European Chemicals Bureau

Institute for Health and Consumer Protection

European Chemicals Bureau

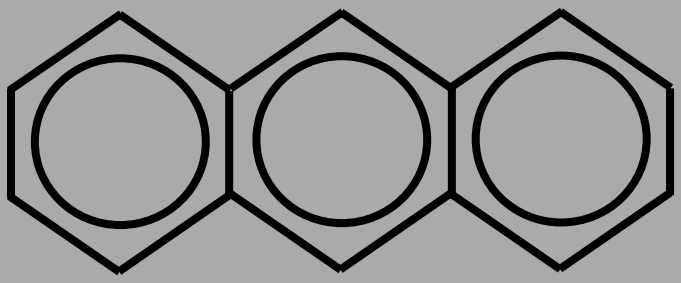
Existing Substances

European Union Risk Assessment Report

CAS No: 120-12-7

EINECS No: 204-371-1

anthracene
part II – human health



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RISK ASSESSMENT

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Part II – Human Health

CAS No: 120-12-7

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RISK ASSESSMENT

Final Report, 2007

Greece

The scientific assessments in this Report have been prepared by the National Hellenic Research Foundation (Unit of Environmental Toxicology), under contract with the Rapporteur.

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Date of Last Literature Search:	**2003**
Review of report by MS Technical Experts finalised:	**2005**
Final report:	**2007**

Foreword

We are pleased to present this Risk Assessment Report which is the result of in-depth work carried out by experts in one Member State, working in co-operation with their counterparts in the other Member States, the Commission Services, Industry and public interest groups.

The Risk Assessment was carried out in accordance with Council Regulation (EEC) 793/93[1] on the evaluation and control of the risks of "existing" substances. "Existing" substances are chemical substances in use within the European Community before September 1981 and listed in the European Inventory of Existing Commercial Chemical Substances. Regulation 793/93 provides a systematic framework for the evaluation of the risks to human health and the environment of these substances if they are produced or imported into the Community in volumes above 10 tonnes per year.

There are four overall stages in the Regulation for reducing the risks: data collection, priority setting, risk assessment and risk reduction. Data provided by Industry are used by Member States and the Commission services to determine the priority of the substances which need to be assessed. For each substance on a priority list, a Member State volunteers to act as "Rapporteur", undertaking the in-depth Risk Assessment and recommending a strategy to limit the risks of exposure to the substance, if necessary.

The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94[2], which is supported by a technical guidance document[3]. Normally, the "Rapporteur" and individual companies producing, importing and/or using the chemicals work closely together to develop a draft Risk Assessment Report, which is then presented at a meeting of Member State technical experts for endorsement. The Risk Assessment Report is then peer-reviewed by the Scientific Committee on Health and Environmental Risks (SCHER) which gives its opinion to the European Commission on the quality of the risk assessment.

If a Risk Assessment Report concludes that measures to reduce the risks of exposure to the substances are needed, beyond any measures which may already be in place, the next step in the process is for the "Rapporteur" to develop a proposal for a strategy to limit those risks.

The Risk Assessment Report is also presented to the Organisation for Economic Co-operation and Development as a contribution to the Chapter 19, Agenda 21 goals for evaluating chemicals, agreed at the United Nations Conference on Environment and Development, held in Rio de Janeiro in 1992 and confirmed in the Johannesburg Declaration on Sustainable Development at the World Summit on Sustainable Development, held in Johannesburg, South Africa in 2002.

This Risk Assessment improves our knowledge about the risks to human health and the environment from exposure to chemicals. We hope you will agree that the results of this in-depth study and intensive co-operation will make a worthwhile contribution to the Community objective of reducing the overall risks from exposure to chemicals.

Roland Schenkel
Director General
DG Joint Research Centre

Mogens Peter Carl
Director General
DG Environment

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1 O.J. No L 084, 05/04/199 p.0001 – 0075

2 O.J. No L 161, 29/06/1994 p. 0003 – 0011

3 Technical Guidance Document, Part I – V, ISBN 92-827-801 [1234]

0 OVERALL RESULTS OF THE RISK ASSESSMENT

CAS No:	120-12-7
EINECS No:	204-371-1
IUPAC Name:	anthracene
Synonyms:	Paranaphthalene, p-naphthalene

This Risk Assessment Report assesses the risks to human health associated with the production and use of the isolated commercial product anthracene. Anthracene is also found as part of complex mixtures in coal tar and products derived there from, as well as in the products of incomplete combustion of organic matter. According to Council Regulation 793/93 non-isolated anthracene is outside the scope of the present Report. However, estimates of the exposures and risks associated with such mixtures are included for illustrative purposes.

Environment

(to be added later)

Human Health

Human Health (toxicity)

Workers

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

This conclusion applies to the induction of dermal phototoxicity as a result of occupational dermal exposure during the production of anthracene from anthracene oil, the packaging of anthracene, and the manufacture of pyrotechnics.

Conclusion (i) There is need for further information and/or testing.

This conclusion applies to

- measured exposure data for workers involved in anthracene production from anthracene oil, anthracene packaging and anthracene use in the manufacture of pyrotechnics;
- testing to determine the reproductive and developmental toxicity of anthracene.

This substance has not been fully tested for reproductive toxicity and consequently this risk assessment does not evaluate the risks to any human populations for this endpoint. The need for a developmental toxicity study to fill this data gap has been identified following OECD 414 (Prenatal developmental toxicity study). However, this risk assessment describes the situation in the EU in 2003, in which there is only one production site in the EU, with 99% of production volume exported outside the EU and only a very minor use in pyrotechnics. There are no consumer exposures to the commercially-produced substance and human environmental exposures are very low. The potential for worker exposure using modelled estimates is low, and limited measured data and control measures, known to be applied at the production site, indicate that the model predictions are probably over-estimates.

On this basis, and taking into account that a) the developmental toxicity of PAHs is at least partly dependent on binding to the Ah receptor, and b) anthracene does not show such binding to any significant extent, the Technical Meeting agreed that there may be grounds on exposure

considerations to waive the requirement on the producer to generate such a study, as long as the exposure situation did not change. Further measured exposure data for workers involved in anthracene production from anthracene oil, anthracene packaging and anthracene use in the manufacture of pyrotechnics, would of course increase the level of confidence in this decision. The situation should be closely monitored and if there are any indications that production and use patterns are changing the potential for increasing exposure should be reconsidered and the need to request a developmental toxicity study revisited.

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

This conclusion applies to the induction of systemic toxicity as a result of exposure during the production of anthracene from anthracene oil, the packaging of anthracene, and the manufacture of pyrotechnics.

Consumers

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

Humans exposed via the environment

Conclusion (ii) There is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already.

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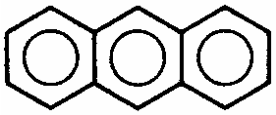
Euses Calculations can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.jrc.it

TABLES

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS No: 120-12-7
EINECS No: 204-371-1
IUPAC Name: Anthracene
Common Name: Anthracene
Synonyms: Paranaphthalene, p-naphthalene
Molecular formula: $C_{14}H_{10}$
Molecular mass: 178.24
Structural formula:



1.2 PURITY/IMPURITIES, ADDITIVES

1.2.1 Purity/impurities

Technical grade anthracene is approximately 97% pure, the main impurities being the following: phenanthrene (1.0%); carbazole (1.0%); naphthothiophene (0.4%); dibenzo[b,c]thiophene (0.3%); acridine (0.2%); acetophenone (0.4%).

Higher-grade anthracene can be obtained by treatment with air to oxidise 9,10-dihydroanthracene to anthracene, and by further recrystallisation, leading to a product with a low nitrogen (carbazole) content. Anthracene can generally be further separated from the higher boiling carbazole (b.p. 354^{o}) by further distillation with a lower-boiling hydrocarbon fraction as reflux medium, or by azeotropic distillation with ethylene glycol. Azeotropic distillation is also used to separate the anthracene-accompanying tetracene (naphthacene) and to obtain very pure anthracene which is used for scintillation counting.

1.3 PHYSICO-CHEMICAL PROPERTIES

1.3.1 Physical state at STP

Anthracene is a colourless crystalline solid, with violet fluorescence.

1.3.2 Melting point

A value of 218^{o}C is reported in IUCLID (Lang and Eigen (1967), in Merck Index (1983), in Ulmann's Encyclopaedia (Collin and Höke, 1985) and in Clar (1964). A closely similar value (217^{o}C) is reported in ECDIN as well as in Sax (1975). IUCLID also reports lower values of 214^{o}C (Hausigk and Koelling, 1968) and 216.4^{o}C (Karcher et al., 1985), while an additional value of 216.2^{o}C is reported in ECDIN. The value of 218^{o}C is adopted in the present Report as the highest value which represents the highest purity material.

1.3.3 Boiling point

Two values (340°C and 342°C) are reported in IUCLID and in several other publications (e.g. 340°C in Lang and Eigen, 1967; 342°C, Lax and Synowietz, 1964). The value of 340°C is reported in CRC (1987) as "corrected", while in ECDIN the value of 339.9°C is reported as the value at 760 mm Hg. Consequently the value of 340°C is adopted in the present Report.

1.3.4 Relative density

IUCLID gives values of 1.252 (25/4°C) (Collin and Höke, 1985) and 1.283 (25/4°C) (Lide, 1991). The same value is given in Lax and Synowietz (1964); while a value of 1.25 (27/4°C) is also reported in ECDIN and in Dean (1979). The value of 1.252 (25/4°C) is adopted in the present Report.

1.3.5 Vapour pressure

Three values are given in IUCLID. Sonnefeld et al. (1983) obtained a value of $8.0 \cdot 10^{-4}$ Pa (25°C) using a method closely similar to one of those recommended by Dir. 67/548/EEC. Their system was based on dynamic coupled-column liquid chromatography that is direct coupling of a gas saturation system to HPLC, used at the ambient temperature range. Commercially available anthracene was employed (purity > 98%). However, through the provisions of the system (pre-washing/conditioning of the saturation column) the measurements concerned pure anthracene.

Jandris and Forcė (1983) measured the vapour pressure of anthracene by analysing the vapour concentration using laser-induced molecular fluorescence. The material employed was 99.9% pure. Fluorescence intensity data over the range 25-150°C were obtained and employed to calculate first the vapour pressure at 101°C, which was then extrapolated to 25°C, yielding a value of $9.1 \cdot 10^{-9}$ atm ($9.2 \cdot 10^{-4}$ Pa).

A third value of 0.026 Pa, is reported in IUCLID citing a secondary reference (Neff, 1979) where no information on the method employed is given.

In the present report, the value of $8.0 \cdot 10^{-4}$ Pa (25°C) is adopted because the method employed by Sonnefeld et al. (1983) is closer to those recommended in Dir. 67/548/EEC.

1.3.6 Water solubility

Among the values reported in IUCLID, the value of 0.041 mg/l (25°C) (Schwartz, 1977) is adopted in the present Report, having been determined at 25°C by direct analysis of a saturated solution using UV and fluorescence analytical methodology. Other values reported in IUCLID are 0.032 mg/l (20°C) (Hashimoto et al., 1984), 0.037 mg/l (22°C) (May et al., 1983) and 0.044 mg/l (25.3°C, but using tap water) (Whitehouse, 1984). A value of 0.073 mg/l (25°C) (Mackay et al., 1977), measured fluorimetrically after extraction of a saturated solution with cyclohexane, was not selected as it was reported in only one study, while the selected value is close to those reported by all other studies.

Values of the solubility of anthracene in saline water are also reported in IUCLID, including 0.0324 mg/l (25.3°C, salinity of 36.5 o/oo; measured by dynamic column liquid

chromatography) (Whitehouse, 1984) and 0.021 mg/l (20°C, salinity of 35 o/oo; measured after extraction of a saturated solution with benzene) (Hashimoto, 1984).

1.3.6.1 Solubility in other solvents

Anthracene is reported to be slightly soluble in benzene, chloroform and carbon bisulfide and less soluble in ether and alcohol, but no quantitative information in given (Collin and Höke, 1985).

1.3.7 Partition coefficient

IUCLID (1995) gives a compilation of measured and calculated values for $\log P_{ow}$ in the range of 3.45-4.8, as reported by Sangster (1989). Among the values reported, two, 4.50 and 4.54, were based on direct measurement (shake-flask), the latter in particular being measured at 25°C (Karickhoff et al., 1979). Yoshida et al. (1983) derived by calculation, using equations related to molar refraction, the values 4.21 and 4.71, and compared them to a measured value of 4.50. In another study, Geyer et al., (1984) a value of 4.54 was reported, derived from measurements carried out in accordance with the Guidelines of Directive 67/548/EEC (OECD method 107). For this reason the value of 4.54 is adopted in the present Report.

1.3.8 Flash point

A single value of 121°C (close cup) is given in IUCLID derived from Sax (1992).

1.3.9 Autoflammability

A single value of 540°C at 1,013 hPa (1 Atm.) is given in IUCLID, derived from Nabert and Schoen (1963).

1.3.10 Explosivity

Information given in IUCLID, derived from Nabert and Schön (1963), indicates a low explosion limit of 45 g/m^3 (20°C, 1 atm) or 0.6% by volume, while no high explosion limit is given. It is also indicated that dust is possibly explosive.

1.3.11 Oxidising properties

Anthracene is not an oxidising agent.

1.3.12 Summary of physicochemical properties

Table 1.1 Summary of physico-chemical properties of anthracene

Property	Value	Reference
Melting point	218°C	Lang and Eigen, 1967, Merck Index, 1983, Collin and Höke, 1985; Clar, 1964
Boiling point	340°C at 1013 hPa (1 Atm.)	Lang and Eigen, 1967; CRC, 1987
Relative density	1.252 at 25°C	Collin and Höke, 1985
Vapour pressure	8.0 · 10-4 Pa at 25°C	Sonnefeld et al., 1983
Water solubility	0.041 mg/l at 25°C	Schwarz, 1977
Partition coefficient (log Pow)	4.54 at 20°C	Karickhoff et al., 1979; Geyer et al., 1984
Flash point	121°C	Sax, 1992
Autoflammability	540°C at 1013 hPa (1 Atm.)	Nabert and Schön, 1963

1.4 CLASSIFICATION

Anthracene has not been classified in the context of Directive 67/548/EEC concerning dangerous substances.

Classification proposed on the basis of the current RAR:

X_i
R38 Irritating to skin
S37 Wear suitable gloves

2 GENERAL INFORMATION ON EXPOSURE

2.1 GENERAL COMMENTS ON RELEASES AND EXPOSURE

Releases of and exposure to anthracene can occur during the production and use of anthracene and anthracene-containing products. Anthracene is produced from light anthracene oil (a fraction of coal tar distillation) and its use is restricted to the industrial production of an aldehyde (which will cease operating in the EU as of 2003), the manufacture of pyrotechnics and in scientific research laboratories.

Several products containing anthracene as part of complex mixtures but not involving addition of isolated commercial anthracene, such as coal tar itself, coal tar-containing products (paints, waterproof membranes etc.) and creosote, are outside the scope of the present Report (Council Regulation 793/93). Nevertheless, all these products may affect, through anthracene releases during their production and use, the background environmental concentrations.

Background environmental concentrations of anthracene can also be affected by releases arising from incomplete combustion of organic matter, as occurring during fossil fuel combustion or in various workplaces (e.g. carbon anode/graphite, silicon carbide, aluminium, iron and steel production plants and others).

2.2 PRODUCTION

Anthracene is present in coal tar, from where it can be recovered efficiently. Hence recovery from coal tar and, in particular, from anthracene oil (one of coal tar's distillate fractions), constitutes the basis for the industrial production of anthracene. In view of the importance of coal tar distillation in anthracene production, and because the production and use of certain coal tar distillation products constitute sources of human exposure to anthracene, coal tar and its distillation products are discussed in some detail below.

2.2.1 Coal tars

Coal tars are by-products of the destructive distillation of coal, called carbonisation or coking. The composition and properties of a coal tar depend mainly on the temperature of carbonisation and, to a lesser extent, on the nature of the coal used as feedstock. Coal tars are complex mixtures of hydrocarbons, phenols and heterocyclic (oxygen-, sulphur- and nitrogen-containing) compounds. Probably as many as 10,000 compounds are actually present in coal-tars, of which over 400 have been identified. Two main classes of coal tars are recognised, depending on the temperature of carbonisation, namely high-temperature ($> 700^{o}C$) and low-temperature coal-tars ($< 700^{o}C$), which differ significantly in their chemical composition. The anthracene content of high-temperature coal tars (low-temperature ones contain negligible amounts of anthracene) has been reported by several sources as shown in **Table 2.1**.

Table 2.1 Anthracene content of different coal tar types

McNeill, 1983		Kleffer et al., 1981		Novotny et al., 1981		Marlich and Leukevitch, 1978		Collin and Höke, 1985	
Coal tar type	**Content**	**Coal tar type**	**Content**	**Coal tar type**	**Content**	**Coal tar type**	**Content**	**Coal tar type**	**Content**
coke-oven (UK)	1%	High tempe-rature	1.5%	coke-oven	5.5%	High tempe-rature	1.1%	High tempe-rature	1.5%
coke-oven (DE)	1.8%								
coke-oven (US)	0.75%								
CVR (UK)	0.26%								
low tempe-rature	0.06%								
Lurgi	0.32%								

Based on the above figures as well as figures from other sources, a value of 1.5% is adopted in the present Report as a representative level for the anthracene content of high temperature coal tars.

2.2.1.1 Coal-tar distillation products (tar oils)

Coal tar distillation is conducted at 10 distillation plants in Europe (1 each in Germany, Belgium, France, the Netherlands, Italy, Denmark, and 2 each in the U.K. and Spain) (Betts, 2000). The amounts of coal-tar produced and distilled in the EU during 1997-1999 are given in **Table 2.2** (the 1998 and 1999 production figures do not include data for Germany) (Betts, 2000).

Table 2.2 Volumes of coal-tar production and distillation in the European Union

Year	Produced (tonnes)	Distilled (tonnes)
1997	**1,266,000**	**1,799,000**
1998	**1,109,000**	**1,810,000**
1999	**825,000**	**1,767,000**

The important common distillation fractions and residues obtained from coal tar by high-temperature processes, including light anthracene oil (the starting material for anthracene production), are shown in **Table 2.3**.

Anthracene oil (distillation temperature 300-450^{o}C) is a semisolid, greenish brown crystalline material. It is obtained in two fractions from the primary distillation of coal tars. The lower-boiling fraction (light anthracene oil) has a high content of phenanthrene, anthracene and carbazole. The higher-boiling fraction (heavy anthracene oil) has a high content of fluoranthene and pyrene (IARC, 1983a; Collin and Zauder, 1982). Light anthracene oil, which makes up

about 20% of coal tar and usually has an anthracene content of 6-7%, is used as the starting material for the production of pure anthracene (Franck and Stadelhofer, 1987; Collin and Höke, 1985). The value of 6% as the anthracene concentration in light anthracene oil is adopted in the present Report and taken forward to risk characterisation.

Table 2.3 Primary distillation fractions and residues obtained from high temperature coal tar distillation

Coal tar fraction		Dist. range	Main components
a	light oil/overheads	<180°C	Mainly toluene, xylene, benzene and indene-naphthalene
b	carbolic oil	180-205°C	Mainly higher alkylbenzenes, phenol and alkylphenols, indene, xylene and naphthalene
c	naphthalene oil	200-230°C	Mainly naphthalene and methylnaphthalene
d	creosote oil/wash oil	230-290°C	Mainly alkynaphthalenes, naphthalene, diphenylacena-phthene, fluorene, plus some higher phenols
e	light anthracene oil	260-310oC	Mainly anthracene, phenan-threne and carbazole, with small amounts of fluorene and pyrene; this fraction is used for anthracene recovery
f	heavy anthracene oil/base oil	>310°C	Mainly polynuclear aromatic compounds of higher molecular weight
g	medium-soft pitch	residue	40-50% polynuclear aromatic compounds of 4-7 rings

2.2.1.2 Creosote

While according to IARC the term "creosote oil" refers to one of the coal-tar distillation fractions (distillation temperature 230-290°C), this term is commonly used to describe the material used for timber impregnation and is made up of a blend of several coal-tar distillation fractions. It is emphasised here that creosote blending does not involve the addition of pure anthracene.

Creosote, in its best known and most commonly used form, is a mid-heavy distillate of coal tar, boiling range 200-400°C, with varying composition because of the different blending procedures employed in its production. It is generally described as a yellow-dark-green-brown oily liquid consisting of aromatic hydrocarbons (including anthracene, naphthalene and phenanthrene derivatives), some tar acids (phenol, cresols and xylenols) and tar bases (e.g. pyridine and lutidine derivatives) (IARC, 1983a; McNeill, 1983). About 160-200 compounds are present in creosote (IARC, 1983a; Nestler, 1974). However, only a limited number (about 30) have been identified, 20 of which are present at levels exceeding 1% and make up the major portion of creosote. Polycyclic aromatic hydrocarbons (mostly unsubstituted) generally account for 75-85% of creosote (Lorenz and Gjovik, 1972). The maximum benzo[a]pyrene content of WEI Grade A creosote is 500 ppm and that of WEI Grades B and C 50 ppm (WEI, 2000).

The anthracene content of some creosotes is given in **Table 2.4**. The anthracene content of "impregnation oil" is said in additional reports to vary from as low as 0.16% to as high as 7% (Lehman et al., 1984; Danish EPA, 1995; Ingram, 1982). In the EU, creosote is generally manufactured to grades specified by the West European Institute for Wood Preservation (WEI). Three creosote types are specified, based on their density, the distillation ranges and other physicochemical characteristics, without any reference to their anthracene content.

Table 2.4 Anthracene content of some creosotes

Component	Creosote type			
	A probably a mixture (classes 3, 4, 5 and 6) (Staesse, 1954)	B classes 3, 4, 5 and 6 (Staesse, 1954)	C average of 9 creosote oil samples (class 3) (Nestler, 1974, Staesse, 1954)	D typical creosote (classes 3, 4, 5 and 6) used for the impregnation of railway sleepers (Andersson et al., 1983)
anthracene	2.0	*	1.5	7.0

* The anthracene content is included in that of phenanthrene (17.4%)

Recent information gives the following picture regarding the anthracene content of creosote preparations:

a) Analyses carried out by WEI for type A and B creosotes show anthracene contents of 1.1% and 1.5%, respectively (Betts, 2000). According to the same source, other analyses gave 1.7% (AWPA P1-65) and 1.3% (P1/P13 Industry composite Test Material).

b) Analyses carried out by the Swiss independent institution EMPA indicate the following concentrations: For two creosote companies, anthracene concentrations of 0.9% and 0.8% (WEI type A), 0.55% and 0.7% (WEI type B) and 1.36% and 1.05% (WEI type C). These figures are in broad agreement with the results of analysis carried out by one of the above companies indicating contents of 0.7% (WEI type A), 0.45% (WEI type B) and 0.8% (WEI type C) (Höke, 2000).

c) The UK Health and Safety Executive have measured the anthracene content of 3 creosote products available to amateur users and found them to depend on the colour of the product as follows (HSE ECOS, unpublished):

Golden Brown	0.07%
Dark Brown	9.9%
Dark Brown	11.6%

Finally, anthracene concentrations in creosote lie at a maximum of 1.5%. A higher content would create problems with crystallisation and workability of the oil (WEI, 2000).

In the present Report the typical anthracene content of commercial creosote is assumed to be 1.5%.

2.2.2 Anthracene production from coal tar

According to information provided by the only European manufacturer of anthracene (operating in Germany), the procedure employed for its production involves, as feedstock, light anthracene oil containing about 6% anthracene (Frank and Stadlhofer, 1987). In the present Report 6% is taken as the anthracene content of light anthracene oil used for the production of anthracene. **Table 2.5** shows a typical composition of this fraction.

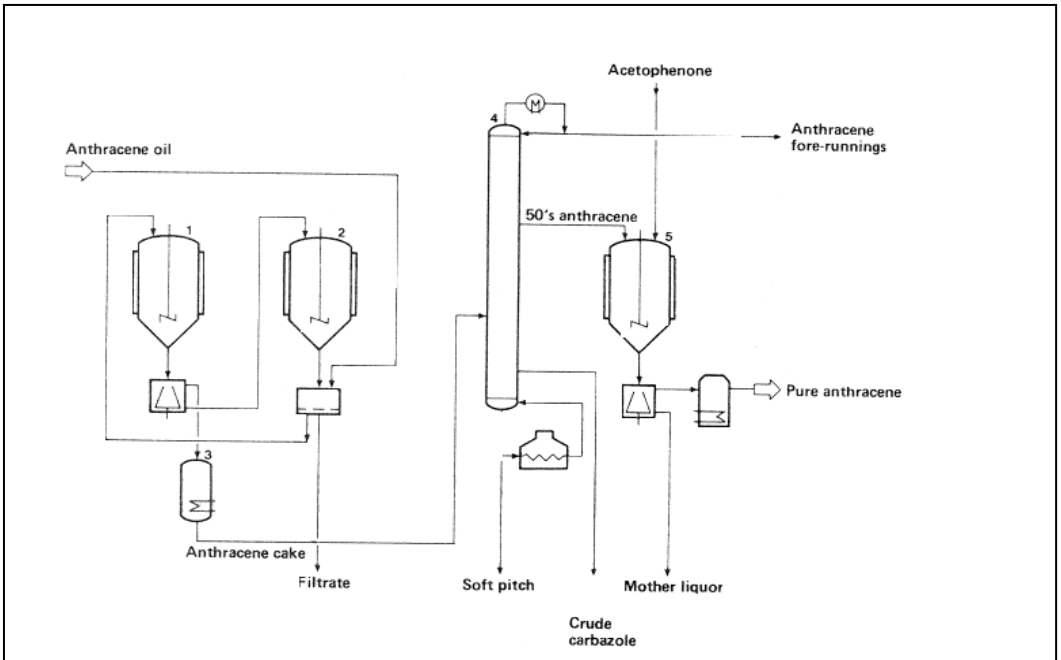
Table 2.5 Composition of light anthracene oil (%) (from Frank and Stadlhofer, 1987)

Component	%
Dimethylnaphthalenes	0.7
Acenaphthenes	3.1
Dibenzofuran	4.0
Fluorene	7.7
Methylfluorene	10.6
Dibenzothiophene	1.9
Anthracene	5.8
Phenanthrene	18.8
Carbazole	3.8
Methylphenanthrenes	12.3
Fluoranthenes	8.0
Pyrene	4 1
Other aromatics	19.2

Anthracene is recovered from anthracene oil by the combined application of crystallisation and distillation (vacuum distillation), while the product is further refined by recrystallisation. **Figure 2.1** shows the flow diagram for the recovery of pure anthracene from anthracene oil.

The first stage in the production of anthracene is the recovery of a concentrate (25-30% anthracene content) by crystallisation, which can be carried out in two stages to increase the yield. The final crystallisate, known as "anthracene cake" or crude anthracene, is generally concentrated to around 50% by vacuum distillation. Subsequent refining to yield anthracene of purity over 95% is normally achieved by recrystallisation. The quality of the anthracene thus obtained is of technical grade with a typical composition shown in **Table 2.6.**

Figure 2.1 Flow diagram for the recovery of anthracene from anthracene oil (from Frank and Stadlhofer, 1987)



1 Crystallizer (1st stage); 2 Crystallizer (2nd stage); 3 Melting vessel; 4 Distillation column; 5 Crystallizer

Table 2.7 shows the amounts of anthracene produced in the EU during recent years (Höke, 2000 and 2002). These data indicate that production of pure anthracene dropped to around 1,000 tpa or less during recent years. Approximately 99% of the 1999 production was exported to outside the EU. No importation of anthracene into the EU appears to take place.

Table 2.6 Typical composition of technical grade anthracene (%)

Component	%
Anthracene	97.0
Phenanthrene	1.0
Carbazole	1.0
Naphthothiophene	0.4
Dibenzo[b,c]thiophene	0.3
Acridine	0.2
Acetophenone	0.4

Table 2.7 Anthracene production volumes in Europe

Year	Production (tonnes)*					
	Pure	40% (liquid) (approx.)	50% (liquid) (approx.)	50% (solid) (approx.)	Total 50% (approx.)	Total crude (approx.)
1987	8,000					
1989	7,500					
1990	1,300					
1991	1,500	-	5,600	-		5,600
1992	3,600	40	420	280	700	740
1993	2,100	600	2,080	1,480	3,550	4,150
1994	2,100	400	2,890	2,490	5,380	5,780
1995	1,900	70	899	480	1,280	1,350
1996	1,800	-	1,030	-	1,030	1,030
1997	1,700	-	780	-	780	780
1998	1,600	-	1,400	-	1,400	1,400
1999	550	-	930	660	1,590	1,590
2000	1,190	-	600	1,330	1,930	1,930
2001	1,150	-	-	400	400	400

* The crude anthracene figures refer to amounts in addition to those of the pure product (Höke, 2000 and 2002).

2.3 USES OF ANTHRACENE AND ANTHRACENE-CONTAINING PRODUCTS

Until recently, the main uses of anthracene which could give rise to releases were two specific types of chemical synthesis. As discussed in the next section, these processes have stopped in recent years. The only known remaining use of anthracene relates to the use of small amounts of anthracene in pyrotechnics and in scientific research laboratories.

Other products containing anthracene are creosote, tar paints, waterproof membranes and related products containing coal tar distillates. These products contain anthracene as part of a complex mixture and do not involve addition of pure anthracene.

Another potential source of exposure to anthracene, which no longer exists and therefore does not need to be considered here, is related to the use of anthracene oil and coal tar in cosmetics products such as soaps, lotions, oils, shampoos and gels. The use of anthracene oil for such purposes was prohibited by Directive 76/768/EC, while more recently Directive 97/45/EC prohibited the use of coal tar in these products.

2.3.1 Uses of anthracene

According to the latest information available, practically all consumption of anthracene in the EU, which until recently was carried out by 2 main industrial users, has now stopped and almost all anthracene produced in Europe is exported. Figures on anthracene consumption during recent years are shown in **Table 2.8**.

Most of the material used by one of these users (User 1, **Table 2.8**) went to the manufacture of anthraquinone. However, production of anthraquinone at this plant has stopped since the end of 1998. User 2 used the quantities of anthracene indicated below for chemical synthesis of anthracene-9-aldehyde. According to information recently provided by this user, as of 2003 this use of anthracene will cease and anthracene-9-aldehyde will no longer be produced (Höke, 2003). Consequently neither of these processes need be further discussed in the present Report. However, in view of the use of anthracene in synthesis of anthracene-9-aldehyde until very recently, this process will be considered in the following Sections for illustrative purposes only.

Table 2.8 Anthracene consumption volumes in Europe

Year	Consumption within EU (tonnes)			Production (pure anthracene; tonnes, from Table 2.7)
	User 1	User 2	Total	
1995	1,937	n.d.	1,937	1,900
1996	1,330	n.d.	1,330	1,800
1997	1,679	19.2	1,699	1,700
1998	1,675	13.5	1,689	1,600
1999	none	6.8	6.8	550
2000	none	none	None	1,190
2001	none	none	None	1,150
2002	none	7.0	7.0	no data available

Small quantities (approximately 0.2 tonnes per year) of anthracene are sold to a company operating in the EU for the manufacture of pyrotechnics.

Small amounts of anthracene are also used in scientific research laboratories. In accordance with Council Directive 79/831, this type of use does not come under the terms of the present Report and for this reason it will not be discussed further.

In conclusion, practically no use of anthracene takes place in Europe. Consequently only the limited use of anthracene for the production of pyrotechnics will be considered in the context of this Report.

2.3.2 Uses of anthracene-containing products

2.3.2.1 Uses of creosote

Creosote is used almost exclusively in wood impregnation. Recent estimates put the amount of creosote used in the EU at approximately 107,000 tpa (Sorgo, 1996). There are 9 bulk wood impregnation plants in the EU (WEI, 2000).

The marketing and use of creosote in the EU are strictly regulated by Directive 2001/90 (adapting to technical process Annex I of Directive 76/769 concerning the restriction of the marketing and use of certain dangerous substances and preparations). This Directive does not permit the use of creosote for wood treatment. By derogation, it permits the use of special creosote (containing < 0.005% benzo[a]pyrene and < 3% water-extractable phenols) only in industrial installations or by professionals for in situ re-treatment. In addition, this kind of creosote may be place on the market only in containers of capacity ≥ 20 l, and may not be sold to consumers. Apart from other labelling restrictions, the packaging of this creosote should mention "For use in industrial installations or professional treatment only". It is concluded from this that creosote cannot be used by consumers.

2.3.2.2 Tar paints, waterproof membranes and related products containing coal tar distillates

Coal tar and its distillates are used in some specialist paints, damp-proofing materials, waterproof membranes, coal tar epoxy paints and coal tar poly-urethane sealers. It is understood that tar paints are no longer used in Germany and that Scandinavian countries are moving away from them. Coal tar paints usually contain 0.5% anthracene, while the anthracene content of other products seems to be below 0.5% (IARC, 1983a).

No information on the number of plants or the production volumes of these products in Europe is available.

2.4 RELEASES OF ANTHRACENE DURING COMBUSTION AND RELATED INDUSTRIAL PROCESSES

Anthracene is produced during incomplete combustion of organic matter. Therefore it is emitted as a component of vehicle exhaust gases, as well as during various industrial processes such as carbon anode/graphite, silicon carbide, aluminium, iron and steel production plants and others.

2.5 SUMMARY OF INFORMATION ON RELEASES DURING PRODUCTION AND USE OF ANTHRACENE AND ANTHRACENE-CONTAINING PRODUCTS

Environmental releases of anthracene can arise mainly through the production and use of anthracene itself, during the production and use of anthracene-containing coal-tar distillates, and during combustion processes. The production of anthracene has been declining significantly during recent years in Europe, ranging around approximately 1,000 tonnes/per annum since 1999. Of this production, 99% was exported to outside the EU. On the other hand, more than 1.7 million tonnes of coal-tar, containing over 25,000 tonnes of anthracene, were distilled in Europe during 1999. Thus the production and use of coal-tar derivatives (especially creosote, 107,000 tpa used for wood treatment in Europe) represents a significantly greater potential source of environmental release of anthracene. In 1998, anthracene production in Europe involved 1,600 tonnes of pure anthracene plus approximately 1,400 tonnes of crude (50%), making a total of 2,300 tonnes of anthracene. In 1999, 550 tonnes of pure anthracene were produced. Taking 1.5% as the typical anthracene content of coal-tar, these quantities would have been derived from the distillation of 153,000 and 37,000 tonnes of crude-coal tar, respectively, corresponding to 8.5% and 2.1% of the total amount of coal-tar distilled in Europe during these two years. Thus, the distillation of coal tar for the ultimate purpose of production of anthracene contributes to fewer than 10% and appears to be following a decreasing trend, and should be seen in this context.

2.6 EXISTING LEGISLATIVE CONTROLS CONCERNING ANTHRACENE AND ANTHRACENE-CONTAINING PRODUCTS

Classification

Anthracene

Anthracene has not been classified in the context of Directive 67/548/EEC concerning dangerous substances.

Anthracene oils

All kinds of anthracene oils (different distillation fractions) are classified according to Directive 94/69 (21st adaptation to technical progress of Directive 67/548/EEC) as

Carcinogen, category 2; R45 - May cause cancer

Labeling: T R45; S53 (Avoid exposure – obtain special instructions before use); S45 (In case of accident or if you feel unwell, seek medical advice immediately - show the label where possible)

Such classification may be considered as not necessary, depending on benzo[a]pyrene content.

Creosote and creosote oils

All types of creosote and creosote oils are classified according to Directive 67/548/EEC as

carcinogen, category 2; R45

labeling T, R45, S53, S45

Such classification may be considered as not necessary, depending on benzo[a]pyrene content.

Occupational Exposure

Directive 91/332 sets a limit value for occupational exposure to "coal tar volatiles" of 0.2 mg/m^3 (8-hour TWA).

Marketing and uses

Creosote

Directive 2001/90 (7th Adaptation to technical progress of Annex I of Directive 76/769) sets strict restrictions on the marketing and use of creosote. Creosote may not be used in the treatment of wood except, by derogation, in the following case:

It may be used for wood treatment in industrial installations, or by professionals covered by Community legislation on the protection of workers for in situ re-treatment, only if it contains < 0.005% benzo[a]pyrene and < 3% water-extractable phenols. Such creosote may be placed on the market only in packaging of capacity ≥ 20 l, and it may not be sold to consumers. It must also be specially labelled as "For use in industrial installations or professional treatment only".

Further provisions restrict the use of creosote-treated wood: The use of wood treated in industrial installations or by professionals as described above, which is placed on the market for the first time or retreated in-situ, is permitted for professional and industrial use only, e.g. on railways, in electric power transmission and telecommunications, for fencing, for agricultural purposes (e.g. stakes for tree support) and in harbours and waterways.

The restrictions concerning creosote-treated wood do not apply to wood which was treated with creosote before this Directive came into operation and which is placed on the second-hand market for re-use. However, such wood may not be used:

- inside buildings, whatever their purpose,
- in toys,
- in playgrounds,
- in parks, gardens, and outdoor recreational and leisure facilities where there is a risk of frequent skin contact,
- in the manufacture of garden furniture such as picnic tables,
- for the manufacture and use and any re-treatment of:
- containers intended for growing purposes,
- packaging that may come into contact with raw materials, intermediate or finished products destined for human and/or animal consumption,
- other materials which may contaminate the products mentioned above.

Cosmetics

According to Directive 76/768 concerning cosmetics, the use of "anthracene oil" is not permitted, while according to Directive 97/45 (adapting to technical progress Directive 74/768) the use of "crude and refined coal tars" is also not permitted.

3 ENVIRONMENT

(to be added later)

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 General discussion

There is a scarcity of measured data on exposures to anthracene. For this reason, in the present Report it was necessary to resort frequently to the use of EASE modelling in order to estimate exposures to anthracene. In applying the EASE model, in addition to the various exposure conditions which are stated analytically in each case, it has been assumed that the processes which result in human exposure (e.g. loading, unloading and cleaning in workplaces) take place at room temperature. It is noted that the output of EASE for inhalation exposure to anthracene is unaffected by the input temperature in the range of values below 120^{o}C and changes above this temperature because the vapour pressure then begins to exceed 1 Pa. In this context it is also important to note that EASE tends to overestimate significantly the vapour concentrations of substances of low volatility such as anthracene. Therefore, when vapour concentrations higher than the concentration of saturated anthracene vapours at room temperature (approximately 60 μg/m^3) were estimated by EASE, they were rejected as an overestimate and only the latter value was carried forward to risk characterisation.

The exposure estimates provided by EASE are 8-hour TWA. Since no information on the duration of specific tasks, likely to be associated with the bulk of exposures, is available, it was not possible to derive estimates of short-term exposures, and for this reason all exposures have been treated as referring to 8-hour TWA.

A complication which may affect the estimation of modelled exposures relates to the fact that the proportion of anthracene in the vapour phase of mixtures such as coal tar and creosote has been assumed to be the same as that in the liquid phase. In reality, the composition of the vapour phase will depend on the temperature of the process concerned.

4.1.1.2 Occupational exposure

4.1.1.2.1 Occupational Exposure during manufacture of anthracene

Exposure to anthracene can take place during coal-tar distillation for the production of anthracene oil, starting material for the production of anthracene. Although this process is not part of anthracene production per se, it is considered here for illustrative purposes.

As far as occupational exposure during anthracene manufacture itself is concerned, it can occur at two stages:

a. manufacture of anthracene from anthracene oil

b. anthracene packaging

Coal-tar distillation and production of anthracene oil

There exist 10 coal-tar distillation plants in Europe. It is expected that in such plants there is exposure of workers to anthracene because of the anthracene content of coal tar (about 1.5%). The total number of exposed employees in Europe is estimated to be no higher than 100.

Worker exposure during coal tar distillation may involve inhalation of vapours and dermal contact which may occur during tank filling, sampling, routine cleaning and maintenance operations. No measured data on occupational exposure to anthracene have been reported. Calculations using the EASE model (non-dispersive use, local exhaust ventilation, direct handling / incidental contact, i.e. once per shift), predict an air concentration of 0-0.1 ppm and a dermal exposure of 0-0.1 mg/cm^2/day. For an anthracene content of 1.5% these values correspond to anthracene exposures of 0-0.0015 ppm (0-11 μg/m^3) and to 0-1.5 μg/cm^2/day. Actual exposures may be lower to the extent to which personal protective equipment is in use. However, for the purposes of the present Report, the upper values of the predicted ranges are taken forward to risk characterisation.

Manufacture of anthracene from anthracene oil

As already discussed (see Section 2.2.2), anthracene is prepared from anthracene oil by the combined application of crystallisation and vacuum distillation. Limited information regarding exposure during the production of anthracene from anthracene oil is available from the single EU plant which produces pure anthracene:

Manufacture is carried out normally in a closed/encapsulated system, and all tanks and apparatus involved (including the centrifuge used during crystallisation) are connected with a waste air treatment plant. The distillation columns are opened usually every second year for approximately one week. Prior to being opened they are washed and their temperature when opened is below 40^{o}C.

Approximately 12 employees are involved in anthracene production; all men aged 20-55. Occupational exposure (dermal or by inhalation) arises through activities such as sampling, loading, cleaning and maintenance. Worker protection includes eye and skin protection, while respiration protection is also used whenever necessary. Air sampling to determine actual occupational exposure is not normally carried out, as it is assumed unnecessary in view of the general exposure controls in place. However, limited measurements concerning exposure during two stages of anthracene production have been made available (Höke, 2003):

a) One of eight workers involved in the production of crude anthracene ("anthracene cake", see Section 2.2.2) was monitored for personal exposure to anthracene during a single 8-hour shift, during which anthracene oil was cooled to form crystals which were removed by filtration and purified by centrifugation. This worker was involved in the filling, emptying and cleaning of vessels and the sampling and loading onto railcars of the crude anthracene thus produced. Gloves and safety glasses were worn. For the purpose of exposure monitoring, a personal pump was carried for the collection of airborne dust (no information on the size of the dust collected was given), and the associated polycyclic aromatic hydrocarbons collected were eluted and analysed by HPLC. The 8-hour time-weighted average concentration of anthracene thus measured was 0.5 μg/m^3.

b) Personal exposure to anthracene during the subsequent stage of the production process (refining of the crude material) was conducted once during an 8-hour shift in a single worker. During this process, crude anthracene was transferred from railcars to a melting system before liquid storage, distillation and further refining. The activities involved

included filling, emptying and cleaning of vessels and loading of the product only railcars. Exposure monitoring again involved collection of airborne dust with a personal pump and HPLC analysis of the associated polycylic aromatic hydrocarbons. The 8-hour time-weighted average concentration of anthracene measured was 0.78 μg/m^3.

The above measurements refer to concentrations of particulate anthracene (anthracene dust or anthracene bound to airborne particulates) and give no indication of the concentration of anthracene vapour. Based on its physicochemical characteristics, airborne anthracene would be expected to exist primarily in the vapour phase. Indeed, analysis of the vapour and the particulate phase of ambient atmospheric polycyclic aromatic hydrocarbons confirmed that 78-98% of anthracene is in the vapour phase (Cautreels and van Cauwenberghe, 1978; Thrane and Mikalsen, 1981). In a study involving measurement of personal occupational exposure to particulate and vapour PAH in plants handling coal tar or creosote-impregnated wood, the following concentrations of airborne anthracene were found (only single, "typical" values are reported) (Andersson et al., 1983):

	Vapour (mg/m^3)	Particulate (mg/m^3)
Coke oven battery top of coke plant	55	<1.0
Handling of creosote-impregnated railroad ties		

A significant predominance of anthracene presence in the vapour, rather than the particulate phase, mostly based on limited numbers of measurements, was also reported in plants carrying out silicon carbide manufacture, basic metal manufacture and iron and steel production (these data are discussed further in Section 4.1.1.2.4). The fraction of anthracene found in the particulate phase, as a percentage of the total airborne amount, reported in various work environments is summarised in **Table 4.1** (overleaf). It is clear that, even if the representativeness of some of these data is limited by the small numbers of measurements, in most cases airborne particulate anthracene constitutes a small fraction of the total airborne concentrations.

Based on the figures in **Table 4.1**, the concentrations of total airborne anthracene during anthracene production will be assumed to be 10 fold higher than the measured particulate concentrations, i.e. 5 μg/m^3 for the preparation and 7.8 μg/m^3 for the refining of crude anthracene. It is also assumed that all this material is respirable.

While the above estimates provide an indication of the order of magnitude of the airborne exposures during anthracene production, their representativeness is limited by the fact that the measurements on which they are based come from monitoring only one worker, and on a single occasion, for each of the two activities considered. For this reason, an estimate of the expected exposures is also obtained by modelling.

Table 4.1 Proportion of anthracene in airborne particulate phase

Activity	Vapour µg/m³	Particulate µg/m³	Particulate as % of total	Ref.
coke plant	55	<1.0	<2	Andersson et al., 1983
handling of creosote-impregnated railroad ties	13.0	4.7	27	
silicon carbide plant	3.5	0.13	4	Norway Competent Authorities
aluminium reduction plants	12.3	0.74	5	Bjorseth et al, 1978a
	3.90	0.1	3	
	2.7	0.13	5	Andersson et al., 1983
basic metals manufacture	0.99	0.49	33	Norway Competent Authorities
	0.42	0.23	33	
iron and steel processing	13.9	0.04	<1	
	0.29	0.41	59	

Calculations using the EASE model to the two processes for which the above exposure measurements were carried out (non-dispersive use, local exhaust ventilation, direct handling / incidental contact, i.e. once per shift) predict an air concentration of 0-0.1 ppm (vapour), no exposure to anthracene dust, and a dermal exposure of 0-0.1 mg/cm^2/day. For the first stage (production of crude anthracene from anthracene oil containing 6% anthracene) these values correspond to anthracene exposures of 0-0.006 ppm (0-44 µg/m^3) and to 0-6 µg/cm^2/day. For the second stage (anthracene refinement from crude anthracene with an upper limit of anthracene content of 30%), the modelled exposures correspond to 0-0.03 ppm (0-222 µg/m^3) and 0-30 µg/cm^2/day, respectively. In view of the use of personal protective equipment as stated by the manufacturer, actual exposure is likely to be on the low side of the modelled range.

For clarity of the comparisons, the total airborne concentrations (in µg/m^3) estimated from the measured data and EASE, are tabulated below:

	Production of crude anthracene	Refining of anthracene
Estim. From measured data	5	7.8
Estim. By EASE	0-44	0-222

It can be seen that in the case of production of crude anthracene the two types of exposure estimates are of similar order of magnitude, while in the case of anthracene refining the EASE estimate is 1-2 orders of magnitude higher than that obtained from the measured data. This difference reflects the conservative assumptions of the exposure scenarios employed and the limitations of EASE in estimating the vapour concentrations of low-volatility chemicals. While it is likely that the measured data reflect more closely the true exposure levels, in view of their limitations both they and the modelled data (with a maximum of 60 µg/m^3 for vapour concentration) will be taken forward to risk characterisation.

Anthracene packaging

Following anthracene manufacture, the final product is packaged manually in paper packages of 25 kg and stored in the dark. No information on measured exposures is available, and, according to information given by the manufacturer, no protection measures are taken during transport and storage of the material.

Calculations using the EASE model (non-dispersive use, local exhaust ventilation, direct handling / intermittent contact, i.e. 2-10 times per shift, non-fibrous, non-aggregating dust, dry manipulation, low tendency to become airborne) predict an air concentration of 2-5 mg/m^3 dust and 0-0.1 ppm (0-741 µg/m^3) vapour, and a dermal exposure of 0.1-1 mg/cm^2/day. The dust particles are likely to be largely of non-respirable size which will be trapped in the nasal region and be carried to the gastrointestinal tract by mucociliary clearance, giving rise to systemic exposure via oral absorption. Actual exposure is likely to be on the low side of this range to the extent to which personal protective equipment is employed during packaging. By analogy with the conclusions drawn in the previous section, it is considered likely that the inhalation exposures predicted by EASE may overestimate the true exposures.

4.1.1.2.2 Occupational exposure during uses of anthracene

Production of anthracene-9-aldehyde

Quantities of anthracene corresponding to 6.8 tonnes in 1999 and 7 tonnes in 2002 were used for chemical synthesis of anthracene-9-aldehyde by one EU manufacturer. No such use was made in 2000 and 2001, and, starting in 2003, the processes will no longer be used. While consideration of this process is consequently not strictly necessary for the purpose of the present Report, in view of its use until very recently it will be examined for illustrative purposes.

According to information provided by the manufacturer, this process was carried out on 20 occasions in 1999, involving approximately 350 kg of anthracene each time and the process lasted 2 hours. The process was carried out in a closed vessel which was filled with anthracene, in the form of lumps, with very little dust formation, via the open manhole at room temperature and under local exhaust ventilation. Subsequently the vessel was closed and reaction took place in a solvent. According to the same source of information, exposure of workers, who were properly protected, was minimal. The number of workers exposed to anthracene in this way was 10-15 in all.

No data on occupational exposure to anthracene during its use in the synthesis of anthracene-9-aldehyde is available. Calculations with the EASE model (non-dispersive use, local exhaust ventilation, direct handling/incidental contact, i.e. 1 time per shift, granular particles) predict an airborne concentration of 0-0.1 ppm (0-741 µg/m^3) and dermal exposure of 0-0.1 mg/cm^2/day. Because the upper end of the latter range exceeds the saturated vapour concentration at room temperature (approximately 60 µg/m^3), the latter value is taken forward to risk evaluation. Actual exposure is likely to be on the low side of this range to the extent to which personal protective equipment is employed.

Production of pyrotechnics

Approximately 0.2 tpa of anthracene are used for the manufacture of pyrotechnics in one plant in Europe. No information on the manufacturing process or related exposures is available.

Calculations using the EASE model (non-dispersive use, local exhaust ventilation, direct handling / intermittent contact, i.e. 2-10 times per shift, non-fibrous, non-aggregating dust, dry manipulation, low tendency to become airborne) predict an air concentration of 2-5 mg/m^3 dust and 0-0.1 ppm (0-741 $\mu g/m^3$) vapour, and a dermal exposure of 0.1-1 mg/cm^2/day. The upper end of the modelled vapour concentration range exceeds the saturated vapour concentration at room temperature (approximately 60 $\mu g/m^3$) and must be rejected as an overestimate. The dust particles are likely to be largely of non-respirable size which will be trapped in the nasal region and be carried to the gastrointestinal tract by mucociliary clearance, giving rise to systemic exposure via oral absorption. For the purposes of this Report, the higher end of the modelled ranges (with a maximum of 60 $\mu g/m^3$ for vapour concentration) is taken forward to risk characterisation.

4.1.1.2.3 Occupational exposure to anthracene via creosote

Exposure to anthracene arising from the manufacture of creosote or creosote-containing products does not strictly come under the terms of the present Report. However, it is considered for illustrative purposes.

Occupational exposure to anthracene present in creosote may occur mainly during the blending and packaging of creosote, treatment of timber at bulk impregnation plants, wood brushing and various other minor uses. Exposure is expected to occur through inhalation and the dermal route.

Creosote blending

Ceosote blending involves the mixing of various fractions of coal-tar distillation which may contain greater or smaller amounts of anthracene. In the EU, creosote blending takes place in 10 tar distillation plants**.** In the UK tar distillation plants, the number of affected workers is of the order of 2-3 per plant, suggesting that the total number of such workers in Europe may reach 20-30. Additional exposure may take place in an unknown number of small plants which blend purchased coal tar distillates.

No data on occupational exposure to anthracene during creosote blending are available. Calculations using the EASE model (non-dispersive use, local exhaust ventilation, direct handling / intermittent contact, i.e. 2-10 times per shift) predict an air concentration of 0-0.1 ppm and a dermal exposure of 0.1-1 mg/cm^2/day. For an anthracene content of 1.5% these values correspond to anthracene exposures of 0-0.0015 ppm (0-11 $\mu g/m^3$) and to 1.5-15 $\mu g/cm^2$/day. Actual exposure is likely to be on the low side of this range to the extent to which personal protective equipment is employed during packaging. However, for the purposes of this Report, the higher end of these ranges is taken forward to risk characterisation

Creosote packaging

Creosote is delivered to packaging plants by road tankers through a piping system and it is packaged in containers for sale. The packaging operation is usually automatic, except for small companies where the procedure is manual and where some exposure can occur. Short-lived exposure is also likely during special, short duration, intermittent tasks related to tanker delivery, removal of drip trays, transfer of wastes or maintenance. According to information available, there are 10 plants packaging creosote in the UK, with 3-4 affected workers in each. The total number of such plants in Europe is not known.

No data on occupational exposure to anthracene during creosote packaging are available. Calculations using the EASE model (non-dispersive use, local exhaust ventilation, direct handling / intermittent contact, i.e. 2-10 times per shift) predict an air concentration of 0-0.1 ppm and a dermal exposure of 0.1-1 mg/cm^2/day. For an anthracene content of 1.5% these values correspond to anthracene exposures of 0-0.0015 ppm (0-11 μg/m^3) and to 1.5-15 μg/cm^2/day. Actual exposure is likely to be on the low side of this range to the extent to which personal protective equipment is employed during packaging. However, for the purposes of this Report, the higher end of these ranges is taken forward to risk characterisation.

Timber impregnation

There are 9 bulk timber impregnation plants in Europe. From the number of affected workers (three to four) known to exist in some of them, a total number of 30-40 for Europe may be estimated.

Measured data on anthracene exposure through creosote timber impregnation are limited:

a) A study of occupational exposure to creosote was carried out at two bulk impregnation plants and also during the handling of creosote-treated wood (stevedores, railway sleepers, welding on track) in Finland (Heikkila et al., 1987). In the context of this study, particulate polycyclic aromatic hydrocarbons were identified and personal exposures quantified. No data on the presence of anthracene in the vapour phase are given. The total concentrations of airborne particulate PAH's (including anthracene) found in the timber impregnation plants varied between 0.2 and 46 μg/m^3. As regards more specific information on anthracene, the following mean exposure values (without information on ranges) were given:

   Impregnation plant workers (18 samples): 1 μg/m^3
   Openings (impregnation plants) (2 samples): 19 μg/m^3
   Cleaning chambers (impregnation plants) (3 samples): 6 μg/m^3
   Switch element assembly (railways) (8 samples): 0.5 μg/m^3
   Manual metal arc welding (3 samples): 1.8 μg/m^3

   Thus, for the activity associated with maximum exposure to anthracene in impregnation plants (openings), the mean air concentration was 19 μg/m^3.

b) In another study conducted in the Netherlands (van Rooij et al., 1993), concerning wood creosoting plants, inhaled pyrene concentrations were found to be in the range 0.3-3 μg/m^3, while average dermal exposure to pyrene was estimated at 0.6 mg/day (range 0.2-1.5 mg/day). Taking into account that the proportion of pyrene in creosote was 3.4% and that of anthracene is 1.5%, and assuming a similar composition of emitted vapours (the vapour pressures at 25^{o}C of pyrene and anthracene are $0.6 \cdot 10^{-3}$ Pa and $0.8 \cdot 10^{-3}$ Pa, respectively (Sonnefeld and Zoller, 1983)), the corresponding exposures to anthracene can be approximately estimated at 0.1-1 μg/m^3 (inhalation) and 265 μg/day (range 88-662 μg/day) (dermal). Assuming that dermal exposure arises mainly through contact with the hands and forearms (surface area 1,980 cm^2 - EASE default), the latter figure would correspond to an average dermal dose rate of 134 ng/cm^2/day (range 44-334 ng/cm^2/day). To the extent to which the exposed areas were in fact lower, the estimated dose rates would be correspondingly higher.

   Calculations using the EASE model (non-dispersive use, local exhaust ventilation, direct handling / intermittent contact, i.e. 2-10 times per shift) give an air concentration of 0-0.1 ppm and a dermal exposure of 0.1-1 mg/cm^2/day. For an anthracene content of 1.5%

these values correspond to anthracene exposures of 0-0.0015 ppm (0-11 μg/m^3) and 1.5-15 μg/cm^2/day. These estimates are in fair agreement with the abovementioned measured values. For the purpose of risk characterisation, the upper range of the measured data will be utilised (inhalation exposure: 19 μg/m^3; dermal exposure: 334 ng/cm^2/day).

Creosote brushing

Although according to Directive 2001/90 creosote brushing of wood is not expected to occur, exposure of professionals in the context of in situ re-treatment of wood may still occur. Such exposure is expected to occur via dermal contact. There are no measured data available on occupational exposure to creosote via its use for wood brushing. However, an indication of the levels of dermal exposure may be obtained by reference to the results of 2 studies on amateur volunteers.

a) In a study by Garrod et al. (2000), volunteers were monitored during the use of commercial preservative or anti-foulant formulations (not related to creosote or anthracene) for brushing wooden fences and panels. Gauze pads were fixed on top and underneath their clothing (to allow estimation of through-clothing penetration), while, when gloves were worn on the hands, additional cotton sampling gloves were worn underneath to allow estimation of through-glove penetration. The most relevant data reported in this study are (actual numbers of measurements are not given):

   i) dermal exposure to the formulation:
   body, potential exposure (amount deposited on clothes) 5 mg/min (median), 63.3 mg/min (upper limit);
   gloved hand (actual skin exposure), 0.015 mg/min (median), 3.2 mg/min (upper limit);
   bare hand, 3.5 mg/min (median), 56.2 mg/min (upper limit)

   ii) penetration through coveralls to the body: 10% (median), 67% (upper limit)

   Applying these data to the case of application of creosote by professionals (anthracene content 1.5%; exposure 8 hours per day), the corresponding skin exposures would be:

- actual body exposure (10% penetration through the clothes; 5,690 cm^2 area of the trunk): 0.6 μg/ cm^2/day (median), 8.0 μg/ cm^2/day (upper limit);
- gloved hand (420 cm^2 per hand): 0.26 μg/cm^2/day (median), 54.9 μg/cm^2/day (upper limit);
- bare hand: 60 μg/ cm^2/day (median), 963 μg/ cm^2/day (upper limit)

b) In the study of Roff (1997), amateur volunteers, wearing different types of clothing, were asked to conduct, for 0.5 or 1 hour, brushing of wooden fences with spirit- or water-based woodworm fluids which contained a colourless fluorescent dye. Body exposure was measured using a fluorescence monitor-based system. Highest contamination was found on the bare hands, while clothing was found to provide a major protective effect. The worst case conditions led a predicted maximal value of total dermal exposure of 5.5 ml after 1 hour brushing, of which 75% (i.e. 4.1 ml) is concentrated on the bare hands. Applying these figures to creosote containing 1.5% anthracene leads to an estimated dermal exposure of the bare hands of 61.5 mg. For a skin area (two hands) of 840 cm^2, this corresponds to 585 μg/cm^2/day. This value compares favourably with the worst-case estimate derived from the Garrod et al. (2000) study (bare hand, upper limit) of 963 μg/cm^2/day.

   In using the above data to obtain an estimate of professional exposure it would be reasonable to expect professionals to be more careful than amateurs and make full use of

protective equipment (gloves, coverall). In this context it should be appreciated that, even though the upper limits of dermal exposure estimated from the data of Garrod et al. (2000) (i.e. 8.0 μg/cm^2/day through the trunk and 54.9 μg/cm^2/day through the gloved hand), being based on measured values, will be taken through to risk characterisation, they must be considered as overestimations.

Calculations using the EASE model (non- dispersive use, dilution ventilation and direct handling, extensive contact, i.e. more than 10 times per shift) predict a dermal exposure of 1-5 mg/cm^2/day. For an anthracene content of 1.5%, these values correspond to an anthracene exposure of 15-75 μg/cm^2/day. The modelled range of dermal exposure is comparable with the worst-case estimates obtained above from the Garrod et al. (2000) study.

4.1.1.2.4 Occupational exposure from other industrial sources

Occupational exposure to anthracene in the context of industrial activities not related to the production or use of anthracene itself. Such exposures do not strictly come under the terms of the present Report. However, they are considered for illustrative purposes.

Most reported data on occupational exposures to PAH in relevant occupations focus on benzo[a]pyrene, while data specific to anthracene are limited (the number of measurements in each case being unspecified in published reports, but often by implication they appear to be single measurements), permitting an estimation of the order of magnitude of exposure but giving little or no indication of the variance of the exposures. Therefore it is not possible to estimate the 90th percentiles or other measures of the upper limits of exposure.

Processing of coal and related activities

Geometric mean values for vapour plus particulate airborne anthracene concentrations of 18.61 μg/m^3 (stationary sampling) and 0.073 μg/m^3 (personal sampling) have been reported for a coke plant and bitumen paving plant, respectively (Bjorseth et al, 1978b). No indication of the range of values measured is given.

Average concentrations of anthracene in 5 static and 7 personal air samples for workers employed at a needle coke plant, during normal operation, were 0.66 μg/m^3 and 0.03 μg/m^3, respectively (Boogaard and Vansittetr, 1995).

In a study involving measurement of personal occupational exposure to particulate and vapour PAH in coal tar-handling plants, the following concentrations of airborne anthracene were reported (only single, "typical" values are reported) (Andersson et al., 1983):

	Vapour (mg/m^3)	Particulated (mg/m^3)
Coke oven battery top of coke plant	55	< 1.0
Handling of creosote-impregnated railroad ties	13.0	4.7

B) Carbon anode/graphite plants

In a plant producing carbon anodes for aluminium electrolysis, total airborne anthracene exposure, as measured by personal monitoring) was as follows for workers employed on different tasks (Petry et al, 1996b):

forming section: 0.83-1.49 μg/m^3
paste plant: 2.76-5.51 μg/m^3
store section (broken green anodes and burned anodes): 0.55-1.14 μg/m^3
forming section: 0.57-0.76 μg/m^3
store section (coke) paste plant: 0.77-1.60 μg/m^3
all worksites: 0.42-1.39 μg/m^3

According to another study, the mean (geometric) airborne concentrations of total airborne anthracene were 0.894 μg/m^3 and 0.042 μg/m^3 in a carbon anode and a graphite plant, respectively (Petry et al, 1996a).

C) Silicon carbide plants

The average workplace air concentration of anthracene in the particulate fraction in a silicon carbide and refractory brick industries was reported as 12 μg/m^3 by Lesage et al, (1987), while the geometric mean total airborne concentration in a silicon carbide plant was reported as 0.006 μg/m^3 by Petry et al. (1996a).

In the furnace area of 2 silicon carbide process plants (plant A and plant B), airborne anthracene concentrations (as measured using personal monitors) were as follows for workers employed on different tasks (Petry et al, 1996a):

foreman, 14-20 ng/m^3 and 8-55 ng/m^3
crane operator, 9-16 ng/m^3 and 4-57 ng/m^3
oven workers operating in close proximity to the oven: 14-20 ng/m^3 and 40-249 ng/m^3
oven workers whose tasks did not involve direct work close to the oven site: 3-15 ng/m^3 and 75-200 ng/m^3.

Anthracene in the air of 2 silicon carbide plants had concentrations in the range 0.01-0.85 μg/m^3 in the gaseous phase and 0.01-139 μg/m^3 in the particulate phase (Dufresne et al, 1987). Stationary air samples collected near the ovens of 2 silicon carbide process plants contained anthracene at concentrations ranging from <1 to 7 ng/m^3 and 100-196 ng/m^3, respectively (Petry et al, 1996a).

Measurements of airborne anthracene in a silicon carbide production plant in Norway gave the following results (Norway CA):

Task	N	Vapour (mg/m^3)		Particulate (mg/m^3)	
		Mean	Range	Mean	Range
Electrolysis cellwork (working conditions: 4 “normal”, 1 “worse”	5	3.5	0.4 – 8.6	0.13	03 – 0.32
Unknown welding	1			3.6	
	1			1.1	

D) Aluminium and other metals production

Anthracene was detected in the air of an aluminium reduction plant: 61% of 28 particulate samples contained anthracene at concentrations ranging from non-detectable to 2.8 μg/m^3

(average 0.74 μg/m^3) and 94% of 18 gaseous samples contained anthracene at concentrations ranging from non-detectable to 32.6 μg/m^3 (average 12.3 μg/m^3) (Bjorseth et al., 1978a).

Anthracene was detected in the workplace atmosphere of an aluminium plant in Norway, at a concentration of 4 μg/m^3 (Becher and Bjorseth, 1985). In another similar study, the amount of anthracene in the gaseous phase was found to be 3.90 μg/m^3, while it was 0.1 μg/m^3 in the particulate phase (Bjorseth et al, 1978a).

"Typical" levels of personal exposure in the pot-room of a Sonderberg aluminium plant were reported as 2.7 μg/m3 (vapour) and 0.13 μg/m3 (particulate) (Andersson et al., 1983).

Measurements of airborne anthracene in a metal manufacture plant in Norway gave the following results (Norway CA):

Task	N	Vapour (mg/m^3)		Particulate (mg/m^3)	
		Mean	Range	Mean	Range
Basic Metals					
Electrolysis	5	0.99	0.48-1.65	0.49	0.03-1.10
Welding	2	0.42	0.17-0.66	0.23	-

Measurements in the context of the same study in the manufacture of "other inorganic basic metals" gave exposures to particulate anthracene of 256 μg/m^3 for one electrolysis worker and traces for another two.

A mean value of 0.040 μg/m^3 was reported for airborne anthracene in a metal recycling plant (Petry et al, 1996a).

E) Iron and steel processing

Measurements of airborne anthracene in an iron and steel processing plant in Norway gave the following results (Norway CA):

Task	N	Vapour (mg/m^3)		Particulate (mg/m^3)	
		Mean	Range	Mean	Range
Electrolysis	3	13.9	1.8-22	0.04	0.01-0.06
Pot making	1			273	
Welding	2	29		0.41	0.26-0.56

Table 4.2 summarises the available data and presents the typical and maximum levels reported in the studies described above. Within the limits of confidence permitted by the fragmentary nature of the available information, it can be seen that highest concentrations have been found in silicon carbide and in iron and steel plants.

Table 4.2 Occupational exposure from other industrial sources – Summary (concentrations in µg/m^3)

Type of industry	Typical range	Maximum levels*	Form	Reference
coal processing and related activities	< 20	52	Total	Bjorseth et al., 1978a
Carbon anode/graphite	< 1.5	5.51	Total	Petry et al., 1996a
Silicon carbide	< 1	139	Particulate	Dufresne et al., 1987
Aluminium	< 20	35.4	Particulate	Bjorseth et al., 1979
Iron and steel	Insuf. data	273	Particulate	Norway CA

* Sum of maximal vapour plus particulate concentrations, where available

4.1.1.2.5 Occupational exposure from consumer products

Occupational exposure to anthracene can occur during the professional use of coal tar-derived paints and related products. Various types of coal tar paints, as well as damp-proofing materials (usually emulsions of rubber and coal-tar pitch), containing 0.5% or less anthracene, find use in various situations including painting of walls and floors or other surfaces, and are normally used in open spaces.

Use of coal tar paints and related products

There are no measured data available on occupational exposure to coal tar paints and related products. A rough indication of exposures may be obtained if it is assumed that the arguments presented in the previous section to derive exposures during creosote brushing from the Garrod et al. (2000) data also apply to the present case. In this way, taking into account that the anthracene content is approximately 0.5%, the upper limits of the extrapolated exposures would be 2.7 µg/cm^2/day through the trunk and 18.3 µg/cm^2/day through the gloved hand.

Calculations using the EASE model (non-dispersive use, dilution ventilation and direct handling, extensive contact, i.e. more than10 times per shift) predict a dermal exposure of 1-5 mg/cm^2/day. For an anthracene content of 0.5%, these values correspond to an anthracene exposure of 5-25 µg/cm^2/day. The modelled range of dermal exposure is comparable with the worst-case estimates extrapolated from the data of the Garrod et al. (2000) study.

4.1.1.3 Consumer exposure

No consumer exposure is expected to occur to commercial anthracene (normal use of pyrotechnics containing anthracene is not expected to lead to significant exposure).

Consumer exposure can occur only during the use of coal tar-derived paints and related products. As already stated, the only significant exposure expected is that through the skin. No measured data for such exposures are available. However, a rough indication of the magnitude of dermal exposure may be obtained if it is assumed that the arguments presented in the previous section to derive exposures during creosote brushing from the data of Garrod et al. (2000) also apply to the present case. Recalling that the upper limit of dermal exposure through the bare hands (it is assumed as a worst case that consumers will work with bare hands) was 56.2 mg/min, and 6.3 mg/min through the trunk, and taking 2.5 hours as a typical time of exposure per day for amateurs, the resulting exposures can be estimated as 100 µg/cm^2/day through each hand and 0.8 µg/cm^2/day through the trunk. These values will be taken forward to risk characterisation.

4.1.1.4 Exposure of the general population via the environment

Exposure of the general population via the environment may occur by the following ways:

a) via inhalation of air polluted with anthracene: Measurements of anthracene concentration in polluted western European cities indicated maximal concentrations (vapour plus particulate) typically in the range below 10 ng/m^3, and a maximum reported level of 34 ng/m^3 (Broman et al., 1991; Smith and Harrison, 1996; Masclet et al., 1988). Incomplete combustion of fossil fuels seems to be the main source of this pollution, while the contribution of industrial activities related the production and use of anthracene or anthracene-containing products is minimal. Concentrations tend to be near the higher end of the range observed during the winter months, whereas they tend to be substantially lower during the summer period. The maximum reported value of 34 ng/m^3, taken to reflect regional exposure, would be expected to contribute 680 ng (9.7 ng/kg) to the daily intake of the general population. It is emphasised once more that only a small fraction of this exposure would be attributable to activities related to the production and use of isolated anthracene.

   No measured data exist regarding atmospheric concentrations of anthracene in the vicinity of the single European anthracene production plant. Application of standard EUSES modelling, and taking air emissions as 25 kg/year (Höke, 2000), leads to a calculated annual average PEC_{local} for anthracene production of 0.1 ng/m3, which would correspond to a daily intake by inhalation of 2 ng (0.03 ng/kg).

b) via intake of drinking water and food. Measured data on drinking water concentrations show that such concentrations are usually below the limit of detection, with detectible levels being in the range below 10 ng/l, and the highest value reported is 30 ng/l (Piet and Morra, 1983; Kvesheth and Sortland, 1982). Thus drinking water consumption is expected to contribute no more than 60 ng to daily intake of anthracene, with only a small fraction of this exposure arising from activities related to the production and use of isolated anthracene. Application of standard EUSES modelling leads to an estimated $PEC_{local,\ surface\ water}$ for anthracene production of 12.9 ng/l which, even if it corresponded to drinking water levels, would contribute 25.8 ng (0.4 ng/kg) to the daily intake.

As regards anthracene intake through the diet, there are no data sufficient to permit the proper estimation of human daily intake. Anthracene is found in relatively large concentrations in smoked food or in food which has been cooked on open fire or broiling. Residues of anthracene have been reported in:

- broiled meats at 4.5—7 μg/kg (US EPA, 1987; Fazio and Howard, 1983; Maga, 1986),
- smoked meats and meat products at 2-20 μg/kg (Lo and Sandi, 1978),
- vegetable oils at concentrations typically of the order of 10 μg/kg or less (Menichini et al., 1991; IARC, 1983b; Santodonato et al., 1981; Speer et al., 1990; Hopia et al., 1986), and
- vegetables up to about 0.2 μg/kg (Wickström et al., 1986).

Taking 10 μg/kg as a conservative, maximal concentration for foodstuffs, and a consumption of 1 kg of food per day, a maximum daily human intake of 10 μg anthracene would be via the diet. This estimate is supported by the results of a calculation using data on food intake from the Dietary and Nutritional Survey of the British population which resulted in an estimated mean anthracene intake of 45 ng/kg/day, i.e. 3.1 μg/day (Health and Safety Executive (UK), 2002). Hence a maximum daily intake via food of 10 μg will be adopted.

The above estimates show clearly that exposure via food dominates exposure of the general population via the environment, and a maximal value of 10 μg (143 ng/kg) for oral daily intake via food and water will be taken forward to risk assessment.

4.1.1.5 Combined exposure

Given the extremely low levels of exposure of the general population via the environment, relative to occupational exposures, and the very limited opportunity of consumer exposure (only via one product), it was not considered useful to produce a combined exposure assessment.

4.1.1.6 Exposure assessment – conclusions and summary

The ranges of exposure levels estimated for the various scenarios related to the production and current uses of anthracene, and the maximal values taken forward to risk assessment, are summarised in **Table 4.3**. The corresponding figures estimated for exposures related to other activities, which do not come under the terms of the present Report but are discussed for illustrative purposes, are summarised in **Table 4.4**.

Occupational exposure

Occupational exposure to anthracene can occur during the manufacture of anthracene from anthracene oil and in the context of the use of anthracene for the manufacture of pyrotechnics. Measured data on these exposures are limited, and in most cases EASE has been used to obtain modelled values which are taken forward to the risk characterisation section. Because in some cases the air concentrations predicted by EASE exceed the concentration of saturated vapours of anthracene at room temperature (a consequence of the overestimation to which EASE leads for compounds of relatively low volatility), the figure of 60 $\mu g/m^3$ (concentration of saturated anthracene vapour at room temperature) has been taken forward to risk characterisation. It is likely that even this figure represents a significant overestimation of the true vapour concentrations.

Additional occupational exposures arise during the production of anthracene oil from coal tar, as a result of the production and use of products which are based on tar distillates and contain anthracene as part of a complex mixture (e.g. creosote and products containing coal tar), as well as in the context of workplace activities where organic material is incompletely combusted. For most of these exposure situations, there are no measured exposure data available, and for this reason modelling had to be employed to estimate exposure by inhalation and dermal exposures.

Consumer exposure

No exposure from products containing commercial anthracene is expected. Consumer exposure to anthracene can come through the use of products based on coal tar (which contains anthracene), used for painting and damp-proofing. No measured data are available on the exposure which such uses entail, and the estimated exposures are taken to be similar to those obtained for the corresponding professional uses. These are calculated by the EASE model. However, it is recognised that such exposures in the case of consumers will be much more limited in frequency and duration.

Exposure of the general population via the environment

Exposure of the general population to anthracene via the environment can come from the inhalation of polluted air and the consumption of polluted water and food. The contribution of activities directly related to the production and use of anthracene to this exposure is probably very limited.

Table 4.3 Exposures related to production and current uses of anthracene

Type of exposure		Measured exposure (maximum values)	Modelled exposure			Values taken forward to risk characterisation	
Manufacture of anthracene			**EASE scenario**	**Air concentration**	**Dermal exposure**	**Air concentration**	**Dermal exposure**
Anthracene production	**Preparation of crude anthracene**	0.5 µg/m^3 (particulate)	non-dispersive use; LEV; direct handling/incidental contact	0-44 µg/m^3 vapour	0-6 µg /cm^2/day	5 µg/m^3 (respirable) Modelled: 44 µg/m^3 (vapour)	6 µg /cm^2/day
	Purification of crude anthracene	0.78 µg/m^3 (particulate)	non-dispersive use; LEV; direct handling/incidental contact	0-222 µg/m^3 * vapour	0-30 µg /cm^2/day	7.8 µg/m^3 (respirable) Modelled: 60 µg/m^3 # (vapour)	30 µg /cm^2/day
Anthracene packaging		none	non-dispersive use; LEV; direct handling/intermittent contact; non-aggregating dust; dry manipulation; low TBA	2-5 mg/m^3 dust 0-741 µg/m^3 vapour *	100-1000 µg/cm^2/day	5 mg/m^3 dust 60 µg/m^3# vapour	1000 µg/cm^2/day
Manufacture of pyrotechnics		none	non-dispersive use; LEV; direct handling/intermittent contact; non-aggregating dust; dry manipulation; low TBA	2-5 mg/m^3 dust 0-741 µg/m^3 vapour *	100-1000 µg/cm^2/day	5 mg/m^3 dust 60 µg/m^3# vapour	1000 µg/cm^2/day
Exposure of the general population through the environment		10 µg/day (oral) 680 ng/day (inhalation)	N/A	N/A	N/A	143 ng/kg/day (oral) 9.7 ng/kg/day (inhalation)	

upper limit rejected as higher than concentration of saturated vapour at room temperature
concentration of saturated vapour at 25°C

Table 4.4 Exposures to anthracene from activities not related to production and current uses

Type of exposure	Measured data (max. values)	EASE scenario	Modelled exposure		Values taken to risk characterisation	
			Air concentration	Dermal exposure	Air concentration	Dermal exposure
Coal-tar distillation	none	non-dispersive use; LEV; direct handling/incidental contact	0-11 µg/m^3 vapour	0-1.5 µg /cm^2/day	11 µg/m^3 vapour	1.5 µg /cm^2/day
Use of anthracene in chemical synthesis	none	non-dispersive use; LEV; direct handling/incidental contact	0-741 µg/m^3 vapour *	0-100 µg/cm^2/day	60 µg/m^3 vapour #	100 µg/cm^2/day
Occupational exposure via creosote						
Creosote blending	none	non-dispersive use; LEV; direct handling/intermittent contact	0-11 µg/m^3 vapour	1.5-15 µg/cm^2/day	11 µg/m^3 vapour	15 µg/cm^2/day
Creosote packaging	none	non-dispersive use; LEV; direct handling/intermittent contact	0-11 µg/m^3 vapour	1.5-15 µg/cm^2/day	11 µg/m^3 vapour	15 µg/cm^2/day
Timber impregnation	19 µg/m^3 (particulate); 334 ng/cm^2/day	non-dispersive use; LEV; direct handling/intermittent contact	0-11 µg/m^3 vapour	1.5-15 µg/cm^2/day	19 µg/m^3 particulate	334 ng/cm^2/day

Upper limit rejected as higher than concentration of saturated vapour at room temperature
Concentration of saturated vapour at 25°C

Table 4.4 continued overleaf

Table 4.4 continued Exposures to anthracene from activities not related to production and current uses (continued)

Type of exposure	Measured data (max. values)	EASE scenario	Modelled exposure		Values taken to risk characterisation	
			Air concentration	Dermal exposure	Air concentration	Dermal exposure
Creosote brushing	8.0 µg/cm²/day through the hands and 54.9 µg/cm²/day through the trunk (indirect estimates)	non-dispersive use; dilution ventilation and direct handling; extensive contact	none	15-75 µg/cm²/day	none	8.0 µg/cm²/day through the hands; 54.9 µg/cm²/day through the trunk; 75 µg/cm²/day (EASE)
Occupational exposure from other industrial sources						
Coal processing & related activities	52 µg/m³ (total)	N/A (not applicable)			52 µg/m³ (total)	-
Carbon anode/graphite	5.51 µg/m³ (total)	N/A			5.51 µg/m³ (total)	-
Silicon carbide	139 µg/m³ (particulate)	N/A			139 µg/m³ (particulate)	-
Aluminium & other metals	256 µg/m³ (particulate)	N/A			35.4 µg/m³ (particulate)	-
Iron and steel	273 µg/m³ (particulate)	N/A			22 µg/m³ (particulate)	-
Occupational exposure from consumer products						
Use of coal tar paints and related products	18.3 µg/cm²/day through the hands and 2.7 µg/cm²/day through the trunk (indirect estimates)	non-dispersive use; dilution ventilation and direct handling; extensive contact	none	5-25 µg/cm²/day	none	18.3 µg/cm²/day through the hands and 2.7 µg/cm²/day through the trunk; 25 µg/cm²/day (EASE)
Consumer exposure						
Use of coal tar paints and related products	100 µg/cm²/day through the hands and 0.8 µg/cm²/day through the trunk (maximum, indirect estimate)	N/A	none	N/A	none	100 µg/cm²/day through the hands and 0.8 µg/cm²/day through the trunk

4.1.2 Effects assessment: Hazard identification and dose-response relationships

Anthracene belongs to the group of (homocyclic) polycyclic aromatic hydrocarbons (PAH), a group of compounds which includes many powerful genotoxic and carcinogenic agents (IPCS, 1998). Most studies of the toxicology of PAH have been carried out with compounds other than anthracene, and indicate that PAH are in general absorbed through the lung, the gastrointestinal tract, and the skin. Once absorbed by any route, they are widely distributed in the body and are found in almost all internal organs, particularly those rich in lipids. They can cross the placenta and have been detected in fetal tissues.

The metabolism of PAH is complex, and involves mainly conversion via intermediate epoxides to phenols, diols, and tetrols, which can subsequently form phase II conjugates (esters with sulfuric or glucuronic acids or with glutathione). Metabolites and their conjugates are excreted via the urine and feces, but conjugates excreted in the bile can be reabsorbed after being hydrolysed by enzymes of the gut flora. After inhalation or intratracheal instillation of PAH, the largest part of metabolites was recovered in the feces, suggesting significant hepatobiliary recirculation following pulmonary absorption. PAH do not persist in the body and their turnover is rapid (IPCS, 1998).

The molecular basis of the genotoxicity and carcinogenicity of PAH has been extensively investigated, and the ability to undergo metabolism to a bay-region diol epoxide is believed to constitute an important structural feature of it. It is important, from this point of view, to note that the anthracene molecule does not contain a bay region.

4.1.2.1 Toxicokinetics, distribution and metabolism

Anthracene is a photosensitive substance and needs to be protected from light during experimental handling. In many of the reported studies it is not explicitly clarified whether suitable precautions had been taken. When such precautions were described they are mentioned in the text below.

4.1.2.1.1 Studies in animals

In vivo studies

Inhalation

No information is available on the absorption, metabolism or excretion of anthracene after inhalation exposure. However, based on data obtained with other polycyclic aromatic hydrocarbons, it can be anticipated that the degree and rate of anthracene uptake and distribution following inhalation can be affected significantly by its physical form, i.e. whether it is in a vapour, aerosol or particulate form or whether it is adsorbed to solid particles (IPCS, 1998; Montizaan et al., 1989). Lung clearance of PAH is significantly slower when they are particulate or particulate-bound (half-life of the order of days) than when they are in a vapour or dissolved form (usually half-life of the order of hours), and depends on the size of the particles and the PAH-to-carrier weight ratio. The degree of penetration of particulate or particle-bound PAH into the lung depends on the size of the particles. Inhaled particles with aerodynamic diameter greater

than 10-20 μm can be intercepted in the nasopharynx and the tracheobronchial part of the lung, while particles < 2.5 μm are respirable, i.e. they can reach the lung alveoli. Depending on the size of different particles, the mucociliary system can contribute to different degrees to their clearance, in turn affecting the degree of elution and absorption of the particulate-adsorbed PAH. For the particle-bound PAH found in the ambient air, the overall degree of absorption through the lungs has been estimated at about 20% (Montizaan et al., 1989). The corresponding figure for other situations (e.g. industrial sites of anthracene production and handling) will depend on the size distribution of the corresponding particulates, for which no information is available.

The lung clearance kinetics of anthracene was examined in rats after intratracheal instillation (Bond et al., 1985). Twenty-four female F344/Crl rats received 1 nmole (178 ng, ~1.2 ng/kg) 9-^{14}C-anthracene (suspended in 250 μl of a vehicle consisting of 10% DMSO in 0.9% saline) by a single intratracheal instillation, and groups of 3 animals were killed 1, 3, 12, 24, 48, 72 and 96 hours later. The lungs were solubilised and the amount of radioactivity they contained measured by scintillation counting. Most (99.7%) of the radioactivity disappeared very rapidly (in less than 1 hour), while the remaining 0.3% was cleared much more slowly (half-life of 25.6 hours). It is not known whether mucociliary clearance contributed to the extremely rapid rate of the first phase. A qualitatively similar picture was reported in the same study for other PAH, and it is noted that broadly similar findings (biphasic and substantial lung clearance after intratracheal instillation or inhalation) have also been described for other PAH (e.g. benzo[a]pyrene) (Weyand and Bevan, 1986; Mitchell, 1982; reviewed by Montizaan et al., 1989). Nevertheless, the data from the Bond et al. (1985) study do not provide a clear answer to important questions such as whether all the material that disappeared from the lung was systemically absorbed and whether similar kinetics would hold after inhalation, or after different doses.

Oral

Information allowing the estimation of the net absorption of anthracene through the gastrointestinal epithelium is missing. In an old study in male white rats, groups of 4 animals were fed diets containing 0.2% or 1% anthracene for two 1-hour periods during the same day (total intake 270-830 mg; ~1-3 mg/kg), and feces were collected during the next 2 days (Chang, 1943). Gravimetric analysis of the feces, based on extraction with ether, saponification with alcoholic potassium hydroxide, and precipitation of the saponified material with water, indicated that an amount of saponifiable material (interpreted by the authors as corresponding to unchanged anthracene) equivalent to 53% and 83% of the administered doses, respectively, was excreted by this route. In the context of the same study, an aqueous starch suspension of 100 mg anthracene was administered by gavage to 2 male white rats. The “unchanged anthracene” found in feces collected during the next 3 days from each of the animals corresponded to 64% or 74% of the administered dose, respectively. The results of positive and negative control experiments reported in this study indicate that, at the level of dosing employed, the material detected in the feces was indeed related to the treatment. However, the crude (by modern standards) nature of the analytical method does not permit any conclusions on the net absorption of anthracene from the GI tract following oral ingestion, other than suggesting that it may not exceed 50%.

Because of their low water solubility, PAH can be physically adsorbed to the mucosal surfaces of the gastrointestinal tract. For this reason (as indicated by studies with PAH's other than anthracene - mainly benzo[a]pyrene), absorption and, hence, tissue concentrations tend to increase exponentially with dose (IPCS, 1998; Montizaan, 1989). For the same reason, systemic absorption of PAH may be aided by bile. To study the role of bile in the intestinal absorption of anthracene following oral intake, conscious rats with bile duct and duodenal catheters were given isotopically labelled anthracene (1 mg in 0.2 ml in corn oil, corresponding to 3.7 mg/kg), and the

recovery of radioactivity in bile and urine was measured (Rahman et al., 1986). One group of animals received via the duodenal catheter only anthracene solution, whereas a second group received the anthracene solution mixed with 0.5 mg bile, followed by 8 further doses of 0.5 ml bile at hourly intervals to simulate normal bile flow. Over the next 24 hours, samples of bile and urine were collected and the amount of radiolabel recovered was measured as an index of the efficiency of absorption. Irrespective of the presence or absence of bile, about two thirds of the radioactivity absorbed was found in the bile and one third in the urine. Cumulative recovery in the presence of bile was 75.55% of the administered dose, while in the absence of bile it was somewhat lower (53.65%), a finding attributed to the relatively low water solubility of anthracene and suggesting that bile-mediated micellar solubilisation facilitates the uptake process. While this study indicates that, over a period of 24 hours, at least 75% of orally administered anthracene is initially absorbed from the intestinal tract of rats with normal bile flow; in the absence of information on the amount of unmetabolised anthracene present in biliary secretions the net systemic absorption of anthracene via the intestine cannot be estimated. Nevertheless, the result of this study is not incompatible with that of Chang (1943) which suggested a net absorption of less than 50%.

In early studies of the metabolism of anthracene, (-)-1,2-dihydroxy-1,2-dihydroanthracene was found in the urine of rats fed a diet containing 4% anthracene (Boyland and Levi, 1935; 1936a; 1936b). While the free 1,2-dihydrodiol was the main metabolite found, additional metabolites detected included its glucuronic acid ester as well as 1-anthrylmercapturic acid. Rabbits treated in the same way excreted in the urine mainly the (+)-stereoisomer of the glucuronic acid ester.

In a more recent, detailed study, a group of 24 male Chester Beatty rats, was given for 3 weeks a diet containing 5% anthracene (Sims, 1964). Examination of metabolites in urine indicated that anthracene was converted to 1,2-dihydroxyanthracene and trans-1,2-dihydro-1,2,-dihydroxyanthracene, which were excreted mainly as sulphuric acid and glucuronic acid conjugates. An additional product of metabolism at the 1 and 2 positions of anthracene was N-acetyl-S-(1,2-dihydro-2-hydroxy-1-anthryl) cystein (a glutathione conjugation product), which was also found in the urine. Anthracene appears to undergo also metabolism at the 9- and 10-positions, as indicated by the detection of trans-9,10-dihydro-9,10-dihydroxy-anthracene as well as its further metabolites 2-hydroxy-9,10-anthraquinone, anthrone and conjugates of 9-hydroxy-, 9,10-dihydroxy- and 2,9,10-trihydroxyanthracene. A possible non-hepatic origin of the metabolites at the 9,10- position was suggested by the fact that *in vitro* metabolism of anthracene using rat liver microsomes led to the formation primarily of trans-1,2-dihydroxy-1,2-dihydroanthracene but not of metabolites at the 9,10-position (Akhtar et al., 1979).

Dermal

The rate of skin absorption of anthracene was examined in 55-day old mice of Strong/A strain (Bock and Burnham, 1961). 0.25 ml of a 1% solution of anthracene in a 99:1 mixture of benzene and mineral oil was applied on an area of shaved skin approximately 6 cm^2., resulting in an estimated dose of roughly 400 $\mu g/cm^2$. After periods of 10 minutes to 4 hours the animals were killed, the application site was cleaned with benzene and a piece of skin removed, homogenised, extracted with benzene and the extract analysed by spectrofluorimetry (no information is given on measures to protect the chemical from photodegradation). The skin concentration of anthracene increased rapidly, reaching its maximal value (10-15 μg/g wet weight of skin, representing roughly 0.2-0.3% of the applied dose) after approximately 1 hour and remained almost unchanged up to 4 hours post-application (no measurements were reported beyond this point). This steady-state concentration was not significantly affected by the sex of the animals. It

is noted that the use as a solvent of benzene, an efficient defattening agent, may have affected the absorption kinetics.

The cutaneous absorption of anthracene was also examined in female Sprague-Dawley rats that were administered a single topical skin application of ^{14}C-anthracene (14.2 μg, 9.3 μg/cm^2) dissolved in 71 μl 1:7 hexane:acetone. The solvent was removed with a stream of air immediately after application (no information is given on measures to protect the chemical from photodegradation) (Yang et al., 1986), and urine and feces were collected daily. Cumulative recovery of the applied radioactivity over a period of 6 days was 29.1% from urine and 21.9% from feces, while another 1.3% was found in tissues (mainly the liver and kidneys) collected when the animals were sacrificed at the end of this period. Absorption was fastest during the first 24 hours (20.1%), while, as indicated above, at 6 days it reached 52.3% and was still rising, albeit at a greatly decreased rate. This figure is compatible with the findings of the study of Bock and Burnham (1961), described in the previous section, which, based on an initial rate of increase of the tissue concentration of anthracene of 0.2-0.3% per hour, would suggest 50% absorption in 5-10 days.

The study of Yang et al. (1986) indicates that, at the relatively low dose used, the absorption rate through the rat skin is approximately 1% per hour. An approximately 2fold faster initial absorption rate, but similar (55.9%) cumulative skin absorption after 6 days, was described in the same report, using an *in vitro* system: To excised slices of rat skin, 350 μm thick, ^{14}C-anthracene was applied at the same concentration as used in the *in vivo* study (9.3 μg/cm^2), and the kinetics of penetration of radioactivity through the skin and into the receptor fluid of Franz-type diffusion cells measured.

Van Rooij et al. (1995) used an isolated blood-perfused pig ear system to study the skin penetration of PAHs applied in the form of coal tar. This test system is considered as a useful model for dermal absorption studies because of the morphological and functional similarity of pig skin to that of humans and because percutaneous absorption rates through the pig skin have been found to be comparable to those through the human skin. Coal tar containing 3.7% anthracene (other PAH present included phenanthrene, fluoranthene, fluorene and pyrene at levels ranging from 6.8% to 2.1%, and various heavier PAH at levels below 1%), was applied at 11 mg/cm^2 (corresponding to 407 μg/cm^2 anthracene) to a 24 cm^2 surface of a pig ear. The latter was perfused with blood for 250 min and blood concentrations of various PAHs measured at intervals. The mean absorption rate of anthracene was 19.6 ng/cm^2 per hour, corresponding to 0.005% of the applied dose per hour. This rate is much slower than the rates reported by the previously described *in vivo* and *in vitro* rat studies, a difference which can be ascribed primarily to the much higher dose employed in the van Rooij (1995) study where even after 200 minutes less than 0.2% of each PAH had been absorbed. In addition, the application of a PAH in the form of a complex mixture is known to increase significantly its dermal residence time (Dankovich et al., 1989). For these reasons the result of this study cannot be used to estimate the absolute value of the rate or degree of skin absorption of anthracene.

Sartorelli et al. (1999) examined the kinetics of absorption of various PAHs, including anthracene, through full-thickness monkey (Cercopithecus aetiops) skin using an *in vitro* static diffusion cell and saline solution with gentamycin sulphate and 4% bovine serum albumin as receptor fluid. Anthracene was applied at a dose of 15.1 nmol/cm^2 (2.7 μg/cm^2) as part of a mixture of 13 PAHs dissolved as a suspension in lubricating oil or dissolved in 30 μl of acetone. In the latter case, following evaporation of the solvent, a few drops of artificial sweat were applied to the residue on the skin surface No information is given on measures to protect the chemical from photodegradation. In the presence of artificial sweat, the anthracene absorption

rate reached a steady state corresponding to 0.35% of the applied dose per hour, while it was approximately 4fold slower when lubricating oil was used.

Other routes

Anthracene (0.4 µmol in 200 µl sesame oil – corresponding to approximately 0.5 µg/kg) was administered to male Sprague-Dawley rats by subcutaneous injection (Myers et al., 1988). The animals were killed 24 hours later and the tissue in contact with the anthracene removed, extracted with organic solvent and analysed by HPLC. The metabolites detected included 9-formylanthracene, 9-methylanthracene, 9-hydroxymethyl-10-methylanthracene, 9-hydroxymethyl-anthracene, 9,10-dimethyl-anthracene, and 9,10-dihydroxymethyl-anthracene. The detection of these metabolites indicates the operation of a pathway leading to methylation of positions 9 and 10 of anthracene, followed by further oxidative metabolism. The same metabolites were observed following *in vitro* incubation of anthracene (taking precautions to avoid photodegradation) with rat liver cytosol fortified with S-adenosylmethionine. In view of the weak tumour initiating activity of 9,10-dimethylanthracene (LaVoie et al., 1985), it was suggested that this type of biomethylation pathway (which was not reported after oral administration), may contribute to the induction of local sarcomas by subcutaneously applied anthracene.

Evidence of hepatobiliary recirculation was provided by the detection, after mild acid hydrolysis, of 1-anthrylglucuronic acid and free anthracene in the bile as well as in aqueous extracts of the duodenum and the intestine of mice (strain A) after intravenous administration of 0.5 mg of a colloidal suspension of anthracene (Harper, 1959). From this finding it was concluded that 2-hydroxy-1,2-dihydro-1-anthrylglucuronic acid is formed during the metabolism of anthracene.

In vitro studies

Two *in vitro* studies have already been mentioned: *In vitro* metabolism of anthracene with rat liver microsomes predominantly results in the formation of trans-1,2-dihydroxy-1,2-dihydroanthracene, with little evidence of metabolism at the 9,10-position (Akhtar et al., 1979). *In vitro* formation of the intermediate 1,2-epoxide during incubation of anthracene with purified cytochrome P450 from rat liver has been shown by van Blanderen et al. (1985). On the other hand, *in vitro* metabolism using rat liver cytosol (post-microsomal supernatant) fortified with S-adenosylmethionine gave metabolites derived from methylation at positions 9 and 10, as well as products of their further oxidative metabolism (Myers et al., 1988), the same metabolites being observed also after skin application.

In vitro metabolism of anthracene by microsomes from the liver and skin of New Zealand White rabbits leads primarily to the 1,2-dihydrodiol, as also observed with rat microsomes (Hall and Grover, 1987).

4.1.2.1.2 Studies in humans

In vivo studies

Five normal adult volunteers without cutaneous disease applied to their skin a 2% solution of crude coal tar in petrolatum, containing 190 mg/l anthracene (Storer et al, 1984). In total, 85 g of the solution were applied for 8-hour periods on two consecutive days. Organic extracts of blood collected after completion of the second application and subjected to gas chromatography and

mass spectrometry yielded evidence of anthracene adsorption in four of the five volunteers, with blood concentrations ranging 0.08-0.47 μg/l.

4.1.2.1.3 Summary

A limited study in human volunteers indicates that anthracene penetrates human skin but does not permit a quantitative estimation of the proportion of dermally applied anthracene which is systemically absorbed by humans. No data on the absorption of anthracene via the gastrointestinal tract or via the pulmonary system in humans are available.

In vivo studies with rats, and *in vitro* studies with rat and monkey skin, suggest that, at doses ranging from a few μg to a few hundreds of μg per cm^2, dermal absorption of anthracene occurs at a rate of 0.3-1% of the applied dose per hour.

Although at least 75% of orally administered anthracene is absorbed from the intestinal tract of rats in 24 hours, the available data do not allow the estimation of the net absorption after oral intake. Data from an old study suggest that net gastrointestinal absorption in rats may not exceed 50%.

Based on data from intratracheal instillation in rats, lung clearance appears to be practically 100% within 1 hour. No information on the extent of systemic absorption of anthracene after inhalation is available. Physical form (particulate, aerosol) and particle size are expected to be important determinants of the rate and degree of such absorption.

Analysis of urinary metabolites, as well as *in vitro* studies, suggest that the metabolism of anthracene after oral intake proceeds initially via epoxidation at the 1,2-position, followed by hydrolysis to the 1,2-dihydrodiol which undergoes further metabolism, mainly to glucuronic or sulphuric acid conjugates. There is also evidence of additional metabolic pathways, at least in rat skin, leading to methylation and oxidation of anthracene at the 9,10 positions. Although there is evidence that anthracene metabolites occur in the bile and the feces, no information on the amounts and nature of such metabolites is available.

In conclusion, the available studies leave significant questions regarding the absorption, distribution and metabolism of anthracene unresolved, including the degree of systemic absorption after inhalation or dermal exposure and the levels and nature of metabolites in the gastrointestinal tract. Although data on other PAH suggest that in general PAH do not persist in the body (IPCS, 1998), given the moderately high log Pow and the low water solubility of anthracene, its potential to accumulate in lipid-rich mammalian tissues also remains to be addressed.

4.1.2.2 Acute toxicity

4.1.2.2.1 Studies in animals

Inhalation

No information is available on the acute toxicity of anthracene after inhalation in animals.

Oral

Anthracene (40% suspension in 0.5% carboxymethylcellulose) was administered intragastrically, at a dose of 16 g/kg, to groups of 5 male and 5 female Wistar rats. No lethality was observed after 14 days of observation, indicating that the LD_{50} is > 16 g/kg (Grote, 1979a). The toxic effects observed included fatigue asthenia, hyperemia of the kidney, liver, heart and lungs, lipid changes in the liver and leukocytosis. A similar result was reported when anthracene was administered to mice (unspecified strain) at 17 g/kg (Nagornyi and Rodionov, 1969).

In another study, groups of 5 male Wistar strain rats were administered single doses of anthracene by gavage at dose levels of 5.0, 10.0 and 20.0 g/kg of body weight (Mellon Institute, 1977). Mortality was observed within 14 days of dosing in 4 animals receiving 10.0 g/kg and in all animals receiving 20.0 g/kg (no toxic symptoms were reported at the dose of 5.0 g/kg). The LD_{50} was calculated to be 8.12 g/kg of body weight (5.90-11.2, 95% confidence interval). Clinical observations included piloerection, sluggishness, prostration, rapid breathing, and bloody eyes. Gross necropsy evaluation revealed hemorrhages of the lungs; mottled livers with prominent acini and a burned white colour; spleens and kidneys pale and mottled; congested kidneys and adrenals; distended, chemical-filled and opaque stomachs; pink pylori; and distended, transparent, gas-filled, and yellowed intestines.

Dermal

An early study in which the ability of various compounds to suppress the sebaceous glands in mice was examined as a marker of skin carcinogenic potential reported anthracene to be negative (Bock and Mund, 1958).

Anthracene (purity 'Anthrazen reinst', dissolved at 0.4 g/ml in polyethylene glycol), was applied, at a single dose of 1,320 mg/kg, in the form of an occlusive patch to the shaved skin of Wistar rats (5 male, 5 female) for 24 hours, and the animals observed for 14 days. No deaths were observed, and it was reported that no local or systemic symptoms of toxicity or pathological findings were observed (although no details of the symptoms or changes looked for are given). This led to the conclusion that the dermal LD_{50} was greater than 1,320 mg/kg body weight (Worstmann, 1981).

Acute toxicity after dermal exposure was evaluated in a group of six male albino rabbits (strain not reported) receiving single occluded applications of anthracene at a dose level of 4.0 g/kg of body weight (Mellon Institute, 1977). The test article was held in contact with the intact skin (under polyethylene sheeting) for a 24-hour period. Mortality was not observed within 14 days of treatment; the LD_{50} was determined to be greater than 4.0 g/kg of body weight. Clinical observations included diarrhoea. Gross necropsy evaluation revealed congestion of the liver and spleen and pale and mottled kidneys. No further details are given in that report.

Intraperitoneal

The LD50 of anthracene after i.p. administration to mice (unspecified strain) was reported to be 430 mg/kg (Salamone, 1981).

Five mice were administered i.p. anthracene dissolved in olive oil, at a dose of 1,000 mg/kg. Sacrifice of 1 animal revealed that the oil had been fully resorbed after 15 days. The remaining 4 animals were without effects 5 months later (Shubik and Della Porta, 1957).

Administration i.p. to mice (unspecified strain) of anthracene at a dose of 1,000 mg/kg was reported in an old study, cited in a secondary reference, to cause a reduction of the growth rate from 4.7 g/day to 2.8 g/day (Elson et al., 1945).

In a study of the mechanism of control of cytochrome P450 expression, a single intraperitoneal injection of 300 mg/kg bw anthracene (dissolved in corn oil) to B6C3F1 mice was found to cause a 10-fold increase in the activity of hepatic microsomal methoxyresofurin O-deethylase (a cytochrome P4501a2-dependent activity) 24 hours later (Chaloupka et al., 1994). It also caused an increase in the mRNA levels of cytochrome P4501A2 by an Ah receptor-independent mechanism. No specific toxicological significance can be attached to these observations.

Other routes

According to a secondary report, 0.5 mg anthracene injected subcutaneously into rats decreased the anti-oxidative activity of the pancreas during the 25 days after injection. Pancreatic insular cells showed increases in the cell, nucleus, and nucleolus size (Clayton and Clayton, 1981).

In a test meant to compare the ability of carcinogenic and non-carcinogenic PAHs to affect the calcium ionophore A23187-induced activation of washed rabbit platelets, measured as biosynthesis of thromboxane B2, anthracene was reported to have an enhancing effect. Other (carcinogenic) PAH's (benz[a]anthracene, chrysene, benzo[a]pyrene, and benzo[ghi]perylene) had an inhibitory effect (Yamazaki et al., 1990).

4.1.2.2.2 Studies in humans

According to a report in a secondary source, which gives no other details, the acute symptoms of anthracene exposure include irritation of the upper airways, lacrymation, photophobia, oedema of the eyelids and conjuctival hyperemia (Volkova, 1983). Other effects described, which could not be associated with a specific route of anthracene exposure, include headache, nausea, loss of appetite, inflammation of the gastrointestinal tract, slow reactions and weakness. These symptoms are said to disappear within several days after cessation of contact.

No specific data are available on the acute toxicity of anthracene to humans.

4.1.2.2.3 Summary

The acute toxicity of anthracene after oral, dermal and i.p. administration is low. Its oral LD_{50} in the rat is 8.12 g/kg, while its dermal LD_{50} was greater than 1,320 mg/kg in the rat and greater than 4 g/kg in the rabbit. No tissue-specific acute toxic effects have been reported. No data on acute toxicity in humans are available.

4.1.2.3 Corrosivity and irritation

Anthracene is known to cause phototoxicity (photoirritation) in the presence of UV radiation (see Section 4.1.2.5). In this section reference is made to studies on the irritating potential of anthracene in the absence of UV radiation.

4.1.2.3.1 Studies in animals

Skin irritation

The induction of primary skin irritation by anthracene was tested in accordance with a method specified in the US Code of Federal Regulations (Title 16, Section 1500.41). To a 1 sq. inch area of intact or abraded skin (clipped free of hair) of 6 albino rabbits, 0.5 g of anthracene (reinst = purest), in the form of a 10% suspension in 0.5% carboxymethlcellulose, was applied under an occlusive gauze for 24 hours (Grote, 1979b). The skin condition was assessed for erythema/eschar and oedema formation, using the standard Draize scale, at the time of removal of the gauze as well as 48 hours later. The values for erythema/eschar formation at the two observation times for intact skin were added to those for abraded skin (4 values), as were the values for oedema formation at the two observation times for intact skin (4 values). The total of the 8 values was divided by 4 to give the primary irritation score. Very slight erythema and/or oedema was observed in five of the six rabbits, giving an overall irritation score of 0.79 and leading to its characterisation as "slightly irritating" according to the criteria of the method used. For classification as a skin irritant under present guidelines a score of 2 would be required. On the other hand, this testing method differs from that of Annex V of Dir. 92/69/EEC in a number of points, the most important of which is that it made use of a diluted formulation, rather than the pure substance.

In a study already described (see Section 4.1.2.2.1), anthracene (purity 'Anthrazen reinst', 0.4 g/ml in polyethylene glycol), was applied in the form of an occlusive patch (5 · 7.5 cm) to the shaved skin of Wistar rats (5 male, 5 female) for 24 hours, at a mean dose of 300 mg (8 mg/cm^2), and the animals observed for 14 days (Worstmann, 1981). No erythema or oedema was observed at any time. The low dose employed in this study is noted.

In a short note, a substance described as "anthracene residues" was reported to have been applied to the inner surface of the ear of white New Zealand rabbits (one male and one female, 500 mg/animal), using an occlusive gauze, for 24 hours. Examination 7-days post exposure did not reveal evidence of "irritating activity" (Thyssen J, 1979). Although this report refers to using this test to look for irritating activity, it is noted that this method (as well as the analogous "Mouse Ear Swelling Method") is normally used as a test for sensitisation. Furthermore, the "anthracene residues" employed in this study consisted of wastes of unknown composition from anthracene production (Höke, 2002). Therefore no conclusions regarding anthracene can be drawn from the study.

Recrystallised anthracene was applied to the skin of the ear of MNRI mice which were examined for evidence of irritation 24 hours later. The ID50 (dose causing irritation to 50% of the animals) was found to be 118 µg per ear (corresponding to 4.7 mg/kg or, assuming 1 cm^2 as the area of the treated area, 118 µg/cm^2) (Brune et al, 1978). No further information on the test method is given.

A quantity of 0.01 ml of 25% (w/v) suspension (described as "poor") of anthracene in corn oil (2.5 mg) was applied to unclipped, uncovered intact belly skin of 5 rabbits (Mellon Institute, 1977). No irritation was reported to be present 24 hours later, but a marginal effect ("moderate capillary injection") was found in one animal. No further details are given in the report. The low dose employed is noted.

Eye irritation

Eye irritation was tested in accordance with a method specified in the US Code of Federal Regulations, Title 16, Section 1500.42. Anthracene (reinst = purest) was administered at 100 mg

per animal to the conjunctival sac of six albino rabbits, and scoring for irritation according to the standard Draize criteria was done after 24, 48 and 72 hours. No effects on the cornea or the iris were observed in any of the tested animals. Slight to moderate redness of the conjunctiva appeared in 4 out of the 6 rabbits, while slightly increased secretion appeared in 1 animal, giving a total Draize irritation score of 1.0, leading to its characterisation as "non-irritant" according to the criteria of the method used. (Grote, 1979c). This test broadly fulfils the criteria of the Annex V of Dir. 92/69/EEC test for eye irritation, and leads to the conclusion that anthracene would be classified as "non-irritant" by the criteria of this method.

In a short note, a substance described as "anthracene residues" was reported to have been administered at 50 mg per animal to the conjunctival sac of white New Zealand rabbits (one male and one female) and the animals observed for 7 days. No evidence of eye irritation was found (Thyssen, 1979). For reasons given above (under Skin Irritation), no conclusions regarding anthracene can be drawn from this study.

Anthracene was instilled into the conjunctival sac of 5 rabbits, as powder (40 mg) or as a 25% suspension in corn oil (0.5 mg anthracene per eye) (Mellon Institute, 1977). Examination of the unstained eyes immediately, and with staining with 5% fluorescein 24 hours after later, did not reveal any corneal injury. No further details of the test procedure or the clinical findings are given in this report.

Corrosivity

The animal studies for skin irritation described above do not provide any evidence to suggest that anthracene is corrosive to the skin or eyes.

4.1.2.3.2 Studies in humans

According to secondary references, which give no further specific information, anthracene is a primary irritant, causing "possible mild irritation of skin, eyes, mucous membranes and the respiratory tract after exposure to anthracene fumes or dust during labour" (Montizaan et al., 1989) and irritation of the upper airways, lacrymation, edema of the eyelids and conjuctival hyperemia (Volkova, 1983). No conclusions can be drawn from these reports in view of their uninformative nature and the fact that they are based on observations in occupational settings which probably involve exposure to complex mixtures.

Skin disorders related to irritation and sensitisation ("occupational skin burns") are relatively common among workers exposed to coal tar and related products (Emmett, 1986; Riala et al., 1998). However, no studies specifically linking anthracene to these effects have been reported.

4.1.2.3.3 Summary

Anthracene has not been tested for skin irritating activity by a method conforming to the criteria of Annex V of Dir. 92/69/EEC. At a dose of 500 mg (as a 10% suspension) it caused slight erythema and oedema to the skin of rabbits. On the other hand, when applied on the skin of rats at a mean dose of 300 mg (as a 40% formulation) for 24 hours, no evidence of skin irritation was observed up to 14 days later. Finally, a report that at a dose of 118 μg/cm^2 it caused irritation to the skin of the ear of 50% of mice cannot be evaluated because of limited reporting. Although these reports do not provide convincing evidence that anthracene has skin irritating activity in the absence of UV light, none strictly fulfils the criteria of Annex V of Dir. 92/69/EEC. On the

other hand, in view of the strong skin phototoxicity potential of anthracene (see Section 4.1.2.5 below), and the proposal that it be classified as a skin irritant on this basis, no further testing of its skin irritating activity in the absence of UV light seems necessary.

Anthracene was negative in a test for eye irritation that closely resembled the corresponding method of Annex V of Dir. 92/69/EEC.

In view of the lack of evidence that anthracene causes skin irritation in the absence of light, no specific recommendation for further studies to examine the induction of lung irritation are necessary.

4.1.2.4 Sensitisation

4.1.2.4.1 Studies in animals

The ability to anthracene to induce contact sensitivity was tested by immunising adult female Hartley guinea pigs on each front foot pad with 125 μg of anthracene in the form of a 1:1 emulsion of a saline solution and complete Freund's adjuvant (Old et al., 1963). Two to three weeks later, each animal was tested for contact sensitivity by applying one drop of a serial two-fold dilution of anthracene (1 – 0.001%) dissolved in an acetone-olive oil mixture to the shaved ventral or dorsal skin. Skin induration and erythyma were examined 24 hours later. Anthracene was negative in this test, in contrast to the (carcinogenic) PAH benzo[a]pyrene, 3-methylcholanthrene and dimethylbenzanthracene which were positive.

4.1.2.4.2 Studies in humans

No information on the sensitising effects of anthracene (in the absence of light) in humans was found. Skin disorders related to irritation and sensitisation ("occupational skin burns") are relatively common among workers exposed to coal tar and related products (Emmett, 1986; Riala et al., 1998). However, no studies specifically linking anthracene to these effects have been reported.

4.1.2.4.3 Summary

There are no studies in humasn on the skin sensitisation potential of anthracene.

A limited report on a test for sensitising activity of anthacene in rabbits was negative. Anthracene has not been tested in animals for skin sensitising activity in accordance with Annex V of Dir. 92/69/EEC. On the other hand, in view of the strong skin phototoxicity potential of anthracene (see Section 4.1.2.5), and the proposal that it be classified as a skin irritant on this basis, no further testing of its skin sensitising activity in the absence of UV light seems necessary.

4.1.2.5 Phototoxicity

Under Commission Directive 2000/33/EC (27th adaptation to technical progress of Council Directive 67/548/EEC), Annex II ("B.41. Phototoxicity – *In vitro* 3T3 NRU phototoxicity text"), photoxicity is defined as a toxic response that is elicited after the first exposure of skin to certain

chemicals and subsequent exposure to light, or that is induced similarly by skin irradiation after systemic administration of a chemical. Photoirritation is defined in the same text as referring only to those phototoxic reactions which are produced at the skin after exposure to chemicals (topically or orally). These phototoxic reactions lead always to non-specific cell damage (sunburn like reactions). Finally, photoallergy is defined as an acquired immunological reactivity which does not occur on first treatment with chemical and light, and needs an induction period of one or two weeks before skin reactivity can be demonstrated.

Anthracene is a photodynamic compound which, in the presence of UV radiation, generates reactive oxygen species (singlet oxygen, superoxide anion) (Joshi and Pathak, 1984) and can elicit toxic effects. A possible mechanistic basis for anthracene's phototoxic effects may be related to its light-mediated interaction with, and modification of, cellular constituents.

Anthracene in combination with UV light has been shown to damage DNA, proteins and lipids. Although oxygen is believed to be important for the phototoxic effects of anthracene, there is also evidence that anthracene can also induce oxygen-independent effects on cellular components. Thus, irradiation of ^{14}C-labelled anthracene with UV light (wavelength > 292 nm) in the presence of calf-thymus DNA led to covalent binding of radioactivity to the DNA, which was not dependent on the presence of oxygen (Sinha and Chignell, 1983). The photoinduced covalent binding of anthracene to DNA *in vitro* and in monkey kidney and human skin epithelial cells in culture has also been demonstrated by the studies of Blackburn et al. (Blackburn et al., 1973; Blackburn and Tausig, 1975). On the other hand, the decrease of the thermal denaturation temperature of calf thymus DNA and the nicking of a circular plasmid (both reflecting induction of DNA strand breaks) by anthracene plus UV light were oxygen dependent, implying the involvement of reactive oxygen species.

A similar oxygen dependence was observed for the UV-induced covalent binding of anthracene to human serum albumin and the accompanying crosslinking of the same protein (Sinha and Chignell, 1983). Glutathione (a quencher of reactive oxygen species as well as electrophilic reactive intermediates) inhibited all the above effects regardless of the dependence or not on oxygen. Irradiation with light of wavelength > 320 nm of a solution containing a mixture of 19 aminoacids in the presence of anthracene was shown to cause modifications only of tryptophan (Schothorst et al., 1979). Similar treatment of a glutathione solution led to loss of -SH groups which, at low anthracene concentrations, was accompanied by formation of the glutathione dimer. The significance of such phenomena lies in the possibility that modification of proteins or peptides may give rise to the induction of an immune response or other toxic effects.

Finally, anthracene plus UV light cause lipid peroxidation in liposomes derived from rat liver microsomes (Sinha and Chignell, 1983). This oxidation reaction was not significantly inhibited by superoxide dismutase or catalase alone or in combination, suggesting that this reaction was not mediated by superoxide, hydroxide radicals or hydrogen peroxide.

4.1.2.5.1 Studies in animals and in *in vitro* cell cultures

In the context of a photocarcinogenicity study, Skh-1 hairless mice treated on their skin (size of painted area not specified) with 40 µl of a 0.01% solution of anthracene in methanol (approximately 4 µg anthracene) and subsequently irradiated with UV radiation (intensity and duration not specified) showed more severe skin inflammation than animals treated only with methanol and UV (Forbes et al., 1976).

Skh-1 hairless mice received a topical application to their backs (size of painted area not specified) of 20 µl of a 0.025% solution of anthracene in 20% pyrrolidone/ isopropyl alcohol 20:80 (approximately 5 µg anthracene), followed by topical irradiation with UV light (320-400 nm) for periods ranging from 100 to 2,000 seconds (total radiance delivered 1.3-26 kJ/m^2) (Argenbright et al., 1980a). A rapid and substantial onset of hyperemia was observed which was not accompanied by any change in permeability of vascular walls to plasma albumin. Hyperemia was prevented by the simultaneous application of histamine H1 and H2 receptor blockers, suggesting that it resulted from primary injury of dermal mast cells and consequent release of histamine which in turn acted to bring about vasodilation.

Analogous results were obtained in 9 white pigs (males and females, 9-15 kg) treated with 12.5 µg anthracene (50 µl of a 0.025% solution in pyrrolidone/ isopropanol 20:80) painted on an area of 6 cm^2. Forty-five minutes later the animals were exposed for 100 – 2,000 sec to UV radiation, receiving 2.6-52 kJ/m^2 of total radiance. Minimal erythema was observed within 2 minutes of irradiation and increased with radiation dose (no more information is given). A radiation dose-related increase of vascular permeability was also observed, which was mediated by histamine and serotonin receptors (Argenbright et al., 1980b).

The possibility that anthracene plus UV light may damage mast cell membranes, thus causing the release of inflammation-mediators, is supported by the observation that anthracene accumulates in the lysosomes of animal and human endothelial cells (Alison et al., 1966). It has been postulated that such accumulation may result, upon photoactivation, in membrane damage permitting the leakage of lytic enzymes and other chemicals which can initiate the inflammatory cascade. The ability of anthracene to cause light-mediated membrane damage is further indicated by its ability to induce photohemolysis (light-mediated lysis of erythrocytes) *in vitro*.

Hairless mice were treated on the skin with anthracene (2 applications of saturated solution, solvent and concentration unspecified) followed by 48 hours of continuous UV irradiation (intensity and wavelength unspecified) (Gloxhuber, 1970). Intense erythema was observed. No erythema was observed when the anthracene (100 mg/kg) was administered i.p., followed by 48 hours of UV irradiation. This finding is in contrast to that described in an abstract by Dayhaw-Barker et al. (1985), according to which oral administration of anthracene (50 mg/ml in corn oil) to mice by gavage, followed by UV irradiation of the skin for 1 hour, resulted in keratitis of the exposed skin. This effect was said to be less pronounced in animals receiving only UV radiation and absent from animals receiving only solvent.

The induction of erythema by combined treatment with anthracene and UV radiation, and the corresponding action spectrum, were investigated in guinea pigs by Kochevar et al. (1982). Groups of 6 Hartley strain female albino guinea pigs had 0.1 ml of a solution of anthracene in methanol (concentrations ranging 0.005 - 5 mM) applied to a site (2.5 · 2.5 cm) on their shaved and depilated back. Thirty minutes later the animals were irradiated with 20-40 W/m^2 UV irradiation (320 - 400 nm), receiving a total of 100 KJ/m^2 of radiance (the duration of UV exposure can be calculated as approximately 40-80 minutes). Twenty hours after irradiation, a dose-related increase in erythema was observed in all animals receiving both anthracene and UV irradiation (but not in any of those receiving only one of the two stimuli). Animals which had received 0.005 mM (corresponding to 14 ng/cm^2) anthracene showed no erythema, 0.05 mM being the lowest dose causing an effect. The action spectrum was found to broadly match the absorption spectrum of anthracene, showing activity in the range 340-380 nm and a maximum around 360 nm, as observed in corresponding studies with humans (Kaidbey and Nonaka, 1984). Thus for the induction of skin irritation by the combination of anthracene and 100 kJ/m^2 of UV light in the guinea pig the NOAEL is 14 ng/cm^2 and the LOAEL is 140 ng/cm^2

In another study, groups of 10 female guinea-pigs (Colworth Dunkin-Lartley) were treated on the hair-clipped dorsal skin with anthracene (10 µl of 0.01% solution in ethanol on a 14-mm diameter area; corresponding to 0.65 µg/cm^2) (Lovell and Sanders, 1992). Thirty minutes later they received a dose of 150 kJ/m^2 UVA (313-400 nm). Skin irritation symptoms were already observed during the irradiation period and were maximal at the first (4 hour post-irradiation) observation point, where a mean erythema score of 5.5 was obtained (score 4 corresponded to slight erythema and score 6 to definite erythema). The effects decreased thereafter, but were still detectible (score of 0.5; score 2 corresponding to faint trace of erythema) after 72 hours. A score of 0.1 was noted 4 hours after application of anthracene without irradiation and faded completely by 24 hours. Varying the UVA dose between 75 kJ/m^2 and 200 kJ/m^2 had no effect on the level of symptoms at 4 hours, but did affect slightly their rate of disappearance. No change in the effects was observed when the ethanol was replaced by acetone or dimethylacetamide-acetone-alcohol as a solvent. Varying the applied dose of anthracene between 0.001% and 1% indicated a minimum photoirritant concentration (at 150 kJ/m^2) of 0.003% (220 ng/cm^2), in broad agreement with the findings of the study of Kochevar et al. (1982).

Burnham and Rahman (1992) treated female C3H/HeN mice on their shaved dorsal skin (approximately 1 cm^2), or a similar area of cultured skin *in vitro*, with 25 µl of a solution of anthracene in 1:1 acetone/olive oil (5 µg/ml), corresponding to 125 ng/cm^2, for 2 hours. Subsequently they were received a dose of 20 kJ/m^2 UVA (365$\pm$10 nm) at 11 J/m^2/sec (over a 30 minute period). Forty hours later, the number of IA^k-expressing Langerhans cells as well as IA^k-negative but Thy-1-positive dendritic cells were enumerated by immunocytostaining and found to be significantly decreased. Depletion of these cells can result in a decreased immune response. No analogous effect was observed with a 10fold lower anthracene dose.

4.1.2.5.2 Studies in humans

According to a report (in a secondary source) which gives no other specific information, the phototoxic effects of anthracene in humans include acute dermatitis with symptoms of burning, itching and edema which are more pronounced in the exposed bare skin regions (Volkova, 1983). Prolonged exposure is said to give rise to pigmentation of the bare skin regions, cornification of its surface layers and telangioectasis. No conclusions can be drawn from this unspecific and limited report.

In 3 human volunteers, a 2% solution of anthracene in benzene was applied twice daily for 2 days on the skin of the forearms, prior to irradiation with long-wavelength UV light (340-380 nm). Urticarial reactions and burning were observed in all 3 subjects, symptoms which persisted for several days, with subsequent pigmentation. In 1 subject erythema also appeared, which persisted for a few days (Crow et al., 1961).

Kaidbey and Nonaka (1984) investigated the action spectrum and UV dose-response relationships governing the induction by anthracene of photoirritation in human volunteers. They applied 10 µl/cm^2 of a 0.25% solution of anthracene (at least 99% pure) (i.e. 25 µg anthracene/cm^2) in equal parts of 95% ethanol and benzene on the untanned backs of 6 Caucasian males of fair complexion. The application sites were covered with non-absorbent cotton cloth for 2 hours, and then uncovered again and allowed to air dry for 15 minutes. Subsequently they were irradiated with UV light of selected wavelength ranges (half-band width 6.6 nm) for different times. The threshold dose of radiation needed for the induction at each wavelength of a) immediate erythema, i.e. erythema localised to the area of exposure, appearing within a few minutes after irradiation and fading after 15 minutes, b) delayed erythema present 22-24 hours after irradiation and c) a weal-and-flare reaction appearing 5-10 minutes after

irradiation, were assessed. The effective wavelengths were in the range 340-380 nm, with maximum activity appearing at 360 nm for all three end-points, an action spectrum paralleling the absorption spectrum of anthracene. Of the three end-points examined, that appearing at the lowest radiation intensity was immediate, transient erythema (mean threshold dose 1.0 $\pm$ 0.6 kJ/m^2), followed by delayed erythema (mean threshold dose 1.9 $\pm$ 1.0 kJ/m^2), and by appearance of flare and wealing (mean threshold dose 2.8 $\pm$ 1.9 kJ/m^2). The observation of different thresholds for the various end-points suggests the existence of different cellular and molecular targets. It has been suggested that the flare and wealing effects may be related mainly to the release of inflammatory mediators from mast cells, as suggested by the fact these effects, but not immediate erythema, were prevented by prior injection of codeine, a mast cell degranulating agent.

A therapeutic use of anthracene phototoxicity to treat psoriasis has been reported in a conference abstract (Rispler and Urbanek, 1978). Forty µl of a 0.025% solution of anthracene (10 µg anthracene; solvent and size of treated area unspecified) were applied to the psoriatic plaques of patients, who were irradiated 1 hour later with long wavelength UV light or natural mid-day sunlight. Phototoxicity was induced by irradiation of the treated area with 0.1-1 J long wavelength UV (which gave rise to erythema and a stinging sensation). After 20-40 treatments the lesions were cleared for up to 1 year, with very little hyperpigmentation of the treated areas. While demonstrating a phototoxic effect of anthracene, this study gives no information on its ability to induce skin photoirritation or photosensitisation.

4.1.2.5.3 Summary

There are no standard validated methods for the assessment of phototoxicity *in vivo*. A standardised *in vitro* method for the assessment of phototoxicity has been defined under Annex II of Commission Directive 2000/33/EC, and added to Annex V of Commission Directive 67/548/EEC, based on the assessment of *in vitro* cytotoxicity in the presence of UV light. This method has not been employed to examine the phototoxicity of anthracene. However, Studies in humans, mice and guineapigs have amply demonstrated that, in combination with long-wavelength UV light (340 - 380 nm), anthracene can lead to photoirritation as defined under Commission Directive 2000/33/EC, with symptoms, in decreasing order of ease of appearance, of transient erythema, delayed erythema and flare-and-wealing. In guinea pigs, the highest amount of anthracene applied to the skin which, in combination with 100 kJ/m^2, did not give rise to erythema (NOAEL) was 14 ng/cm^2, while the corresponding LOAEL was 140 ng/cm^2.

In humans, a single skin application of 25 µg anthracene/cm^2 was sufficient to cause skin irritation after exposure to UVA radiation in the range 1-2.8 kJ/m^2 (depending on the wavelength). With the radiant flux of the global solar radiation (defined as the total solar radiation reaching the earth's surface (WHO, 1994) in the mid- or southern European region being of the order of 800-1,000 W/m^2, and with UVA making up approximately 5-6% of solar radiation (i.e. 40-60 W/m^2), a person exposed to natural sunlight can receive 1 kJ/m^2 of UVA within a period of seconds to minutes (1 J = 1 W.sec) (Moseley et al., 1981). Because 25 µg/cm^2 was the only dose applied in the corresponding study, it is concluded that this corresponds to the human LOAEL, although, in view of the findings in guinea pigs, it effects in humans may occur at substantially lower levels. Consequently the animal LOAEL (140 ng/cm^2) and NOAEL (14 ng/cm^2) will also be considered in Risk Characterisation.

4.1.2.6 Repeated dose toxicity

4.1.2.6.1 Studies in animals

Inhalation

In a report in secondary source, which gives no other specific information, it is mentioned that chronic inhalation of anthracene aerosol by albino rats, at concentrations of 0.05 and 0.01 mg/l, is associated with a reduced gain in body weight and blood changes (decrease in hemoglobin, reticulocytosis, leukopenia, and increase in residual blood nitrogen) (Volkova, 1983). The same blood changes were observed after intragastric administration. No conclusions can be drawn from this report in view of its uninformative nature.

Oral

In a study mentioned in a secondary reference, repeated intragastric exposure of rats with anthracene at unspecified doses and duration was said to produce a decrease in hemoglobin, reticulosis, leukopenia and an increase in residual blood nitrogen (Volkova, 1983).

In a study on enzyme induction by polycyclic aromatic hydrocarbons, intragastric administration of anthracene (100 mg/kg/day) to rats for 4 days was found to induce an increase in microsomal carboxylesterase activity in the gastrointestinal mucosa but not in the kidney (Nousiainen et al., 1984), and a slight increase in cytosolic aldehyde dehydrogenase activity in the liver (Torronen et al., 1981). These changes do not have any obvious toxicological significance.

In a detailed study, conducted under GLP conditions for the US EPA (US EPA, 1989), anthracene dissolved in corn oil was administered to groups of 20 male and female CD-1 (ICR)BR mice by oral gavage, at doses of 0, 250, 500, and 1,000 mg/kg/day for 13 weeks. Mortality, clinical signs, body weights, food consumption, ophthalmology findings, hematology and clinical chemistry results, organ weights, organ-to-body weight ratios, gross pathology, and histopathology findings were evaluated. No significant treatment-related effects on any of these parameters were noted. A statistically significant increase in mean ovary weight (absolute and relative to terminal body weight) for the group receiving 500 mg/kg/day (but not any of the other doses), as well as non-dose-related changes in serum globulin and total protein concentrations, and numbers of segmented neutrophils, were considered incidental and of no pathological significance.

In a chronic bioassay, a group of 28 BD I and BD III rats received anthracene in the diet, starting when the rats were approximately 100 days old (Schmahl, 1955). The daily dosage was initially 5 mg/rat, later increased to 15 mg/rat (corresponding to 17-50 mg/kg/day, assuming average animal weight of 300 g), and the experiment was terminated on the 550th experimental day, when a total dose of 4.5 g/rat had been achieved. The rats were observed until they died, with some living more than 1,000 days. No treatment-related effects on lifespan or gross and histological appearance of tissues were observed. No data on a control group were reported, body weights were not mentioned, and hematological parameters were not measured, making the standard of this old study lower than would be desirable.

Diet containing 1 mg/kg anthracene was fed ad libitum to a group of 7 Swiss mice (unspecified sex) for 17 days (Rigdon and Giannukos, 1964). Subsequently, the anthracene content of the diet was increased to 5 mg/kg for days 18-24 and then to 25 mg/kg for days 25-32. The daily intakes of anthracene during these periods were approximately 150 mg/kg/day (day 1-17),

750 mg/kg/day (day 18-24) and 3,750 mg/kg/day (day 25-32). A control group was concurrently fed the same diet without anthracene. The anthracene-treated group had a slightly higher food consumption than in the controls and showed a correspondingly increased gain in weight. Histological examination of the kidneys and the liver did not reveal any significant anthracene-induced changes.

No effect on liver regeneration was observed in partially hepatectomised rats fed anthracene (514 mg/kg bw per day) in the diet for 10 days (Gershbein, 1975).

Other routes

Daily i.p. administration of anthracene (28.5 mg/kg/day; in corn oil) for 14 days to B6C3F1 mice did not significantly affect their immune response as indicated by their antibody-forming cell response to sheep erythrocytes (White et al., 1985).

An old study mentioned in a secondary reference indicates that treatment-related lymphoid effects, including increases in reticulum cells, accumulation of iron, decreased lymphoid cells and dilated lymph sinuses were seen in albino mice receiving weekly subcutaneous injections of a 0.05% colloidal solution of anthracene in gelatine for 40 weeks (Hoch-Ligeti, 1941).

4.1.2.6.2 Studies in humans

No information on the repeated dose toxicity of anthracene in humans is available. It seems likely that the "acute effects" discussed in Section 4.1.2.2.2 refer also to effects seen after repeated human exposure.

4.1.2.6.3 Summary

According to an old and rather poorly described study, administration of anthracene to rats in the diet for up to 550 days, at a daily dose of up to 50 mg/kg, did not reveal any adverse effects. On the other hand, a well-conducted study showed that daily administration of anthracene by gavage to mice for at least 90 days, at doses up to 1,000 mg/kg/day, did not result in any treatment-related effects of toxicological significance (NOEL).

There is lack of information on the effects on animals or humans of anthracene after inhalation is available. However, in view of the absence of any toxic effects after a 90-day oral exposure study, the generally low toxicity of anthracene, and the low levels of human inhalation exposure (see Section 4.1.3, Risk Characterisation), it is not considered that an inhalation study is justified.

4.1.2.7 Genetic toxicity

The genetic toxicity of anthracene has been examined in a large number of studies, too numerous to discuss individually. In the following discussion, only representative negative studies and rare studies reporting positive results are discussed, where appropriate, and the overall conclusions presented.

As is the case with other studies with anthracene, the use of adequate protection from UV radiation is not always described in the reports examined. No reports specifically intended to assess the genotoxicity of photodegradation products of anthracene have been found. However, as has already been mentioned (see Section 4.1.2.5.1), in the presence of UV radiation

anthracene can form DNA adducts *in vitro* as well as in monkey kidney and human skin epithelial cells in culture (Sinha and Chignell, 1983; Blackburn et al., 1973; Blackburn and Tausig, 1975). On the other hand, no results on the induction of anthracene-related DNA damage in the presence of UV *in vivo*, or of the induction of genetic end-points other than DNA adducts (e.g. gene or chromosome mutations) in cell cultures have been reported.

4.1.2.7.1 *In vitro* studies

Studies in bacteria and lower eukaryotes

Anthracene has been tested for the induction of genotoxicity (DNA damage and mutations) in a large number of bacterial systems, including Escherichia coli, Salmonella typhimurium and Bacillus subtilis, with and without metabolic activation, giving negative results in the great majority of cases. Results on its testing for mutagenicity in Salmonella typhimurium has been described in tens of reports, involving use of strains TA1535, TA1536, TA1537, TA1538, TA97, TA98 and TA100, without or with S9 metabolic systems from the liver of rats and guinea pigs subjected to various enzyme-inducing pre-treatments (no reports of genotoxicity testing using metabolic systems other than S9 have been traced). Almost invariably, clearly negative results were reported in there studies. For example, it was tested in Salmonella typhimurium TA1535, TA1538, TA98 and TA100 with S9 extract from Arochlor-induced rat liver, with negative results (Purchase et al., 1976). Rare reports of positive mutagenic activity in Salmonella typhimurium were based on marginal activity observed in TA97 or TA100 with metabolic activation (less than 3fold increase over spontaneous mutation frequency – the use of UV protection was not mentioned) (Sakai et al., 1985; Carver et al., 1986).

Anthracene was also negative in a large number of tests for the induction of gene mutations or cytogenetic damage in Saccharomyces cerevisiae and Saccharomyces pombe.

Studies in mammalian cells

Anthracene did not induce DNA damage in human peripheral blood leukocytes *in vitro*, without metabolic activation. Also, it failed in a large number of studies to induce unscheduled DNA synthesis in primary rat hepatocytes (Williams, 1988), Chinese hamster ovary cells, human HeLa cells with metabolic activation (Martin et al., 1978), while it gave a marginally positive, non-dose-related response in primary human skin epithelial cells (the use of UV protection was not mentioned) (Lake at al., 1978).

It was negative for the induction of gene mutations in a large number of studies, including studies using Chinese hamster ovary cells and human lymphoblast cells. In mutagenesis studies with mouse lymphoma L5178/TK+/-cells it was negative in most cases. However, in one study it gave weak mutagenicity when tested (with protection from UV) in the presence of S9 extract from C57Bl/6J mouse liver (but not with 6 other types of S9 extract) (Amacher and Turner, 1980).

Anthracene has been tested for the induction of sister chromatid exchanges in Chinese hamster ovary cells with metabolic activation, in a rat liver epithelial cell line and in a combined *in vitro*/*in vivo* test using Chinese hamster V79 cells implanted into mice. All studies reported negative results except for one which was marginally positive (Perry and Thomson, 1981).

Anthracene was negative for the induction of chromosomal aberrations in one study with Chinese hamster ovary cells and one with rat liver RLL cells. However, it was reported to give a

positive result using Chinese hamster ovary cells with (but not without) metabolic activation when tested at concentrations up to 0.02 mg/ml (Sofuni et al., 1985).

In tests for the induction of cell transformation *in vitro*, sometimes followed by examination of the *in vivo* growth potential of the transformed foci obtained, anthracene was reported to be negative in over one dozen studies. For example, it was clearly negative for the induction of morphologically transformed foci of cells capable of forming a tumour after s.c. injection into syngeneic animals when tested up to a concentration of 10 µg/ml in mouse BALB/3T3 cells (DiPaolo et al., 1972), and in the induction of transformed foci in Syrian hamster embryo cells after exposure for 7 days at 50 µg/ml (LeBoeuf et al., 1996). However, it was reported positive in a study with Syrian hamster kidney cells BHK 21 C13/HRC 1, with and without metabolic activation (the use of UV protection was not mentioned) (Purchase et al., 1976). It was also reported to be positive in an assay measuring the acquisition of attachment independence of Rauscher leukemia virus-infected rat embryo cells (2FR450) (Traul et al., 1981). Finally, in a test involving treatment with anthracene (at concentration 0.001-50 µg/ml) of Fischer rat embryonal cell line F1706 P88, infected with Rauscher leukemia virus, followed by inoculation of transformed cells into newborn Fischer rats and analysis of tumour induction, an ambiguous result was obtained (marginally positive in one experiment but negative in a subsequent one). The use of UV protection was not mentioned (Freeman et al., 1973)

4.1.2.7.2 *In vivo* studies

Studies in animals

Anthracene did not induce sex-linked recessive lethal mutations in Drosophila melanogaster. However, it tested positive in the wing somatic mutation and recombination test (SMART), causing the appearance of small single spots in a high bioactivation (but not in the normal) strain of insects (no information on the use of light protection is given) (Delgado-Rodriguez et al., 1995).

All *in vivo* tests for genotoxicity of anthracene in mammals have given negative results. It has been tested with negative results for the induction of unscheduled DNA synthesis in various tissues (including liver, kidney and testes) of male C57Bl mice after i.p. doses up to 125 mg/kg (Friedman and Straub, 1976). It was also negative for the induction of mouse micronuclei in bone marrow 96 hours after a single dose of 344 mg/kg (Salamone, 1981) as well in peripheral blood erythrocytes 24 hours after 4 daily administrations of up to 2,500 mg/kg/day (Oshiro et al., 1992). Administration of 2 i.p. doses of 450 mg/kg to mice and Chinese hamsters gave no increase in the frequency of sister-chromatic exchanges and chromosome aberrations in bone marrow cells (Roszinsky-Koecher et al., 1979).

Anthracene was also negative for the induction of transformed cell colonies in an *in vivo-in vitro* test system involving i.p. administration (10-30 mg/kg) to pregnant Syrian golden hamsters on days 10-11 of gestation, excision of embryos 2-3 days later and *in vitro* cultivation of embryo cells (DiPaolo et al., 1973). A number of carcinogenic compounds tested in parallel were positive in this system.

No DNA adducts could be detected in mouse skin, using the sensitive ^{32}P-postlabelling assay, after 4 applications (at 0, 6, 30 and 54 hours) of 0.21 mg anthracene (dissolved in acetone) to the skin of Balb/c mice, followed by sacrifice 24 hours later (no information on the use of light protection is given) (Reddy et al., 1984).

It is recalled that one study, discussed in Section 4.1.2.1.1, reported detecting the formation of 9,10-dimethylanthracene, a weakly genotoxic (Fujikawa et al., 1993; Spano et al., 2001) and carcinogenic (LaVoie et al., 1985) compound, in rat skin in contact with anthracene after subcutaneous application, as well as after *in vitro* incubation of anthracene with an extract of rat liver fortified with the methylating agent S-adenosylmethionine (Myers et al., 1988).

Studies in humans

No data on the genotoxicity of anthracene in humans exist.

4.1.2.7.3 Summary

The genotoxicity of anthracene has been examined in a large number of studies. The great majority of these studies, which involved examination of its ability to induce DNA damage, point mutations, chromosome aberrations, sister chromatid exchanges and morphological cell transformation, using systems of varying complexity ranging from bacteria *in vitro*, through host-mediated bacterial studies, lower eukaryotes, and mammalian cells *in vitro*, to *in vivo* rodent studies, have negative results. Many of the genotoxicity tests involving anthracene were conducted in the context of inter-laboratory and assay-comparison studies, based on common, well defined protocols (e.g. Bridges et al., 1981; Brookes and Preston, 1981) and, for this reason, the trend towards negative outcomes must be considered valid. Occasional reports of marginally or inconsistent positive responses do not seem sufficient to overturn the overall conclusion that anthracene is not genotoxic. Furthermore, the consistent absence of any genotoxic activity in a range of *in vivo* tests strongly suggests that the formation of the weakly genotoxic 9,10-dimethylanthracene as a metabolite of anthracene probably does not have any significant biological consequences in terms of genotoxicity.

Limited studies indicate that, in the presence of UV light, anthracene can bind to DNA, but no *in vitro* or *in vivo* biological consequences of such binding have been demonstrated.

4.1.2.8 Carcinogenicity

4.1.2.8.1 Studies in animals

Anthracene has been examined in a large number of studies of varying design and validity. These studies have been assessed in detail by IARC (1983b). The overall conclusion of IARC was that these data provide no evidence that anthracene is carcinogenic to experimental animals and that anthracene cannot be classified as to its carcinogenicity in humans.

Inhalation

No information on the inhalation carcinogenicity of anthracene was found.

Oral

A group of 28 BDI or BDIII rats of unspecified sex, 14 weeks old, was administered in its diet initially 5 mg and later 15 mg anthracene “without impurities” per rat on 6 days per week for 78 weeks, so that the total dose received by each rat was 4.5 g (Schmahl, 1955). No control group was used. The animals were observed for life, and had a mean survival time of 700 days. One

animal developed a liver sarcoma after 18 months and another had an adenocarcinoma of the uterus after 25 months. None of these tumours was attributed by the investigators to anthracene. The absence of controls and the relatively low doses used in this old study mean that it is not adequate for the assessment of anthracene carcinogenicity.

Dermal

Anthracene has been tested for carcinogenicity by skin application in a number of studies using different types of protocols aimed at the detection of full carcinogenic potential, tumour initiating activity or photocarcinogenicity. Many of these studies are old, of poor quality and/or poorly reported.

In an early study, 100 mice of unspecified strain, sex or age had a 40% suspension of anthracene in lanolin painted on their skin (Kennaway, 1924a). No details of the purity, dose or number of applications were given. No skin tumours were found among 45 animals which survived more than 6 months.

Skin application (of unspecified number or dose) of anthracene in benzene or sesame oil on the skin of 41 albino mice of unspecified strain, sex or age did not produce any skin tumours (Pollia, 1939). Tumours were produced in a positive control group treated with 1,2,5,6-dibenzanthracene in the same experiment.

Five female Swiss mice of unspecified age received skin applications of a 10% solution of anthracene in acetone (the purity and dose of anthracene were not reported) 3 time per week for life (Wynder and Hoffman, 1959). No skin tumours were observed in any of the animals, all of whom died within 10-20 months of the start of the experiment. Benzo[a]pyrene, employed as a positive control in the same study, produced a high yield of skin papillomas and carcinomas.

The tumour initiating activity of anthracene was examined by painting on the skin of 20 "S" mice, of unspecified sex or age, 0.3 ml 0.5% anthracene (unspecified purity) in acetone twice with an interval of 30 minutes, 3 times per week, so that each animals received a total of 30 mg anthracene (Salaman and Roe, 1956). This was followed by 18 weekly skin applications of the tumour promoter croton oil in acetone, beginning 25 days after the first anthracene application, as follows: one 0.3 ml application of 0.17% croton oil, two 0.3 ml applications of 0.085% croton oil and a further 15 0.3 ml applications of 0.17% croton oil. Control animals received only the croton oil treatments. All surviving animals (17/20 anthracene-treated and 19/20 controls) were killed after the end of the croton oil treatment. No skin tumour induction by anthracene was found, as 3 of anthracene-treated animals exhibited a total of 4 skin papillomas, while among the control animals 4 had a total of 4 skin papillomas.

In another initiation-promotion study, 30 female CD-1 mice, 8 weeks old, received a single skin application of 1,782 μg anthracene (chromatographically purified) in benzene, followed 1 week later by skin application of the tumour promoter TPA (probably 5 μg and not 5 μmol as indicated in the relevant publication) 2 times per week for 34 weeks (Scribner, 1973). A control group received only TPA. At the end of treatment, 4 out of the 28 surviving anthracene-treated animals had one skin papilloma each, as did 1 of the 30 surviving controls. The author concludes that this indicates "borderline initiating activity", but no statistical analysis is included.

Anthracene has also been tested in a number of studies for skin carcinogenicity in combination with UV or visible radiation. In one such study (Miescher, 1942), 2 groups of 44 mice of unspecified strain, sex or age, received skin applications (on the back of the ears) of 5% anthracene (of unspecified purity and dose) in petroleum jelly-olive oil 3 times per week for life. One of the groups also received UV radiation (wavelength > 320 nm) for 40 or 60 min, 2 hours

after each skin application. A third group of 100 mice was treated in a similar way with anthracene but received UV irradiation for 90 min. In all groups most animals died within 7-11 months. While the group receiving the combined anthracene and UV treatment showed "broadness of the epidermis", but no skin papillomas or carcinomas were observed in either group.

In another photocarcinogenesis study (Heller, 1950), white mice were treated on the skin with 10% anthracene (of unspecified purity) in petroleum jelly-olive oil, followed by irradiation for 5 hours with UV light (wavelength 405-320 nm,) alone or in combination with visible light. No information was given on the dose of anthracene and the duration of treatment. A high incidence of skin tumours (including carcinomas) were observed within 5-8 weeks in the group receiving the combined treatment of anthracene plus UV and visible radiation, but none in those receiving either anthracene or UV radiation alone or UV plus visible radiation alone. The unusually short latency time and the poor reporting make it difficult to draw reliable conclusions from this study.

In a relatively recent, well designed and reported photocarcinogenicity study (Forbes, 1976), a group of 24 outbred Skh:hairless-1 mice (mixed males and females), 3 weeks old, were administered skin applications of 4 μg anthracene (of unspecified purity) dissolved in 40 μl methanol once per day, 5 days per week, for 38 weeks, followed after each application by 2 hours of UV irradiation (300 J/m^2, wavelength > 290 nm). Each test animal received a total of 0.76 mg anthracene. Similar groups of negative and positive controls received only methanol or 4 μg 8-methoxypsoralen, respectively, as well as the UV radiation. After 38 weeks, 20, 19 and 16 animals survived from the vehicle control, anthracene-treated and positive control groups, respectively. The times to 50% tumour incidence were 27.2 and 28.2 weeks for the negative controls and the anthracene-treated group, respectively, the difference not being statistically significant. In contrast, the time to 50% tumour incidence for the group of positive controls was significantly shorted at 20.0 weeks. The tumours observed in all groups were mainly squamous-cell carcinomas.

Subcutaneous

In an old study with a small number of animals, 10 rats (unspecified strain, sex, age and body weight) were given weekly s.c injections of 2 ml of a 0.05% suspension of anthracene (unspecified purity) in water for life (Boyland and Burrows, 1935). The maximum total dose administered was 103 mg per animal. Mortality rates were 0/10 after 6 months, 7/10 after 12 months and 8/10 after 18 months. No subcutaneous sarcomas were reported. Groups of positive controls treated in a similar way with 1,2,5,6-dibenzanthracene developed s.c. sarcomas in at least 6/10 and 9/18 rats.

In a small study of short duration, 5 Wistar rats (unspecified sex, age 6-8 weeks) were given s.c injections of 0.5 ml of a solution of anthracene (unspecified purity) in sesame oil (5 mg anthracene/injection) once per week (Pollia, 1941). At 10 months, 4 of the animals were killed. No tumours were reported, in contrast to the positive control groups of animals treated with 1,2,5,6-dibenzanthracene, where s.c tumours were seen.

To a group of 10 BDI and BDII rats (unspecified sex), 14 weeks old, s.c. injections of 1 ml of 2% highly purified anthracene in oil (unspecified type) were administered (total dose 660 mg per animal) once a week for 33 weeks, and the animals observed for life (Schmahl, 1955). Fibrosarcomas (partly with sarcomatous areas) at the site of injection were observed in 5/9 animals, with a mean latency of 26 months. No concurrent vehicle control was used. However, a group of rats similarly treated with naphthalene dissolved in oil (of unspecified type) did not develop any tumours.

Anthracene (8 mg per mouse, dissolved in refined sunflower oil) was given s.c. daily or as a single intragastric dose to BALB/C, C3H/A and C57BlxCBAF1 hybrid strains during the last week of gestation (Shabad et al., 1972). Fragments of embryonic kidney were cultured. In contrast to the control cultures, cultures from the anthracene-treated animals showed an increase in survival and hyperplastic epithelial changes. The changes seen were qualitatively similar but less strong that those produced by treatment with the carcinogen 7,12-dimethylbenz[a]anthracene. While the observed changes were considered by the authors as indicative of pre-malignancy, the lack of a consistent correlation between the effects of known carcinogens and non-carcinogenic analogues and of consistent dose-response relationships makes the significance of these effects difficult to assess.

In the assessment of carcinogenicity of anthracene after subcutaneous administration, it is relevant to recall (see Section 4.1.2.1.1) that one metabolism study demonstrated the formation of 9,10-dimethylanthracene, a weak carcinogen, after subcutaneous administration of anthracene to rats as well as during *in vitro* metabolism with a rat liver extract fortified with S-adenosylmethionine (Myers et al., 1988).

Intraperitoneal

To a group of 10 BDI and BDII rats (unspecified sex), 14 weeks old, i.p. injections of 1 ml of 2% highly purified anthracene in oil were administered (total dose 660 mg per animal) once a week for 33 weeks, and the animals observed for life, the mean survival time being over 2 years. One rat developed a spindle-cell sarcoma of the abdominal cavity. No concurrent vehicle control was used (Schmahl, 1955).

Implantation

Sixty female Osborne-Mendel rats, 3-6 months old, were given 1 pulmonary implant of 0.05 ml of 0.5 mg anthracene (unspecified purity) in 1:1 beeswax:tricaprylin. No lung tumours were observed when "nearly half" of the animals were killed after 1 year. Lung epidermoid carcinomas were observed in groups of rats treated under similar conditions with 3-methylcholanthrene (Stanton et al., 1972).

In a study that was too small to yield useful results, 9 rabbits of various breeds, ages and weights (unspecified strain, sex, age and bodyweight received an implant of a pellet of 4-20 mg anthracene (purity unspecified) into the cerebrum, cerebellum or eye. Animals died or were killed 20-54 weeks after implantation. No gliomas were found (Russel, 1947).

4.1.2.8.2 Studies in humans

Among workers handling crude anthracene (40%, no other information on composition), 3 were reported to have developed epitheliomas of the hand, cheek and wrist, respectively (Kennaway, 1924a,b). Two of these workers had been exposed for 30 and 32 years, respectively. Workers in the same factory who had contact only with purified anthracene did not develop tumours or other skin lesions.

No other information on the carcinogenicity of anthracene in humans was found.

4.1.2.8.3 Summary

Anthracene has been tested for complete carcinogenicity, tumour initiating activity and photocarcinogenicity (in combination with UV light) by various routes of administration (oral, dermal, subcutaneous, intraperitoneal, pulmonary implantation) in a large number of studies using various strains of rats and mice. Many of these studies were carried out many years ago and were of small size or poor quality. This is particularly true of the skin carcinogenicity studies other than those looking for photocarcinogenicity.

All the mouse skin application studies gave negative results for complete carcinogenicity and for tumour-initiating activity. Of 3 studies of photo-carcinogenicity, 2 (including the most recent and best conducted study) did not yield evidence of carcinogenicity, while the third, positive study was poorly reported and exhibited an unusually short tumour induction latency period.

Oral, subcutaneous and intrapulmonary administration to rats gave negative results, except for one subcutaneous injection study which showed induction of fibrosarcomas at the sight of injection. It is noted, in this context, that a metabolism study reported the formation of 9,10-dimethylanthracene, a weak carcinogen, after subcutaneous application of anthracene to rats or after *in vitro* metabolism in the presence of added S-adenosylmethionine. These observations would be compatible with a potential of anthracene to cause local sarcomas after sub-cutaneous administration. However, the consistent absence of any genotoxic activity in a range of *in vivo* tests strongly suggests that the production of this metabolite does not have any significant biological consequences in terms of genotoxicity and carcinogenicity.

Despite the fact that most of the carcinogenicity studies described above were not up to present day standards, overall, the available data do not provide evidence of carcinogenicity for anthracene alone or in combination with light. This conclusion is further supported by the consistent absence of evidence of genotoxic activity of anthracene in *in vitro* and *in vivo* test systems (see section 4.1.2.7 - Genetic Toxicity).

Having in mind the negative outcome of the available carcinogenicity studies, the absence of genotoxicity, and the relatively low levels of human inhalation exposure (see Section 4.1.3, Risk Characterisation), it is not considered that a long-term inhalation study is justified.

4.1.2.9 Reproductive and developmental toxicity

4.1.2.9.1 Studies in animals

Few studies on the reproductive and developmental effects of PAH have been reported. However, studies with PAH other than anthracene demonstrate that PAH are able to cross the placenta, and benzo[a]pyrene is embryotoxic and teratogenic and causes reduced fertility in mice (IPCS, 1998). These effects were partly dependent on the genetically determined modulation (inducibility) by PAH of PAH-metabolising enzymes in the mother and the fetus, mediated by interaction with the Ah receptor. In this context it is useful to note that anthracene does not bind to the Ah receptor (Machala et al., 2001).

No formal tests of the reproductive and developmental effects of anthracene in animals appear to have been conducted.

In the context of the 90-day oral exposure study already described (see Section 4.1.2.6.1), the weights and histology of the testes and ovaries, as well as clinical chemistry and haematology

values, were examined after treatment of CD-1 mice with daily doses of 0, 250, 500 and 1,000 mg/kg/day for 90 days (US EPA, 1989). Although a statistically significant increase in the mean ovary weight and the ovary-to-terminal body weight ratio of animals fed 500 mg/kg/day (but not the other two treated groups) was noted, this was considered incidental and of no toxicological relevance. The clinical chemistry and hematology analyses did not include any parameters which could be of use in the further assessment of this finding, the only changes observed being an increase in total protein in all male treated groups, and decreases in serum globulin and segmented neutrophils in the group of males treated with the low dose. All these changes were also judged to be incidental and of no toxicological relevance. No histological changes in any organs, including the testes and the ovaries, were observed.

In the context of a transplacental carcinogenicity study already described (see Section 4.1.2.8.1), anthracene (8 mg per mouse, dissolved in refined sunflower oil) was given s.c. daily or as a single intragastric dose to BALB/C, C3H/A and C57BlxCBAF1 hybrid strains during the last week of gestation (no information on maternal toxicity is given) (Shabad et al., 1972)**.** Fragments of embryonic kidney from the embryos were cultured. In contrast to the control cultures, cultures from the anthracene-treated animals showed an increase in survival and hyperplastic epithelial changes. The changes seen were qualitatively similar but less strong that those produced by treatment with the carcinogen 7,12-dimethylbenz[a]anthracene. While the observed changes were considered by the authors as indicative of pre-malignancy, the lack of a consistent correlation between the effects of known carcinogens and non-carcinogenic analogues, and of consistent dose-response relationships, makes the significance of these effects difficult to assess. In a similar study, the transplacental effect of anthracene in mice was examined by oral administration of 8 mg of the substance per animal, followed by organ cultures of embryonic kidneys (Sorokina, 1971). Hyperplasia of individual tubules and outgrowths of atypical epithelial structures were observed in 15.6% of the tissues from animals given anthracene, compared to 1.8% seen in tissues from control animals.

In the context of a study of the effects of components of cigarette smoke on the metabolic activity of the placenta, it was shown that oral treatment of 18-day pregnant rats (unspecified strain or age) with 40 mg/kg anthracene resulted 24 hours later in a greater-than-6fold increase in the levels of benzo[a]pyrene hydroxylase activity in the placenta (Welch et al., 1969). However, no change in the levels of the same enzyme, or of 3-methyl-4-monomethylaminoazobenzene demethylase, was observed in the liver of F1 Sprague-Dawley rats after intragastric administration of 60 mg/kg anthracene (dissolved in DMSO) to pregnant animals (age unspecified) on the 19th day of gestation (Welch et al., 1972). These data cannot be utilised for the assessment of the reproductive or developmental toxicity of anthracene.

4.1.2.9.2 Studies in humans

No information on the reproductive and developmental effects of anthracene in humans was found.

4.1.2.9.3 Summary

Anthracene did not cause any detectable toxic effects on the reproductive system of mice during a 90-day feeding study On the other hand, limited studies suggest that, when administered to pregnant mice or rats, anthracene may possibly exert toxic effects on the developing embryo, including the induction of morphological changes and the upregulation of PAH-metabolising

enzymes. However, the poor quality of the data and the absence of any quantitative information do not permit the derivation firm qualitative or dose-response-related conclusions.

In view of the very limited data on reproductive toxicity, the lack of any studies of the ability of anthracene to affect pregnancy outcome or the development of mammalian organisms, the limited evidence of induction in rat embryos of toxic effects in an *in vivo*/*in vitro* study, and the established ability of other members of the PAH family to cross the placenta and cause embryotoxic and teratogenic effects (IPCS, 1998), it is concluded that further data on the reproductive and developmental toxicity of anthracene are needed. In evaluating the importance of the current absence of such data, one should take into account the fact that, as already indicated at the beginning of Section 4.1.2.9.1, the developmental toxicity of PAHs is at least partly dependent on binding to the Ah receptor, and that anthracene does not show such binding to any significant extent.

4.1.3 Risk characterisation

4.1.3.1 General aspects

Human exposure to anthracene can occur during the production and packaging of the pure compound and during the use of anthracene in the manufacture of pyrotechnics. Until recently, exposure could also take place in the context of the use of anthracene for the production of anthracene-9-aldehyde, a process which has now ceased to operate in Europe. Exposure can also occur during additional activities and processes which do not involve the production or use of anthracene, such as the distillation of coal tar for purposes other than the production of anthracene, the production and use of creosote, the production and use of coal tar- or creosote-containing products, the combustion of organic materials and certain industrial processes.

4.1.3.1.1 Exposure

In Europe about 100 workers appear to be involved in the distillation of coal tar to give various products, including light anthracene oil from which anthracene is produced. Anthracene production from light anthracene oil takes place in one plant in Europe, where 12 workers, all males, are involved. Until recently, use of anthracene in chemical synthesis took place at 1 plant in Europe, where 10-15 workers were involved in relevant activities. This production has now ceased.

Information on human exposure associated with the production and uses of anthracene is extremely limited and in most cases does not permit the use of measured data for risk characterisation. Consequently most exposure data employed for this purpose in the present Report have been derived using the EASE modelling programme. Although information for the derivation of specific exposure scenarios for the different occupation- or consumer-related activities is also limited, reasonable worst-case assumptions have been made and used to model the corresponding exposures (see Section 4.1.1 and its sub-sections). The quantitative conclusions of this exposure assessment are summarised in **Table 4.2** and **Table 4.3**.

4.1.3.1.2 Toxicity

Absorption and metabolism

Human exposure to anthracene occurs mainly via the dermal or inhalation routes, and to a limited degree via the oral route (the latter arising mostly through the ingestion of dust cleared from the nasopharyngeal and the tracheobronchial compartments by the mucociliary mechanism). While some animal toxicity data after oral or dermal administration are available, practically no inhalation toxicity data exist. The scarcity of toxicological information is even more severe when it comes to human data.

a) Absorption after inhalation

A short reference in a secondary source to reduced body weight and changes in blood biochemistry after chronic inhalation of rats to an anthracene aerosol, is impossible to assess or utilise further. However, the possibility that anthracene undergoes significant systemic absorption via the lung is supported by the finding that 99.7% of a dose of dissolved anthracene given to rats intratracheally disappears rapidly from the lung. Thus, although it is likely that absorption of particulate anthracene via the lung will be less than 100%, in the absence of other information, complete absorption of inhaled anthracene (vapour, aerosol, or particulate of respirable size) will be assumed.

b) Absorption after dermal exposure

Studies in humans and experimental animals indicate that anthracene is absorbed from the skin and enters systemic circulation, but do not permit the estimation of the rate or degree of systemic absorption in humans. Studies in rodents suggest that dermally applied anthracene (applied in solution form) is absorbed at a rate of the order of 0.3-1% per hour during the first 12-24 hours, the rate thereafter decreasing, thus resulting in an overall absorption of approximately 50% over a period of 5-6 days.

Human occupational exposure via the skin is expected to involve anthracene in dissolved form (e.g. coal tar, anthracene oil) as well as in particulate form (e.g. during packaging or handling of solid anthracene). It is reasonable to expect that systemic absorption via the skin of particulate anthracene will be lower than that of dissolved anthracene. In the absence of other information, the figure of 10% per day (i.e. per 24 hours) will be taken as a conservative estimate of the rate of absorption after dermal exposure to anthracene solution, and 2% per day after dermal exposure to particulate anthracene. When estimating systemic absorption in workers, it is assumed that the time during which the substance remains on the skin is that of the working shift (8 hours), after which the material remaining on the skin surface is removed by washing, However, in view of the lipophilicity of anthracene ($\log P_{ow}$ = 4.54), material passing through the epidermis it is likely to accumulate in the stratum corneum and form a reservoir from which it will continue to diffuse into the systemic circulation after the remaining anthracene has been washed from the skin surface. Therefore systemic uptake will continue for longer than the 8 hour exposure period, and a 24 hour period is considered as more appropriate for estimating the dose absorbed as a result of exposure during an 8-hour working shift.

c) Absorption after oral exposure

There are no data on the systemic absorption of anthracene after oral ingestion in humans, and the corresponding studies in animals are limited and of poor quality. A single, old study suggests that systemic absorption in rats following oral intake of anthracene mixed with the diet does not

exceed 50%. In the absence of other information, this figure will adopted for systemic absorption after oral ingestion of anthracene by humans.

The values of systemic absorption which will be adopted for the purpose of estimating the absorbed body burden after the various exposures are summarised in **Table 4.5**.

Table 4.5 Systemic absorption in humans after different routes of anthracene exposure

Exposure route	% absorption
Inhalation (all forms)	100%
Dermal: dissolved anthracene particulate	10% per 24 hours 2% per 24 hours
Oral	50%

Metabolism

Data are available on the metabolism of anthracene *in vitro* and in rats *in vivo*, suggesting that the major route followed is based on 1,2-epoxidation followed by epoxide hydrolysis and conjugation of the resulting dihydrodiol. There is also some evidence that, in the rat, methylated metabolites (including the weakly tumourigenic 9,10-dimethylanthracene) may also be formed by a different metabolic route. Information on anthracene metabolites other than those found in the urine is almost completely lacking. Given that significant metabolism of PAH occurs in the gastrointestinal tract, the absence of data on bile and feces metabolites is notable.

Information regarding toxicokinetics and metabolism in humans is completely lacking. However, the pattern of anthracene metabolism in the rat broadly follows that of other polycyclic aromatic hydrocarbons, for which human metabolism is known to be qualitatively similar to that of the rat (IPCS, 1998). This suggests that, on a qualitative level, human metabolism of anthracene may also be comparable to that seen in the rat. On the other hand, it is clear that no evaluation of the relative quantitative importance of competing metabolic pathways in humans can be made. In the absence of other information, it will be assumed that the metabolic pathways of anthracene in humans are not different from those observed in the experimental animal systems investigated.

Toxicological end-points and critical values

Systemic toxicity after oral, inhalation and dermal exposure

Anthracene exhibits low acute systemic toxicity in animals after oral exposure, with LD_{50} of 8.12 g/kg in the rat. Repeated dose systemic toxicity data from rats (life-time exposure) and mice (90-day exposure) also suggest low toxic potential by the oral route. No specific targets are revealed by these studies, and a small increase in ovary weight in mice receiving 500 mg/kg/day for 90 days, lacking dose-dependence, is not considered to have toxicological significance. Thus values of oral NOEL's of 50 mg/kg (rat; highest dose tested) and 1,000 mg/kg (mouse) have been derived. Although the latter value is derived from 90-day, rather than life-time exposure, it is considered more reliable as it was based on a more recent and better conducted study and for this reason it will be adopted for risk assessment.

With 50% systemic absorption, an oral NOEL of 1,000 mg/kg corresponds to a daily body burden of 500 mg/kg/day. As no data suitable for estimating limit values for systemic toxicity after inhalation or dermal exposure are available, in subsequent sections this value of the body burden will be employed as a limit value corresponding to a NOEL for systemic exposure, and

compared with the body burdens arising from exposure from other routes in order to derive the corresponding MOS values.

Skin irritation and sensitisation after dermal exposure and eye irritation

Limited references to skin irritating activity of anthracene in humans, usually in the context of occupational medicine reports, are impossible to evaluate or utilise further. On the other hand, in view of the strong phototoxic potential of anthracene under normal daily conditions, any limit values adopted for this endpoint are likely to provide protection from any dermal toxicity in the absence of UV light.

Anthracene was negative in a test for eye irritation that closely resembles that of Annex V of Dir. 92/69/EEC. Therefore it is considered that all exposures to anthracene examined do not raise concern over the induction of eye irritation. **Conclusion (ii)**.

Phototoxicity

In contrast to the situation regarding the ability of anthracene to induce irritation or sensitisation in the absence of light, extensive studies in animals and human volunteers demonstrate its potential to induce, in combination with UV radiation, skin irritation, including immediate and delayed erythema as well as weal-and-flare reaction. Such studies, are in agreement with occupational medicine reports of the occurrence of photodermatitis in workers involved in handling tar and other petroleum-derived products.

No formal *in vivo* test for phototoxicity is foreseen under Directive 67/548/EEC. However, the data of Kaidbey and Nonaka (1984) clearly demonstrate induction of phototoxicity in humans after a single skin application of 25 μg of dissolved anthracene per cm^2 of skin in combination with a minimum of 1 kJ/m^2 of UVA radiation. Although the derivation of a true LOAEL or NOAEL would require extensive data obtained with varying doses of both anthracene and irradiation, the outcome of the abovementioned study, in combination with the ease with which sufficient UVA energy on eliciting phototoxicity can be received by a person exposed to moderate sunlight (a few seconds to minutes), justifies consideration of classification anthracene as an irritant, with a practical LOAEL of 25 $\mu g/cm^2$ (for dissolved anthracene). This value, being derived from a study which utilised only a single anthracene dose level, provides a weak basis from which to extrapolate to a NAEL. Indeed, the possibility that effects may occur at levels substantially lower than 25 $\mu g/cm^2$ finds support in the results of a well reported study in guinea pigs, which indicates that a much lower dose (140 ng/cm^2), in combination with 100 kJ/m^2, can still cause skin irritation, while no effects were observed at 14 ng/cm^2. As no information is available on the relative sensitivities of humans and guinea pigs, the human as well as animal limit values will be considered for the calculation of MOS.

Genotoxicity, carcinogenicity

Although anthracene belongs to the category of polycyclic aromatic hydrocarbons, which includes a large number of well known genotoxic and carcinogenic members, it appears to lack such activity. It has been tested for genotoxicity in a large number of well-validated assays, involving systems ranging from bacteria to whole animals and end-points ranging from DNA damage to gene mutations and clastogenicity. Many of the tests were conducted in the context of multi-laboratory trials, which were based on strictly defined methodologies and must be considered reliable. Although occasional positive or inconclusive results were obtained, the great majority yielded negative results, supporting an overall conclusion that anthracene is not genotoxic. The absence of explicit clarification regarding the use or not of protection against

UV-induced photodegradation in many of the reported genotoxicity studies is not sufficient to overturn this conclusion.

Anthracene has been examined for carcinogenicity in rats, mice and rabbits, using assays designed to test complete carcinogenicity or tumour initiating activity. Many of these studies are old and do not come up to the standards currently considered acceptable. However, when assessed collectively, and taking into account the lack of genotoxic activity, these studies do not provide evidence of anthracene carcinogenicity by any of the exposure routes employed (oral or dermal). Although no inhalation carcinogenicity study has been conducted, the overall balance of available evidence supports the conclusion that anthracene lacks carcinogenic activity by any route. Assays to examine the potential of anthracene to induce skin cancer in combination with UV light (including some relatively recent and well-conducted studies) have also given negative results. Therefore it is considered that all exposures to anthracene examined do not raise concern over the induction of cancer. **Conclusion (ii)**.

Reproductive/developmental toxicity

No Studies in humans on the reproductive or developmental effects of anthracene are available.

Anthracene has not been examined in a formal reproductive toxicity study. However, a 90-day oral toxicity study did not demonstrate any clear toxicological effects on the gonads.

Studies in animals indicate that anthracene can pass the placenta, but no information suitable for the qualitative or quantitative evaluation of reproductive and developmental toxicity of anthracene is available. The limited evidence from an *in vivo* treatment/*in vitro* organ cultures study, while suggesting a possible embryotoxic potential, cannot be utilised to assess the potential of anthracene to exert developmental toxicity. In view of these observations and having in mind the established ability of other members of the PAH family to cross the placenta and cause embryotoxic and teratogenic effects, the lack of adequate information on the developmental toxicity of anthracene constitutes a hurdle in the risk assessment and it is concluded that a developmental toxicity study would ideally be needed. On the other hand, the absence of binding by anthracene to the Ah receptor, which appears to at least partly mediate the developmental toxicity of PAHs, suggests that anthracene may possess weak, if any, developmental toxicity.

4.1.3.1.3 Summary of critical values used in risk characterisation

Table 4.6 summarises the important quantitative data regarding the toxic effects of anthracene in animals and humans. It can be seen that most of them are based on studies in animals, whereas limit values obtained from observations in humans are also available only for skin phototoxicity.

Table 4.6 Limit values and conclusions taken forward to risk assessment

End-point	Value	Type of study	Limit value taken forward to risk characterisation
systemic, oral toxicity	NOEL: 1,000 mg/kg/day	mouse 90-day repeated dose	Body burden: 500 mg/kg/day
skin irritation	no information		None (but see phototoxicity)
eye irritation	Negative		No concern
sensitisation	no information		None (but see phototoxicity)
phototoxicity	NOAEL: 14 ng/cm^2	guinea pig	NOAEL: 14 ng/cm^2
	LOAEL: 140 ng/cm^2	guinea pig	LOAEL: 140 ng/cm^2
	LOAEL: 25 µg/cm^2	Human	LOAEL: 25 µg/cm^2
mutagenicity	Negative	*in vitro* and mouse *in vivo*	No concern
carcinogenicity	Negative	rat, mouse	No concern
reproductive toxicity	no direct information		Information needed
	no effects on gonads	Mouse	
developmental toxicity	no information		Information needed

4.1.3.1.4 Minimal MOS

In the present Section, the toxicological limit values adopted in the previous section will be compared with the maximum exposure levels (or, where appropriate, the corresponding body burdens) adopted for the various exposure scenarios previously examined (summarised in **Table 4.2 and Table 4.3**), and MOS values will be calculated. The latter will be assessed by comparison with the minimal MOS values which are considered acceptable, obtained by using the safety factors described in **Table 4.7**.

The uncertainty factors of 10 adopted for inter- and intraspecies variability and 5 adopted for extrapolation from 90-day to chronic exposures are widely used, standard values. For the extrapolation from LOAEL (human) to NAEL for phototoxicity, an uncertainty factor of 100 is considered necessary in view of the fact that the study from which the LOAEL was derived utilised only a single dose level. The overall minimal MOS is obtained by multiplying the relevant uncertainty factors, depending on the type of extrapolation concerned.

Table 4.7 Uncertainty factors employed in the estimation of minimal MOS

Source of uncertainty	Uncertainty factor
Interspecies variability	10
Intraspecies variability	10
Exposure duration (90-day to chronic exposure)	5
LOAEL to NAEL (phototoxicity)	100

4.1.3.2 Workers

Occupational exposure to anthracene is expected to occur during the purification of anthracene oil for the manufacture of anthracene and during anthracene packaging.

4.1.3.2.1 Manufacture of anthracene from anthracene oil

In the context of the assessment of exposure during the manufacture of anthracene from anthracene oil, two stages at which worker exposure can occur are recognised, the first referring to the preparation of crude anthracene and the second referring to the refining of the latter.

Exposure to anthracene during both stages can occur by inhalation and by skin contact during loading and unloading as well as during cleaning and maintenance operations.

Systemic toxicity

Inhalation exposure may involve exposure to anthracene vapour or in particulate form. Assuming that particulate anthracene is in respirable form, an inhalation rate of 10 m^3/shift and 100% systemic absorption, the body burden for workers exposed for 8 h per shift to the airborne concentrations derived from measurement and from modelling shown in **Table 4.3** have been calculated (**Table 4.8**). In the calculations it has been assumed that a worker spends a full shift on only one of the two stages of the process. However, the broadly similar levels of exposure (measured or modelled) expected at the two stages, in combination with the large MOS estimated, indicate that the overall conclusion of the risk characterisation is not dependent on the proportion of the shift time spent on each job.

Dermal exposure may involve anthracene in a dissolved state as well as solid anthracene (during removal of solidified anthracene from pipelines and vessels), and is likely to take place via contact with the hands and forearms (total area = 1,980 cm^2). It is not possible to estimate the proportion (duration or amount) of skin contact with dissolved or solid anthracene. Using the levels of dermal contact predicted by EASE, the resulting body burdens have been calculated assuming 10% absorption per 24 hours for dissolved anthracene. If contact is with particulate anthracene (2% absorption), the body burden and MOS would be 5 fold lower (not shown in **Table 4.8**).

Based on the fact that the limit value of the body burden (corresponding to the NOEL) is derived from the sub-chronic mouse feeding study, a minimal MOS of 500 is adopted. As seen in **Table 4.8**, the estimated MOS values exceed the minimal MOS for inhalation, dermal and combined exposures not only for the measured air concentrations but also for the much higher (and probably substantially exaggerated) ones predicted by EASE. **Conclusion (ii)**.

Skin photoirritation

The dermal exposure levels estimated by EASE for the two stages of the process considered are similar to or approximately 4 times lower than the human LOAEL of 25 μg/cm^2. They are also substantially higher than the animal LOAEL and NOAEL. This suggests that **Conclusion (iii)** applies.

Table 4.8 Risk characterisation for anthracene production

Systemic toxicity							
Inhalation	**Air conc. (µg/m³)**	**Body burden[1] (µg/kg/day)**	**Mean life-time body burden[3] (µg/kg/day)**	**MOS[4]**		**Min. MOS[5]**	**Concl.**
Preparation of crude anthracene	Estimated from Measurement: 5	0.71	0.33	$1.5 \cdot 10^6$		500	ii
	Modelled: 44	6.3	2.9	$1.7 \cdot 10^5$			
Purification	Estimated from Measurement: 7.8	1.1	0.51	$9.8 \cdot 10^5$			
	Modelled: 60	8.6	3.9	$1.3 \cdot 10^5$			
Dermal	**Dermal exposure (µg/cm²/day)**	**body burden[2] (µg/kg/day)**					
Preparation of crude anthracene	Modelled: 6	17.0	7.8	$6.4 \cdot 10^4$		500	ii
Purification	Modelled: 30	84.9	39.0	$1.3 \cdot 10^4$			
Combined							
Preparation of crude anthracene	Inhal^n from measurement	17.7	8.1	$6.2 \cdot 10^4$		500	ii
	Inh. Modelled	23.3	10.7	$4.7 \cdot 10^4$			
Purification	Inhal^n measured	85.6	39.6	$1.3 \cdot 10^4$			
	Inhal^n modelled	93.5	42.9	$1.2 \cdot 10^4$			
Dermal phototoxicity	**Dermal exposure (µg/cm²/day)**			**Limit value**	**MOS**	**Min MOS[6]**	
Preparation of crude anthracene	Modelled: 6	N/A	N/A	Human LOAEL	4	100	iii
				Animal LOAEL	$2 \cdot 10^{-2}$		
				Animal NOAEL	$2 \cdot 10^{-3}$		
Purification	Modelled: 30	N/A	N/A	Human LOAEL	0.8	100	iii
				Animal LOAEL	$5 \cdot 10^{-3}$		
				Animal NOAEL	$5 \cdot 10^{-4}$		

1 Exposure · (inhalation rate 10 m³/8-hour shift) · (100% systemic absorption) / (70 kg bd.wt.)

2 Exposure · (1,980 cm²) · (10% systemic absorption) / (70 kg bd.wt.)

3 Body burden · (5/7 days/week) · (45/70 years)

4 Compared to mouse NOEL body burden (500 mg/kg/day)

5 Interspecies variability · intraspecies variability x subchronic-to-chronic extrapolation

6 LOAEL-to-NAEL extrapolation

4.1.3.2.2 Anthracene packaging

Exposure during the packaging of pure anthracene is expected to occur primarily by skin contact or oral ingestion of airborne, non-respirable particles cleared by the mucociliary system and subsequently ingested. To a small extent it may also occur by inhalation of anthracene vapours, although it is recognised that the value of vapour concentration brought forward from the modelled estimation of exposure (concentration corresponding to saturated vapour pressure at room temperature) is likely to represent a serious overestimation.

Systemic toxicity

The body burdens resulting from the modelled exposures have been calculated using the absorption rates adopted and assuming that the all of the inhaled dust is cleared by the mucociliary system and is eventually ingested. Dermal exposure is expected to involve solid anthracene and is likely to take place via contact with the hands and forearms (total area = 1,980 cm^2). As can be seen in **Table 4.9**, the MOS values calculated for systemic toxicity exceed the minimal MOS for all three routes considered individually or combined. Taking into account that the modelling procedure employed probably leads to significant overestimation of the exposure, it is concluded that **Conclusion (ii)** applies.

Skin photoirritation

The maximal dermal exposure level estimated by EASE (1 mg/cm^2) is significantly higher than the human LOAEL of 25 $\mu g/cm^2$ (MOS = $2.5 \cdot 10^{-2}$), as well as the animal LOAEL and NOAEL, indicating that **Conclusion (iii)** applies.

Table 4.9 Risk characterisation for anthracene packaging

Systemic toxicity						
	Air conc. ($\mu g/m^3$)	**Body burden[1] ($\mu g/kg/day$)**	**Mean life-time body burden[3] ($\mu g/kg/day$)**	**MOS[4]**	**Min. MOS[5]**	**Concl.**
Ingestion of non-respirable dust	5,000	357	164	$3.0 \cdot 10^3$	500	ii
Inhalation of vapour	60	8.6	3.9	$1.3 \cdot 10^5$	500	ii
Dermal	**Dermal exposure ($\mu g/cm^2/day$)**	**Body burden[2] ($\mu g/kg/day$)**				
	1,000	566	260	$1.9 \cdot 10^3$	500	ii
Combined exposure			428	$1.2 \cdot 10^3$	500	ii

Table 4.9 continued overleaf

Table 4.9 continued Risk characterisation for anthracene packaging

dermal phototoxicity	Dermal exposure (µg/cm²/day)			Limit value	MOS	Min. MOS[6]	
Dermal	1,000	N/A	N/A	Human LOAEL	$2.5 \cdot 10^{-2}$	100	iii
				Animal LOAEL	$1.4 \cdot 10^{-4}$	-	
				Animal NOAEL	$1.4 \cdot 10^{-5}$		

1 Exposure · (inhalation rate 10 m³/8 hour shift) · (systemic absorption) / (70 kg bd.wt.); absorption: 50% for ingested dust, 100% for inhaled vapour
2 Exposure · (1,980 cm²) · (2% systemic absorption) / (70 kg bd.wt.)
3 Body burden · (5/7 days/week) · (45/70 years)
4 Compared to mouse NOEL body burden (500 mg/kg/day)
5 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation
6 LOAEL-to-NAEL extrapolation

4.1.3.2.3 Use of anthracene in the manufacture of pyrotechnics

Exposure during the manufacture of pyrotechnics is expected to occur primarily by skin contact or oral ingestion of airborne, non-respirable particles cleared by the mucociliary system and subsequently ingested. To a small extent it may also occur by inhalation of anthracene vapours, although it is recognised that the value of vapour concentration brought forward from the modelled estimation of exposure (concentration corresponding to saturated vapour pressure at room temperature) is likely to represent a serious overestimation.

Systemic toxicity

The body burdens resulting from the modelled exposures have been calculated using the absorption rates adopted and assuming that all of the inhaled dust is cleared by the mucociliary system and is eventually ingested. Dermal exposure is expected to involve solid anthracene and is likely to take place via contact with the hands and forearms (total area = 1,980 cm^2). As can be seen in **Table 4.10**, the MOS values calculated for systemic toxicity exceeds the minimal MOS for all three routes considered individually or combined. Taking into account that the modelling procedure employed probably leads to significant overestimation of the exposure, it is concluded that **Conclusion (ii)** applies.

Skin photoirritation

The maximal dermal exposure level estimated by EASE (1 mg/cm^2) is significantly higher than the human LOAEL of 25 µg/cm^2 (MOS = $2.5 \cdot 10^{-2}$), as well as the animal LOAEL and NOAEL, indicating that **Conclusion (iii)** applies.

Table 4.10 Risk characterisation for manufacture of pyrotechnics

Systemic toxicity							
	Air conc. (µg/m³)	**Body burden[1] (µg/kg/day)**	**Mean life-time body burden[3] (µg/kg/day)**	**MOS[4]**		**Min. MOS[5]**	**Concl.**
ingestion of non-respirable dust	5,000	357	164	$3.0 \cdot 10^3$		500	ii
inhalation of vapour	60	8.6	3.9	$1.3 \cdot 10^5$		500	ii
Dermal	**Dermal exposure (µg/cm²/day)**	**Body burden[2] (µg/kg/day)**					
	1,000	566	260	$1.9 \cdot 10^3$		500	ii
Combined exposure			428	$1.2 \cdot 10^3$		500	ii
Dermal phototoxicity	**Dermal exposure (µg/cm²/day)**			**Limit value**	**MOS**	**Min. MOS[6]**	
Dermal	1,000	N/A	N/A	human LOAEL	$2.5 \cdot 10^{-2}$	100	iii
				animal LOAEL	$1.4 \cdot 10^{-4}$	-	
				animal NOAEL	$1.4 \cdot 10^{-5}$		

1 Exposure x (inhalation rate 10 m³/8 hour shift) x (systemic absorption) / (70 kg bd.wt.); absorption: 50% for ingested dust, 100% for inhaled vapour
2 Exposure x (1,980 cm²) x (2% systemic absorption) / (70 kg bd.wt.)
3 Body burden x (5/7 days/week) x (45/70 years)
4 Compared to mouse NOEL body burden (500 mg/kg/day)
5 Interspecies variability x intraspecies variability x subchronic-to-chronic extrapolation
6 LOAEL-to-NAEL extrapolation

4.1.3.3 Consumers

There is no consumer exposure to anthracene produced as an industrial product or to products containing added anthracene.

4.1.3.4 Exposure of the general population via the environment

Exposure of the general population via the environment is likely to result in a maximal oral intake (via the diet and drinking water) of 143 ng/kg/day and a maximal likely airborne exposure of 9.7 ng/kg/day. These intakes would correspond a total body burden of 81.2 ng/kg/day, leading to a MOS = $6.2 \cdot 10^6$ (compared with a minimal MOS of 500) (**conclusion (ii)**) (**Table 4.11**). The large MOS indicates that this conclusion will not be affected even if the level of exposure is significantly higher.

Table 4.11 Risk characterisation for the general population exposed via the environment

Systemic toxicity				
	Body burden[1] (ng/kg/day)	**MOS[2]**	**Min. MOS[3]**	**Concl.**
Oral intake (ng/kg/day): 143	71.5	$7.0 \cdot 10^6$	500	ii
Inhalation intake (ng/kg/day): 9.7	9.7	$5.2 \cdot 10^7$		ii
Combined exposure	81.2	$6.2 \cdot 10^6$		ii

1 Intake · (50% absorption rate)
2 Intake · (100% absorption rate)
3 Compared to mouse NOEL (500 mg/kg/day)
4 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation

4.1.3.5 Combined exposure

Given the extremely low levels of exposure of the general population via the environment, relative to occupational exposures, and absence of consumer exposure, it was not considered useful to produce a combined exposure assessment.

4.1.3.6 Exposures to anthracene not related to the production and current uses of anthracene

The following discussion on exposures arising from sources NOT related to the production and current use of anthracene does not directly come under the terms of reference of the present Report, and is presented for illustrative purposes. For this reason, formal conclusions are not included in this Section.

4.1.3.6.1 Occupational exposure during use of anthracene during chemical synthesis

Even though the use of anthracene for chemical synthesis appears to have now ceased, it is also discussed for illustrative purposes given its use until very recently.

Exposure during chemical synthesis could occur by inhalation of airborne anthracene vapours as well as by skin contact with dissolved anthracene during loading, sampling and routine cleaning and maintenance operations. It is recognised that the value of the vapour concentration brought forward from the estimation of exposure (concentration corresponding to saturated vapour pressure at room temperature) is likely to represent a serious overestimation.

Systemic toxicity

As can be seen in **Table 4.12**, the body burden resulting from the modelled exposure leads to MOS values greater than 10^4 for systemic toxicity from inhalation and dermal exposure individually and combined.

Skin photoirritation

The maximal dermal exposure level estimated by EASE (100 µg/cm^2) is 4 times higher than the human LOAEL, and also substantially higher than the animal LOAEL and NOEL, indicating concern.

Table 4.12 Risk characterisation for use of anthracene in chemical synthesis

Systemic toxicity					
	Air conc. (µg/m^3)	**Body burden[1] (µg/kg/day)**	**Mean life-time body burden[3] (µg/kg/day)**	**MOS[4]**	**Min. MOS[5]**
Vapour	60	8.6	3.9	$1.3 \cdot 10^5$	500
Dermal	**Dermal exposure (µg/cm^2/day)**	**Body burden[2] (µg/kg/day)**			
	100	283	130	$3.8 \cdot 10^3$	500
Combined exposure		292	134	$3.7 \cdot 10^3$	500
Dermal phototoxicity	**Dermal exposure (µg/cm^2/day)**			**Limit value**	**Min. MOS[6]**
Dermal	100	N/A	N/A	Human LOAEL	0.25
				Animal LOAEL	$1.4 \cdot 10^{-3}$
				Animal NOEL	$1.4 \cdot 10^{-4}$

1 Exposure · (inhalation rate 10 m^3/8 hour shift) · (systemic absorption) / (70 kg bd.wt.); absorption: 50% for ingested dust, 100% for inhaled vapour

2 Exposure · (1,980 cm^2) · (10% systemic absorption) / (70 kg bd.wt.)

3 Body burden · (5/7 days/week) · (45/70 years)

4 Compared to mouse NOEL (500 mg/kg/day)

5 Interspecies variability · intraspecies variability x subchronic-to-chronic extrapolation

6 LOAEL-to-NAEL extrapolation

4.1.3.6.2 Coal tar distillation

Exposure during coal tar distillation is expected to occur by inhalation of anthracene vapours as well as by skin contact with dissolved anthracene during loading, sampling and routine cleaning and maintenance operations.

Systemic toxicity

As can be seen in **Table 4.13**, the body burden resulting from the modelled exposure leads to MOS values greater than 10^4 for systemic toxicity from inhalation and dermal exposure individually and combined.

Skin photoirritation

The maximal dermal exposure level estimated by EASE (0.1 mg/cm^2) is 4 times higher than the human LOAEL and substantially higher than the animal LOAEL and NOEL, indicating concern.

Table 4.13 Risk characterisation for coal tar distillation

Systemic toxicity						
	Air conc. (µg/m³)	**Body burden[1] (µg/kg/day)**	**Mean life-time body burden[3] (µg/kg/day)**	**MOS[4]**		**Min. MOS[5]**
Vapour	11	1.6	0.7	$6.9 \cdot 10^5$		500
Dermal	**Dermal exposure (µg/cm²/day)**	**Body burden[2] (µg/kg/day)**				
	1.5	4.2	1.9	$2.6 \cdot 10^5$		500
Combined exposure		5.8	2.7	$1.9 \cdot 10^5$		500
Dermal phototoxicity	**Dermal exposure (µg/cm²/day)**			**Limit value**	**MOS**	**Min. MOS[6]**
Dermal	1.5	N/A	N/A	Human LOAEL	17	100
				Animal LOAEL	$9 \cdot 10^{-2}$	-
				Animal NOEL	$9 \cdot 10^{-3}$	

1 Exposure · (inhalation rate 10 m³/8 hour shift) · (systemic absorption) / (70 kg bd.wt.); absorption: 50% for ingested dust, 100% for inhaled vapour

2 Exposure · (1,980 cm²) · (10% systemic absorption) / (70 kg bd.wt.)

3 Body burden · (5/7 days/week) · (45/70 years)

4 Compared to mouse NOEL (500 mg/kg/day)

5 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation

6 LOAEL-to-NAEL extrapolation

4.1.3.6.3 Occupational exposures via creosote

Creosote blending

Exposure during creosote blending is expected to occur by inhalation of anthracene vapours as well as by skin contact with dissolved anthracene during loading, sampling and routine cleaning and maintenance operations.

Systemic toxicity

As can be seen in **Table 4.14**, the body burden resulting from the modelled exposure leads to MOS values greater than 10^4 for systemic toxicity from inhalation and dermal exposure individually and combined.

Skin photoirritation

The maximal dermal exposure level predicted by EASE (15 µg/cm²) is comparable with the human LOAEL, leading to a MOS of 1.7 as compared to the minimal MOS of 100. It is also substantially higher than the animal LOAEL and NOEL, indicating concern.

Table 4.14 Risk characterisation for creosote blending

Systemic toxicity						
	Air conc. (µg/m³)	**Body burden[1] (µg/kg/day)**	**Mean life-time body burden[3] (µg/kg/day)**	**MOS[4]**		**Min. MOS[5]**
Vapour	11	1.6	0.73	$6.9 \cdot 10^5$		500
Dermal	**Dermal exposure (µg/cm²/day)**	**Body burden[2] (µg/kg/day)**				
	15	42.5	19.5	$2.6 \cdot 10^4$		500
Combined exposure		44.1	20.2	$2.5 \cdot 10^4$		500
Dermal phototoxicity	**Dermal exposure (µg/cm²/day)**			**Limit value**	**MOS**	**Min. MOS[6]**
Dermal	15	N/A	N/A	Human LOAEL	1.7	100
				Animal LOAEL	$9 \cdot 10^{-3}$	-
				Animal NOEL	$9 \cdot 10^{-4}$	

1 Exposure · (inhalation rate 10 m³/8 hour shift) · (systemic absorption) / (70 kg bd.wt.); absorption: 50% for ingested dust, 100% for inhaled vapour

2 Exposure · (1,980 cm²) · (10% systemic absorption) / (70 kg bd.wt.)

3 Body burden · (5/7 days/week) · (45/70 years)

4 Compared to mouse NOEL (500 mg/kg/day)

5 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation

6 LOAEL-to-NAEL extrapolation

Creosote packaging

Exposure during creosote packaging is expected to occur by inhalation of anthracene vapours as well as by skin contact with dissolved anthracene during loading, sampling and routine cleaning and maintenance operations.

Systemic toxicity

As can be seen in **Table 4.15**, the body burden resulting from the modelled exposure leads to MOS values greater than 10^4 for systemic toxicity from inhalation and dermal exposure individually and combined.

Skin photoirritation

The maximal dermal exposure level estimated by EASE (15 µg/cm²) is comparable with the human LOAEL, leading to a MOS of 1.7 as compared to the animal MOS of 100. It is also substantially higher than the animal LOAEL and NOEL, indicating concern.

Table 4.15 Risk characterisation for creosote packaging

Systemic toxicity						
	Air conc. (µg/m³)	**Body burden[1] (µg/kg/day)**	**Mean life-time body burden[3] (µg/kg/day)**	**MOS[4]**		**Min. MOS[5]**
Vapour	11	1.6	0.73	$6.9 \cdot 10^4$		500
Dermal	dermal exposure (µg/cm²/day)	body burden[2] (µg/kg/day)				
	15	42	19.5	$2.6 \cdot 10^4$		500
Combined exposure		43.6	20.2	$2.5 \cdot 10^4$		500
Dermal phototoxicity	**Dermal exposure (µg/cm²/day)**			**Limit value**	**MOS**	**MOS[6]**
Dermal	15	N/A	N/A	human LOAEL	1.7	100
				animal LOAEL	$9 \cdot 10^{-3}$	-
				animal NOEL	$9 \cdot 10^{-4}$	

1 Exposure · (inhalation rate 10 m³/8 hour shift) · (100% systemic absorption) / (70 kg bd.wt.); absorption: 50% for ingested dust, 100% for inhaled vapour

2 Exposure · (1,980 cm²) · (2% systemic absorption) / (70 kg bd.wt.)

3 Body burden · (5/7 days/week) · (45/70 years)

4 Compared to mouse NOEL (500 mg/kg/day)

5 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation

6 LOAEL-to-NAEL extrapolation

Timber impregnation

Exposure during timber impregnation is expected to occur by inhalation of anthracene in particulate form as well as by skin contact with dissolved anthracene during loading, sampling and routine cleaning and maintenance operations. No information is available on the size of the anthracene-containing particles, and they are assumed to be respirable, leading to 100% absorption.

Systemic toxicity

As can be seen in **Table 4.16**, the body burden resulting from the exposures estimated from measured values leads to MOS values greater than 10^3 for systemic toxicity from inhalation and dermal exposure individually and combined.

Skin photoirritation

The maximal dermal exposure level leads to a MOS of $7 \cdot 10^{-2}$ compared to the human LOAEL. It is also substantially higher than the animal LOAEL and NOEL, indicating concern.

Table 4.16 Risk characterisation for timber impregnation

Systemic toxicity						
	Air conc. (µg/m³)	**Body burden[1] (µg/kg/day)**	**Mean life-time body burden[3] (µg/kg/day)**	**MOS[4]**		**Min. MOS[5]**
Particulate	19	2.7	1.2	$4.2 \cdot 10^5$		500
Dermal	Dermal exposure (µg/cm²/day)	Body burden[2] (µg/kg/day)				
	334	945	435	$1.1 \cdot 10^3$		500
Combined exposure		948	436	$1.1 \cdot 10^3$		500
Dermal phototoxicity	**Dermal exposure (µg/cm²/day)**			**Limit value**	**MOS**	**Min. MOS[5]**
Dermal	334	N/A	N/A	Human LOAEL	$7 \cdot 10^{-2}$	100
				Animal LOAEL	$4 \cdot 10^{-4}$	-
				Animal NOEL	$4 \cdot 10^{-5}$	

1 Exposure · (inhalation rate 10 m³/8 hour shift) · (100% systemic absorption) / (70 kg bd.wt.)
2 Exposure · (1,980 cm²) · (10% systemic absorption) / (70 kg bd.wt.)
3 Body burden · (5/7 days/week) · (45/70 years)
4 Compared to mouse NOEL (500 mg/kg/day)
5 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation
6 LOAEL-to-NAEL extrapolation

Creosote brushing

Exposure of professionals (e.g. gardeners) during creosote brushing is expected to occur by dermal contact with dissolved anthracene.

Systemic toxicity

In **Table 4.17** the body burden has been calculated based on the dermal exposures to the hands (taken to have an area of 840 cm^2) and the trunk (area 5,690 cm^2) estimated from an experimental study on volunteers, as well as based on the predictions of the EASE model (in this case taking the area exposed as the sum of the hands and trunk, i.e. 6,530 cm^2). The body burden figures indicated, and on which the calculations of MOS for systemic toxicity are based, is that corresponding to continuous lifetime exposure. It can be seen that the MOS values thus obtained are greater than 10^2. Actual exposure for consumers is not expected to exceed a few days per year, at most, leading to a substantially greater MOS value.

Skin photoirritation

It has been assumed that risk of photoirritation exists for the part of the body most likely to be exposed to the light, i.e. the hands. The dermal exposure of the hands leads to a MOS of 3.1 relative to the human LOAEL, while it is substantially lower than the animal LOAEL and NOEL. Furthermore, the exposure predicted by EASE is comparable to the human LOAEL (MOS = 0.3) and substantially higher than the animal LOAEL and NOEL. These observations indicate concern.

Table 4.17 Risk characterisation for creosote brushing

	Dermal exposure (µg/cm²/day)	**Body burden[1] (µg/kg/day)**	**MOS[2]**			**Min. MOS[3]**
Systemic toxicity	Estimated from measurements Through the hands: 8 Through the trunk: 54 Modelled by EASE 75	449 700	$1.1 \cdot 10^3$ 715			500
Dermal phototoxicity	Estimated from measurements Through the hands: 8 Modelled by EASE 75	N/A	Limit value	Exposure	MOS	Min. MOS[4]
			Human LOAEL	Measure-ments	3.1	100
				EASE	0.3	
			Animal LOAEL	Measure-ments	$1.7 \cdot 10^{-2}$	-
				EASE	$1.8 \cdot 10^{-3}$	
			Animal NOEL	Measure-ments	$1.7 \cdot 10^{-3}$	
				EASE	$1.8 \cdot 10^{-4}$	

1 [hand exposure · (840 cm²) + (trunk exposure x (5,690 cm²)] · (10% systemic absorption)/ (70 kg bd.wt.); for EASE-derived exposure, body burden = exposure · (6,530 cm2) · (10% systemic absorption)/(70 kg bd.wt.)
2 Compared to mouse NOEL (500 mg/kg/day)
3 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation
4 LOAEL-to-NAEL extrapolation

4.1.3.6.4 Occupational exposure from consumer products

Use of coal tar paints and related products

Exposure during the use of coal tar paints and related products is expected to occur by dermal contact with dissolved anthracene.

Systemic toxicity

As can be seen in **Table 4.18**, the body burden has been calculated based on the dermal exposures to the hands (taken to have an area of 840 cm^2) and the trunk (area 5,690 cm^2) estimated from an experimental study on volunteers. It has also been estimated using the modelled dermal exposure obtained using the EASE programme (in this case taking the area exposed as the sum of the hands and trunk, i.e. 6,530 cm^2). The body burden figures indicated, and on which the calculations of MOS for systemic toxicity are based, is that corresponding to continuous lifetime exposure. It can be seen that the MOS values thus obtained are greater than 10^4. Actual exposure for consumers is not expected exceed a few days per year, at most, leading to a substantially greater MOS value.

Skin photoirritation

It has been assumed that risk of photoirritation exists for the part of the body most likely to be exposed to the light, i.e. the hands. The dermal exposure of the hands, estimated from the experimental data, lead to a MOS of 1.4 relative to the human LOAEL, while it is substantially lower than the animal LOAEL and NOEL. On the other hand, the exposure level modelled by EASE is equal lead to the human LOAEL (MOS = 1), and substantially lower than the animal LOAEL and NOEL. These observations indicate concern.

Table 4.18 Risk characterisation for use of coal tar paints and related products

	Dermal exposure (µg/cm²/day)	**Body burden[1] (µg/kg/day)**	**MOS[2]**			**Min. MOS[3]**
Systemic toxicity	Estimated from measurements Through the hands: 18.3 Through the trunk: 2.7	43.9	$1.1 \cdot 10^4$			500
	Modelled by EASE: 25	233	$2.1 \cdot 10^3$			
Dermal phototoxicity	Estimated from measurements Through the hands: 18.3	N/A	limit value	expo-sure	MOS	min. MOS[4]
			Human LOAEL	measure-ments	1.4	100
				EASE	1	
	Modelled by EASE: 25		Animal LOAEL	measure-ments	$7.7 \cdot 10^{-3}$	
				EASE	$5.6 \cdot 10^{-3}$	
			Animal NOEL	measure-ments	$7.7 \cdot 10^{-4}$	
				EASE	$5.6 \cdot 10^{-4}$	

1 [hand exposure · (840 cm²) + (trunk exposure · (5,690 cm²)] · (10% systemic absorption) / (70 kg bd.wt.); for EASE-derived exposure, body burden = exposure · (6,530 cm2) · (10% systemic absorption) / (70 kg bd.wt.)
2 Compared to mouse NOEL (500 mg/kg/day)
3 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation
4 LOAEL-to-NAEL extrapolation

4.1.3.6.5 Occupational exposure from other industrial sources

Inhalation exposure to anthracene can occur in the context of industrial sources not related to the production of use of anthracene. **Table 4.19** presents the body burdens estimated for various occupational activities, based on the maximal exposures estimated from the limited data available. In all cases, the calculated MOS exceeds the minimal MOS for systemic toxicity by many orders of magnitude, indicating no concern.

Table 4.19 Risk characterisation for occupational exposure from other industrial sources

activity	Air conc. (µg/m³)	body burden[1] (µg/kg/day)	Mean life-time body burden[3] (µg/kg/day)	MOS[4]	Min. MOS[5]
Coal processing and related activities	52	7.4	3.4	$1.5 \cdot 10^5$	500
Carbon anode/graphite	5.51	0.8	0.4	$1.3 \cdot 10^6$	
Silicon carbide	139	19.9	9.1	$5.5 \cdot 10^4$	
Aluminium and other metals	256	36.6	16.8	$3 \cdot 10^4$	
Iron and steel	22	3.1	1.4	$3.6 \cdot 10^5$	

1 Exposure · (inhalation rate 10 m³/8 hour shift) · (100% systemic absorption) / (70 kg bd.wt.)

2 Body burden · (5/7 days/week) · (45/70 years)

4 Compared to mouse NOEL (500 mg/kg/day)

5 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation

4.1.3.6.6 Consumer exposure during use of coal tar paints and related products

Consumer exposure to anthracene can only occur in the context of using coal tar paints and related products, and is expected to occur via skin contamination.

Systemic toxicity

In **Table 4.20**, the body burden has been calculated using the maximal levels which have been estimated indirectly from measured data, and assuming exposures to the hands to involve an area of 840 cm^2 and those to the trunk an area of 5,690 cm^2.

Skin photoirritation

It has been assumed that risk of photoirritation exists for the part of the body most likely to be exposed to the light i.e. the hands. The dermal exposure of the hands leads to a MOS of 0.4 relative to the human LOAEL, while it is substantially lower than the animal LOAEL and NOEL.

Table 4.20 Risk characterisation for consumer use of coal tar paints and related products

	Dermal exposure (µg/cm²/day)	**Body burden[1] (µg/kg/day)**	**MOS[2]**		**Min. MOS[3]**
Systemic toxicity	Through the hands: 100 Through the trunk: 0.8	127	$4.0 \cdot 10^4$		500
Dermal phototoxicity		N/A	Limit value	MOS	Min. MOS[4]
			Human LOAEL	0.25	100
			Animal LOAEL	$1.4 \cdot 10^{-3}$	-
			Animal NOEL	$1.4 \cdot 10^{-4}$	

1 [hand exposure · (840 cm^2) + (trunk exposure · (5,690 cm^2)] · (10% systemic absorption) / (70 kg bd.wt.)
2 Compared to mouse NOEL (500 mg/kg/day)
3 Interspecies variability · intraspecies variability · subchronic-to-chronic extrapolation
4 LOAEL-to-NAEL extrapolation

4.2 HUMAN HEALTH (PHYSICOCHEMICAL PROPERTIES)

No need for further information or for classification according to Directive 67/548/EEC arises in connection with the physicochemical properties of anthracene.

5 RESULTS

5.1 EXPOSURES RELATED TO THE PRODUCTION AND USE OF ANTHRACENE

Table 5.1 summarises the outcome of the risk assessment as regards exposures related to the production and use of anthracene. These conclusions are the following:

a) **Conclusion (ii)** has been reached for systemic toxicity via all routes of exposure considered with regard to occupational exposure during production and packaging of anthracene, during the use of anthracene for manufacture of pyrotechnics and with regard to exposure of the general population via the environment. This conclusion was reached on the basis of MOS values which in most cases exceeded the minimal MOS substantially. Furthermore, in those cases (the majority of scenarios) where modelled, rather than measured, maximum exposure levels were utilised, these levels are likely to have been highly conservative. Consequently adoption of **Conclusion (ii)** is based on a high confidence level.

b) **Conclusion (iii)** has been reached for skin phototoxicity via dermal exposure with regard to occupational exposure during anthracene production and packaging. In all cases, the maximal exposures estimated are higher than the human LOAEL as well as the animal LOAEL and NOEL, and the calculated MOS values are substantially smaller than the minimal MOS. Although the studies from which these limit values were derived were not based on a formally approved protocol, they appear to have been well conducted and well reported, providing clear evidence of induction of skin irritation after a single application of anthracene in combination with a dose of UVA radiation which can be readily received by a person exposed for a short time to natural sunlight.

Even if estimated exposures may exceed the true ones due to the conservative nature of the assumptions made during modelling, the degree by which the estimated MOS is exceeded by the minimal MOS is such as to suggest that there is significant concern for adverse effects and a need for limiting risks.

c) A significant lack of measured exposure data has been identified for workers involved in anthracene production from anthracene oil, anthracene packaging and anthracene use in the manufacture of pyrotechnics.

d) There is need for further information regarding the reproductive and developmental toxicity of anthracene, and studies (e.g. a test based on OECD TG 414 (Prenatal Developmental Toxicity Study)) would be required to fill this information gap.

On the other hand, it is noted that, as far as the situation in the EU in 2003 is concerned, only one production site exists in the EU, with 99% of production volume exported outside the EU and only a very minor use in pyrotechnics. There are no consumer exposures to the commercially-produced substance and human environmental exposures are very low. The potential for worker exposure using modelled estimates is low, and limited measured data and control measures, known to be applied at the production site, indicate that the model predictions are probably over-estimates. Finally, mechanistic considerations (absence of Ah receptor binding by anthracene) make it likely that any reproductive toxicity of anthracene would probably be weak. On this basis, the execution of the abovementioned reproductive toxicity study may not be required as long as the exposure situation does not change.

Further measured exposure data for workers involved in anthracene production from anthracene oil, anthracene packaging and anthracene use in the manufacture of pyrotechnics, would of course increase the level of confidence in this decision.

The situation should be closely monitored and if there are any indications that production and use patterns are changing the potential for increasing exposure should be reconsidered and the need to request a developmental toxicity study revisited.

e) Although anthracene has not been formally tested for the induction of skin irritation or sensitisation in the absence of UVA light, no convincing data have been found to support the suggestion that it has such activity. On the other hand, as stated above, in combination with UVA light it has clear photoirritating activity for the skin. Classification of substances as “phototoxic” is not currently foreseen by Directive 67/548/EEC or any of its derivative legislation. Because the levels of irradiant energy of a magnitude sufficient to elicit anthracene photoirritation can be received easily through short exposures to sunlight, it is proposed that anthracene must be considered in practice as a skin irritant and be classified as "irritating to the skin". In this case there would not be a need for further tests on its skin irritating or sensitising activity in the absence of UVA light.

5.2 EXPOSURES NOT DIRECTLY RELATED TO THE PRODUCTION OR USE OF ANTHRACENE

Table 5.2 summarises the outcome of risk assessment as regards exposures which are not related to the production or use of anthracene. This assessment has been included for illustrative purposes, and covers occupational activities such as use of anthracene for chemical synthesis (which was conducted in a European plant until recently), coal tar distillation, occupational exposure during creosote production, packaging and use in timber impregnation and wood brushing, occupational exposure during use of coal tar paints and related products and occupational exposure associated with industrial sources involving combustion of organic materials. It also includes consumer exposure during the use of coal tar paints and related products. In all cases, there was no concern for systemic toxicity, with a high degree of confidence, arising from exposure via inhalation or dermal contact. However, there were concerns for skin phototoxicity in all cases where dermal exposure was considered.

5.3 PHYSICOCHEMICAL PROPERTIES (HUMAN HEALTH)

No need for further information or for classification according to Directive 67/548/EEC arises in connection with the physicochemical properties of anthracene.

Table 5.1 Summary of risk assessment conclusions

Exposure/toxicity end-point	Conclusion
Occupational exposures	
Manufacture of anthracene from anthracene oil	
Systemic toxicity by inhalation	ii
Systemic toxicity by dermal exposure	ii
Systemic toxicity by combined inhalation and dermal exposure	ii
Dermal phototoxicity	iii
Anthracene packaging	
Systemic toxicity by ingestion of airborne dust	ii
Systemic toxicity by inhalation	ii
Systemic toxicity by dermal exposure	ii
Systemic toxicity by combined inhalation, oral and dermal exposure	ii
Dermal phototoxicity	iii
Use of anthracene in the manufacture of pyrotechnics	
Systemic toxicity by ingestion of airborne dust	ii
Systemic toxicity by inhalation	ii
Systemic toxicity by dermal exposure	ii
Systemic toxicity by combined inhalation, oral and dermal exposure	ii
Dermal phototoxicity	iii
Exposure of the general population via the environment	ii

Table 5.2 Summary of scenarios for which information can be found in this report regarding exposures not related to production and current uses of anthracene

Occupational exposure during use of anthracene for chemical synthesis (not in operation in Europe)
Systemic toxicity by inhalation
Systemic toxicity by dermal exposure
Systemic toxicity by combined inhalation and dermal exposure
Dermal phototoxicity
Coal tar distillation
Systemic toxicity by inhalation
Systemic toxicity by dermal exposure
Systemic toxicity by combined inhalation and dermal exposure
Dermal phototoxicity

Table 5.2 continued overleaf

Table 5.2 continued Summary of scenarios for which information can be found in this report regarding exposures not related to production and current uses of anthracene

Occupational exposure via creosote	
Creosote blending	
Systemic toxicity by inhalation	
Systemic toxicity by dermal exposure	
Systemic toxicity by combined inhalation and dermal exposure	
Dermal phototoxicity	
Creosote packaging	
Systemic toxicity by inhalation	
Systemic toxicity by dermal exposure	
Systemic toxicity by combined inhalation and dermal exposure	
Dermal phototoxicity	
Timber impregnation	
Systemic toxicity by inhalation	
Systemic toxicity by dermal exposure	
Systemic toxicity by combined inhalation and dermal exposure	
Dermal phototoxicity	
Creosote brushing	
Systemic toxicity by dermal exposure	
Dermal phototoxicity	
Occupational exposure from other industrial sources	
Coal processing and related activities	Systemic toxicity by inhalation
Carbon anode/graphite	Systemic toxicity by inhalation
Silicon carbide	Systemic toxicity by inhalation
Aluminium and other metals	Systemic toxicity by inhalation
Iron and steel	Systemic toxicity by inhalation
Occupational exposure from consumer products	
Exposure during creosote brushing	
Systemic toxicity by dermal exposure	
Dermal phototoxicity	
Exposure during the use of coal tar paints and related products	
Systemic toxicity by dermal exposure	
Dermal phototoxicity	
Consumer exposure during use of coal tar paints and related products	
Systemic toxicity by dermal exposure	
Dermal phototoxicity	

6 REFERENCES

Akhtar MN, Hamilton JG, Boyd DR, Braunstein A, Seifried HE and Jarina DM (1979) Anthracen 1,2-oxide: Synthesis and role in the metabolism of anthracene by mammals. J. Chem. Soc. Perkin Trans. **1**, 1442-1446.

Alison AC, Magnus IA and Yound MR (1966) Role of lysosomes and of cell membranes in photosensitization. Nature **209**, 874.

Amacher DE and Turner GN (1980) Promutagen activation by rodent-liver postmitochondrial fractions in the L5178YT/K cell mutation assay. Mutat. Res. **74**, 485-501.

Andersson K, Levin J-O and Nilsson C-A (1983) Sampling and analysis of particulate and gaseous PAH's from coal-tar sources in the working environment. Chemosphere **12**, 197-204.

Argenbright LW, Forbes PD and Stewart GJ (1980a) Quantitation of phototoxic hyperemia and permeability to protein: II. Inhibition by histamine (H1 and H2) receptor antagonists in mouse skin. J. Invest. Dermatol. **75**, 417-420.

Argenbright IW, Forbes PD and Stewart GJ (1980b) Quantitation of phototoxic hyperemia and permeability to protein: I. Inhibition by histamine (H1 and H2) and serotonin receptor antagonists in pig skin. Exp. Molec. Pathol. **32**, 154-161.

Becher G and Bjorseth A (1985) A novel method for the determination of occupational exposure to polycyclic aromatic hydrocarbons by analysis of body fluids. In: Cooke M, Dennis AJ, eds. Polynuclear aromatic hydrocarbons: Mechanisms, methods and metabolism. Columbus, OH: Battelle Press, 145-155.

Betts (2002) Personal communication with Betts.

Bjorseth A, Bjorseth O and Fjeldstad P (1978a) Polycyclic aromatic hydrocarbons in the work atmosphere: I. Determination of area specific concentrations and job specific exposure in a vertical pin Sonderberg aluminium plant. Scand. J. Work Environ. Health **4**, 212-223.

Bjorseth A, Bjorseth O and Fjeldstad P (1978b) Polycyclic aromatic hydrocarbons in the work atmosphere: II. Determination in a coke plant. Scand. J. Work Environ. Health **4**, 224-236.

Blackburn GM, Buckingham J, Fenwick RG, Taussig P and Thompson MH (1973) Photochemical binding of anthracene and other aromatic hydrocarbons to deoxyribonucleic acid with attendant loss of tritium. J. Chem. Soc. Perkin I, 2809-2813.

Blackburn GM and Taussig PE (1975) The photocarcinogenicity of anthracene: photochemical binding to deoxyribonucleic acid in tissue culture. Biochem. J. **149**, 289-291.

Bock FG and Burnham M (1961) The effect of experimental conditions upon the concentration of hydrocarbons in mouse skin after cutaneous application. Cancer Res. **21**, 510-515.

Bock FG and Mund R (1958) A survey of compounds for activity in the suppression of mouse sebaceous glands. Cancer Res. **18**, 887-892.

Bond JA, Baker SM and Bechtold WE (1985) Correlation of the octanol/water partition coefficient with clearance half-times of intratracheally instilled aromatic hydrocarbons in rats. Toxicology **36**, 285-95.

Boogaard PJ and van Sittert NJ (1995) Urinary 1-hydroxypyrene as biomarker of exposure to polycyclic aromatic hydrocarbons in workers in petrochemical industries: baseline values and dermal uptake. Sci. Total Environ. **163**, 203-9.

Boyland, E and Burrows H (1935) The experimental production of sarcoma in rats and mice by a colloidal aqueous solution of 1:2:5:6-dibenzanthracene. J. Pathol. Bacteriol. **41**: 231-238.

Boyland E and Levi AA (1935) Metabolism of polycyclic compounds. I. Production of dihydroxydihydroanthracene from anthracene. Biochem. J. **29**, 2679-2683.

Boyland E and Levi AA (1936a) Metabolism of polycyclic compounds. II. Production of dihydroxydihydroanthracene glycuronic acid from anthracene. Biochem. J. **30**, 728-731.

Boyland E and Levi AA (1936b) Metabolism of polycyclic compounds. III. Anthrylmercapturic acid. Biochem. J. **30**, 1225-1227.

Bridges BA, McGregor DB and Zeiger E. et al. (1981) Summary report on the performance of bacterial mutation assays. **In**: Evaluation of Short-term Tests for Carcinogens. Report of the International Collaborative Program. Progress in Mutation Research, Vol. 1, F.J. de Serres and J. Ashby, Ed. Amsterdam, Elsevier, North Holland. 49-67.

Broman D, Naef C and Zebuehr Y (1991) Long-term high and low-volume air sampling of polychlorinated dibenzo-p-dioxins and dibenzofurans and polycyclic aromatic hydrocarbons along a transect from urban to remote areas on the Swedish Baltic coast. Env. Sci. Technol. **25**, 1841-1850.

Brookes P and Preston RJ (1981) Summary report on the performance of in vitro mammalian assays. **In**: Evaluation of Short-term Tests for Carcinogens. Report of the International Collaborative Program. Progress in Mutation Research, Vol. 1, de Serres FJ and Ashby J (eds), Amsterdam, Elsevier, North Holland. 77-85.

Brune K, Kalin H, Schmidt R and Hecker E (1978) Inflammatory, tumor initiating and promoting activities of polycyclic aromatic hydrocarbons and diterpene esters in mouse skin as compared with their prostaglandin releasing protency in vitro. Cancer Lett. **4** (1978), 333-342.

Burnham K and Rahman M (1992) Effects of petrochemicals and ultraviolet radiation on epidermal IA expression in vitro. J. Toxicol. Environ. Health **35**, 175-85.

Carver JH, Machado ML and MacGregor JA (1986) Application of modified Salmonella/microsome prescreen to petroleum-derived complex mixtures and polynuclear aromatic hydrocarbons (PAH). Mutat Res, **174**, 247-253.

Cautreels W and van Cauwenberghe K (1978) Experiments on the distribution of organic pollutants between airborne particulate matter and the corresponding gas phase. Atmos. Environ. **12**, 1133-1141.

Chaloupka K, Santosstefano M, Goldfarb IS, Liu G, Myers MJ, Tsyrolv IB, Gelboin HV, Krishnan V and Safe S (1994) Aryl hydrocarbon (ah) receptor-independent induction of Cyp1a2 gene expression by acenaphthylene and related compounds in B6C3F1 mice. Carcinogenesis **15**, 2835-2840.

Chang LH (1943) The fecal excretion of polycyclic hydrocarbons following their administration to rats. J. Biol. Chem. **151**, 93-99.

Clar E (1964) Polycyclic Hydrocargbons, Academic Press **1**, 288-307.

Clayton GD and Clayton FE (1981) Patty's Industrial Hygiene and Toxicology, Volume 2A, 2B, 2C, Toxicology. 3rd ed. New York, John Wiley Sons.

Collin G and Zauder M (1982) Tar and Pitch. **In**: Ullmann's Encyclopedia of Technical Chemistry.

Collin G and Höke H (1985) Anthracene. In: Ullman's Encyclopedia of Industrial Chemistry, 5th Ed., Vol. 2.

CRC Handbook of Chemistry and Physics, (1987) CRC Press.

Crow KD, Alexander E, Buck WHL, Johnson BE, Magnus IA and Porter AD (1961) Photosensitivity due to pitch. Brit. J Dermatol, **73**, 220-232.

Danish EPA (1995) Human health and environmental concerns of creosote. Danish EPA, Copenhagen.

Dankovich DA, Wright CW, Zangar RC and Springer DL (1989) Complex mixture effects on the dermal absorption of benzoa]pyrene and other polycyclic aromatic hydrocarbons from mouse skin. J. Appl Toxicol. **9**, 239-244.

Dayhaw-Barker P, Sambuco CP, Forbes PD and Barker FM (1985) Development of an animal model to study the phototoxic effects of anthracene and UV in skin and ocular tissues. Photochem. Photobiol. **41**, 122S.

Dean J (1979) Lange's Handbook of Chemistry, 12th ed., Dean J (ed.).

Delgado-Rodriguez A, Ortiz-Marttelo R, Graf U, Villalobos-Pietrini R and Gomez-Arroyo S (1995) Genotoxic activity of environmentally important polycyclic aromatic hydrocarbons and their nitro derivatives in the wing spot test of Drosophila melanogaster. Mutat. Res. **341**, 235-47.

DiPaolo JA, Takano K and Popuscu NC (1972) Quantitation of chemically induced neoplastic transformation of BALB/3T3 cloned cell lines, Cancer Res. **32**, 2686-2695.

DiPaolo JA, Nelson RL, Donovan PJ and Evans CH (1973) Host-mediated in vivo-in vitro assay for chemical carcinogenesis, Arch. Pathol. **95**, 380-385.

Dufresne A, Lesage J and Perrault G (1987) Evaluation of occupational exposure to mixed dusts and polycyclic aromatic hydrocarbons in silicon carbide plants. Am. Ind. Hyg. Assoc. J. **48**, 160-6.

Elson LA et al. (1945) Biochem. J. **39**, 301-308.

Emmett EA (1986) Cutaneous and ocular hazards of roofers. Occup. Med. **1**, 307-22.

Fazio T and Howard JW (1983) **In**: Handbook of Polycyclic Aromatic Hydrocarbons, Bjoresth A (ed.), Marcel Dekker, Inc., New York.

Forbes PD, Davies RE and Urbach F (1976) Phototoxicity and photocarcinogenesis: comparative effects of anthracene and 8-methoxypsoralen in the skin of mice. Fd. Cosmet. Toxicol. **14**, 303-306.

Franck H-G and Stadlhofer JW (1987) Industrial Aromatic Chemistry, Raw Materials, Processes and Products.

Freeman AE, Weisburger EK, Weisburger JH, Wolford RG, Maryak JM and Huebner RJ (1973) Transformation of cell cultures as an indication of the carcinogenic potential of chemicals. J. Natl. Cancer Inst. **51**, 799-808.

Friedman MA and Staub J (1976) Inhibition of mouse testicular DNA synthesis by mutagens and carcinogens as a potential sample mammalian assay for mutagenesis. Mutat. Res. **37**, 67-76.

Fujikawa K, Fort FL, Samejima K and Sakamoto Y (1993) Genotoxic potency in Drosophila melanogaster of selected aromatic amines and polycyclic aromatic hydrocarbons as assayed in the DNA repair test. Mutat. Res. **290**, 175-82.

Garrod AN, Guiver R and Rimmer DA (2000) Potential exposure of amateurs (consumers) through painting wood preservative and antifoulant preparations. Ann. Occup. Hyg. **44**, 421-6.

Gershbein LL (1975) Liver regeneration as influenced by the structure of aromatic and heterocyclic compounds. Res. Commun. Chem. Pathol. Pharmacol. **11**, 445-466.

Geyer H, Politzki G and Freitag D (1984) Prediction of ecotoxicological behaviour of chemicals: relationship between n-octanol/water partition coefficient and bioaccumulation of organic chemicals by *alga chlorella*. Chemosphere **13**, 269-284.

Gloxhuber H (1970) Phototoxicity testing of cosmetic materials, J. Soc. Cosmetic Chemists **21**, 825-833.

Grote D (1979a) Űberprüfung des toxischen Wirkungsbildes nach einmaliner, oraler Applikation von 16,0 g/kg Kg2. Auftragsnummer 335a, S. 1-3, Huntingdon Research Centre, Deutschland, Münster, Upublished Report.

Grote D (1979b), Prüfung der Hautverträglichkeit nach einmaliger Applikation auf die intakte oder skarifizierte Haut beim Kaninchen, Auftragsunummer 335b, Huntington Research Centre, Deutschland, Münster, Upublished Report.

Grote D (1979c), Verträglichkeitspruefung am Auge nach einmaliger Applikation beim Kaninchen, Auftragsnummer 335c, Huntington Research Centre, Deutschland, Münster, Upublished Report.

Hall M and Grover PL (1987) Differential stereoselectivity in the metabolism of benzo[a]pyrene and anthracene by rabbit epidermal and hepatic microsomes. Cancer Letters **38**, 57-64.

Harper KH (1959) The intermediary metabolism of polycyclic hydrocarbons. Brit. J. Cancer **13**, 718-731.

Hashimoto Y, Tokura K, Kishi H and Strachan WMJ (1984) Prediction of seawater solubility of aromatic compounds. Chemosphere **13**, 881-888.

Hausigk D and Koelling G (1968) Űber Reaktionen von partiell hydrierten mehrkernigen aromatischen Verbindungen mit 1,4-dichlor-butan. Chem. Ber. **101**, 469-472.

Heikkila PR, Hameilae M, Pyy L and Raunu P (1987) Exposure to creosote in the impregnation and handling of impregnated wood. Scan. J. Work Environ. Health **13**, 431-437.

Heller W (1950) Experimental study on tumours produced by light. 2. Tumours produced by light through photosensitisation (Ger.). Strahlentherapie **81**, 529-548. Cited in IARC (1983b).

Hoch-Ligeti C (1941) Studies on the changes in the lymphoid tissue of mice treated with carcinogenic and non-carcinogenic hydrocarbons. Cancer Res. **1**, 484-488. Described in: Faust RA (1991) Toxicity summary for antrhacene. Report prepared for the Oak Ridge Reservation Environmental Restoration Program.

Höke (2000) Personal communication with Höke.

Höke (2002) Personal communication with Höke.

Höke (2003) Personal communication with Höke.

Hopia A, Pyysalo H and Wickström K (1986) Margarines, butter and vegetable oils as sources of polycyclic aromatic hydrocarbons. J. Am. Oil Chem. Soc. **63**, 889-93.

HSE (2002) Personal communication from the Health and Safety Executive (UK).

IARC (1983a) International Agency for Research on Cancer Monographs on the Evaluation of Carcinogenic Risks of Chemicals to Humans. Vol. 32, Bitumens, coal-tars and derived products, shale-oils and soots, Part 1.

IARC (1983b) International Agency for Research on Cancer Monographs on the Evaluation of Carcinogenic Risks of Chemicals to Humans, Vol. 32, Polynuclear Aromatic Compounds, Part 1, Chemical, Environmental and Experimental Data. Anthracene, 105.

Ingram LL Jr, McGinnis GD, Gjovik KR et al. (1982) Migration of creosote and its components from treated piling sections in marine environments. Proceedings of the American Wood Preservation Association, **78**, 120-128.

IPCS (International Programme of Chemical Safety) (1998) Environmental Health Criteria. 202. Selected non-heterocyclic polycyclic aromatic hydrocarbons. World Health Organisation, Geneva.

Jandris LJ and Forcė RK (1983) Determination of polycyclear aromatic hydrocarbons in vapor phases by laser-induced molecular fluorescence. Anal. Chim. Acta **151**, 19-27.

Joshi PC and Pathak MA (1984) The role of active oxygen ($^1O_2$ and O_2^{-}) induced by crude coal tar and its ingredients used in photochemotherapy of skin diseases. J. Invest. Dermatol. **82**, 67-73.

Kaidbey KH and Nonaka S (1984) Action spectrum for anthracene-induced photosensitization of human skin, Photochem. Photobiol. **39**, 375-378.

Karcher W et al. (eds.) (1985) .Spectral Atlas of Polycyclic Aromatic Compounds, Karcher W. et al. (eds.).

Karickhoff SW et al. (1979), Sorption of hydrophobic pollutants on natural sediments. Water Res. **13**, 241-248.

Kennaway FL (1924a) On cancer-producing factor in tar. Brit. Med. J. **1**, 564-567. Cited in IARC (1983b).

Kennaway FL (1924b) On cancer-producing tars and tar-fractions. J. Ind. Hyg. **5**, 462-488. Cited in IARC (1983b).

Kleffner HW, Talbiersky J and Zander M (1981), Simple scheme for the estimation of concentrations of polycyclic aromatic hydrocarbons in tars. Fuel **60**, 361-362. Cited in IARC (1983a).

Kochevar IE, Armstrong RB, Einbinder J, Walther RR and Harber LC (1982) Coal tar photoxocitiy: active compounds and action spectra. Photochem. Photobiol. **36**, 65-69.

Kveseth K and Sortland B (1982) Polycyclic aromatic hydrocarbons in sewage, mussels and tap water. Chemosphere **11**, 623-39.

Lake RS, Kropko ML, Pezzutti MR, Shoemaker RH and Igel HJ (1978) Chemical induction of unscheduled DNA synthesis in human skin epithelial cell cultures. Cancer Res. **38**, 2091-2098.

Lang KF and Eigen I (1967), Forstschr. Chem. Forsch. **8**, 91-141.

LaVoie JE, Coleman DT, Rice JE, Geddie NG and Hoffmann D (1985) Tumor-initiating activity, mutagenicity and metabolism of methylated anthracenes. Carcinogenesis **10**, 1483-1488.

Lax E and Synowietz C (1964) Taschenbuch für Chem. und Physicker. Lax E and Synowietz C (eds.).

LeBoeuf RA, Kerckaert GA, Aardema MJ, Gibson DP, Brauninger R and Isfort RJ (1996) The pH 6.7 Syrian hamster embryo cell transformation assay for assessing the carcinogenic potential of chemicals. Mutat. Res. **21**, 85-127.

Lehman E, Auffarth J and Hager J (1984) Determination of selected polycyclic aromatic hydrocarbons in coal-tar, coal-tar pitch and tar products. Staub-Reinhalt. Luft **44**, 452-455.

Lesage J, Perrault G and Durand P (1987) Evaluation of worker exposure to polycyclic aromatic hydrocarbons. Am. Ind. Hyg. Assoc. J. **48**, 753-9.

Lide DR (1991) CRC Handbook of Chemistry and Physics, 72nd ed., Lide DR (ed.), CRC Press, Boca Raton.

Lo M and Sandi E (1978) Polycyclic aromatic hydrocarbons in foods. **In**: Gunter FA (ed.) Residue Review. Springer-Verlag, New York, **69**, 35-86.

Lorenz LJ and Gjovik LR (1972) Analysing creosote by gas chromatography. **In**: Proceedings of the Annual Meeting of the American Wood-Preservers' Association, 32-42.

Lovell WW and Sanders DJ (1992) Phototoxicity testing in guinea-pigs. Food Chem. Toxic. **30**, 155-160.

Machala M, Vondracek J, Blaha L, Ciganek M and Neca JV (2001) Aryl hydrocarbon receptor-mediated activity of mutagenic polycyclic aromatic hydrocarbons determined using in vitro reporter gene assay. Mutat. Res. **497**, 49-62.

Mackay, D. and Shiu, W. Y., "Aqueous Solubility of Polynuclear Aromatic Hydrocarbons", J. Chem. Eng. Data, **22(4)**, 399-402 (1977).

Maga JA (1986) Polycyclic aromatic hydrocarbon (PAH) composition of mesquite (Prosopis fuliflora) smoke and grilled beef. J. Agric. Food Chem. **34**, 249-51.

Marlich LI and Leukevitch ZK (1973) Capillary chromatograph as a method for the rapid determination of the main components in coal tar and coal tar fractions. Zh. ana. Khim. **28**, 1193-1198. Cited in IARC (1983a).

Martin CN, McDermid AC and Garner RC (1978) Testing of known carcinogens and noncarcinogens for their ability to induce unscheduled DNA synthesis in HeLa cells, Cancer Res. **38**, 2621-2627.

Masclet P, Pistikopoulos P, Beyne S and Mouvier G (1988) Long range transport and gas-particle distribution of polycyclic aromatic hydrocarbons at a remote site in the Mediterranean sea, Atmos. Environ. **22**, 639-50.

May W, Walik SP, Miller MM, Tewari UB, Brown-Thomas JM and Goldgerg RN (1983) Solution thermodynamics of some slightly soluble hydrocarbons in water. J. Chem. Eng. Data **28**, 197-200.

McNeil D (1983) Tar and Pitch. **In**: Encyclopedia of Chemical Technology. Kirk RE and Othmer DF (eds.), 3rd edn.

Mellon Institute (1977) Range Finding Toxicity Tests on Rabbits and Rats, EPA Doc. No. 86-870001568, Fiche No. OTS0516149.

Menichini E, Bocca A, Merli F, Ianni D and Monfredini F (1991) Polycyclic aromatic hydrocarbons in olive oils on the Italian market. Food Addit. Contam. **8**, 363-69.

Miescher G (1942) Experimental studies on the formation of tumours by photosensitisation (Ger.) Schweiz. med. Wochenschr. **72**, 1082-1084. Cited in IARC (1983b).

Mitchell CE (1982) Distribution and retention of benzo[a]pyrene in rats after inhalation. Toxicol. Lett. **11**, 35-42.

Montizaan GK, Kramers PGH, Janus JA and Posthumus R (1989) Integrated criteria document PAH: Effects of 10 selected compounds. Appendix to Report No. 758474011. Bilthoven, National Institute of Public Health and Environmental Protection.

Moseley H, Diffey BL, Marks JM and Mackie RM (1981) Personal solar UV-A doses received by patients undergoing oral psoralen photochemotherapy for psoriasis. Brit. J. Dermatol. **105**, 573-7.

Myers SR, Blake JW and Flesher JW (1988) Bioalkylation and biooxidation of anthracene, in vitro and in vivo. Biochem. Biophys. Res. Comm. **151**, 1441-1445.

Nabert K and Schön G (1963) Sickerheitstechnische Kennzahlen brennbarer Gase und Dämpfe, 2nd ed.

Nagornyi PA and Rodionov GA (1969) Data on the toxicology of anthracenetoluolphenol-formaldehyde resin. Gig. Tr. Prof. Zabol. **13**, 59-61 (Russ.).

Neff JM (1979) Polycyclic aromatic hydrocarbons in the aquatic environment. Sources, fates and biological effects. Neff JM (ed.), Applied Science Publisheres Ltd., London.

Nestler FHM (1974) The characterization of wood-reserving creosote by physical and chemical methods of analysis (USDE Forest Service Research Paper FPL 195), U.S. Department of Agriculture.

Nousiainen U, Torronen R and Hanninen O (1984) Differential induction of various carboxylesterases by certain polycyclic aromatic hydrocarbons in ther at. Toxicology **32**, 243-251.

Novotny M, Strand JW, Smith SL, Wieslder D and Schwende FJ (1981) Compositional studies of coal tar by capillary gas chromatograph/mass spectrometry. Fuel 60, 213-220. Cited in IARC (1983a).

Old LJ, Benacerraf B and Carswell E (1963) Contact reactivity to carcinogenic polycyclic hydrocarbons. Nature, **198**, 1215-1216.

Oshiro Y, Balwierz PS, Soelter SG, Guzzie PJ and Rohrbacher E (1992) Evaluation of mouse peripheral blood micronucleus assay. Environm. Molec. Mutagen. **19**, 42.

Perry PE and Thomson EJ (1981) Evaluation of the sister chromatid exchange method in mammalian cells as a screening system for carcinogens, in: evaluation of short-term tests for carcinogens: Report of the International Collaborative Program. Prog. Mutat. Res. 1, (F.J. de Serres, J. Ashby, eds.), p. 560-569, Elsevier North-Holland, New York, Amsterdam, Oxford.

Petry T, Schmid P and Schlatter C (1996a) The use of toxic equivalency factors in assessing occupational and environmental health risk associated with exposure to airborne mixtures of polycyclic aromatic hydrocarbons (PAHs). Chemosphere **32**, 639-48.

Petry T, Schmid P and Schlatter C (1996b) Airborne exposure to polycyclic aromatic hydrocarbons (PAHs) and urinary excretion of 1-hydroxypyrene of carbon anode plant workers. Ann. Occup. Hyg. **40**, 345-57.

Piet GJ and Morra CF (1983) **In**: Artificial Groundwater Recharge. Huisman L and Olsthorn TN (eds.) Pitman Publ, 29-42.

Pollia JA (1939) Investigations on the possible carcinogenic effect of anthracene and chrysene and some of their compounds. J. Indust. Hyg. **21**, 219-220. Cited in IARC (1983b).

Pollia JA (1941) Investigations on the possible carcinogenic effect of anthracene and chrysene and some of their compounds. II. The effect of subcutaneous injection in rats. J. Ind. Hyg. Toxicol. **23**, 449-451.

Purchase IFH, Longstaff E, Ashby J, Styles JA, Anderson D, Lefevre PA and Westwood FR (1976) Evaluation of six short term tests for detecting organinc chemical carcinogens and recommendations for their use. Nature **264**, 624-627.

Rahman A, Barrowman JA and Rahimtula A (1986) The influence of bile on the bioavailability of polynuclear aromatic hydrocarbons from the rat intestine. Can. J. Physiol. Pharmacol. **64**,1214-8.

Reddy MV, Gupta RC, Randerath E and Randerath K (1984) ^{32}P-Postlabeling test for covalent DNA binding of chemicals in vivo: application to a variety of aromatic carcinogens and methylating agents. Carcinogenesis **5**, 231-43.

Riala R, Heikkila P and Kanerva L (1998) A questionnaire study of road pavers' and roofers' work-related skin symptoms and bitumen exposure. Int. J. Dermatol. **37**, 27-30.

Rigdon RH and Giannukos NJ (1964) Effect of carcinogenic hydrocarbons on growth of mice. Arch. Path. **77**, 112-118.

Rispler J and Urbanek RW (1978) Photodynamic induction of remission in psoriasis with anthracene and long ultraviolet irradiation. Photochem. Photobiol. **41**, 103A.

Roff MW (1997) Dermal exposure of amateur or non-occupational users to wood-preservative fluids applied by brushing outdoors. Ann. Occup. Hyg. **41**, 297-343.

Roszinksy-Koecher G, Basler A and Roehrborn G (1979) Mutagenicity of polycyclic aromatic hydrocarbons. 5. Induction of sister-chromatid exchanges in vivo. Mutat. Res. **66**, 65-67.

Russel H (1947) An unsuccelful attempt to induce gliomata in rabbits with chloanthrene. J. Pahtol. Bacteriol. 59, 481-483. Cited in IARC (1983b).

Sakai M, Yoshida D and Mizusaki S (1985) Mutagenicity of polycyclic aromatic hydrocarbons and quinones on Salmonella typhimurium TA97. Mutat. Res. **156**, 61-67.

Salaman MH and Roe FJC (1956) Further tests for tumour-initiating activity: N,N-Di-(2-chloroethyl)-p-aminophenyl-butyric acid (CD1348) as an initiatior of skin tumour formation in the mouse. Br. J. Cancer **10**, 363-378.

Salamone MF (1981) Toxicity of 41 carcinogens and noncarcinogenic analogs. **In**: Evaluation of short-term tests for carcinogens, Progress in mutation research, de Serres FJ and Ashby J (eds.), Elsevier North-Holland, New York, Amsterdam, Oxford. **1**, 682-685.

Sangster J (1989) Octanol-water partition coefficients of simple organic compounds. J. Phys. Chem. Reference Data **18**, 111-1129.

Santodonato J et al. (1981) Hazard Profiles on PAH. Syracuse, NY: Syracuse Res Corp p. 53 TR 81-633.

Sartorelli P, Cenni A, Matteucci, Montomoli L, Novelli MT and Palmi S (1999) Dermal exposure assessment of polycyclic aromatic hydrocarbons: in vitro percutaneous penetration from lubricating oil. Int. Arch. Occup. Environ. Health **72**, 528-232.

Sax NI (1975) Dangerous properties of industrial materials, van Nostrand Reinhold Company, New York; 8th edition.

Sax NI (1992) Dangerous properties of industrial materials, van Nostrand Reinhold Company, New York; 8th edition.

Schmahl D (1955) Examination of the carcinogenic action of naphthalene and anthracene in rats. Z. Krebsforsch. **60**, 697-710.

Schothorst AA, Suurmond D and de Lijster A (1979) A biochemical screening test for the photosensitizing potential of drugs and disinfectants. Photochem Photobiol. **29**, 531-7.

Schwartz FP (1977) Determination of temperature dependence of solubilities of polycyclic aromatic hydrocarbons in aqueous solutions by a fluorescence method. J. Chem. Eng. Data **22**, 273-277.

Scribner JD (1973) Tumor initiation by apparently noncarcinogenic polycyclic aromatic hydrocarbons, J. Natl. Cancer Inst. **50**, 1717-1719.

Shabad LM, Sorikina JD, Golub NI and Bogovski SP (1972) Transplacental effect of some chemical compounds on organ cultures of embryonic kidney tissue. Cancer Res. **32**, 617-627.

Shubik P and Della Porta G (1957) Carcinogenesis and acute intoxication with large doses of polycyclic hydrocarbons. Am. Med. Ass. Arch. Path. **64**, 691-703.

Sims P (1964) Metabolism of polycyclic compounds. 25. The metabolism of anthracene and some related compounds in rats. Biochem. J. **92**, 621-631.

Sinha and Chignell (1983) Binding of anthracene to cellular macromolecules in the presence of light. Photochem. Photobiol. **37**, 33-37.

Smith DJT and Harrison RM (1996) Concentrations, trends and vehicle source profile of polynuclear aromatic hydrocarbons in the U.K. atmosphere. Atmosph. Environ. **30**, 2513-25.

Sofuni T, Hayashi M, Matsuoka A, Sawada M, Hatanaka M and Ishidate M (1985) Mutagenicity tests on organic chemical contaminants in city water and related compounds. II. Chromosome aberration tests in cultured mammalian cells. Bull. Natl. Inst. Hyg. Sci. (Tokyo), 64-75.

Sonnefeld WJ, Zoller WH and May WE (1983) Dynamic coupled-column liquid chromatographic determination of ambient temperature vapor pressures of polynuclear aromatic hydrocarbons. Anal. Chem. **55**, 275-280.

Sorgo PM (1996) Report of the European Commission (DG III) on the justification of the Danish position concerning the Directive on creosote.

Sorokina ID (1971) Transplacental effect of 7,12-dimethylbenz(a)anthracene and its non-carcinogenic analog-anthracene in organ cultures of mouse embryonal kidneys. Bull. Eksp. Biol. Med. **72**, 86-9.

Spano MA, Frei H, Wurgler FE and Graf U (2001) Recombinagenic activity of four compounds in the standard and high bioactivation crosses of Drosophila melanogaster in the wing spot test. Mutagenesis **16**, 385-94.

Speer K, Steeg E, Horstmann P, Kühn Th and Montag A (1990) Determination and distribution of polycyclic aromatic hydrocarbons in native vegetable oils, smoked fish products, mussels and oysters, and bream from the River Elbe. J. High Resol. Chromatogr. **13**, 104-11.

Stanton MF, Miller E, Wrench C and Blackwell R (1972) Experimental induction of epidermoid carcinoma in the lungs of rats by cigarette smoke condensate. J. Natl. Cancer Inst. **49**, 867-877.

Staesse HL (1954) Fractional distillation of creosote and composition of preservatives used in the cooprative creosote programme. Proc. American Wood Preservers' Association **50**, 13-40.

Storer JS, DeLeon I, Millikan LE, Laseter JL and Griffing C (1984) Human absorption of crude coal tar products. Arch. Dermatol. **120**, 874-7.

Thrane KE and Mikalsen A (1981) High-volume sampling of airborne polycyclic aromatic hydrocarbons using glass fiber filters and polyurethane foam. Atmos. Environ. **15**, 909-918.

Thyssen J (1979) Bayer AG, Untersuchung zur Haut- und Schleimhautverträglichkeit, Institut für Toxikologie, Wuppertal-Elberfeld.

Torronen R, Nousiainen U and Hanninen O (1981) Induction of aldehyde dehydrogenase by polycyclic aromatic hydrocarbons in rats. Chem.- Biol. Interact. **36**, 33-44.

Traul KA, Takayama K, Kachevsky V, Hink RJ and Wolff JS (1981) A rapid in vitro assay for carcinogenicity of chemical substances in mammalian cells utilizing an attachment-independence endpoint. 2 - Assay validation. J. Appl. Toxicol. **1**, 190-5.

US EPA (1987) Health and Environmental Effects Profile for Anthracene, US Environmental Protection Agency, Washington, DC.

US EPA (1989) Subchronic toxicity study in mice with anthracene. HLA Study No. 2399-131. Final Report. Prepared by Hazelton Laboratories America, Inc., Rockville, MD, for the Office of solid Waste, US Environmental Protection Agency, Washington, DC.

van Bladeren PJ, Sayer JM, Ryan DE, Thomas PE, Levin W and Jerina DM (1985) Differential stereoselectivity of cytochromes P-450b and P-450c in the formation of naphthalene and anthracene 1,2-oxides. The role of epoxide hydrolase in determining the enantiomer composition of the 1,2-dihydrodiols formed. J. Biol. Chem. **260**, 10226-35.

van Rooij JG, van Lieshout MA, Bodelier-Bade MM and Jongeneelen FJ (1993) Effect of the reduction of skin contamination on the internal dose of creosote workers exposed to polycyclic aromatic hydrocarbons. Scand. J. Work Environ. Health **19**, 200-207.

van Rooij JG, Vinke E, De Lange J, Bruijnzeel PL, Bodelier-Bade MM, Noordhoek J and Jongeneelen FJ (1995) Dermal absorption of polycyclic aromatic hydrocarbons in the blood-perfused pig ear. J. Appl. Toxicol. **15**, 193-200.

Volkova NI (1983) Anthracene and derivatives. **In**: Encyclopaedia of Occupational Health and Safety. Parmeggiani L (ed.), International Labour Office, Geneva, **1**, 162-163.

WEI (2000) Personal communication from the West European Institute for Wood Preservation.

Welch RM, Harrison YE, Gommi BW, Poppers PJ, Finster M and Conney AH (1969) Stimulatory effect of cigarette smoking on the hydroxylation of 3,4-benzpyrene and the N-demethylation of 3-methyl-4-monomethylaminoazobenzene by enzymes in human placenta, Clin. Pharm. Therapeut. **10**, 100-109.

Welch RM, Gommi B, Alvares AP and Conney AH (1972) Effect of enzyme-induction on the metabolsim of benzo(a)pyrene and 3-methyl-4-monomethylaminoazobenzene in the pregnant and fetal rat. Cancer Res, **32**, 973-978.

Weyand EH and Bevan DR (1986) Benzo(a)pyrene disposition and metabolism in rats following intratracheal instillation. Cancer Res. **46**, 5655-61.

White KL, Lysy HH and Holsapple MP (1985) Immunosuppression by polycyclic aromatic hydrocarbons. A structure-activity relationship in B6CeF1 mice and DBA/2 mice. Immunopharmacol. **9**, 155-164.

Wickström K, Pyysalo H, Plaami-Heikkilä S and Tuominen J (1986) Polycyclic aromatic compounds (PAC) in leaf lettuce. Z. Lebensm. Unters Forsch. **183**, 182-5.

Williams GM (1988) Detection of chemical carcinogens by unscheduled DNA synthesis in rat liver primary cell cultures, Cancer Res. **37**, 1845-1851.

Whitehouse BG (1984) The effects of temperature and salinity on the aqueous solubility of polynuclear aromatic hydrocarbons. Marine Chem. **14**, 319-332.

WHO (1994) Ultraviolet Radiation. Environmental Health Criteria (2^{nd} edition), vol. 160, World Health Organisation, Geneva.

Worstmann W (1981) Akute Toxizität von Produkt-Nr. 110.147 (Anthracen) an männlichen und weiblichen Ratten nach dermaler Applikation, Auftragsnummer 874/4/81, S. 1-8, Huntingdon Research Centre Deutschland, Münster, Unpublished Report.

Wynder EL and Hoffman D (1959) A study of tobacco carcinogenesis. VII. The role of higher polycyclic hydrocarbons. Cancer **12**, 1079-1086.

Yamazaki H, Imamura E, Kamei S, Yamauchi A, Kakiuchi Y and Tai HH (1990) Polycyclic aromatic hydrocarbons affect the calcium ionophore induced activation of rabbit platelet. Chemosphere **21**. 21-28.

Yang JJ, Roy TA and Mackerer CR et al. (1986) Percutaneous absorption of anthracene in the rat: comparison of in vivo and in vitro results.Tox. Ind. Health **2**, 79-84.

Yoshida K, Shigeoka T and Yamauchi F (1983), Relationship between molar refraction and n-octanol/water partition coefficient. Ecotox. Environ. Safety **7**, 558-565.

ABBREVIATIONS

ADI	Acceptable Daily Intake
AF	Assessment Factor
ASTM	American Society for Testing and Materials
ATP	Adaptation to Technical Progress
AUC	Area Under The Curve
B	Bioaccumulation
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft
BCF	Bioconcentration Factor
BMC	Benchmark Concentration
BMD	Benchmark Dose
BMF	Biomagnification Factor
BOD	Biochemical Oxygen Demand
bw	body weight / *Bw*, *bw*
C	Corrosive (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
CA	Chromosome Aberration
CA	Competent Authority
CAS	Chemical Abstract Services
CEC	Commission of the European Communities
CEN	European Standards Organisation / European Committee for Normalisation
CEPE	European Committee for Paints and Inks
CMR	Carcinogenic, Mutagenic and toxic to Reproduction
CNS	Central Nervous System
COD	Chemical Oxygen Demand
CSTEE	Scientific Committee for Toxicity, Ecotoxicity and the Environment (DG SANCO)
CT_{50}	Clearance Time, elimination or depuration expressed as half-life
d.wt	dry weight / dw
dfi	daily food intake
DG	Directorate General
DIN	Deutsche Industrie Norm (German norm)
DNA	DeoxyriboNucleic Acid
DOC	Dissolved Organic Carbon
DT50	Degradation half-life or period required for 50 percent dissipation / degradation
DT90	Period required for 90 percent dissipation / degradation
E	Explosive (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
EASE	Estimation and Assessment of Substance Exposure Physico-chemical properties [Model]

EbC50	Effect Concentration measured as 50% reduction in biomass growth in algae tests
EC	European Communities
EC10	Effect Concentration measured as 10% effect
EC50	median Effect Concentration
ECB	European Chemicals Bureau
ECDIN	Environmental Chemicals Data and Information Network
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECVAM	European Centre for the Validation of Alternative Methods
EDC	Endocrine Disrupting Chemical
EEC	European Economic Communities
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EN	European Norm
EPA	Environmental Protection Agency (USA)
ErC50	Effect Concentration measured as 50% reduction in growth rate in algae tests
ESD	Emission Scenario Document
EU	European Union
EUSES	European Union System for the Evaluation of Substances [software tool in support of the Technical Guidance Document on risk assessment]
F(+)	(Highly) flammable (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
FAO	Food and Agriculture Organisation of the United Nations
FELS	Fish Early Life Stage
foc	Organic carbon factor (compartment depending)
GLP	Good Laboratory Practice
HEDSET	EC/OECD Harmonised Electronic Data Set (for data collection of existing substances)
HELCOM	Helsinki Commission -Baltic Marine Environment Protection Commission
HPLC	High Pressure Liquid Chromatography
HPVC	High Production Volume Chemical (> 1000 tonnes/annum)
IARC	International Agency for Research on Cancer
IC	Industrial Category
IC50	median Immobilisation Concentration or median Inhibitory Concentration
ILO	International Labour Organisation
IPCS	International Programme on Chemical Safety
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database (existing substances)
IUPAC	International Union for Pure and Applied Chemistry
JEFCA	Joint FAO/WHO Expert Committee on Food Additives

JMPR	Joint FAO/WHO Meeting on Pesticide Residues
Koc	organic carbon normalised distribution coefficient
Kow	octanol/water partition coefficient
Kp	solids-water partition coefficient
L(E)C50	median Lethal (Effect) Concentration
LAEL	Lowest Adverse Effect Level
LC50	median Lethal Concentration
LD50	median Lethal Dose
LEV	Local Exhaust Ventilation
LLNA	Local Lymph Node Assay
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
LOED	Lowest Observed Effect Dose
LOEL	Lowest Observed Effect Level
MAC	Maximum Allowable Concentration
MATC	Maximum Acceptable Toxic Concentration
MC	Main Category
MITI	Ministry of International Trade and Industry, Japan
MOE	Margin of Exposure
MOS	Margin of Safety
MW	Molecular Weight
N	Dangerous for the environment (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC
NAEL	No Adverse Effect Level
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
NOEC	No Observed Effect Concentration
NTP	National Toxicology Program (USA)
o/oo	Parts per thousand
O	Oxidising (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
OC	Organic Carbon content
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational Exposure Limit
OJ	Official Journal
OSPAR	Oslo and Paris Convention for the protection of the marine environment of the Northeast Atlantic
P	Persistent

PAH	Polycyclic aromatic hydrocarbons
PBT	Persistent, Bioaccumulative and Toxic
PBPK	Physiologically Based PharmacoKinetic modelling
PBTK	Physiologically Based ToxicoKinetic modelling
PEC	Predicted Environmental Concentration
pH	logarithm (to the base 10) (of the hydrogen ion concentration $\{H^+\}$
pKa	logarithm (to the base 10) of the acid dissociation constant
pKb	logarithm (to the base 10) of the base dissociation constant
PNEC	Predicted No Effect Concentration
POP	Persistent Organic Pollutant
PPE	Personal Protective Equipment
QSAR	(Quantitative) Structure-Activity Relationship
R phrases	Risk phrases according to Annex III of Directive 67/548/EEC
RAR	Risk Assessment Report
RC	Risk Characterisation
RfC	Reference Concentration
RfD	Reference Dose
RNA	RiboNucleic Acid
RPE	Respiratory Protective Equipment
RWC	Reasonable Worst-Case
S phrases	Safety phrases according to Annex IV of Directive 67/548/EEC
SAR	Structure-Activity Relationships
SBR	Standardised birth ratio
SCE	Sister Chromatic Exchange
SCHER	Scientific Committee on Health and Environmental Risks
SDS	Safety Data Sheet
SETAC	Society of Environmental Toxicology And Chemistry
SNIF	Summary Notification Interchange Format (new substances)
SSD	Species Sensitivity Distribution
STP	Sewage Treatment Plant
T(+)	(Very) Toxic (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
TDI	Tolerable Daily Intake
TG	Test Guideline
TGD	Technical Guidance Document
TNsG	Technical Notes for Guidance (for Biocides)
TNO	The Netherlands Organisation for Applied Scientific Research
ThOD	Theoritical Oxygen Demand

UC	Use Category
UDS	Unscheduled DNA Synthesis
UN	United Nations
UNEP	United Nations Environment Programme
US EPA	Environmental Protection Agency, USA
UV	Ultraviolet Region of Spectrum
UVCB	Unknown or Variable composition, Complex reaction products of Biological material
vB	very Bioaccumulative
VOC	Volatile Organic Compound
vP	very Persistent
vPvB	very Persistent and very Bioaccumulative
v/v	volume per volume ratio
w/w	weight per weight ratio
WHO	World Health Organisation
WWTP	Waste Water Treatment Plant
Xn	Harmful (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)
Xi	Irritant (Symbols and indications of danger for dangerous substances and preparations according to Annex II of Directive 67/548/EEC)

European Commission

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anthracene – part II – human health, **Volume 78**

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The report provides the comprehensive risk assessment of the substance Anthracene. It has been prepared by Greece in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to humans and the environment, laid down in Commission Regulation (EC) No. 1488/94.

Part I - Environment

This part of the evaluation has not been finalised yet.

Part II – Human Health

This part of the evaluation considers the emissions and the resulting exposure to human populations in all life cycle steps. The scenarios for occupational exposure, consumer exposure and humans exposed via the environment have been examined and the possible risks have been identified.

The human health risk assessment concludes that there is concern for workers with regard to skin phototoxicity as a consequence of dermal exposure. There is a need for further information and for testing (on hold) on reproductive and developmental toxicity.

For consumers, humans exposed via the environment and for human health (physico-chemical properties) there is no concern.

The conclusions of this report will lead to risk reduction measures to be proposed by the Commission's committee on risk reduction strategies set up in support of Council Regulation (EEC) N. 793/93.

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Part II – human health

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