

Contaminants in Soil: Collation of Toxicological Data and Intake Values for Humans. Naphthalene

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CONTAMINANTS IN SOIL:

**COLLATION OF TOXICOLOGICAL DATA AND
INTAKE VALUES FOR HUMANS.**

NAPHTHALENE

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Statement of Use

This publication details the derivation of health criteria values for naphthalene. The report has been written for technical professionals who are familiar with the risks posed by land contamination to human health but who are not necessarily experts in risk assessment. It is expected to be of use to all parties involved with or interested in contamination, but in particular to those concerned with the assessment of land contamination.

Keywords

Tolerable daily intake, tolerable daily soil intake, land contamination, risk assessment, human health, naphthalene.

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Contents

1	Introduction	1
2	Identity	2
3	Toxicity	3
4	Carcinogenicity and genotoxicity	6
5	Derivation of tolerable daily intakes	7
	The recommendations of the EU Scientific Committee on Food (SCF)	7
	The recommendations of the EU risk assessment report	7
	The IPCS Environmental Health Criteria Document	8
	The recommendations of the USEPA	8
	The recommendations of the ATSDR	9
	Conclusions	9
6	Intake of naphthalene from food, water and air	11
7	Other sources	13
8	Conclusions	14
	References	15

1 Introduction

- 1.1 This report is one of a number of reports on the assessment of risks to human health from contaminants in soil. Key data and expert opinion are presented on the toxicology of naphthalene and its intake, by the general population, from background environmental exposure. It may be necessary to update this report in the future to incorporate new toxicological data as scientific knowledge advances.
- 1.2 The aim of this report is to set out authoritative health criteria values for naphthalene, which have been established through a review of the scientific literature and a subsequent peer review process. The health criteria values that are presented herein will be used to derive Soil Guideline Values (SGVs) for naphthalene; these are concentrations of naphthalene in soil below which there will be no significant risk to human health.
- 1.3 The overall framework for this review and associated underlying principles are set out in CLR9 *Contaminants in Soil: Collation of Toxicological Data and Intake Values for Humans* (Department for Environment, Food and Rural Affairs (Defra) and Environment Agency, 2002a). Reference to CLR9 is necessary to understand the concepts, terms and approach used in this report.
- 1.4 The computer model used for deriving Soil Guideline Values is described in CLR10 *The Contaminated Land Exposure Assessment Model (CLEA): Technical Basis and Algorithms* (Defra and Environment Agency, 2002b). SGVs for naphthalene will be published in *SGV 19 Guideline Values for Naphthalene Contamination* (Defra and Environment Agency, in preparation).
- 1.5 This report is principally based on the literature published up to November 1996. The report has been updated following a further review of key review publications up to December 2002.

2 Identity

2.1 Naphthalene (CAS No 91-20-3) consists of two fused benzene rings; the chemical formula is $C_{10}H_8$. Naphthalene is a white, crystalline solid, quite volatile, lipophilic and only very slightly soluble in water (about 31 mg L^{-1} at 25°C) (Mackay *et al*, 1991).

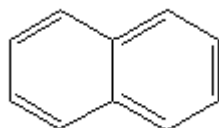


Figure 2.1 The Structure of Naphthalene

2.2 Naphthalene, like the family of polycyclic aromatic hydrocarbons (PAHs), is formed mainly as a result of pyrolytic processes, especially the incomplete combustion of organic materials (IPCS, 1998). Natural sources include volcanoes and forest fires; crude oil and coal tar contain small amounts of naphthalene. Man-made sources include motor vehicle engine exhausts, coal and wood fires, refuse incineration and cigarette smoke. The principal commercial use of naphthalene is as an intermediate in the production of phthalic anhydride; it is also used in the production of the insecticide carbaryl and a number of other organic chemicals (IPCS, 1998).

2.3 In soils, naphthalene is biodegraded to carbon dioxide, with salicylate as an intermediate product; adsorption to soil organic matter reduces the bioavailability and hence the biodegradability of naphthalene. The estimated half-life in a solid waste site has been estimated to be 3.6 months, but more rapid biodegradation is expected in typical soils (Howard, 1989).

2.4 Where studies have reported atmospheric naphthalene concentrations in ppm, a conversion factor of $1 \text{ ppm} = 5.2 \text{ mg m}^{-3}$ (ATSDR, 1995) has been used to ensure consistency throughout the report.

3 Toxicity

- 3.1 Reviews of the literature on the toxicity of naphthalene have been published by the European Commission (EC-JRC, 2003), the International Programme on Chemical Safety (IPCS, 1998), the US Agency for Toxic Substances and Disease Registry (ATSDR, 1995) and the US Environmental Protection Agency (USEPA, 1998). This section is largely based on these reviews (as is Section 4). Particular mention is made of those studies that have been used in deriving tolerable daily intakes (TDIs). In general, the primary publications have not been consulted.
- 3.2 **Absorption.** Lipophilic PAHs can be absorbed through the lungs, the gastrointestinal tract and the skin (IPCS, 1998). The systemic toxicity seen following ingestion, inhalation and dermal exposure to naphthalene is evidence that this general statement holds true for naphthalene. However, there do not appear to be sufficient human or laboratory animal data to form estimates of the fractions absorbed in any of these routes. A figure of 85% for absorption following oral exposure has been claimed, but the basis of this is not clear (Hassauer *et al*, 1993). Toxicological evidence from animal studies suggests that absorption in the gastrointestinal tract is enhanced when the naphthalene is dissolved in a lipophilic medium such as corn oil (ATSDR, 1995). A dermal study, using shaved rat skin, showed that absorption of the naphthalene was slowed when mixed with soil prior to application to the skin (Turkall *et al*, 1994). The limited data available indicate that naphthalene is readily absorbed by all exposure routes in humans (EC-JRC, 2003).
- 3.3 **Distribution.** There are very few data concerning the distribution of naphthalene in either human or animal tissues, but rodent studies on PAHs found the parent compounds and metabolites in almost all tissues, particularly those rich in lipids (IPCS, 1998). In studies with young pigs given oral doses of naphthalene, very different results were found in a single-dose study compared with daily administration over a month. In the former, the highest percentage of the administered dose was in fat, whereas in the latter the highest was in lungs, liver and heart, with very little in the fat tissue (Eisele, 1985).
- 3.4 **Metabolism and elimination.** Metabolism is complex and generally involves cytochrome P450-dependent epoxidation of double bonds, then rearrangement or hydration to yield phenols, diols, and tri- and tetra-hydroxylated compounds, which subsequently undergo conjugation (IPCS, 1998). Naphthalene metabolism differs between species and tissues, and about 20 metabolites (oxidised derivatives and conjugates) have been identified in the urine of animal species. Most metabolites are excreted in the faeces or urine (IPCS, 1998). Following ingestion of naphthalene by rats, metabolism was extensive and urinary elimination was rapid (76% of a dose within 24 hours, in one study) (EC-JRC, 2003).
- 3.5 **Acute toxicity.** In humans, the deliberate ingestion of naphthalene mothballs has caused nausea, vomiting, lethargy, ataxia, convulsions, abdominal pain, haemolytic anaemia (resulting from red cell breakdown), liver toxicity, renal failure, coma and death (ATSDR, 1995; EC-JRC, 2003; IPCS, 1998). Acute lethal oral doses of 2000 mg in a child and 5000 to 15,000 mg for adults have been reported. Haemolytic anaemia was also seen following inhalation or dermal exposure. Infants have died due to haemolysis resulting from exposure to naphthalene-treated clothing, nappies or blankets (ATSDR, 1995; IPCS,

- 1998). There are genetically based differences in human susceptibility to haemolytic anaemia arising from naphthalene exposure (ATSDR, 1995).
- 3.6 Oral toxicity was moderate in mice (LD_{50} of 400 to 700 mg kg^{-1} bw (milligrams per kilogram body weight)) and moderate to low in rats (LD_{50} about 500 to 9400 mg kg^{-1} bw) (EC-JRC, 2003; IPCS, 1998). An 8-hour LC_{50} value of greater than 0.5 mg L^{-1} (500 mg m^{-3}) air for inhalation has been reported for rats (IPCS, 1998). Bronchiolar necrosis was seen in mice exposed for 4 hours at 0.1 mg L^{-1} (100 mg m^{-3}) (Buckpitt and Franklin, 1989). Acute dermal toxicity in rats was low ($LD_{50} > 2500$ g kg^{-1} bw; probably 24/48-hour covered contact) (EC-JRC, 2003; IPCS, 1998). Rodents do not appear to be sensitive to the blood effects of naphthalene, and this should be considered when using rodent data to derive tolerable naphthalene exposure levels for humans. Naphthalene-induced haemolytic anaemia has been reported in dogs (Zuelzer and Apt, 1949).
- 3.7 **Repeated toxicity.** Individuals living in houses where large numbers of mothballs were distributed have suffered anaemia and kidney effects (ATSDR, 1995; EC-JRC, 2003; IPCS, 1998). There is limited evidence linking occupational inhalation of naphthalene with cataracts in humans, but the studies are old and typically involved co-exposure to other substances (ATSDR, 1995; EC-JRC, 2003; IPCS, 1998). No reports of lung damage to humans exposed to naphthalene by the inhalation (or any other) route were found during this review. A woman who ingested 400 mg of naphthalene per day for 7 days (for medicinal purposes) suffered numb extremities and enlarged liver and spleen, while haemoglobin and albumin were detected in the urine (MacGregor, 1954).
- 3.8 The key animal studies are summarised below, including two-year inhalation studies with rats and mice carried out as part of the US National Toxicology Program (NTP, 1992a, 2000) and several sub-chronic oral studies with rodents and rabbits (Battelle, 1980a,b; Shopp *et al*, 1984; IPCS, 1998).
- 3.9 The two-year NTP study in mice involved exposure to atmospheres containing 0, 10 or 30 ppm (0, 52 or 156 mg m^{-3}) of naphthalene, for 6 hours per day, 5 days per week, and the key finding was benign lung tumour induction (paragraph 4.3). Animals of both sexes, in both dose groups, showed non-neoplastic pathology in the nose and lungs (NTP, 1992a).
- 3.10 The two-year study in rats involved inhalation exposures at 0, 10, 30 or 60 ppm (0, 52, 156 or 312 mg m^{-3}) for 6 hours per day, 5 days per week. The main effects were neuroblastoma of the nasal olfactory epithelium and adenoma of nasal respiratory epithelium (paragraph 4.3). Non-neoplastic pathology was seen in the nose in all exposed groups (NTP, 2000).
- 3.11 In a rat inhalation study, signs of nasal olfactory inflammation and proliferative repair were reported in rats exposed to 5 mg m^{-3} , 6 hours per day, 5 days per week for 4 weeks. Higher concentrations administered over 4–13 weeks induced more severe local nasal damage (HRC, 1993a,b).
- 3.12 No effects on the eyes, respiratory tract, blood picture or liver and kidney function were found when naphthalene was given at up to 200 mg kg^{-1} bw day^{-1} (milligrams per kilogram body weight per day), 5 days per week, for 13 weeks to mice by gavage in corn

oil (Battelle, 1980a). In a corresponding rat study, a no observed adverse effect level (NOAEL) of $100 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ was derived, with reduced body weight and possible kidney and thymus damage at higher doses (Battelle, 1980b).

- 3.13 Biochemical indications of possible slight changes in liver function (reduced protein/nitrogen metabolism) were seen in mice given naphthalene at $5.3 \text{ mg kg}^{-1} \text{ bw day}^{-1}$, 7 days per week, for 13 weeks by gavage, in corn oil. At $133 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ there was also a possible minor effect on the blood (an increase in eosinophils, of uncertain clinical significance) and the females showed increased liver weight (Shopp *et al*, 1984).
- 3.14 IPCS briefly mentions a Japanese study where rats ingesting $150\text{--}220 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ for 14 weeks experienced reduced growth, enlarged, fatty liver and kidney inflammation. Cataracts developed in rats and rabbits fed $1000 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ for 46–60 days in the diet (IPCS, 1998).
- 3.15 **Reproductive and developmental effects.** No studies of the potential of naphthalene to affect reproduction in humans have been found. Transplacental exposure of the foetus to naphthalene that had been ingested by the mother has been reported to result in neonatal (and presumably foetal) haemolytic anaemia. No estimates of dose are available (ATSDR, 1995; EC-JRC, 2003).
- 3.16 Fertility studies in laboratory species were not identified. Rat and rabbit studies have not found any evidence of developmental toxic potential. No foetotoxicity or developmental effects were seen when naphthalene was given, by gavage, at up to $450 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ to rats on days 6–15 of pregnancy (NTP, 1991). Transient maternal neurotoxicity was seen, however, even at the lowest dose level of $50 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ (NTP, 1991). No convincing evidence of adverse effects on the foetus was seen in three studies where rabbits were given, by gavage, up to 120, 400 or $500 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ on days 6–18 or 6–19 of pregnancy. The dose ranges included maternally toxic doses (EC-JRC, 2003; IPCS, 1998; NTP, 1992b). Gavage treatment of mice at $300 \text{ mg kg}^{-1} \text{ bw day}^{-1}$ on days 6–13 or days 7–14 of pregnancy caused reduced growth and some deaths in the mothers, and a reduction in the numbers of live births (Hardin *et al*, 1987; Plasterer *et al*, 1985). The limitations of the latter study have been noted (EC-JRC, 2003).

4 Carcinogenicity and genotoxicity

- 4.1 In 2002, an International Agency for Research on Cancer (IARC) Working Group classified naphthalene in Group 2B (“possibly carcinogenic to humans”), based on “inadequate evidence” in humans but “sufficient evidence” in laboratory animals (IARC, 2002). The USEPA has classified naphthalene in Group C, as a “possible” human carcinogen (USEPA, 1998). This conclusion was based on inadequate data in humans and limited evidence in animals exposed by inhalation, but was reached prior to the publication of the two-year rat inhalation study (NTP, 2000).
- 4.2 Information on naphthalene and human cancer is extremely limited. Two brief reports refer to four cases of laryngeal cancer occurring in workers involved in the purification of naphthalene. All four cases were smokers and were exposed to other substances, including coal tar volatiles (Wolf, 1976, 1978). No conclusion can be drawn from these reports regarding the role, if any, of naphthalene in the induction of these cancers (EC-JRC, 2003).
- 4.3 Naphthalene has been tested for carcinogenic potential in mice (NTP, 1992a) and rats (NTP, 2000) as part of the US National Toxicology Program. When mice were exposed to the vapour at 0, 10 or 30 ppm (0, 52 or 156 mg m⁻³, respectively) for 6 hours per day, 5 days per week for two years, the incidence of (benign) lung tumours was significantly increased in the females at the highest concentration. In both groups of exposed males, the incidence of these tumours was higher than in the concurrent controls, but not to a statistically significant extent. A few haemangiosarcomas (malignant cancer of the liver) were found in the top-dose females, but the incidence in this group (3.7%) matched the mean historical control incidence (3.6%) and thus does not constitute evidence of a naphthalene-related effect (NTP, 1992a). Exposure in the rat study was essentially the same except that there was an additional exposure concentration (60 ppm, 312 mg m⁻³). Neuroblastomas of the nasal olfactory epithelium (a very rare tumour type not seen in concurrent or historical controls) were seen in all exposed groups except the 10 ppm females. Adenomas of the nasal respiratory epithelium, another rare type of tumour, developed in all exposed groups except the 10 ppm males (NTP, 2000).
- 4.4 The earlier studies involving exposure of rats or mice by oral, inhalation, dermal, injection or implantation routes gave no convincing evidence of carcinogenicity, but were all of limited sensitivity (EC-JRC, 2003; IARC, 2002; IPCS, 1998).
- 4.5 Naphthalene did not induce chromosome damage (micronuclei) in two mouse studies or DNA damage or unscheduled DNA synthesis (UDS) in rats, and no increases in mutation rates were seen in (about a dozen) Ames bacterial assays (EC-JRC, 2003; IPCS, 1998). However, chromosome aberrations were induced in cultures of hamster cells (when S9 activation was included) and mouse embryo cells (EC-JRC, 2003; IARC, 2002; IPCS, 1998). IARC noted that the results of *in vitro* assays were consistent with an ability to induce chromosome damage (IARC, 2002). However, the available evidence from short-term screening tests has led other expert groups to conclude that, on balance, naphthalene is not an *in vivo* genotoxin (EC-JRC, 2003; IPCS, 1998; SCF, 2002a,b).

5 Derivation of tolerable daily intakes

The recommendations of the EU Scientific Committee on Food (SCF)

5.1 The SCF has recently produced a report on PAHs including naphthalene, having been asked to advise the EU Commission on health risks relating to PAHs in food. The report does not mention the NTP studies where rats and mice inhaled naphthalene for two years. SCF concluded that naphthalene was probably not genotoxic, based on limited negative (i.e. clean) data *in vivo* and mainly negative results *in vitro*. No TDIs were proposed (SCF, 2002a,b).

The recommendations of the EU risk assessment report

5.2 Naphthalene has undergone an in-depth risk assessment at European Community level as a priority substance covered by Council Regulation (EEC) 793/93 on the evaluation and control of the risks of “existing” substances. A draft Risk Assessment Report was prepared by the UK Rapporteur and was peer-reviewed by the EC Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE). The final report did not present any TDI figures for naphthalene. The key health effects were considered to be haemolytic anaemia, local damage resulting from repeated inhalation toxicity and carcinogenicity. A NOAEL could not be derived for haemolytic anaemia because human data are inadequate (and rodents are not suitable models) (EC-JRC, 2003).

5.3 For repeated inhalation exposure, a NOAEL could not be identified, as local damage was seen in the nasal tissue of rats at the lowest tested concentration of 5 mg m^{-3} (about 1 ppm) in a 28-day study involving exposure for 6 hours per day, 5 days per week (paragraph 3.11). Naphthalene was concluded to be non-genotoxic *in vivo*, and the tumours seen in animal bioassays were considered to have arisen via a non-genotoxic mechanism as a consequence of chronic tissue injury. The mouse lung adenomas were considered unlikely to have relevance for humans due to species differences in pulmonary metabolism. There was uncertainty regarding the relevance of the rat nasal tumours to human health, largely because of the possible differences in rat and human metabolism, and the known difference in anatomy and breathing pattern (rats being obligate nose breathers). Despite these differences, it was not possible to dismiss these tumours as being of no relevance for humans. Although a tolerable concentration in air was not derived, the highest airborne environmental exposure of $4 \text{ } \mu\text{g m}^{-3}$ (near a mothball manufacturing site) was three orders of magnitude lower than the 5 mg m^{-3} lowest observed adverse effect level (LOAEL) for local respiratory effects in rats and believed to be of no concern for human health (EC-JRC, 2003).

5.4 The estimated intake of naphthalene from regional environmental exposure ($6.55 \times 10^{-5} \text{ mg kg}^{-1} \text{ bw day}^{-1}$) to naphthalene in air, drinking water and foods was believed to be of no concern, but a similar conclusion could not be reached for environmental exposure in the locality of grinding wheel plants ($0.25 \text{ mg kg}^{-1} \text{ bw day}^{-1}$) (EC-JRC, 2003).

- 5.5 In reviewing the draft report, the CSTE generally agreed with the overall conclusions. However, the Committee noted that an epoxide may be formed in the nasal cavity of exposed rats, pointing to the possible involvement of a genotoxic mechanism alongside chronic inflammation in rat nasal tumour formation. It was agreed that the mouse lung tumours were of little relevance to humans. The Committee concluded that mutagenicity was not of concern in respect of occupational and consumer exposures (CSTEE, 2002).

The IPCS Environmental Health Criteria Document

- 5.6 The IPCS review of selected PAHs (the Task Group met in 1995) did not derive a quantitative estimate of any human cancer risk arising from exposure to naphthalene. In a table appearing in an appendix dedicated to risk assessment approaches (particularly in regard to cancer), two publications are cited as suggesting (on the basis of published experimental studies) a “relative potency” of 0.001 for naphthalene relative to benzo[*a*]pyrene (BaP). IPCS estimated that lifetime exposure to BaP at 1 ng m⁻³ air might be associated with an excess lung cancer risk of 1 in 100,000 (IPCS, 1998).

The recommendations of the USEPA

- 5.7 The USEPA established a reference dose (RfD)¹ in 1998 for chronic oral exposure of 20 µg kg⁻¹ bw day⁻¹. This RfD was derived by applying an uncertainty factor of 3000 (10 each for inter- and intra-species differences, 10 for extrapolating from sub-chronic to chronic exposure, and 3 for database deficiencies) to the NOAEL of 71 mg kg⁻¹ bw day⁻¹ (adjusted from 100 mg kg⁻¹ bw day⁻¹ to account for dosing on only 5 days per week) seen in a 13-week rat gavage study (paragraph 3.12) (USEPA, 1998).
- 5.8 A reference concentration (RfC)² was derived for chronic inhalation exposure. The RfC of 0.003 mg m⁻³ was derived by applying an uncertainty factor of 3000 to the LOAEL of 9.3 mg m⁻³ seen in the two-year mouse study (paragraph 3.9). The 9.3 mg m⁻³ figure was a “human equivalent concentration”, derived from the study LOAEL of 52 mg m⁻³ (10 ppm), adjusted to account for the 6 hours per day, 5 days per week study exposure protocol. The uncertainty factor of 3000 consisted of specific factors of 10 each for inter- and intra-species differences, 10 to extrapolate from a LOAEL to a NOAEL, and 3 for database deficiencies (USEPA, 1998).
- 5.9 The USEPA did not derive quantitative estimates of carcinogenic risk from oral exposure (due to the lack of chronic oral studies) or inhalation exposure (because of the weakness of the evidence for human carcinogenicity). USEPA noted that, while the mechanism of

¹ The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily population exposure that is likely to be without an appreciable risk of deleterious, non-carcinogenic effects during a lifetime.

² The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of non-carcinogenic effects during a lifetime.

induction of the benign mouse lung tumours is not fully understood, the results of genotoxicity tests made a genotoxic mechanism unlikely (USEPA, 1998).

The recommendations of the ATSDR

- 5.10 The ATSDR considered that the data were not sufficient to derive a chronic oral minimal risk level (MRL)³, but an intermediate MRL (for human exposures of up to a year) of 20 $\mu\text{g kg}^{-1} \text{ bw day}^{-1}$ was recommended. This is based on a sub-chronic mouse study in which minor effects on the liver were observed at the lowest dose level used (5.3 $\text{mg kg}^{-1} \text{ bw day}^{-1}$) (paragraph 3.13). The intermediate MRL was calculated from this LOAEL using an uncertainty factor of 300 (3 for use of a minimal LOAEL, and 100 for inter- and intra-species variations) (ATSDR, 1995).
- 5.11 The ATSDR recommended an MRL for chronic inhalation exposure of 0.002 ppm (10 $\mu\text{g m}^{-3}$), based on the NTP's two-year mouse study (paragraph 3.9), in which a LOAEL of 10 ppm (52 mg m^{-3}) for lung effects was identified. This concentration was normalised by adjusting for the 6 hours per day, 5 days per week exposure pattern. An uncertainty factor of 1000 (10 for the use of a LOAEL and 100 for inter- and intra-species variations) was then applied to arrive at the 10 $\mu\text{g m}^{-3}$ figure (ATSDR, 1995).

Conclusions

- 5.12 No good-quality oral carcinogenicity data were identified for naphthalene, but two high-quality inhalation studies have shown carcinogenic potential in rats and mice. The observation of local tissue damage in the cancer target organs, and at the doses producing the tumours, together with the lack of convincing genotoxic potential in screening assays, has led expert groups to conclude that the tumours seen following inhalation did not arise by a directly genotoxic mechanism. The tumour findings, therefore, are not considered to dictate the application of a non-threshold approach to naphthalene risk assessment, and threshold health criteria values have been derived.
- 5.13 Two US expert groups have derived an oral health criteria value and both based their efforts on 13-week gavage studies, albeit in different species. The USEPA applied an uncertainty factor of 3000 to an NOAEL in a 13-week rat study, whereas the ATSDR, in developing an MRL relevant to human exposures lasting for up to a year, favoured application of an uncertainty factor of 300 to a minimal LOAEL (a very minor effect on liver function) reported in a mouse study. Both approaches resulted in a health criteria value of 20 $\mu\text{g kg}^{-1} \text{ bw day}^{-1}$, and this figure is adopted here as the oral TDI.
- 5.14 Following chronic inhalation exposure, naphthalene was carcinogenic to rats and mice. Most of the expert bodies cited above only assessed the mouse study, the exception being the EU risk assessment report, the rat study being available by that time. This report concluded that naphthalene was considered not to have *in vivo* genotoxic activity

³ An MRL is an estimate of the daily human exposure to a substance that is likely to be without appreciable risk of adverse non-cancer health effects over a specified duration of exposure.

and that the tumours resulted from chronic tissue injury; thus exposures that do not induce local tissue damage will not pose any cancer risk.

- 5.15 The USEPA and ATSDR selected the two-year mouse study as the critical study, and agreed that the lowest exposure level of 10 ppm (52 mg m^{-3}), 6 hours per day, 5 days per week, was a LOAEL. After adjustment to an equivalent continuous exposure concentration (9.3 mg m^{-3}), a total uncertainty factor of 1000 (in the case of the ATSDR for the chronic MRL) or 3000 (in the case of the USEPA) was applied to generate (after rounding) health criteria values of $10 \text{ } \mu\text{g m}^{-3}$ (ATSDR) and a reference concentration of $3 \text{ } \mu\text{g m}^{-3}$ (USEPA).
- 5.16 The difference between the two evaluations is an additional factor of 3 favoured by the USEPA to take account of the inadequacy of the database. Considering the insensitivity of rodents to haemolytic anaemia, a key characteristic of naphthalene's hazard profile in humans, this extra conservatism seems appropriate. Caution is also recommended by the observation of effects (proliferative repair in the nasal respiratory epithelium) in rats exposed at 5 mg m^{-3} , 6 hours per day, 5 days per week, for 4 weeks, in a study not cited by USEPA and ATSDR (HRC, 1993a,b). This would be equivalent to a continuous exposure concentration of 0.9 mg m^{-3} , a concentration that is 10 times lower than that derived from the two-year mouse study. The more conservative USEPA figure is, therefore, preferred to the ATSDR value. As a 70 kg adult inhales some 20 m^3 air daily, the USEPA RfC for naphthalene of $3 \text{ } \mu\text{g m}^{-3}$ corresponds, assuming 100% systemic absorption, to an inhalation TDI of $0.86 \text{ } \mu\text{g kg}^{-1} \text{ bw day}^{-1}$.

6 Intake of naphthalene from food, water and air

- 6.1 There are few data on naphthalene in food within the literature. Neither the recent Total Diet Study (TDS) of PAHs in food (FSA, 2002), nor the earlier MAFF TDS study of PAHs (Dennis *et al*, 1983) measured naphthalene. The reviews presented in the EU risk assessment (EC-JRC, 2003) and by the IPCS (1998) provide a few measurements for fish and shellfish, largely in the context of significant oil contamination of the sea or proximity to heavy industry.
- 6.2 The EU risk assessment (EC-JRC, 2003) presents a total daily human dose⁴, equivalent to 4.2 $\mu\text{g day}^{-1}$ for a 70 kg adult, of which 2.2 $\mu\text{g day}^{-1}$ (52%) is considered to come from food. This is on the basis of modelled concentrations in fish, meat, milk and plants using predicted biotransfer factors⁵. For comparative purposes a dietary mean daily intake (MDI) has been calculated for the purposes of this study, based on measured food concentrations and consumption rates, as described below.
- 6.3 Fatty food samples from urban retail outlets (petrol stations, stalls and shops) situated next to busy roads and from other areas with predicted lower air concentrations were tested for a range of aromatic hydrocarbons, including naphthalene (MAFF, 1996). This was to establish whether proximity to motor vehicle exhaust emissions could cause an increase in contaminant concentrations in food. The purchasing of food from locations on busy roads is fairly typical behaviour (particularly given the location of many “out-of-town” supermarkets close to busy road junctions). For the purposes of this study, therefore, data relating to samples taken from locations on busy roads are considered to be the most appropriate for use in estimating the oral MDI. The mean concentration of naphthalene in “butter and cheese” samples from shops on busy roads was 14 $\mu\text{g kg}^{-1}$ and the mean concentration in “lard and margarine” samples was 16 $\mu\text{g kg}^{-1}$. The overall mean concentration was 15 $\mu\text{g kg}^{-1}$. In estimating an MDI, it has been assumed that this is the concentration of naphthalene in fatty foods, including meat and poultry.
- 6.4 The EU risk assessment (EC-JRC, 2003) cites Vogt *et al* (1988), who gave a mean concentration in North Sea fish close to oil platforms of 60 $\mu\text{g kg}^{-1}$, while that from the reference points was 10 $\mu\text{g kg}^{-1}$. This range in concentration is similar to that found in fish caught in the Bay of Naples (Cocchieri *et al*, 1990, cited in EC-JRC, 2003) and so the value of 60 $\mu\text{g kg}^{-1}$ has been used in the calculation of the MDI. It has been assumed that all of the “miscellaneous cereal” consumed has a concentration of 4.3 $\mu\text{g kg}^{-1}$, which is the highest measured concentration in barley (Kirchmann and Tengsved, 1991, cited in EC-JRC, 2003). Wild and Jones (1991, cited in EC-JRC, 2003) measured the concentrations of naphthalene in uncooked and tinned carrots and found levels of 7.8 μg

⁴ Based on the “indirect exposure via the environment” for the regional exposure scenario. This does not include occupational exposure or exposure via consumer products.

⁵ The modelled concentrations are based on reasonable worst-case scenarios. It is assumed that all meat and milk come from cattle grazing on contaminated grass and soil, that fish are exposed to surface waters 1 km from effluent treatment works, and that all plants are grown on agricultural soil to which waste-water treatment sludge has been applied and which are subject to aerial deposition.

kg^{-1} and $12.4 \mu\text{g kg}^{-1}$, respectively. These data have also been used in the derivation of the MDI⁶. The lipophilicity and volatility of naphthalene mean that its presence in other foods is less likely, and hence it has been assumed that it is present in other foods in trace amounts only.

- 6.5 Using the above data on naphthalene concentrations in food and data on adult food consumption rates (Gregory *et al*, 1990), adjusted for a 70 kg adult, a mean dietary intake of approximately $7 \mu\text{g day}^{-1}$ has been calculated. The figure of $7 \mu\text{g day}^{-1}$ is consistent with, although slightly higher than, the figure from the EU risk assessment and is the recommended value for use in this report.
- 6.6 The Drinking Water Inspectorate does not currently report speciated data for PAHs. Data are unlikely to be available because EC Directive 98/83/EC (EC, 1998), which is due to come into force in 2003, does not include naphthalene. The IPCS (1998) reported pre-1982 drinking-water concentrations of naphthalene in Canada, Scandinavia and USA ranging from 1.2 ng L^{-1} to 8.8 ng L^{-1} . The EU risk assessment (EC-JRC, 2003) considered further measurements from Zurich and Osaka in their estimation of 30 ng L^{-1} . Using the more conservative EU figure, a daily consumption rate of 2 L per day (Defra and Environment Agency, 2002a) would give rise to a daily intake from drinking water of 60 ng. This is considered to be negligible when compared to the food intake value of $7 \mu\text{g day}^{-1}$ and has not been considered in further calculations.
- 6.7 Releases from vehicle exhaust fumes are a major source of naphthalene in the environment (CSTEE, 2002). The 1997 Toxic Organic Micropollutants Study (DETR, 1998) recorded concentrations of PAHs throughout the UK, but did not include the measurement of naphthalene. The EU risk assessment (EC-JRC, 2003) estimated environmental airborne levels at a regional level to be $0.14 \mu\text{g m}^{-3}$ based on predicted air concentrations for a number of sites. Indoor air concentrations may be of significance, with a study cited in the EU risk assessment (EC-JRC, 2003) reporting a naphthalene concentration of $80 \mu\text{g m}^{-3}$. Few data on indoor air concentrations are available, however, and those presented are not considered to be suitably representative for determining a UK average exposure concentration. The EU regional air concentration of $0.14 \mu\text{g m}^{-3}$ has therefore been used to calculate an adult inhalation MDI⁷ of $2.8 \mu\text{g day}^{-1}$, assuming an inhalation rate of $20 \text{ m}^3 \text{ day}^{-1}$ (Defra and Environment Agency, 2002a).

⁶ The Wild and Jones (1991) paper provides dry weight concentrations. These have been converted to fresh weight by multiplying by the dry weight conversion factor of 0.097 for carrots provided in CLR10 (Defra and Environment Agency, 2002b).

⁷ The EU risk assessment report calculates an exposure of $2.93 \text{ mg kg}^{-1} \text{ bw day}^{-1}$, equivalent to $2.05 \mu\text{g day}^{-1}$ for a 70 kg adult. This is likely to have been estimated using different assumptions on daily inhalation rate and body weight from those in CLR9. To ensure consistency between TOX publications, the approach presented in CLR9 has been used in this review to provide the MDI of $2.8 \mu\text{g day}^{-1}$.

7 Other sources

- 7.1 Ambient air levels in the surroundings of industrial plants and processes, such as aluminium smelters, coke works, incinerators, mothball manufacture, or where there are releases from grinding wheels, may be significantly higher than those found at regional levels (CSTEE, 2002; IPCS, 1998).
- 7.2 In their opinion on the draft EU risk assessment, the Scientific Committee on Toxicity, Ecotoxicity and the Environment of the European Union (CSTEE, 2002) stated that the combined intake of naphthalene from moth repellents, from tar shampoos and soaps, and through damp-proofing operations was the equivalent to 53.9 mg day^{-1} . They did not distinguish between dermal exposure and indoor air inhalation. They also commented that infrequent additional exposure may also arise from creosote or consumers laying damp-proof courses themselves. They considered that significant exposure may occur from exposure of infants to clothing and bedding stored with naphthalene mothballs, but state that no quantitative data are available.

8 Conclusions

- 8.1 The tolerable daily soil intake (TDSI) is defined as the difference between the tolerable daily intake (TDI) and the mean daily intake (MDI) (i.e. $TDSI = TDI - MDI$). The only exception to this is when the MDI is close to, or exceeds, the TDI, in which case the TDSI is set at 20% of the TDI. "Close to" is defined as greater than or equal to 80% of the TDI (Defra and Environment Agency, 2002a). TDSI values are rounded to two significant figures (2SF).
- 8.2 The oral MDI for a 70 kg adult is equivalent to $0.1 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$. Subtracting this value from the TDI_{oral} of $20 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$ results in an adult oral TDSI of approximately $20 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$ (rounded to 2SF). However, the TDSI for a child may be lower as a result of differences in dietary intake and bodyweight. For example, it is estimated that a 20 kg six-year-old child ingests 62% of the adult dietary intake (Defra and Environment Agency, 2002a). Therefore, the oral MDI for a 20 kg six-year-old child is equivalent to $0.22 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$. Subtracting this value from the TDI_{oral} of $20 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$ results in an oral TDSI of approximately $20 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$ (rounded to 2SF). The TDI_{oral} and the oral MDI of naphthalene are given in Table 8.1.

Table 8.1 TDI_{oral} and oral MDI and TDSI for an adult and a six-year-old child

TDI_{oral} ($\mu\text{g kg}^{-1} \text{ bw day}^{-1}$)	Oral MDI for an adult ($\mu\text{g day}^{-1}$)	Oral TDSI for an adult ($\mu\text{g kg}^{-1} \text{ bw day}^{-1}$)	Oral TDSI for a six-year-old child ($\mu\text{g kg}^{-1} \text{ bw day}^{-1}$)
20	7	20	20

- 8.3 The inhalation MDI for a 70 kg adult is equivalent to $0.04 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$. Subtracting this value from the TDI_{inh} of $0.86 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$ results in an adult inhalation TDSI of about $0.82 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$. However, the TDSI for a child may be lower as a result of differences in inhalation intake and body weight. For example, it is estimated that a 20 kg six-year-old child inhales 50% of the adult inhalation intake (Defra and Environment Agency, 2002a). Therefore, the inhalation MDI for a 20 kg six-year-old child is equivalent to $0.07 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$. Subtracting this value from the TDI_{inh} of $0.86 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$ results in an inhalation TDSI of approximately $0.79 \mu\text{g kg}^{-1} \text{ bw day}^{-1}$. The TDI_{inh} and the inhalation MDI of naphthalene are given in Table 8.2.

Table 8.2 TDI_{inh} and inhalation MDI and TDSI for an adult and a six-year-old child

TDI_{inh} ($\mu\text{g kg}^{-1} \text{ bw day}^{-1}$)	Inhalation MDI for an adult ($\mu\text{g day}^{-1}$)	Inhalation TDSI for an adult ($\mu\text{g kg}^{-1} \text{ bw day}^{-1}$)	Inhalation TDSI for a six-year old child ($\mu\text{g kg}^{-1} \text{ bw day}^{-1}$)
0.86	2.8	0.82	0.79

- 8.4 No authoritative assessments of the health risks posed by dermal exposures to naphthalene were identified.

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