is a trade name for chlorinated naphthalenes.

ADDITIONAL INFORMATION

LEGAL NOTICE

Neither the EC nor the IPCS nor any person acting on behalf of the EC or the IPCS is responsible for the use which might be made of this information

CAS No: 2234-13-1
RTECS No: QK0250000

Perchloronaphthalene
 $C_{10}Cl_8$
Molecular mass: 403.7

TYPES OF HAZARD/ EXPOSURE	ACUTE HAZARDS/SYMPTOMS	PREVENTION	FIRST AID/FIRE FIGHTING
FIRE	Not combustible. Gives off irritating or toxic fumes (or gases) in a fire.		In case of fire in the surroundings: all extinguishing agents allowed.
EXPLOSION			

EXPOSURE		STRICT HYGIENE!	
Inhalation		Local exhaust or breathing protection.	Fresh air, rest. Refer for medical attention.
Skin	MAY BE ABSORBED! Chloracne.	Protective gloves. Protective clothing.	Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention.
Eyes		Safety goggles, or face shield, or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
Ingestion		Do not eat, drink, or smoke during work. Wash hands before eating.	Rinse mouth. Refer for medical attention.

SPILLAGE DISPOSAL	PACKAGING & LABELLING
Sweep spilled substance into containers. Carefully collect remainder, then remove to safe place. (Extra personal protection: P3 filter respirator for toxic particles).	

EMERGENCY RESPONSE	STORAGE

IMPORTANT DATA

Physical State; Appearance

WAXY, YELLOW SOLID IN VARIOUS FORMS, WITH CHARACTERISTIC ODOUR.

Chemical dangers

The substance decomposes on heating producing toxic fumes including hydrogen chloride.

Occupational exposure limits

TLV: 0.1 mg/m³ (as TWA);
0.3 mg/m³ (as STEL) (skin) (ACGIH 2000).

Routes of exposure

The substance can be absorbed into the body by inhalation, through the skin and by ingestion.

Effects of short-term exposure

The substance may cause effects on the liver, resulting in tissue lesions.

Effects of long-term or repeated exposure

The substance may have effects on the liver.

PHYSICAL PROPERTIES

Boiling point: 440°C
Melting point: 192°C
Relative density (water = 1): 2.0

Solubility in water: none
Vapour pressure, kPa at 20°C: 0.13
Relative density of the vapour/air-mixture at 20°C (air = 1): 1.01
Octanol/water partition coefficient as log Pow: 5.88-6.2

ENVIRONMENTAL DATA

In the food chain important to humans, bioaccumulation takes place, specifically in fish.
It is strongly advised not to let the chemical enter into the environment because it persists in the environment.

NOTES

ADDITIONAL INFORMATION

LEGAL NOTICE

Neither the EC nor the IPCS nor any person acting on behalf of the EC or the IPCS is responsible for the use which might be made of this information

RÉSUMÉ D'ORIENTATION

Ce CICAD relatif aux naphthalènes chlorés a été préparé par le *Centre for Ecology and Hydrology* de Monks Wood (Royaume-Uni) et par l'Institut Fraunhofer de toxicologie et de recherche sur les aérosols de Hanovre (Allemagne). Il s'appuie sur le document *Environmental hazard assessment : Halogenated naphthalenes* du Royaume-Uni (Crookes & Howe, 1993) et sur les travaux de la Commission allemande pour l'étude des risques pour la santé liés aux composés chimiques sur les lieux de travail (Greim, 1997), ainsi que sur une recherche documentaire effectuée en juin 2000. On trouvera à l'appendice 1 des indications sur les modalités de l'examen par des pairs et sur les sources documentaires. Les renseignements concernant l'examen du CICAD par des pairs font l'objet de l'appendice 2. Ce CICAD a été approuvé en tant qu'évaluation internationale lors d'une réunion du Comité d'évaluation finale qui s'est tenue à Genève (Suisse) du 8 au 12 janvier 2001. La liste des participants à cette réunion figure à l'appendice 3. Les fiches d'information internationales sur la sécurité chimique pour le trichloronaphtalène (ICSC 0962), le tétrachloronaphtalène (ICSC 1387), le pentachloronaphtalène (ICSC 0935), l'hexachloronaphtalène (ICSC 0997) et l'octachloronaphtalène (ICSC 1059) établies par le Programme international sur la Sécurité chimique (IPCS, 1993a,b,c, 1999a,b) sont également reproduites dans ce document.

La série des naphthalènes chlorés compte 75 homologues possibles. Les produits commerciaux sont en général des mélanges de plusieurs homologues et vont de liquides de faible viscosité à des solides de température de fusion élevée en passant par des cires dures. Ils sont principalement utilisés pour l'isolation des câbles électriques, pour la conservation du bois, dans les condensateurs, et comme additifs pour les huiles de moteur, produits de masquage en galvanoplastie, huiles de référence pour la mesure de l'indice de réfraction et charges pour la fabrication de colorants.

Les principales sources de rejet de naphthalènes chlorés dans l'environnement sont probablement l'incinération des déchets et la mise en décharge de produits qui contiennent ces substances.

Les naphthalènes chlorés devraient en principe être largement adsorbés sur les sols, les sédiments et les particules en suspension dans l'eau. Les prévisions concernant les coefficients de partage carbone organique/eau dans les sols montrent qu'ils augmentent avec le degré de chloration des naphthalènes chlorés. Il est donc probable que la tendance à la sorption sera modérée pour les homologues peu chlorés et forte pour les homologues hautement chlorés.

Il a été démontré que les naphthalènes chlorés ont fortement tendance à s'accumuler chez les poissons, mais dans une plus faible mesure chez les crevettes et les algues. Le niveau de bioaccumulation observé augmente avec le degré de chloration, mais les naphthalènes les plus hautement chlorés (par exemple les octachloronaphtalènes) ne semblent pas s'accumuler car ils sont très peu absorbés.

Les monochloronaphtalènes sont facilement biodégradables en aérobiose par les micro-organismes présents dans le sol et dans les eaux. On ne dispose pas de données sur la biodégradation des naphthalènes hautement chlorés.

Un des rapports indique une demi-vie de 2,7 jours dans l'atmosphère pour le 1,4-dichloronaphtalène. On n'a pas trouvé d'autres données sur le devenir des autres naphthalènes chlorés dans l'atmosphère. Comme tous les naphthalènes chlorés absorbent la lumière à des longueurs d'onde compatibles avec les conditions environnementales, une photolyse directe peut se produire dans l'eau, dans l'air ou sur le sol.

Dans le passé, des concentrations de naphthalènes chlorés pouvant atteindre 14,5 mg/m³ ont été mesurées sur les lieux de travail et des concentrations de 25 à 2900 ng/m³ dans l'air ambiant au voisinage de sites de fabrication. Plus récemment, des études de surveillance ont mis en évidence des concentrations de naphthalènes chlorés atteignant 150 pg/m³ dans des sites « semi-ruraux » et de 1 à 40 pg/m³ dans des sites reculés. Les homologues prédominants dans l'air ambiant étaient les tri- et tétrachloronaphtalènes. Dans les années 70, des concentrations atteignant 5,5 µg/litre ont été mesurées dans les eaux de surface à proximité de sites de fabrication des naphthalènes chlorés, et des taux encore plus élevés ont été trouvés dans les eaux souterraines. Des études récentes ont montré des taux de l'ordre de quelques ng/litre dans les eaux de surface. Une étude réalisée sur de l'eau du robinet chlorée a révélé des concentrations de naphthalènes chlorés de 0,15 ng de dichloronaphtalène et 0,44 ng de monochloronaphtalène par litre. Dans les sédiments et particules en suspension, des teneurs allant jusqu'à 100 mg/kg ont été enregistrées dans le passé; des mesures récentes ont indiqué des concentrations de 0,2 µg/kg dans des sites non pollués et de 250 µg/kg dans des sites pollués. De même, des teneurs allant jusqu'à 1300 mg/kg ont été mesurées dans les sols de sites contaminés au début des années 80, tandis qu'une mesure récente effectuée dans une ancienne fabrique de chlore et de soude caustique a donné une concentration de 18 mg/kg de poids sec. Chez les poissons, les concentrations de naphthalènes chlorés peuvent atteindre un maximum de 300 µg par kg de lipides. Le tétra- et le pentachloronaphtalène tendent à prédominer dans les biotes. Des études de surveillance sur des oeufs d'oiseaux de mer ont mis en évidence une diminution des teneurs en naphthalènes chlorés entre 1974 et 1987.

Les naphthalènes chlorés, notamment ceux qui se rapprochent des dioxines, ont été trouvés dans les tissus adipeux, le foie, le sang et le lait maternel dans la population générale à des concentrations de l'ordre de quelques ng par kg de lipides. Le profil des homologues et isomères de naphthalènes chlorés trouvés dans les prélèvements humains est sensiblement différent de celui des mélanges commerciaux de ces produits. Dans la quasi-totalité des prélèvements humains examinés, les homologues prédominants étaient deux isomères de penta- et hexachloronaphthalènes, à savoir le 1,2,3,5,7- et le 1,2,4,6,7-pentachloronaphthalène et le 1,2,3,4,6,7- et le 1,2,3,5,6,7-hexachloronaphthalène; on a également trouvé, mais en plus petite quantité, des isomères tétrachlorés.

Les naphthalènes chlorés peuvent être absorbés par voie orale, par inhalation et par voie cutanée, avec résorption et distribution dans tout l'organisme après administration orale. Les principaux organes cibles sont, avec les reins et les poumons, le foie et les tissus adipeux, ces deux derniers montrant une forte rétention de ces substances, en particulier des homologues hautement chlorés comme le 1,2,3,4,6,7- et le 1,2,3,5,6,7-hexachloronaphthalène. On a calculé que chez le rat, la demi-vie du 1,2,3,4,6,7- et du 1,2,3,5,6,7-hexachloronaphthalène était de 41 jours dans les tissus adipeux et 26 jours dans le foie. D'après des calculs effectués à partir des données de surveillance de prélèvements de sang humains, la demi-vie de ces isomères hexachlorés chez l'homme serait de 1,5 à 2,4 ans. Des métabolites hydroxylés ont été identifiés chez l'animal d'expérience, surtout avec les naphthalènes les moins chlorés (mono- à tétrachlorés). On dispose également de données préliminaires indiquant la présence de métabolites de type méthylthio- ou méthylsulfoxyde dans les fèces de rats. L'élimination des composés de départ et/ou des métabolites se fait par voie fécale et urinaire. On a également observé un transfert du 1,2,3,4,6,7-chloronaphthalène à la descendance de rats par voie placentaire et par le lait maternel.

Les valeurs de la DL_{50} de certains naphthalènes chlorés allaient de >3 (2,3,6,7-tétrachloronaphthalène) à 1540 (1-monochloronaphthalène) mg/kg de poids corporel. L'exposition à court terme à des naphthalènes hautement chlorés provoquait la mort ou des lésions hépatiques, une dégénérescence rénale, etc. chez des rats, lapins et bovins. Chez les bovins, une atteinte générale grave (hyperkératose bovine) apparaissait lors d'une exposition orale de 5 à 10 jours à des penta-, hexa-, hepta- ou octachloronaphthalènes à raison de 1,7-2,4 mg/kg de poids corporel. Des symptômes analogues (mort, perte de poids importante et lésions hépatiques) ont été observés lors d'expositions subchroniques par voie orale ou par inhalation chez des animaux domestiques et de laboratoire. Les homologues les plus chlorés étaient les plus toxiques. L'inhalation de $1,4 \text{ mg/m}^3$, 8 heures par jour, d'un mélange de penta- et d'hexachloronaphthalène pendant 143 jours a entraîné des lésions histologiques du foie légères à modérées chez le rat.

Il n'a pas été réalisé d'études à long terme ni d'études de cancérogénicité sur les naphthalènes chlorés.

Les naphthalènes chlorés ayant fait l'objet de tests de mutagénicité (1-monochloronaphthalène et 1,2,3,4-tétrachloronaphthalène) n'étaient pas mutagènes dans le test d'Ames sur *Salmonella*.

Le 1,2,3,4,6,7-hexachloronaphthalène accélérail le début de la spermatogenèse chez les descendants mâles de rats lorsqu'il était administré aux mères à raison de $1 \text{ } \mu\text{g/kg}$ de poids corporel par jour les jours 14 à 16 de la gestation.

Comme les composés apparentés, les naphthalènes chlorés sont des inducteurs des enzymes microsomiques dépendant du cytochrome P-450 (CYP). Deux hexachloronaphthalènes très persistants (et souvent rencontrés dans les prélèvements humains et environnementaux), le 1,2,3,4,6,7- et le 1,2,3,5,6,7-hexachloronaphthalène, provoquaient une induction des CYP1A1 – typique des composés de type dioxines – dans plusieurs systèmes *in vitro* et *in vivo*. On a également observé que les naphthalènes chlorés modifiaient l'activité oxydante des enzymes et leur activité de peroxydation des lipides chez le rat, d'une manière indiquant une augmentation du stress oxydatif. On pense qu'au moins certaines des réponses biologiques et toxiques aux naphthalènes chlorés sont médiées par le récepteur Ah du cytosol, comme avec la 2,3,7,8-tétrachlorodibenzo-*p*-dioxine (TCDD) et les composés apparentés.

Tous les naphthalènes chlorés testés provoquaient une irritation cutanée, et les penta- et hexachloronaphthalènes montraient une activité hyperkératosique dans les tests sur oreille de lapin et sur souris « hairless », ce qui rejoint les observations faites sur les bovins (hyperkératose bovine ou maladie X) et chez l'homme (chloracné).

Des réactions cutanées sévères (chloracné) et des atteintes hépatiques ont été observées après exposition professionnelle aux naphthalènes chlorés. La chloracné était fréquente chez les travailleurs manipulant ces substances au cours des années 30 et 40.

Les autres symptômes décrits chez les travailleurs exposés aux naphthalènes chlorés consistaient en irritation oculaire, fatigue, céphalées, anémie, hématurie, impuissance, anorexie, nausées, vomissements et parfois douleurs abdominales sévères. Au moins 10 décès ont été rapportés à la suite d'une atrophie aiguë du foie. Des effets généraux conduisant à une maladie hépatique n'ont été rapportés qu'avec l'inhalation de naphthalènes chlorés.

Après application cutanée de divers échantillons de Halowax chez des adultes, seul le Halowax 1014, qui contient des penta- et des hexachloronaphthalènes, provoquait une chloracné; cet effet ne s'observait pas

avec les échantillons de Halowax contenant des mono-, di-, tri-, tétra-, hepta- et/ou octachloronaphtalènes.

Une étude de cohorte portant sur la mortalité chez les travailleurs exposés aux naphtalènes chlorés dans une fabrique de câbles a montré un excès de décès par cirrhose du foie. Cependant, la mortalité par cirrhose du foie n'était pas plus forte chez les sujets qui avaient présenté une chloracné que chez les autres. La mortalité par cancers de toutes localisations était légèrement, mais significativement, plus élevée parmi l'ensemble des hommes exposés (ratio standardisé de mortalité : 1,18), mais non dans la sous-cohorte présentant une chloracné. Cette sous-cohorte montrait un excès statistiquement significatif de mortalité par cancer de l'oesophage et par « néoplasmes bénins sans précision ».

Seuls quelques rapports mentionnent les effets d'une exposition accidentelle aux naphtalènes chlorés dans la population générale. A une exception près, il s'agit de l'ingestion d'huile contaminée par d'autres produits chimiques aussi bien que par des naphtalènes chlorés, et qui entraînait des symptômes généraux suivis d'une chloracné.

Les naphtalènes chlorés semblent présenter une toxicité aiguë modérée à forte pour les organismes aquatiques.

RESUMEN DE ORIENTACIÓN

Este CICAD sobre los naftalenos clorados, preparado por el Centro de Ecología e Hidrología de Monks Wood (Reino Unido) y el Instituto Fraunhofer de Toxicología y de Investigación sobre los Aerosoles de Hannover (Alemania), está basado en la *Evaluación del peligro para el medio ambiente: Naftalenos halogenados del Reino Unido* (Crookes & Howe, 1993) y en la labor de la Comisión Alemana de Investigación de los Peligros para la Salud de las Sustancias Químicas en el Entorno de Trabajo (Greim, 1997), complementados por una búsqueda bibliográfica (junio de 2000). La información sobre el carácter del examen colegiado y la disponibilidad de los documentos originales se presenta en el apéndice 1. La información acerca del examen colegiado de este CICAD aparece en el apéndice 2. Este CICAD se aprobó como evaluación internacional en una reunión de la Junta de Evaluación Final, celebrada en Ginebra (Suiza) del 8 al 12 de enero de 2001. La lista de participantes en esta reunión figura en el apéndice 3. Las Fichas internacionales de seguridad química para el tricloronaftaleno (ICSC 0962), el tetracloronaftaleno (ICSC 1387), el pentacloronaftaleno (ICSC 0935), el hexacloronaftaleno (ICSC 0997) y el octacloronaftaleno (ICSC 1059), preparadas por el Programa Internacional de Seguridad de las Sustancias Químicas (IPCS, 1993a,b,c, 1999a,b), también se reproducen en el presente documento.

Hay 75 posibles compuestos de naftalenos clorados. Los productos comerciales suelen ser mezclas de varios de ellos y sus características varían, pudiendo ser desde líquidos ligeros hasta ceras duras y sólidos de punto de fusión elevado. Se han utilizado principalmente en el aislamiento de cables, la conservación de la madera, aditivos para el aceite de los motores, compuestos de revestimiento galvánico, condensadores y aceites de prueba para el índice de refracción y como materia prima para la producción de colorantes.

Las fuentes principales de emisión de naftalenos clorados al medio ambiente probablemente son la incineración de desechos y la eliminación de artículos con naftalenos clorados en vertederos.

Es previsible una adsorción elevada de naftalenos clorados en el suelo y los sedimentos. Los coeficientes de reparto carbono orgánico/agua del suelo previstos aumentan con su grado de cloración. Así pues, los compuestos menos clorados probablemente presentarán una tendencia a la sorción moderada y los más clorados intensa.

Se ha puesto de manifiesto que los naftalenos clorados alcanzan un elevado grado de bioacumulación en los peces, pero menos en los camarones y las algas. La intensidad de la bioacumulación observada aumenta con

el grado de cloración de los naftalenos clorados, aunque los más clorados (por ejemplo, el octacloronaftaleno) no parecen bioacumularse debido a su capacidad de absorción muy limitada.

En condiciones aerobias, los microorganismos del suelo y el agua parecen degradar fácilmente los monocloronaftalenos. No se encontró información acerca de la biodegradación por los microorganismos de los compuestos más clorados.

En un informe figuraba una semivida atmosférica de 2,7 días para el 1,4-dicloronaftaleno. No se encontró ninguna otra información relativa al destino en la atmósfera de otros naftalenos clorados. Dado que todos los naftalenos clorados absorben luz de las longitudes de onda habituales en el medio ambiente, se puede producir fotólisis directa en el agua, el aire y el suelo.

En el pasado se han medido concentraciones de naftalenos clorados de hasta 14,5 mg/m³ en lugares de trabajo, mientras que en el aire exterior circundante de las fábricas se han registrado concentraciones de 25-2900 ng/m³. En estudios de vigilancia más recientes se han observado concentraciones de naftalenos clorados de hasta 150 pg/m³ en zonas "semirurales" y de 1-40 pg/m³ en zonas remotas. Los compuestos predominantes en el aire exterior fueron los tricloronaftalenos y los tetracloronaftalenos. En los años setenta se midieron concentraciones de hasta 5,5 µg/litro en aguas superficiales cercanas a fábricas de naftalenos clorados, habiéndose registrado concentraciones más elevadas en el agua freática. En estudios recientes se han obtenido en aguas superficiales concentraciones correspondientes a la gama baja de ng/litro. En un estudio único de agua de grifo clorada se observaron concentraciones de naftalenos clorados de hasta 0,15 ng de dicloronaftaleno/litro y de hasta 0,44 ng de monocloronaftaleno/litro. En el pasado se han registrado concentraciones en los sedimentos de hasta 100 mg/kg; sin embargo, en resultados recientes se han obtenido concentraciones de 0,2 µg/kg en lugares no contaminados y de 250 µg/kg en los contaminados. Igualmente, a comienzos de los años ochenta se determinaron concentraciones en el suelo de hasta 1300 mg/kg en zonas contaminadas, en comparación con un valor más reciente en una antigua fábrica de clorálcis de 18 mg/kg de peso seco. Las concentraciones de naftalenos clorados en los peces alcanzan hasta un máximo de unos 300 µg/kg de peso de lípidos. En la biota tienden a predominar el tetracloronaftaleno y el pentacloronaftaleno. En estudios de vigilancia con huevos de aves marinas se ha puesto de manifiesto una disminución de las concentraciones de naftalenos clorados entre 1974 y 1987.

Se han detectado naftalenos clorados, especialmente compuestos semejantes a las dioxinas, en muestras de tejido adiposo, hígado, sangre y leche materna en la población general, en concentraciones del orden de

varios ng/kg de lípidos. La distribución de los compuestos/isómeros de naftalenos clorados presentes en muestras humanas era muy diferente de la observada en las mezclas de naftalenos clorados comerciales. Los compuestos predominantes en casi todas las muestras humanas examinadas fueron dos pentaisómeros y dos hexaisómeros, a saber, el 1,2,3,5,7/1,2,4,6,7-pentacloronaftaleno y el 1,2,3,4,6,7/1,2,3,5,6,7-hexacloronaftaleno, y en menor medida algunos tetraisómeros.

Los naftalenos clorados se pueden absorber por vía oral, respiratoria y cutánea, con absorción y distribución en todo el organismo después de la administración oral. Los principales órganos destinatarios son el hígado y el tejido adiposo (además del riñón y el pulmón), presentando ambos una elevada retención, en particular de los compuestos más fuertemente clorados, como el 1,2,3,4,6,7/1,2,3,5,6,7-hexacloronaftaleno. Para el 1,2,3,4,6,7/1,2,3,5,6,7-hexacloronaftaleno se calculó una semivida de 41 días en el tejido adiposo y de 26 días en el hígado de ratas. Los cálculos realizados para estos isómeros hexaclorados con los datos de vigilancia obtenidos de muestras de sangre humana parecían indicar una semivida de 1,5-2,4 años. En los animales de experimentación se han identificado metabolitos hidroxilados fundamentalmente para los naftalenos menos clorados (de monoclorados a tetraclorados). Hay también indicios preliminares de la presencia de metabolitos de metiltiocloronaftaleno o metilsulfóxidocloronaftaleno en las heces de ratas. La eliminación de los compuestos de origen y/o los metabolitos se produce en las heces y la orina. También se observó una transferencia de 1,2,3,4,6,7-hexacloronaftaleno a las crías de ratas por vía placentaria o mamaria.

Los valores de la DL₅₀ de algunos naftalenos clorados oscilaban entre >3 (2,3,6,7-tetracloronaftaleno) y 1540 (1-monocloronaftaleno) mg/kg de peso corporal. La exposición breve a los naftalenos más clorados produjo mortalidad, lesiones hepáticas, degeneración renal, etc., en ratas, conejos y ganado vacuno. En el ganado vacuno apareció una enfermedad sistémica grave (hiperqueratosis bovina) durante una exposición por vía oral de 5-10 días a 1,7-2,4 mg/kg de peso corporal al día de naftalenos pentaclorados, hexaclorados, heptaclorados u octaclorados. Se han observado asimismo síntomas semejantes (muerte, pérdida grave de peso y lesiones hepáticas) durante la exposición subcrónica por vía oral o respiratoria de animales de laboratorio y domésticos. Los compuestos más fuertemente clorados parecen ser más tóxicos que los menos clorados. La inhalación de 1,4 mg/m³ (8 horas/día) de una mezcla de naftaleno pentaclorado/hexaclorado durante 143 días produjo en el hígado de ratas lesiones histológicas de ligeras a moderadas.

No se han realizado estudios prolongados ni de carcinogenicidad con los naftalenos clorados.

Los escasos naftalenos poco clorados con los que se han realizado pruebas de mutagenicidad - 1-mono-cloronaftaleno y 1,2,3,4-tetracloronaftaleno - no han resultado mutagénicos en la prueba Ames con *Salmonella*.

Se ha observado que el 1,2,3,4,6,7-hexacloronaftaleno acelera el comienzo de la espermatogénesis en las crías machos de ratas tratadas con 1 µg/kg de peso corporal al día en los días 14-16 de la gestación.

Como otros compuestos análogos, se ha demostrado que los naftalenos clorados inducen la producción de enzimas microsomales dependientes del citocromo P-450 (CYP). Dos isómeros muy persistentes (y frecuentemente identificados en muestras de personas y del medio ambiente) de naftalenos hexaclorados (es decir, el 1,2,3,4,6,7/1,2,3,5,6,7-hexacloronaftaleno) provocaron la inducción de CYP1A1 - característica de los compuestos semejantes a las dioxinas - en varios sistemas de prueba *in vitro* e *in vivo*. También se observó que los naftalenos clorados cambiaban la peroxidación de los lípidos y las actividades de las enzimas antioxidantes en ratas, lo que indica un aumento de la tensión oxidativa. Se considera que por lo menos algunas respuestas biológicas y tóxicas de los naftalenos clorados están mediadas por el receptor citosólico Ah de manera parecida a las de la 2,3,7,8-tetraclorodibenzo-*p*-dioxina y compuestos afines.

Todos los naftalenos clorados sometidos a prueba provocaron irritación cutánea y los naftalenos penta-clorados y hexaclorados mostraron actividad hiperqueratósica en la prueba de la oreja de conejo y de ratones sin pelo, en consonancia con los resultados obtenidos en el ganado vacuno (hiperqueratosis bovina) y en las personas (cloracné).

Se han notificado reacciones cutáneas graves (cloracné) y enfermedades hepáticas tras la exposición ocupacional a los naftalenos clorados. El cloracné era común entre los trabajadores que manipulaban naftalenos clorados en los años treinta y cuarenta.

Otros síntomas descritos en los trabajadores expuestos a los naftalenos clorados fueron: irritación ocular, fatiga, dolor de cabeza, anemia, hematuria, impotencia, anorexia, náusea, vómitos y ocasionalmente dolor abdominal intenso. Se notificaron al menos 10 muertes por atrofia aguda del hígado. Se han notificado efectos sistémicos con el resultado de enfermedades hepáticas sólo a partir de la inhalación de cloronaftalenos.

Tras la aplicación cutánea de varias muestras de Halowax a personas adultas, sólo produjo cloracné el Halowax 1014, que contiene pentacloronaftaleno y hexacloronaftaleno; las muestras de Halowax que contenían monocloronaftaleno, dicloronaftaleno, tricloro-

naftaleno, tetracloronaftaleno, heptacloronaftaleno y/u octacloronaftaleno no tuvieron ese efecto.

En un estudio de mortalidad de cohortes en trabajadores expuestos a naftalenos clorados en una fábrica de cables se observó un exceso de muertes por cirrosis hepática. Sin embargo, las personas que habían manifestado síntomas de cloracné no mostraron una mortalidad más alta debido a la cirrosis hepática en comparación con otros trabajadores. La mortalidad derivada de todos los tipos de cáncer registró una elevación ligera, pero significativa, entre todos los hombres expuestos (razón normalizada de mortalidad = 1,18), pero no fue más elevada en la subcohorte con cloracné. En esta subcohorte se puso de manifiesto un exceso de mortalidad estadísticamente significativo por cáncer de esófago y por "neoplasmas benignos y no especificados."

Sólo hay algunos informes diversos sobre los efectos de la exposición accidental a naftalenos clorados en la población general. Con una sola excepción, se trata de la ingestión de aceite contaminado con otras sustancias químicas, así como naftalenos clorados, con el resultado de síntomas sistémicos generales seguidos de cloracné.

La toxicidad aguda de los naftalenos clorados para los organismos acuáticos parece ser de moderada a alta.

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