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IEH report on

BENZENE IN THE ENVIRONMENT:

AN EVALUATION OF EXPOSURE OF THE UK GENERAL POPULATION AND POSSIBLE ADVERSE HEALTH EFFECTS

1999 **REPORT R12**

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The views expressed here do not necessarily represent those of any Government Department or Agency.

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Executive summary

Benzene has long been recognised as a carcinogen and has historically caused great concern as an occupational health hazard. Current interest, however, is centred on the effects of continuous low-level exposure to benzene both occupationally and environmentally. In response to this concern the Department of the Environment, Transport and the Regions commissioned the MRC Institute for Environment and Health to evaluate exposure of the general UK population to environmental levels of benzene and any potential associated risk to health. A review paper was presented by IEH to an expert workshop in October 1997 and the present report, based on that review paper, takes account of comments and additional information provided by the workshop participants. This report presents a synopsis of the current knowledge about human exposure to benzene in the UK population based on recently published data, summarises the known human health effects and uses this information to assess potential risks to human health.

In the UK, benzene emissions to air are predominantly derived from road transport, mainly petrol; the most important sources include evaporative losses, refuelling emissions and combustion of petrol. Benzene may also enter the environment through fugitive emissions from chemical manufacturing and processing operations and from refining and distribution of fuels, principally petrol. As benzene is primarily found in the atmosphere, human exposure is mainly through inhalation which accounts for >95% of the total daily intake. Ambient air concentrations are generally in the range of 1–6 $\mu g/m^3$ (0.31–1.9 ppb)*.

Given the very minor contribution that non-inhalation sources make to the overall daily intake of benzene to humans, only exposure via inhalation has been considered when estimating the daily exposure of the general population to benzene. Exposure of adults, children and infants to benzene has been estimated for different exposure scenarios by using time–activity patterns and inhalation

* Units used throughout are $\mu g/m^3$ with values in ppb indicated in parenthesis; where the original figures were reported in ppb a conversion factor of 1 ppb = 3.2 $\mu g/m^3$ has been used.

and absorption rates in conjunction with measured benzene concentrations for each micro-environment. Exposures during re-fuelling and driving as well as the contribution of active and passive tobacco smoking have been considered as part of the general population risk characterisation. The analysis shows that infants (<1 year old), the average child (11 years old) and non-occupationally exposed adults, receive average daily doses of 15–26, 29–50 and 75–522 μg of benzene, respectively, which corresponds to an average range of benzene in air of 3.40–5.76 μg/m^3 (1.06–1.80 ppb), 3.37–5.67 μg/m^3 (1.05–1.77 ppb) and 4.47–40.95 μg/m^3 (1.40–12.80 ppb) for infants, children and adults respectively. Infants and children exposed to environmental tobacco smoke (ETS) have benzene exposure levels comparable to those of an adult passive smoker. ETS is a significant source of exposure; a 1995 UK survey showed that 47% of children aged 2–15 years live in households where at least one person smokes. The consequence of benzene exposure in infants is more significant than for children or adults owing to their lower body weight; this is reflected in the higher daily intake (1.68–2.85 μg/kg bw/day) of infants compared with children (0.71–1.20 μg/kg bw/day) or non-smoking adults (1.07–2.1 μg/kg bw/day). The worst-case scenario for benzene exposure in the general population is that of an urban smoker who works adjacent to a busy road for 8 hours/day (e.g. a maintenance worker) who can receive an average daily exposure of approximately 820 μg (equal to an estimated exposure of 41 μg/m^3). This represents a physically active individual whose inhalation rate is higher than that of a person in a more sedentary occupation.

The major health risk associated with low-level exposure to benzene is leukaemia and the strongest link in humans is with acute non-lymphocytic leukaemia (ANLL). To date little information has been found relating adverse health effects among women, children or the elderly to benzene exposure, as most studies have involved exposure of male workers. The lowest level of exposure at which an increased incidence of ANLL among occupationally exposed workers has been reliably detected appears to be in the range of 32–80 mg/m^3 (10–25 ppm). Although some studies have suggested that effects may occur at lower levels, clear estimates of risk have not been determined, partly because of the inadequacy of exposure data and the small number of cases. Overall the evidence from human studies suggests that any risk of leukaemia to adults at general population exposure levels of 3.8 to 41 μg/m^3 (1.19–12.80 ppb), that is at levels three orders of magnitude less than the occupational lowest observed effect level, is likely to be exceedingly small and probably not detectable using current methodology. There is no evidence to suggest that continuous exposure to environmental levels of benzene manifests as any other adverse health effect.

General introduction

Benzene is a well known genotoxic carcinogen and has caused great concern historically as an occupational health hazard. Progressive reduction in benzene use and continual reduction in the occupational exposure limits has ensured that effects due to high levels of benzene in the workplace should no longer present a serious problem. Current interest focuses on the effects of long-term continuous low-level exposure to benzene both occupationally and environmentally.

In response to this concern, the Department of Environment, Transport and Regions (DETR), formerly known as the Department of Environment (DoE), requested the Medical Research Council's (MRC) Institute for Environment and Health (IEH) to evaluate, for the general population, total exposure to environmental levels of benzene and any potential associated risks to health.

This report is based on a report prepared by IEH for an expert workshop in October 1997. The report incorporates the views presented at the workshop and additional information provided by workshop participants. A list of participants is provided at the end of the report.

The aim of this report is not to provide a complete toxicological review of benzene (as many of these are currently available) but to report on the available UK data on environmental exposure in the general population, to summarise the known health effects in humans and then to use this information to assess the potential risks to human health.

The report comprises three sections: an environmental exposure assessment for benzene, a summary of the known health effects of benzene, and an evaluation of the risk to human health arising from exposure to environmental levels of benzene. It also provides extensive references and a glossary explaining the terms and abbreviations used in the text.

2 Environmental exposure assessment

2.1 INTRODUCTION

This section presents a synopsis of the current knowledge on human exposure to benzene based on recently published data. Individuals can be exposed to benzene in three ways: workers who are exposed in the work-place (i.e. occupational exposure); consumers exposed during the normal use of benzene-containing substances (consumer exposure); and the general population who may be exposed to contaminated air, soil and water, and via the food-chain (indirect exposure; CONCAWE, 1997). This report is primarily concerned with non-occupational exposure.

Restrictions on the marketing and use of benzene were first enforced in the UK in 1982 through the implementation of the amended European directive 82/806/EEC (CEC, 1982, OJ* L339 1.12.82), which banned the use of benzene in toys (where concentration exceeded 5 mg per kg weight of toy or part of toy). Further restrictions were introduced in 1989, whereby benzene concentrations in all consumer products were restricted to less than 0.1% by mass (89/677/EEC in CEC, 1989, OJ L398 30.12.89). The exceptions to this include the use of benzene in industrial processes and benzene in petrol (petrol is regulated to an upper limit of 5% by volume by EC legislation; Directive 85/210/EEC in CEC, 1985, OJ L96 3.4.85). The amount of benzene in petrol in the UK is currently on average about 2% by volume (DoE, 1997).

Much of the work conducted in the UK and elsewhere has shown that the general population is exposed to benzene primarily through inhalation of contaminated air (particularly in areas with heavy road traffic, and in petrol stations while re-fuelling) and tobacco smoke (both active and passive smoking; EBS, 1996; Wallace 1996a; Crump, 1997; Leung & Harrison, 1998). Petrol is the only product marketed to the general public in the UK in which benzene is present in more than trace amounts; consumer exposure to benzene should thus be negligible. As a consequence, only indirect exposure is considered here.

* Council Directive, published in the Official Journal of the European Communities (OJ)

Sections 2.2–2.5 below summarise the information available on sources of human exposure to benzene, current legislation and the effects that stricter regulations may have on future benzene emissions, the environmental fate and behaviour of benzene, and measured environmental concentrations. Section 2.6 provides estimates of the typical exposure of the general population in the UK, using published time–activity data and typical concentrations of benzene in air, water, food and tobacco smoke for various exposure scenarios.

2.2 SOURCES OF BENZENE AND ANNUAL EMISSIONS

Benzene is a simple cyclic organic compound which is found naturally in the environment at low concentrations. The magnitude of benzene emissions from natural sources is unknown; however, on the basis of concentrations reported in remote areas, these are believed to be low in comparison with anthropogenic sources. Benzene occurs naturally in crude oil and as a consequence is a natural constituent of petrol. It is also formed during incomplete combustion of fossil fuels (petroleum products, coal and, to a lesser extent, wood). In addition, it is a commercially important intermediate in the manufacture of many chemicals (Nielsen *et al.*, 1991). Details of its chemical structure and main physicochemical properties are summarised in the Annex.

During 1995, an estimated 35 kilotonnes (kt) of benzene were emitted to the UK environment (see Table 2.1 and Figure 2.1). Emissions to air have increased significantly in the period 1960–1990 as a consequence of the rapid increase in vehicle numbers. Some 70% of emissions are currently derived from road transport, mainly from petrol (Salway *et al.,* 1997); the most important sources include evaporative losses, refuelling emissions and combustion of petrol. Benzene from car exhaust is likely to be a mixture of unburned benzene and benzene produced during the combustion of other aromatic components of petrol (EBS, 1996). Benzene may also enter the environment through fugitive emissions from industrial and non-combustion processes and from refining and distribution of fuels, principally petrol, although these account for only 12% of total emissions.

In the past, benzene was widely used as a solvent, mainly in industrial paints, paint removers, adhesives, degreasing agents, denatured alcohol, rubber cements and arts and crafts supplies (Young *et al.*, 1978; WHO, 1993). The imposition of lower occupational exposure limits led to a reduction in these uses. An exposure limit for benzene in the UK was first established in 1966 when a guideline value of 80 mg/m^3 (25 ppm) 8-hour time-weighted average (TWA) was recommended.

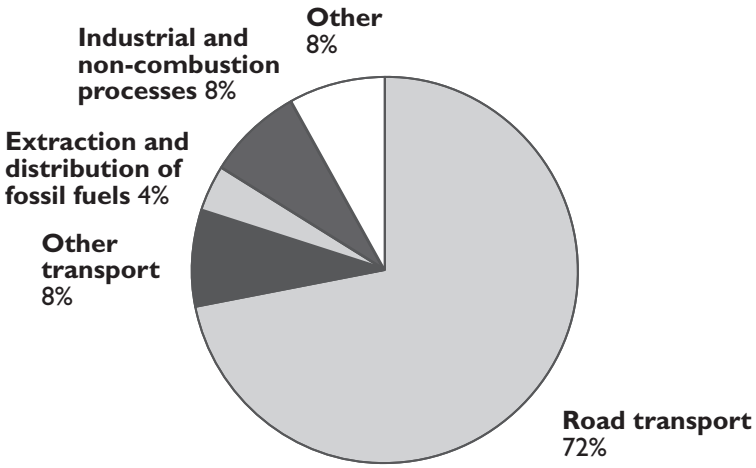
Table 2.1 Benzene emissions inventory (kt) for the UK for 1995[a]

Location	Emission	%
Road transport – diesel fuel (DERV)	0.44	1.3
Road transport – petrol	22.84	65.3
Petrol evaporation	2.02	5.8
Other transport (inc. shipping, railways and civil aircraft)	0.20	0.6
Off-road (inc. naval shipping and military aircraft)	2.50	7.1
Power stations and other stationary combustion processes	2.40	6.9
Extraction and distribution of fossil fuels	1.29	3.7
Industrial and non-combustion processes[b]	2.89	8.3
Solvent use	0.26	0.7
Waste treatment	0.16	0.5
Total	35	

Data from Salway *et al.* (1997)

[a] Total UK emissions ±50%, as data relating to individual industrial processes and solvents are currently incomplete
[b] Including processes in oil refineries, iron and steel rolling mills, road construction, chemical industry, bread baking and food production (including alcoholic beverages)

Figure 2.1 Percentage contribution of sources of benzene to total emissions in 1995



From Salway *et al.* (1997)

Total emissions for 1995 were 35 kt
'Other' includes other combustion, waste treatment and solvent use

Occupational exposure limits were further reduced to 32 mg/m^3 (10 ppm) in 1977 and to 16 mg/m^3 (5 ppm) in 1991. (see Krstic, 1996 for a summary of UK legislation and HSE, 1999 for current occupational exposure limits*). Currently only 0.7% of benzene is used as a solvent in the UK (Table 2.1), mainly as a laboratory reagent (various authors, summarised in WHO, 1993). Building materials and certain furnishing materials may contain trace levels of benzene. For example, a recent study conducted by the Building Research Establishment (BRE) detected trace amounts of benzene in polymeric materials such as vinyl, PVC and rubber floorings as well as nylon carpets and SBR-latex-backed carpets, which may be used in UK homes (Yu & Crump, 1998). Benzene (along with many other volatile organic compounds) is also produced as a fungal metabolite, is present in environmental tobacco smoke, and arises from photocopied and laser-printed paper and associated equipment, particleboard furniture, flooring adhesives, paints, wood panelling, caulking and paint remover (various authors, summarised by Etkin, 1996). Thus it is likely that there is a wide range of potential low-level sources of benzene in homes.

Although thousands of tonnes of benzene are emitted annually by outdoor sources, tobacco smoke has been attributed as a major source of general population exposure to benzene, and smoke inhalation may account for a large proportion of the total exposure in smokers (EPAQS, 1994). Therefore, tobacco smoke is a far more important source of human exposure to benzene than either car exhaust or emissions from stationary sources.

* Until 1984 the Health and Safety Executive (HSE) proposed exposure limits for benzene based on those of the American Conference Industrial Hygienists (ACGIH; Guidance Note EH 15/80). In 1984 these were replaced with a new Guidance Note (EH 40/84) which no longer used the ACGIH exposure limits (HSE, 1984).

2.3 CURRENT LEGISLATION AND ESTIMATED FUTURE EMISSIONS

The UK Government has published a National Air Quality Strategy with the aim of meeting the recommended ambient Air Quality Standard (AQS) of 16 μg/m^3 (5 ppb as a running annual mean; EPAQS, 1994) by the year 2005 (DoE, 1997). As current benzene emissions to the UK environment arise primarily from road transport, stricter regulations have been introduced in recent years to control benzene (and other hydrocarbons) in motor vehicle and fuel emissions.

With the aim of discussing the effects that the implementation of stricter legislation may have on future emissions, the relevant regulations are briefly outlined below.

- Tighter emission limits for gaseous pollutants emitted from heavy duty vehicles were implemented in 1991 through the adoption of Directive 91/542/EEC (CEC, 1991a, OJ L295 25.10.91).

- Stricter emission limits for all new passenger cars (petrol and diesel) were introduced under the Consolidated Directive 91/441/EEC (CEC, 1991b, OJ L242 30.8.91); to meet these standards, new petrol-engined cars registered after 1 January 1993 had to be fitted with three-way catalytic converters.

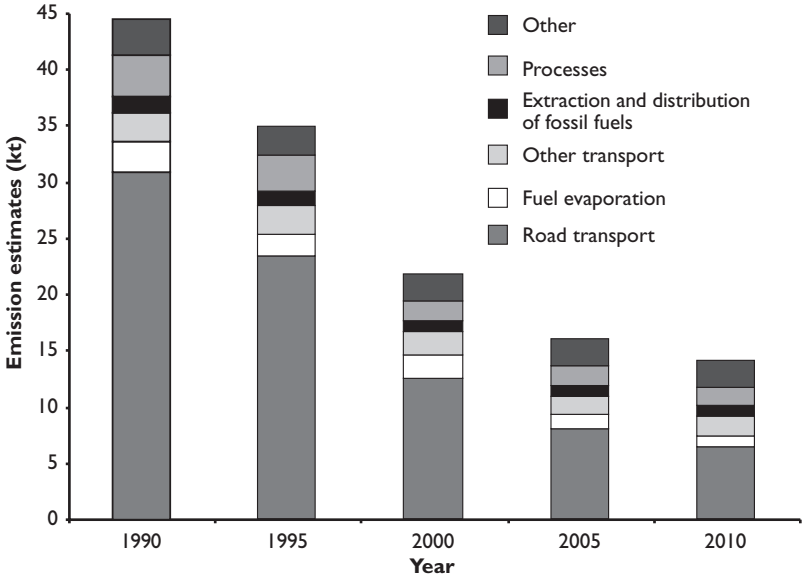
- Emission limits for new light commercial vehicles, off-road vehicles and heavy cars were implemented from 1 October 1994 under Directive 93/59/EEC (CEC, 1993, OJ L86 28.7.93). Petrol-engined vehicles had to be fitted with three-way catalytic converters (to meet the exhaust limits) and with carbon canisters (to control evaporative hydrocarbon emissions); diesel-engined vehicles needed engine modifications or two-way catalytic converters.

- Volatile organic compound (VOC) emissions resulting from the storage of petrol and its distribution from terminals to service stations are in the process of being implemented, as outlined under Directive 94/63/EC ('Stage I' controls; European Parliament and Council of the European Union, 1994, OJ L365 31.12.94). This Directive also covers the loading of petrol onto rail or new oil tanker lorries and inland waterways' vessels. The aim is to reduce emissions from these sources by 80–90% over 10–15 years through the use of technical measures, such as vapour recovery, painting of storage tanks with high reflectance paint and bottom loading of tankers (NSCA, 1997. New storage installations had to comply with the new regulation by 1996; for existing installations various dates have been given: larger facilities have to comply by the year 1999 while smaller facilities have a longer period to make the necessary changes.

- DETR is currently preparing a consultation paper for a scheme to implement Stage II of the petrol vapour recovery process, which will control VOC emissions during the process of car refuelling. It is likely to recommend that active petrol vapour recovery systems, which use a vacuum pump to retrieve and recycle emissions, will form an integral part of the scheme, which may be implemented by regulation.

DoE (1997) has recently estimated the reductions in benzene emissions likely to occur in future years as a consequence of the implementation of current UK policies. These estimates are based on the assumption that all policies mentioned above (with the exception of Stage II) have been fully implemented. It was also assumed that sales of diesel-engined cars would level off at 20% of all car sales from 1994. On this basis, it is estimated that future benzene emissions will decline by almost 40% by the year 2000, by more than 50% by 2005, and by approximately 60% by the year 2010, compared to 1995 levels (Figure 2.2). The significant reductions in emissions from motor vehicles obtained through the implementation of vehicle exhaust emission limits will be offset to an extent through the increase in traffic activity forecast over the next decade or so (DoE, 1997).

Figure 2.2 Annual emissions of benzene in the UK for the period 1990–2010



From DoE (1997)

Processes are industrial processes including iron and steel manufacture
Road transport includes petrol and diesel exhaust emissions
Emissions for 2000–2010 are estimates

2.4 ENVIRONMENTAL TRANSPORT, FATE AND BEHAVIOUR

The volatility and water solubility of benzene greatly influence its environmental transport and partitioning. Benzene is considered to be highly volatile, with a vapour pressure of 12.7 kPa at 25°C. It is also soluble in water, with a solubility of 1780 mg/l at 25°C. The Henry's Law constant for benzene (550 Pa.m^3 per mole at 25°C) suggests that benzene will have a tendency to volatilise into the atmosphere from surface water (WHO, 1993; EBS, 1996).

As highlighted in Section 2.2, benzene primarily enters the environment from vehicle exhaust emissions, industrial sources and as an evaporative component of petrol. Mackay *et al.* (1992) have estimated that, following emission, partitioning of benzene is primarily to air (99%), with some partitioning to surface waters via waste water treatment plant effluents (0.9%) and soil (0.1%). As a consequence, the atmosphere plays a determining role in the ultimate fate of this compound in the environment. However, as benzene is quite mobile between phases, any discussion of its fate, behaviour and occurrence should take into consideration other compartments, such as water, soil, sediment and biota (Nielsen *et al.*, 1991). The fate and behaviour of benzene in these compartments is outlined in Sections 2.4.1–2.4.5 and its occurrence in these matrices is presented in Section 2.5.

2.4.1 AIR

Benzene in air exists predominantly in the vapour phase, with residence times typically of a few days in the UK atmosphere. The main pathway of degradation

is through photo-oxidation by reaction with the hydroxyl radical. Measurements of the rate constant for reaction of vapour phase benzene with hydroxyl radical lie within the range 1.15×10^{-12} to 1.59×10^{-12} $cm^3/molec^{-1}$ $second^{-1}$ (reviewed by Nielsen *et al.,* 1991). The concentration of hydroxyl radical in air is closely linked to the intensity of sunshine, with typical noontime mid-latitude concentrations in the northern hemisphere ranging from 4×10^4 molecules/cm^3 in winter to 3.7×10^6 molecules/cm^3 in summer. Singh and Zimmerman (1992) estimate a lifetime for benzene of 4.8 days in the tropics where hydroxyl radical concentrations are typically high, rising to a global average of 16 days. At a hydroxyl radical concentration considered characteristic of a polluted atmosphere, the lifetime of benzene is about 9 days (Finlayson-Pitts & Pitts, 1986). Products of benzene oxidation in the atmosphere have not been fully characterised, but oxidation products include phenol, nitrobenzene, glyoxal, methylglyoxal and biacetyl (Finlayson-Pitts & Pitts, 1986). With an atmospheric lifetime of several days, benzene is capable of transport in the atmosphere over large distances, typically hundreds or thousands of kilometres. Because of its modest water solubility, wet deposition is not a very effective mechanism for removing benzene from the atmosphere, but will lead to some contamination of surface waters and soils, from which repartition into the atmosphere is a strong possibility.

2.4.2 WATER

Volatilisation and biodegradation are the major processes involved in the removal of benzene from water. Mackay and Leinonen (1975) used thermodynamic calculations to estimate the evaporation of benzene from a one-metre thick water column. Half-lives ($t_{1/2}$) of 4.81 hours (at 25°C) and 5.03 hours (at 10°C) were estimated for still water conditions; well mixed water will have a lower residence half-life than still water at the same temperature. Another study reported lower volatilisation rates during the spring ($t_{1/2}$ = 23 days; 8–16°C) than in summer ($t_{1/2}$ = 3.1 days; 20–22°C) and winter ($t_{1/2}$ = 13 days; 3–7°C) conditions (Wakeham *et al.*, 1983). Although evaporation was the primary mechanism for benzene loss, biodegradation became important during the warmer months.

Microbial degradation of benzene in aquatic environments is influenced by many factors such as microbial population, dissolved oxygen, nutrients, other sources of carbon, temperature and pH (ATSDR, 1993). Benzene is susceptible to biodegradation under both aerobic and anaerobic conditions, with a reported $t_{1/2}$

of 33 hours–16 days, under aerobic biodegradation in surface water (van der Linden, 1978; Tabak *et al.*, 1981; Vaishnav & Babeu, 1987). Under anaerobic conditions, bacterial degradation is slow, with a reported $t_{1/2}$ of 23–720 days in deep waters and groundwater. In the absence of bacterial degradation, benzene can be persistent and may require a lag period of weeks before degradation takes place (Horowitz *et al.*, 1982; Vaishnav & Babeu, 1987; Howard *et al.,* 1991).

Hydrolysis of benzene at typical environmental conditions is not likely owing to the lack of reactive functional groups in the molecule (Nielsen *et al.*, 1991).

The available data seem to suggest that volatilisation can lead to rapid elimination of benzene from the aquatic environment, although it should be noted that benzene in the atmosphere can be returned to water by washout in precipitation and by diffusion across the air:water interface (Hedgecott & Lewis, 1997).

2.4.3 SOIL

Benzene released to soil surfaces can pass into the atmosphere through volatilisation, into surface waters through run off and into groundwater as a result of leaching. Because of its volatility, any benzene released in the top layers of soil is liable to evaporate; however, information on its persistence in and rate of volatilisation from soils is lacking (Nielsen *et al.*, 1991). A useful parameter for investigating the leachability of a chemical is the soil organic carbon partition coefficient (K_{oc}). Compounds that have log K_{oc} values of <2 are considered to be moderately to highly mobile in soils (reviewed by Wilson *et al.*, 1996). With a log K_{oc} of 1.8–1.9 (see Annex) benzene is considered highly mobile in soils. Other parameters that influence the leaching potential include soil type, the amount of rainfall, the height of the water table and the extent of degradation (ATSDR, 1993). Under aerobic conditions biodegradation may also account for a small proportion of loss, although in general benzene is likely to dissipate quickly to the atmosphere and will therefore not remain on the soil long enough for biodegradation to take place (Korte & Klein, 1982). When benzene is buried or released well below the surface, it may be transported into groundwater (see Section 2.4.2 above). However, problems associated with significant leaching of benzene down to aquifers are likely to be localised (e.g. near contaminated sites such as landfills or following accidental spills).

2.4.4 BIOTA

Benzene has a low *n*-octanol/water partition coefficient (K_{ow}; log K_{ow} = 2.13), which indicates a low potential for accumulation in aquatic biota. Geyer *et al.* (1984) have reported an experimental bioconcentration factor (BCF) value of 30 for the green alga *Chlorella fusca*, after exposure to benzene at a concentration of 0.05 mg/l over a 24-hour period. Herman *et al.* (1991) also reported a low experimental BCF of 43 for the alga *Selenastrum capricornutum* exposed for intervals of between 0.5 and 12 hours. As this value was based on dry weights of algae, it probably overestimates fresh-weight BCFs by approximately one order of magnitude. Trucco *et al.* (1983) reported a maximum BCF of 225 for the invertebrate *Daphnia pulix*. Once the organisms were removed from the contaminated water, benzene was rapidly cleared, with 85% of the accumulated benzene being removed during the following 72 hours.

Depuration in fish is also rapid. Half-lives have been estimated as being less than 0.5 days in eel (*Anguilla japonica*) and less than 1 day in some species of striped bass (Ogata & Miyake, 1978; Niimi, 1987). Park and Lee (1993) reported a predicted BCF for fish of 9, which compared well with an experimentally determined value of 13. Most data therefore suggest that bioconcentration of benzene in aquatic food-chains does not appear to be important.

2.4.5 SUMMARY

Most of the benzene released from anthropogenic sources enters the atmospheric compartment directly and, if released to soil or aquatic systems, will reach the atmosphere fairly rapidly owing to its high volatility. Chemical degradation reactions, primarily photo-oxidation reactions with hydroxyl radicals, limit the residence time of benzene in air, with half-lives of 4.8 in the tropics where hydroxyl radicals are typically high, rising to a global average of 16 days under ambient air conditions. Volatilisation and, to a lesser extent, biodegradation are the main processes involved in the removal of benzene from water and soil. Benzene is unlikely to accumulate in aquatic organisms.

2.5 ENVIRONMENTAL CONCENTRATIONS

Benzene has been reported in a variety of matrices including air, water (fresh and marine), sediment, soil, foodstuffs and biota (Nielsen *et al.*, 1991). Concentrations in environmental compartments relevant to this assessment are summarised below. As benzene is primarily found in the atmosphere and human exposure is mainly through inhalation, most monitoring programmes have concentrated on measuring levels in air. Therefore, most data presented here relate to this compartment. Where available, UK data are given. No attempt has been made to cover the vast amount of data available in the literature, but rather to present typical environmental concentrations for key matrices. It should be noted that the data may come from different sources and may therefore not be directly comparable owing to differences such as the reasons for setting up the monitoring programme, sampling and analytical methodologies, quality assurance/quality control procedures, accuracy of measurements, and temporal and spatial variability of the data. Furthermore, when assessing exposure, fundamental information is needed concerning the statistical properties of the distribution of exposure, which are often not provided in the published literature. These points are discussed below.

The Government established the Automotive Hydrocarbon Network in 1991 for the continuous measurement of 25 hydrocarbon species, including benzene, in ambient air. As of 1998, the network comprised 12 urban sites and one rural site.

- Other UK monitoring campaigns are generally designed for specific research activities which have clearly-defined objectives and take place at specific locations and points in time, so levels may not be typical and may not account for temporal and spatial variability.

- Numerous sampling and analytical methods exist for measuring benzene and other VOCs in air and other environmental matrices; there will

therefore be differences in quality assurance/quality control procedures and accuracy of measurements.

Details of the main sampling and analytical methodologies used in the UK for monitoring benzene in ambient air have recently been reviewed by QUARG (1993) and are briefly summarised below. Two basic types of air quality monitoring equipment can be used, passive sampling and continuous automatic monitors. The use of passive samplers, developed in recent years, is a simple and inexpensive technique that provides long-term averaging times, typically of 24 hours–1 month. It is also a convenient way of identifying the spatial distribution of pollution, highlighting hotspots and identifying trends in average concentrations (QUARG, 1993). Benzene and other hydrocarbons are usually collected using passive diffusion tubes containing an adsorbent such as the polymeric resins Tenax and Chromosorb or a graphitised carbon. It is also possible to draw a measured volume of air through an adsorbent tube by use of a pump (active sampling); sampling times range from 30 minutes to several hours. Cryogenic trapping of hydrocarbons is used for some continuous monitors, with a typical sampling period of 30 minutes in every hour.

Once the sample has been collected it is most commonly analysed by gas chromatography. Benzene is usually recovered from the adsorbent by thermal desorption followed by cryogenic trapping. Benzene collected in the cryogenic trap is driven onto the separating column of the gas chromatograph by rapid heating in a flow of helium. The benzene is separated from the mixture of other hydrocarbons collected from the air and detected by flame ionisation detection (FID), photo-ionisation detection (PID), electron capture detection (ECD) or mass spectrometry (MS).

Benzene can also be collected by direct on-column cryogenic trapping, or samples may be analysed directly by using continuous automatic monitors that give instantaneous measurements of air pollution concentrations by transferring the data to a central computer system using telemetry. Continuous monitors provide better resolution than passive samplers as they allow for measurements of short-term peak concentrations. In the UK, analysis is generally by GC-FID or GC-ECD (QUARG, 1993). The limits of detection for these techniques are in the low ppb to low ppt ranges. Monitoring can either be in batch mode, with remote air sampling, or quasi-continuously, with a typical sampling period of 30 minutes in every hour. Data regarding the comparability of different methods of monitoring

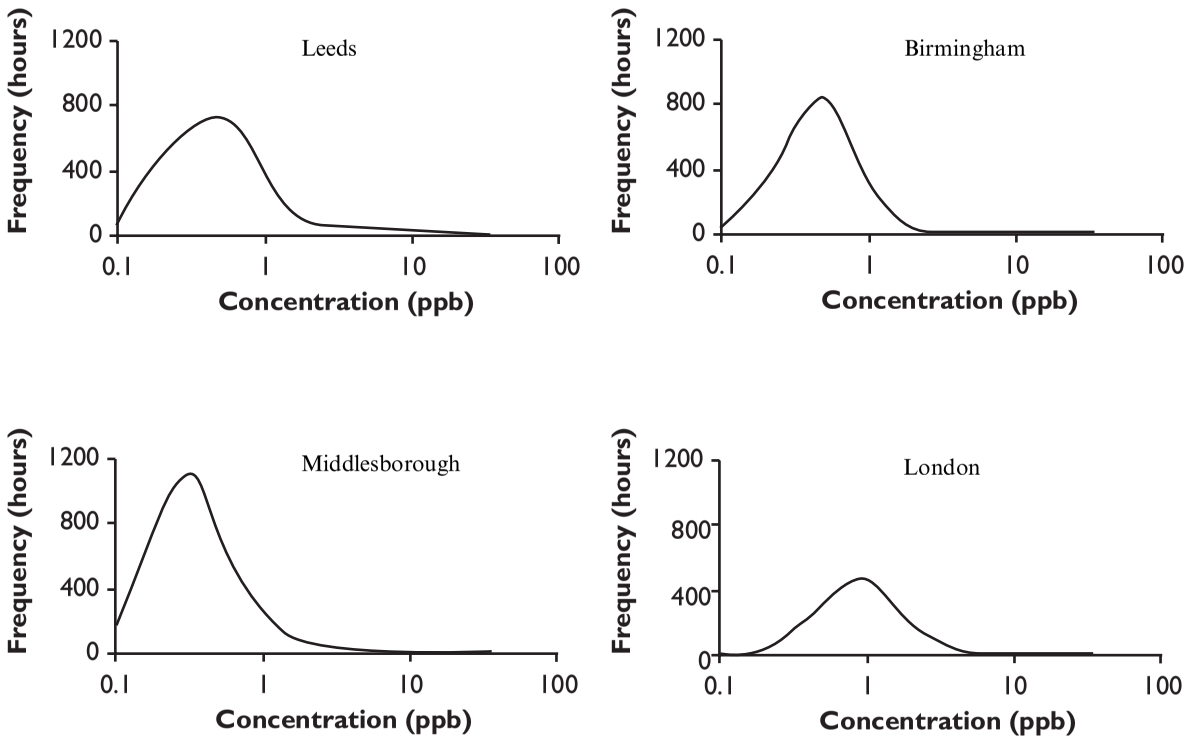
are currently inadequate and there are no UK or international standards describing the required performance, although some relevant standards are in preparation.

- The information on monitoring provided in the published literature is often insufficient to permit evaluation of the significance of results. For example, studies may summarise the data, reporting only the mean and/or range of concentrations, with no further details of the frequency, duration and number of samples collected (CONCAWE, 1997).

  It has long been argued that acceptable exposure levels should be defined with reference to the exposure distribution. To obtain environmental concentrations which are representative of the general population good sampling designs are needed, moving away from methods which are biased (e.g. sampling only the worst-case scenario). The distribution of environmental data is usually log-normal. Examples of such distributions are shown in Figure 2.3, which indicates that hourly outdoor air concentrations at four UK sites are generally in the range 0.32–3.2 $\mu g/m^3$ (0.1–1.0 ppb), although high peak concentrations are also measured occasionally. The distribution can become more extreme when measured exposures include numerous zeros or are below the limit of detection, as is the case for benzene concentrations measured in water (see Section 2.5.4 for further details). For a log-normal distribution a geometric mean is often used as a summary measure (Seixas *et al*., 1988); however, geometric means are not always reported in the literature.

  The best summary measure of long-term exposure has been shown to be given by the arithmetic mean of the distribution (Rappaport, 1991), since the distribution of the individual mean values is usually skewed to the right, and the arithmetic mean of this distribution is more sensitive than the geometric mean to contributions of heavily exposed workers (i.e. those in the right tail). Thus the risk of chronic disease is generally related to the arithmetic mean exposure received by an individual over time. Sampling strategies must allow for the distribution of individual mean exposures to be characterised across the population at risk. Some studies of occupational groups, where exposure is intermittent rather than continuous, have indicated that the use of short-term peak rather than long-term average exposure may be a more appropriate exposure metric.

Figure 2.3 Frequency distribution for outdoor air benzene concentrations at four UK sites in 1996



Data supplied by AEA Technology

Birmingham and Leeds are urban background sites; Middlesborough is an urban background site influenced by local non-motor vehicle sources; the London site is at a roadside location (closer to the source)

These paragraphs have highlighted the importance of data interpretation. However as long as the data are treated with caution, they provide a useful source of information in assessing the main sources of exposure and likely risks to humans.

2.5.1 AMBIENT AIR CONCENTRATIONS

Numerous studies have demonstrated that inhalation is the dominant pathway of human exposure to benzene, accounting for more than 95% of the total daily intake (see Section 2.6). Consequently, most monitoring programmes have aimed at measuring benzene concentrations in air. UK data for 1995[a] are summarised in Tables 2.2 and 2.3. These tables only include recent measurements; historical data are unlikely to be representative of current environmental concentrations owing to the introduction of stricter regulations on benzene emissions (see Section 2.3).

Benzene has been monitored in ambient outdoor air since 1991 as part of the DoE's Automatic Hydrocarbon Monitoring Network (AEA, 1997). Each monitoring station uses instruments which sample and analyse the ambient air continuously to provide hourly levels of resolution for 25 speciated hydrocarbons. In 1995 benzene was monitored at a total of 12 sampling stations, 11 urban and one rural[b]. Data for 1995, summarised in Table 2.2, show that annual mean concentrations at urban sites (urban, suburban, city centre and urban industrial) were in the range of 2.2–8.0 μg/m^3 (0.7–2.5 ppb), the lowest level being reported at an urban background location and the highest in an urban centre. However, the annual mean for Southampton and Liverpool were not representative for that year as a whole since these sites were only commissioned in September and December 1995 respectively. Therefore a more representative range is 2.2–3.8 μg/m^3 (0.7–1.2 ppb). Mean annual concentration at a roadside location was 5.4 μg/m^3 (1.7 ppb). Data from a rural site showed a mean annual concentration of 1.3 μg/m^3 (0.4 ppb), which is approximately 30–35% of the current levels measured at most urban background locations (AEA, 1997). In 1995 the Expert Panel for Air Quality Standards (EPAQS) recommended a running annual mean standard for benzene of 16 μg/m^3 (5 ppb) which was not exceeded, though the EPAQS recommended target concentration for benzene of 3.2 μg/m^3 (1 ppb) was exceeded at all urban sites except Edinburgh.

[a] Subsequent to the workshop data from 1996 became available: see the DETR web site at http://www.environment.detr.gov.uk/airq/aqinfo.htm

[b] By 1998 benzene was monitored at 12 urban sites and 1 rural site

Table 2.2 UK outdoor air benzene concentrations (μg/m^3) for 1995 from the Automatic Hydrocarbon Monitoring Network

Location	Site	Start date	1995 mean concentration	Max. hourly concentration	Data capture (%)
Middlesborough	Urban industrial	Jan 1993	3.5	139	95
London	Roadside	Feb 1993	5.4	60	91
London	Suburban	Mar 1993	3.2	49	91
Belfast	Urban background	Aug 1993	2.9	109	95
Birmingham	Urban background	Aug 1993	3.2	108	95
Edinburgh	Urban background	Aug 1993	2.2	36	90
Cardiff	Urban background	Nov 1993	3.8	78	86
Bristol	Urban background	May 1994	3.8	100	93
Harwell	Rural	Jan 1995	1.3	15.4	74
Leeds	Urban background	Jan 1995	3.2	76	94
Southampton	Urban centre	Sep 1995	8.0[a]	89	28
Liverpool	Urban background	Nov 1995	5.1[b]	34	10

From AEA (1997); values reported as ppb

[a] Mean concentration is a 4-monthly average as sampling was only conducted from September to December 1995

[b] Mean concentration is a 1-monthly average as sampling was only conducted during December 1995

Another study measured levels of background ambient benzene concentrations at both rural and urban sites during 1992 (Downing *et al.,* 1994). This survey was conducted over a 6-month period and measured various hydrocarbons at 59 sites, using diffusion tubes. Mean concentrations were in the range 1.6–7.04 μg/m^3 (0.5–2.20 ppb), although in most areas concentrations were below 3.2 μg/m^3 (1.0 ppb; Table 2.3). It was concluded that benzene concentrations were slightly higher in and around London, and in close proximity to roads. Benzene monitoring has also been conducted by Manchester City Council at seven locations since 1994, including semi-rural, urban background, roadside and petrol service station sites (Drabble & Hodgson, 1997). The methodology involves passive sampling to obtain 2-weekly as well as annual running averages. Data for the period January 1995–July 1997 are summarised in Table 2.3. Mean concentrations at the semi-rural site were in the range 0.86–1.95 μg/m^3 (0.27–0.61 ppb) with higher values being reported in urban locations and adjacent to main roads.

A large amount of benzene monitoring has been carried out in the London area using diffusion tubes (DoE, 1997). Mean benzene concentrations of up to 118 μg/m^3 (37 ppb) have been reported at roadside sites in close proximity to the

Table 2.3 UK benzene outdoor concentrations (μg/m^3) from passive monitoring networks

Location	No. of sites	Concentration	Comment	Reference
Outdoor, general	59	1.6–7.04[a]	Mean ranges over 6 months	Downing *et al.* (1994)
Outdoor, Avon	13	5	Annual mean	Brown & Crump (1996)
Roadside (<20 m)	NR	10–45[a]	Averaging time not reported	DoE (1997)
Semi-rural, Manchester	2	0.86–1.95[a,b]	Annual running mean	Drabble & Hodgson (1997)
Urban, Manchester	3	1.28–3.14[a,b]	Annual running mean	"
Roadside, Manchester	2	1.92–6.85[a,b]	Annual running mean	"

NR, not reported

[a] Values reported as ppb

[b] Based on data supplied by Environmental Health Division, Technical Services Department, Manchester City Council, Town Hall, Manchester M60 2JT

kerbside. Typical mean benzene concentrations at sites within 20 m of busy roads appear to cover the range 10–45 μg/m^3 (3.13–14.1 ppb), although levels generally lie in the mean range 30–37 μg/m^3 (9.4–11.6 ppb). Thus benzene concentrations in outdoor air are usually highest adjacent to busy urban streets and lowest in remote locations, reflecting traffic density.

There is a marked seasonal variation in outdoor air concentrations of benzene; in the winter they are approximately 1.5–3 times higher than during the summer (AEA, 1997; Crump, 1997), possibly owing to the higher prevalence of cold, still weather conditions at this time of year. Typical average concentrations in the Avon area for the period June 1991–May 1992, for example, were 3 μg/m^3 (0.94 ppb) during the spring and summer and 5 and 8 μg/m^3 (1.56 and 2.5 ppb) during the autumn and winter months, respectively (Crump, 1997).

Ambient UK levels are within the ranges reported elsewhere. Recent large-scale studies in the USA and Canada, for example, have shown that mean outdoor air concentrations are in the range 1–8 μg/m^3 (0.3–2.5 ppb; see Table 2.4). In the Netherlands, studies have shown that in streets where cars are parked, levels of benzene in indoor air and at the front of houses can be 1.5–2 times higher than those measured at the back of the houses (Bloeman *et al.*, 1993). This has been attributed to the evaporation of benzene from petrol tanks and engines. The increase is likely to be as significant in the UK, as highlighted by the higher benzene levels reported near busy roads.

Table 2.4 Mean benzene concentrations (μg/m^3) in North America reported in recent studies

Location	n	Personal exposure	Indoor air	Outdoor air
US TEAM study	800	15	10	6
Alaska	112	24	20	8
California	3000			7
California	1000			4
California	120	5	4	1
California	161		8.3	6
Canada	754		5.4	
Ohio	49	3.2		

From Wallace (1996a)

TEAM, Total Exposure Assessment Methodology

Since the early 1980s, measures have been put in place in the UK to reduce vehicle exhaust hydrocarbon emissions progressively (see Section 2.3). These measures, which have largely involved combustion modifications, are believed to have accounted for a reduction in benzene concentrations observed in outdoor air at a site in central London since the early 1970s (EPAQS, 1994). However, reduction has not been as marked at rural locations. Although a slight downward trend in benzene concentrations was noted between 1986 and 1990 at Harwell (Oxfordshire), with levels fluctuating between 1.28 and 5.44 μg/m^3 (0.4 and 1.7 ppb), expressed as a running 3-month average, measurements made at two other rural sites in southern England during 1989 and 1991 have shown rises in annual average concentrations, reaching mean values of 2.88–3.2 μg/m^3 (0.9–1.0 ppb) in 1991 (EPAQS, 1994).

Although traffic is likely to increase in the UK over the next few years, recent legislation requiring the introduction of catalytic converters in new cars and the introduction of a check on exhaust emissions as part of the Ministry of Transport (MOT) test is expected to prevent an increase in emissions over the next 15–20 years (EPAQS, 1994).

To summarise the information presented in this section, values of 1.3 μg/m^3 (0.4 ppb; AEA, 1997), 4.0 μg/m^3 (1.25 ppb; mean of nine urban sites; AEA, 1997) and 33 μg/m^3 (10.3 ppb; DoE, 1997) are assumed to be typical UK rural, urban and roadside background concentrations, respectively, for the purpose of estimating exposure of the general population to benzene in outdoor air.

2.5.2 INDOOR AIR CONCENTRATIONS

BRE has recently undertaken a major study to determine the levels of specific pollutants, including benzene, in a sample of homes in the Avon area (Brown & Crump, 1996). This study, known as the BRE Indoor Environment Study, involved 174 households of participants in the Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC). Women were recruited to this study during early pregnancy, with the intention of monitoring the health of their children for 7 years from birth (Crump, 1997). The Avon area was chosen because it comprises a mixture of environmental conditions from open country to dense central urban housing. However, benzene concentrations in these houses may not be typical of the whole population, as the study monitored levels in homes with young families (i.e. expecting mothers and babies under 6 months of age). Indoor air was monitored in the living room and main bedroom of all 174 homes, and in other rooms in some of these homes, using passive samplers containing Tenax tubes (Perkin-Elmer; passive sampling); 13 outdoor sites were also monitored. Samplers were each exposed for one month and monitoring continued for up to 12 months at each sampling location. Table 2.5 summarises the results. The mean indoor concentration was 8 $\mu g/m^3$ (2.5 ppb; n = 3000 samples) compared with an outdoor mean of 5 $\mu g/m^3$ (1.6 ppb; n = 125). Similar results were found in six homes in Hertfordshire where mean indoor concentrations were higher (11–13 $\mu g/m^3$; 3.4–4.1 ppb) than the mean concentration measured at one outdoor site (7 $\mu g/m^3$; 2.2 ppb; Brown & Crump, 1996). These values seem to be in agreement with those reported for other countries (see Table 2.4).

Table 2.5 Summary of benzene measurements ($\mu g/m^3$) in homes in Avon

	Mean of monthly readings in each house				
Room	n	Mean	SD	Minimum	Maximum
Main bedrooms	173	8	4	2	32
Living rooms	173	8	6	2	46
Kitchens	6	6	2	3	8
Bathrooms	6	6	3	3	8
Second bedrooms	20	5	2	2	11
Outside	13	5	1	3	8

From Crump (1997)

SD, standard deviation

Mean indoor concentrations in different rooms were 1–1.6 times the values measured outside. In eight homes (5% of those studied), mean benzene concentration in at least one room exceeded the UK air quality standard of 16 μg/m^3 (5 ppb; as a running annual average), and in 48 homes at least one monthly mean reading was above 16 μg/m^3 (Crump, 1997). The difference between mean benzene concentrations in the main bedrooms of homes in urban (mean = 9.03 μg/m^3; 2.8 ppb) and rural (mean = 6.4 μg/m^3; 2.0 ppb) locations was statistically significant ($p<0.05$), suggesting that levels indoors are influenced by the higher concentrations of benzene in the outdoor air in cities. Similar trends, though not statistically significant, where also found in living rooms.

Another factor associated with higher concentrations of benzene in indoor air was the presence of an attached garage, the difference being more pronounced when the car was kept in the garage (Table 2.6). The presence of the car resulted in an 80% increase in indoor air concentrations in the home. High levels of benzene (144.7 μg/m^3; 45 ppb, measured over 28 days) were also found inside a garage in a BRE study that measured exposure to a number of indoor pollutants over 30 months (Mann *et al.*, 1997; see Section 2.5.9 and Table 2.12). Of the

Table 2.6 Mean benzene concentrations (μg/m^3; and standard deviations) in indoor air in households with attached garages and with occupants who smoke

	Main bedroom	Statistical significance	Living room	Statistical significance
Garage				
Garage attached	9.73 (6.52)	$p<0.05$	10.02 (7.15)	$p<0.05$
No garage or garage not attached	6.87 (3.3)		7.47 (4.96)	
Use of car with attached garage				
Car in attached garage	12.02 (7.6)	$p<0.05$	12.3 (8.48)	$p<0.05$
Car never in attached garage	6.58 (2.36)		6.9 (2.76)	
Smoker living in home				
Smoker	8.18 (4.26)	$p>0.05$ (NS)	9.58 (7.32)	$p<0.05$
No smokers	7.06 (4.37)		7.15 (4.23)	
Heavy smoker living in home				
Heavy smoker (>50 cigarettes/week)	9.18 (4.93)	$p<0.05$	9.99 (6.47)	$p<0.05$
No smokers (or visitors who smoke)	7.13 (4.53)		7.28 (4.41)	

From Crump (1997)

NS, not statistically significant

households participating in the Avon study, 22% were reported as having attached garages. This will therefore represent an important variable in determining the exposure to benzene in a significant proportion of the UK population. These results are in agreement with those reported in the USA, where benzene concentrations have also been found to be higher in homes with attached garages than in those without (reviewed by Ashmore & Loth, 1994).

The BRE Indoor Environment Study also reported a seasonal variation in indoor air concentrations, which was due to the higher levels in the outdoor air that infiltrated the building and the greater influence of indoor sources during winter compared with summer months, probably due to the lower rates of ventilation (Crump, 1997). Differences in concentrations in indoor environments between smoking and non-smoking households have also been reported. These are discussed below.

SMOKING AND PASSIVE SMOKING

Cigarette smoke contributes significant amounts to the levels of benzene reported in indoor air. The BRE Indoor Environment Study (see above for further details of this study) reported a statistically significant increase in benzene concentrations in the living rooms of homes with one or more occupants who smoke when compared with a non-smoking environment; the increase was lower in main bedrooms (Table 2.6), possibly because fewer cigarettes are smoked there (Crump, 1997). Differences in concentrations were more pronounced in homes where more than 50 cigarettes were smoked by an occupant per week; based on the means of monthly readings, benzene levels were 73% higher in homes with heavy smokers relative to no-smoking homes.

Another study in the UK, conducted by Leung and Harrison (1998), reported higher daily exposures (active sampling over 12 hours during the day) to benzene for smokers (23.0 $\mu g/m^3$; 7.2 ppb) relative to non-smokers (11.52 $\mu g/m^3$; 3.6 ppb). Regular smoking (i.e. where smoking occurred every hour throughout the sampling period) led to elevated concentrations of up to a maximum of 57 $\mu g/m^3$ (17.8 ppb). Further details of this personal monitoring study are provided in Section 2.5.9. Factors such as the number of smokers per household, how many cigarettes are smoked each day and household characteristics such as room size and ventilation rates will clearly influence exposure in the home (Ashmore & Loth, 1994). The fact that in 1995, in the UK, an average of 29% of men and 27% of women were current smokers and that 47% of children (2–15 years) lived in households with at least one person who smoked (Prescott-Clarke & Primatesta, 1997) highlights the importance of this source of indoor air exposure to benzene in passive smokers.

Various large-scale studies from other countries have also highlighted the contribution that cigarette smoke makes to indoor air benzene levels. The US Total Exposure Assessment Methodology (TEAM) studies have reported median levels of benzene in 200 homes without smokers to be 7 μg/m^3 (2.2 ppb), compared with 10.5 μg/m^3 (3.3 ppb) in 300 homes with one or more smokers (Wallace, 1989a). Measurements in 230 homes in West Germany found very similar results, with median values of 6.9 μg/m^3 (2.2 ppb) in no-smoking homes and 9.3 μg/m^3 (2.9 ppb) in homes with smokers (Krause *et al.,* 1987).

In summary, based on the studies described above, concentrations of 7 μg/m^3 and 10 μg/m^3 (2.5 and 3.4 ppb) are representative of indoor air benzene levels in no-smoking and smoking homes, respectively.

2.5.3 REFUELLING AND IN-VEHICLE CONCENTRATIONS

Refuelling at petrol stations and in-vehicle exposure are likely to contribute to increased benzene exposure.

REFUELLING

During refuelling, petrol station exposure will vary according to the benzene content of fuel, the presence or absence of vapour control devices and the amount of time spent at such locations.

An in-depth study has been conducted on behalf of AgipPetroli in Italy to determine the exposure of service station employees to benzene*. A total of 72 service stations were monitored throughout Italy covering motorway, suburban and urban areas to ensure that the measurements were applicable to all types of petrol stations. Benzene levels in air were measured in each petrol station during three consecutive working days, randomly chosen, during both the summer and

* The results of the study, *Evaluation of Benzene Exposure of Employees and Customers in Filling Stations of the AgipPetroli Sector*, were presented to a meeting held in Rome, Italy in February 1993. The data are available from AgipPetroli, Sede Centrale, Via Laurentina 449, 00142 Rome, Italy.

winter, using active sampling monitoring equipment. The results obtained were grouped as follows for each sampling position: petrol station attendants, monitored using personal sampling devices that measured the exposure levels to vapours in air collected from their breathing zone; next to petrol pump column units; close to the entrance of nearby buildings such as coffee shops (motorway areas only) or cash or managers' offices; in the perimeter of the petrol station, usually at the edge of the road away from the petrol pump units; and background sites situated a few hundred metres away from the service area on the opposite side of the road. Concentrations are summarised in Table 2.7. The highest benzene levels were reported in the breathing zone of petrol station attendants, who were exposed to an average concentration over 3 days of 482 μg/m^3 (151 ppb); 52% were exposed to an average of 320 μg/m^3 (100 ppb) while 8% received maximum exposure levels in the region of 2000–3200 μg/m^3 (625–1000 ppb). Exposures varied widely, not only between different petrol stations, but also for the same petrol attendants at different times. Exposure to benzene was found to be related to the car type and pressure within the petrol tank and ambient conditions.

Average air concentrations over 3 days next to the petrol pump column were 110 μg/m^3 (34 ppb). As expected, the values also varied depending on the type of fuel. Air concentrations next to petrol pump columns supplying leaded and lead free petrol and diesel fuel had median values of 95, 80 and 46 μg/m^3 (30, 25 and 14 ppb), respectively, reflecting their benzene content; lead-free petrol, for example, contained 1.2–2.5% benzene by volume, while leaded petrol contained 1.25–3.5% by volume. [These values are approximate as the original paper only presented the results graphically.] This difference was also reflected in the exposure received by the petrol attendants which, on average, ranged from approximately 50 to 300 μg/m^3 (16–94 ppb), while working at a diesel fuel pump column, and from 750 to 1100 μg/m^3 (234–344 ppb), while refuelling vehicles with leaded petrol.

The study also included an assessment to determine the exposure of petrol attendants during refuelling. The refuelling operation was divided into three phases to include:

- removal of the tank cap, unhooking of nozzle and introduction of this into the opening of the tank (average time for this phase was approximately 10 seconds);
- fuel inflow (average time 40 seconds); and
- removal of nozzle from the tank, replacement of this into the column unit and screwing the tank cap before closure (average time approximately 10 seconds).

Table 2.7 Studies reporting benzene concentrations (μg/m^3) in air in and around petrol stations

Location	No of sites	Concentration					Comment	Reference
		Mean	GM	Median	Min	Max		
Italy[a]								
Personal monitoring, service station attendants	72	482	336	371		~3200	Active sampling	Data available from AgipPetroli
Air next to petrol pump	72	110	74	72		~440	Sampling time corresponds to average fuelling time	
Coffee shop entrance	72	51	36	36		~140		
Road	72	42	31	30		~150		
Background	72	24	20	22		~90		
Various European countries								
Petrol attendants	5	2100			<160	5200	Active sampling Sampling time corresponds to average fuelling time	CONCAWE (1994a)
UK[b]								
Petrol station	4	3.8			1.6	6.9	Passive sampling	CONCAWE (1996)
Roadside	4	1.4			1.0	1.8	Data refer to range of annual running averages	
Semi-rural background site	1	<1.0						
Outside vehicles during refuelling, Birmingham	15	190					Active sampling Sampling time corresponds to average fuelling time	Leung & Harrison (1998)
Petrol station courtyard, Manchester	2	11–28					Passive sampling Data refer to range of annual running averages	Based on data supplied by Manchester City Council[c]

GM, geometric mean

[a] Maximum concentrations presented only as histograms; AgipPetroli, Sede Centrale, Via Laurentina 449, 00142 Rome, Italy

[b] Subsequent to the IEH workshop the results of a study on benzene concentrations in the vicinity of petrol stations was published (Uren, 1997)

[c] Environmental Health Division, Technical Services Department, Manchester City Council, Town Hall, Manchester M60 2JT

The atmospheric concentrations were measured during these phases by placing three personal sampling devices side by side on the shoulder of petrol attendants, each of which was activated during one of the above three phases in order to collect three samples of air. The time spent by each operator on each refuelling operation, the number of refuelling operations and the volume of fuel supplied were also recorded.

Results (summarised in Table 2.8) showed that a single refuelling operation lasted approximately one minute, and the mean air concentration to which the petrol attendant was exposed was 3709 μg/m^3 (1160 ppb), most of the benzene (88%) being emitted while supplying fuel to vehicle (i.e. phase 2)*. By taking into account the variety in shape of vehicle tank caps, erroneous manoeuvres by petrol attendants, accidental dysfunction of the system, and so on, the AgipPetroli study estimated that the introduction of vapour-recovery systems would be capable of reducing the exposure of benzene emissions by 80% and 50% during phases 2 and 3, respectively. This would reduce air concentrations during the whole refuelling operation to 930 μg/m^3 (290 ppb; Table 2.8). Though the aim of this study was focused on the exposure of petrol station employees, these values may provide an estimate of likely exposure to motor vehicle drivers in the UK, where refuelling is mainly carried out by the customer.

An Industrial Hygiene Sub-group of the Oil Companies' European Organization for Environment, Health and Safety (CONCAWE) collated and summarised data from member companies on short-term exposures (2–5 minutes) in the breathing zone of five service station attendants for the period 1986–1992 (CONCAWE, 1994a). The mean air concentration was 2144 μg/m^3 (670 ppb), with a range of <160–5200 μg/m^3 (<50–1630 ppb), which seems to be in general agreement with the values reported for petrol attendants in the Italian study.

Three studies have recently been conducted in the UK to determine benzene concentrations in petrol stations, although none of these measured short-term personal exposures and only one (Leung & Harrison, 1998) measured benzene levels whilst refuelling, using a sampling time corresponding to average refuelling times. A CONCAWE study reported annual average benzene concentrations in air

* The AgipPetroli study estimated exposure based on the assumption that a proposed EU Directive on petrol vapour recovery would be implemented. The aim of the Directive was to fit vapour recovery equipment in filling necks and petrol pump nozzles to ensure hermetic seals, initially capable of recovering 70% of vapour, and eventually (by January 2006), 95% (NSCA, 1997). However it now appears the proposed Directive is not to be implemented.

Table 2.8 Benzene concentration in the breathing zone of petrol attendants during refuelling (values expressed in µg/m^3) before and after vapour-recovery measures

Refuelling phase	Current concentration	Estimated concentration[a]
1	110	110
2	3262	652
3	337	168
Total	3709	930[b]

Data available from AgipPetroli, Sede Centrale, Via Laurentina 449, 00142, Rome, Italy

[a] Assuming 80% of vapour is recovered during phase 2 (fuel inflow) and 50% during phase 3 (removal of fuel nozzle and closure of petrol tank)

[b] In original report this value is incorrectly given as 920 µg/m^3

at a UK petrol station in 1995 (CONCAWE, 1996). Continuous ambient air samples were taken at nine locations over 26 consecutive, 2-week periods, using diffusion monitors; four sites were located within the petrol station, four around a nearby site to assess the effects of passing road traffic, and a further sample at a background location. Annual mean levels around the petrol station (summarised in Table 2.7) were in the range 1.6–6.9 µg/m^3 (0.5–2.2 ppb), with a mean annual average concentration from four sampling points of 3.8 µg/m^3 (1.2 ppb). The results indicated that the service station activities contributed approximately 2.4 µg/m^3 (0.75 ppb; 65%) to the overall mean concentration in air at the service station, 0.5 µg/m^3 (0.16 ppb; 15%) arose from adjacent road traffic and 0.9 µg/m^3 (20%) was associated with background levels of exposure. Two other recent UK studies reported benzene concentrations in air outside vehicles during refuelling. Leung & Harrison (1998) measured an average of 190 µg/m^3 (59.5 ppb; sampling time corresponded to average refuelling time) at 15 sites in Birmingham, and Manchester City Council found annual running averages of 11–28 µg/m^3 (3.45–8.8 ppb) at two sites. The concentrations reported by these three UK studies are lower than those found in the Italian study and the earlier CONCAWE study because they are presented as annual running averages and/or did not monitor personal exposure in the breathing zone while refuelling.

On the basis of the information presented above, a value of 3700 µg/m^3 (1156 ppb) is considered to represent exposure during refuelling without evaporative emissions controls, and a value of 930 µg/m^3 (290 ppb) to represent likely exposure once this type of equipment has been installed in petrol pumps. These values were chosen as being the most representative of exposure available, as they were obtained from a relatively large personal monitoring study which took into account average refuelling time.

IN VEHICLES

Benzene found in the air inside vehicles is largely derived from exhaust or evaporation and varies in concentration according to the vehicle type and age, the fuel used, traffic variables, such as density and speed, and ventilation, that is whether windows are open and ventilation fans or heaters are switched on (SCAQMD, 1989). Older vehicles tend to have slightly higher concentrations of vehicular pollutants than new vehicles. Slower average speeds, due to increased traffic, also tend to raise benzene concentrations inside the vehicle. The air turbulence created by moving vehicles is influenced by traffic density, vehicle speeds and vehicle design. At faster speeds there will be greater turbulence, thereby diluting pollutant concentrations (SCAQMD, 1989). Similarly, concentrations appear to be lower with windows closed and vents opened and with windows closed and air conditioning on (SCAQMD, 1989).

A UK study monitoring personal exposure to benzene, conducted by Mann *et al.* (1997), highlighted the importance of transport as a source of benzene exposure (further details of this study are provided in Section 2.5.9 below). A mean in-vehicle concentration of 55 $\mu g/m^3$ (17.2 ppb) was reported for three BRE employees compared with an outdoor background level of 5 $\mu g/m^3$ (1.56 ppb; Table 2.9). Thus individuals participating in this study were exposed to 11 times higher benzene levels while driving.

Leung and Harrison (1999) conducted a study to determine in-vehicle benzene concentrations in a car being driven along six major roads in Birmingham (Table 2.9) and a rural road in Wales. In-vehicle concentrations were measured within the breathing zone of front passengers. Measurements were also taken from immediately outside the car and at the roadside. Sorbent tubes were positioned inside the vehicle within the breathing zone of front passengers and outside attached to the front of the vehicle. Static sampling sites were located adjacent to one section of each road. Although most samples were collected using a 1990 vehicle, another four cars (year of manufacture ranging from 1984 to almost new) were also used to investigate differences related to the age of the vehicle. For the majority of cars, in-vehicle concentrations recorded while driving on busy roads and along a rural road were similar to those measured outside. However, in urban traffic, in-vehicle levels were higher than those measured at the roadside. This led to the conclusion that benzene levels inside the car were derived from pollution drawn into the vehicle through the ventilation system. Comparison of in-vehicle concentrations with suburban levels shows that in-vehicle levels are 5–38 times higher than those measured outside.

In an older car, in-vehicle concentrations were found to exceed those immediately outside by a factor of 2.3 (compared with a factor of 0.48–1.28 measured in other cars), indicating probable contamination arising from the car itself (e.g. petrol leakages from engine and petrol tanks). Benzene levels were also found to build up in a very new car while stationary without ventilation, especially in warm conditions (in- to out-vehicle ratio = 2.6). Since benzene is only expected to be present as a small percentage in vehicle interior solvents and furnishings, the authors suggested that these levels may arise from petrol evaporation from fuel lines at higher ambient temperatures (Leung & Harrison, 1999).

Leung and Harrison (1999) also assessed in-vehicle concentrations in relation to traffic density by monitoring a number of London taxis. This type of vehicle was chosen because it is diesel-fuelled and therefore 'self-contamination' from fuel is likely to be less important. Measurements inside the taxis showed that concentrations were influenced by the area within which the taxi was driven, the traffic density and the presence of passengers smoking cigarettes. Table 2.9 summarises the mean concentrations for no-smoking taxis. Dense traffic

Table 2.9 Benzene concentration (μg/m^3) inside and outside vehicles and at the roadside

Location	n	Mean	SD	Max	Reference
BRE					
Inside vehicle	3	55	34	80.3	Mann *et al*. (1997)[a]
Outdoor background	3	5.0	2.7		
Birmingham[b]					
Inside vehicle	53	24.7	12		Leung & Harrison[c]
Outside vehicle	53	20.2	11		(1999)
Roadside	53	9.3	7.3		
Outside suburban		0.64–4.8			
London, no-smoking taxis[b]					
Busy traffic density	27	17.9	8.6		Leung & Harrison
Quiet traffic density	19	14.4	10.9		(1999)
Area travelled, central	34	17.9	9.0		
Area travelled, suburban	8	12.2	11.5		
Los Angeles basin[b]					
Inside vehicle	191	42.6	31	268	SCAQMD (1989)[d]
Ambient background air during peak commuting	19	17.0	8.6	35.2	

SD, standard deviation
[a] Sampling over consecutive 28-day exposure periods
[b] Concentrations reported as ppb in original study
[c] Sampling for six 1-hour periods in one day
[d] In-vehicle average concentrations during commuting time; ambient background 4-hour sampling periods

accounted for 25% higher benzene concentrations compared to light traffic. During rush-hours, elevated levels were measured in all areas, indicating that the main source of in-vehicle pollution was from nearby vehicle emissions as opposed to background sources. This study did not measure concentrations immediately outside the vehicles.

In-vehicle levels reported in UK studies are within the range of those reported elsewhere. The largest study to date was conducted in Los Angeles, USA, where exposure to an average benzene concentration in air of 43 μg/m^3 (13.4 ppb) was reported for commuters during the rush-hour (Table 2.9). This was approximately three times the concentration measured by fixed long-term outdoor monitoring stations (SCAQMD, 1989). Other smaller US studies have shown that average in-vehicle benzene exposure can be in the order of three to ten times the background ambient levels (various authors, summarised by Wallace, 1996a). A recent Australian study reported benzene levels inside cars as being around 11 times higher than ambient levels (Duffy & Nelson, 1997). This value was even higher for older cars without catalytic converters, where an average in-vehicle concentration of 154 μg/m^3 (48 ppb), 27 times higher than ambient background levels, was measured during city driving. However, levels dropped sharply in faster-flowing motorway traffic. In general, in-vehicle concentrations were about twice as high for cars without catalytic converters as for newer models with catalytic converters. This study showed that the pollution inside cars was a result of a combination of the cars' own exhaust emissions and those from the other vehicles on the road.

Based on data presented for in-vehicle concentrations, a value of 11 times the average urban concentration of 4 μg/m^3 (1.25 ppb) is believed to be representative of typical exposure while driving and therefore typical in-vehicle concentration can be assumed to be 44 μg/m^3 (13.75 ppb).

2.5.4 WATER CONCENTRATIONS

Benzene is not found in significant amounts in water. Levels reported in fresh water, seawater, groundwater and drinking-water are summarised in Table 2.10. In one UK survey, the benzene content of 80 surface water bodies (rivers and estuaries) collected throughout the UK during 1988–1989 was measured. Average (for samples with levels above the detection limit) and maximum concentrations of 7.05 and 89.4 μg/l, respectively, were reported. However, in 60% of samples

(n = 154) benzene content was below the detection limit of 0.1 μg/l; by using 0.1 μg/l as the level for these samples, an overall average of 2.85 μg/l was calculated (Nielsen *et al.*, 1991). More recently Hedgecott and Lewis (1997) have summarised the levels reported by the Environment Agency in three UK regions (Anglian, North West and North East) in river and coastal waters, groundwater, abstracted water and effluents. For estuarine and coastal waters, higher concentrations were generally detected in relation to both industrial releases and releases during oil extraction and transport. Mean values (expressed as the mean of the detected levels) in these three regions ranged from 1.96 μg/l in the North-East region to 25 μg/l in the North-West region (Table 2.10).

The frequency distribution of benzene concentrations in water is not log-normal, as in most samples the benzene concentration is below the detection limit (Table 2.10). As the mean values summarised in Table 2.10 are the mean of the detected levels, they are overestimates of the actual mean. For example, the high average values reported in the Anglian and North-East regions were a consequence of a very small number of high concentrations being recorded; in 72% of samples levels were below the detection limit. Thus none of the reported average concentrations in surface waters exceeded the annual average Environmental Quality Standard of 30 μg/l benzene in fresh and salt waters proposed by Hedgecott and Lewis (1997), although a number of spot samples did exceed that level. For example, in the North-East region 23% of 823 river and estuary samples collected during 1993–1994 contained benzene, with a mean concentration of 1.96 μg/l. Only two had levels that exceeded the proposed Environmental Quality Standard; concentrations of 312 and 54 μg/l were measured.

In seawater, concentrations of benzene reported by various monitoring programmes in the UK have generally been below the detection limit (Table 2.10). A maximum concentration of 18 μg/l was reported during a survey conducted by the Ministry of Agriculture, Fisheries and Food (MAFF) in 1984 along the East coast of the UK (Nielsen *et al.*, 1991). However, more recent surveys have measured levels of <0.01–0.34 μg/l, with less than 4.3% of samples having levels above the detection limit (Table 2.10; Dawes & Waldock, 1994).

Concentrations in groundwater and abstracted water are generally in the range <0.1–1.5 μg/l (Table 2.10). However, a maximum value of 12 476 μg/l, was recorded at one highly contaminated aquifer in the North-East region; exclusion of this measurement gave a mean value of 0.9 μg/l (Hedgecott & Lewis, 1997). Some concentrations in effluent were very high, with a maximum value of 900 mg/l being reported (Table 2.10).

To summarise, freshwater, groundwater and abstracted water concentrations generally have a mean concentration of benzene (and range) of 0.64 (<0.1–35) µg/l, although in the majority of samples levels are below the detection limit. Higher benzene concentrations of up to 12.5 mg/l may be detected at contaminated sites.

Table 2.10 Benzene concentrations in water (µg/l)

Location	n	Mean[a]	Range	%<DL[b]	Reference
Freshwater					
UK rivers and estuaries	154	7.05 2.85[c]	<0.1–89.4	60	Nielsen *et al*. (1991)
Anglian region, rivers	97	9.3	<0.7–35.4		Hedgecott & Lewis
NE region, rivers/estuaries	823	1.96	<0.3–312	77	(1997)
NW Region, rivers	348	25.1	<10–35.3	98	
Saline waters, estuaries					
Humber, Tees, Tyne, Thames			<1–18		Nielsen *et al*. (1991)
Various sites, UK	48	<0.01	<0.01–0.033	95.8	Dawes & Waldock (1994)
Seawater					
Anglian region	2		<0.02		Hedgecott & Lewis
NE region	26	0.34	<0.3–0.34	96.2	(1997)
NW region	86		<10		
Groundwater					
Anglian region	75	0.64	<0.1–1.5[d]		Hedgecott & Lewis
NE region	156	890 0.9[e]	<0.3–12 476	72	(1997)
Abstracted water					
Anglian region	16		<0.1		Hedgecott & Lewis (1997)
Effluents					
Anglian region	15	0.2	<0.2–0.2		Hedgecott & Lewis
NE region	487	4183	<0.3–900 000		(1997)

[a] Mean of detected levels, unless otherwise specified

[b] Percentage of samples in which the benzene concentration was below the limit of detection (DL)

[c] Value calculated by assuming that values below detection are equal to the detection limit of 0.1 µg/l

[d] In original report this range is incorrectly given as <10–1.5 µg/m^3

[e] Value calculated by excluding the maximum reported concentration of 12 476 µg/l

2.5.5 SOIL CONCENTRATIONS

No data for benzene in soil have been found in the literature. Partitioning of benzene (e.g. from fallout in rain) into this compartment is expected to be extremely small owing to its volatility and low K_{ow}. As this is not an important route of exposure for humans it is not considered further.

2.5.6 CONCENTRATIONS IN FOOD

Using the Total Diet Study, MAFF (1995) has investigated benzene levels in foodstuffs in the UK. This involved the collection of samples in 20 food groups from 10 UK locations, collected in 1993 (Table 2.11). Each food group consisted of retail food products, prepared as for consumption and then combined in amounts reflecting their relative importance in the average UK diet. As shown in Table 2.11 benzene was detected in most samples of carcass meat, offal, meat products, poultry, fish and nuts, but was not detected in most other food groups. This table also summarises the average daily intakes of benzene through food consumption; these are fully explained in Section 2.6.1.

2.5.7 CONSUMER PRODUCTS

Benzene is no longer permitted in products marketed to the general public (see Section 2.1), with the exception of petrol; therefore, any exposure from trace amounts of benzene in consumer products remaining in the home will be accounted for in the levels measured in indoor air. Exposure from any benzene in petrol should be taken into consideration in general population scenarios.

No recent publications were found concerning benzene levels in consumer products. However, this does not mean that benzene is not present in consumer products, but rather that there are currently no monitoring schemes aimed at measuring these levels. There was no significant effect on mean monthly benzene concentrations in the homes of participants in the BRE Indoor Environment Study when painting and decorating activities took place and new furnishings were purchased (Crump, 1997).

Table 2.11 Concentrations and daily intake of benzene in ten samples of each food group from the 1993 Total Diet Study

Food group	Concentration[a] (μg/kg)		Average weight as eaten[b] (kg/day)	Daily intake (μg/person/day)	
	Mean (n = 10)	Range		Lower bound daily intake	Upper bound daily intake
Carcass meat	3	1–7	0.028	0.084	0.084
Offal	6	3–18	0.001	0.006	0.006
Meat products	5	2–8	0.045	0.225	0.225
Poultry	3	1–4	0.018	0.054	0.054
Fish	6	2–13	0.013	0.078	0.078
Eggs	<1	<1	0.016	0	0.016
Milk	<1	<1	0.285	0	0.285
Dairy products	1	<1–1	0.057	0	0.057
Bread	<1	<1	0.113	0	0.113
Other cereals	<1	<1	0.099	0	0.099
Oils and fats	<1	<1–1	0.03	0	0.030
Sugars	<1	<1	0.069	0	0.069
Green vegetables	<1	<1	0.039	0	0.039
Potatoes	<1	<1	0.137	0	0.137
Other vegetables	<1	<1–1	0.073	0	0.073
Canned vegetables	<1	<1	0.036	0	0.036
Fruit	<1	<1	0.065	0	0.065
Fruit products	1	<1–3	0.043	0	0.043
Beverages	<1	<1	0.861	0	0.861
Nuts	3	1–7	0.002	0.006	0.006
Total food	2.03		2.03	0.5	2.4

Lower and upper bound daily intakes for individual food groups have been calculated by using food concentrations as reported in MAFF (1995) and consumption rates as reported in MAFF (1994). For an explanation of how the lower and upper bound intakes were estimated, see text.

[a] Detection limit 1 μg/kg; values <1 in the range column indicate that all samples were below the detection limit

[b] Average weight has been derived from weight purchased, taking into consideration gain or loss of weight in preparation and cooking

2.5.8 SKIN EXPOSURE

Dermal uptake of benzene following dermal contact has been studied by several researchers. Hanke *et al.* (1961), for example, exposed the skin of human volunteers to liquid benzene for a period of 1.5–2 hours and reported a low percutaneous absorption rate of 0.4 mg/cm^2/hour. However, although skin exposure to benzene may be highly relevant in an occupational environment, it is unlikely to be of significance for the general public as benzene is no longer

marketed in consumer products. Exceptions to this may occur when petrol, which in the UK contains an average of 2% benzene by volume (DoE, 1997), is splashed onto the skin during refuelling or misused for cleaning purposes (e.g. cleaning car parts); this may result in avoidable skin exposure (Young *et al.*, 1978).

2.5.9 PERSONAL EXPOSURE MONITORING (INHALATION)

The exposure of individuals to pollutants is dependent upon the time spent in a particular micro-environment and the concentration of the pollutant in that micro-environment. As people spend most of their time indoors, their exposure to benzene is strongly influenced by the concentrations of this compound in the indoor environment (Mann *et al.*, 1997). Exposure can also be enhanced by personal activities which result in higher concentrations in the breathing zone than in the general indoor environment (e.g. through smoking).

The inhaled dose of benzene from cigarettes has been reported to be in the range 16–75 µg/cigarette (Brunnemann *et al.*, 1989). Guerin *et al.* (1992) reported levels of 45.2 µg/cigarette, while Wallace (1995) suggested a value of 55 µg/cigarette. On the basis of these values, using a figure of 40 µg/cigarette to estimate exposure to smokers from this source and assuming that 50% of inhaled benzene is absorbed/retained in the body, smoking 20 cigarettes/day would result in an exposure of 800 µg/day and a retained dose of 400 µg/day (see also Section 2.6.4).

Two studies have recently been conducted in the UK which aimed to determine human personal exposure to benzene (and other VOCs); neither looked at exposure through active smoking (Mann *et al.*, 1997; Leung & Harrison, 1998). In both studies, personal exposure was measured directly as well as indirectly (by combining activity diary data with measures of concentrations in a number of micro-environments).

Mann *et al.* (1997) monitored the exposure of four BRE employees over a period of 12–30 months using passive diffusion samplers. As only a small number of individuals (all office workers) participated in this study, personal exposure may not necessarily be representative of the general population. However, monitoring was conducted over a long period of time providing a good insight into daily

exposure to benzene, as well as long-term information on time–activity data. In addition to personal sampling, measurements were also taken in air at fixed locations, including the workplace, inside and outside the home and inside an attached garage and during transport, to provide information on benzene levels in these micro-environments. Results, summarised in Table 2.12, show that mean personal exposure ranged from 7.3 to 11.0 μg/m^3 (2.3–3.4 ppb). Highest benzene concentrations were found in the garage, inside vehicles and while riding a bicycle. Levels were lowest in the office (which was situated on the third floor of a building, far away from traffic) and outside. By using time–activity data and levels of benzene in air in the different micro-environments, Mann *et al.* (1997) estimated that for individuals living in a non-smoking environment the main exposure to benzene was due to indoor air, owing to the high proportion of time spent in this micro-environment. Exposure during transport was also relatively high; a short time (5–8% of the day) spent in the vehicle resulted in 34–44% of the total daily exposure to benzene.

In the study conducted by Leung and Harrison (1998), active air sampling was used to monitor the personal exposure of 50 volunteers who were divided into four main categories: office workers (15 volunteers), students (15 volunteers), elderly (5 volunteers) and individuals who spend the largest proportion of their time at home, excluding the elderly (15 volunteers). Only one 12-hour period per subject was studied and the whole sampling campaign took one year to complete (summer 1995 to summer 1996). The authors commented that it may not be appropriate to extrapolate these results directly to the general public as the population sampled was not randomly selected. Furthermore, the numbers of individuals within each population category were not evenly distributed between urban and non-urban areas. Nonetheless, this study provides valuable information on personal exposure as well as on a number of micro-environments, some of which have not been measured previously in the UK. The study found that indoor and in-vehicle concentrations generally exceeded those measured at background outdoor locations (Table 2.12). Personal exposures determined indirectly from activity diaries and micro-environment measures (some of which are summarised in Table 2.12) correlated well with those obtained directly from personal samplers. Personal exposures in day time (both urban and rural) were higher than in night time (urban and rural). Elevated exposures were experienced during refuelling and driving, especially in areas where dispersion was limited (e.g. road tunnels and multistorey car parks). Exposure was further increased in volunteers who commuted during rush-hour or travelled in congested traffic. Results from both UK studies are broadly similar, though exposure while driving was not as significant (<5% of total benzene exposure) for the specific groups of volunteers who participated in the

Table 2.12 Average benzene concentrations (μg/m^3) measured by personal and fixed-site monitors for two UK studies

Study location	BRE study[a]		Birmingham study[b,c]			
	Number of employees	Range of means	Number of observations	Mean	SD	Range
Living room[d]	4	5.5–7.2	15	11.52	2.241	
Main bedroom	4	8.5–17.8				
Smoky pub			16	79	21.12	-
Outside	3	2.9–7.3	10	14.08	2.24	-
Pedestrian area			15	18.24	2.88	-
In-vehicle	3	19.0–80.3	52	41.3	34.9	-
On bicycle	1	16.1	15	12.48	4.16	-
Office	4	3.5–5.0				-
Refuelling			15	190	155	-
Garage	1	144.7	-	-	-	-
Personal exposure						
Annual average	4	7.3–11.0	-	-	-	-
12 h day time exposure						
Urban	-	-	28	15	-	2.3–283
Non-urban	-	-	16	9.5	-	0.73–54
12 h night time exposure						
Urban	-	-	5	10.8	-	1.95–18
Non-urban	-	-	6	7.1	-	3.2–15.2

SD, standard deviation

[a] Data from Mann *et al.* (1997); sampling at fixed locations was for consecutive 28-day exposure periods

[b] Data from Leung & Harrison (1998); micro-environment sampling periods were between 10 and 30 minutes. Outside refers to Birmingham city centre

[c] Values reported as ppb in original papers

[d] No-smoking house

In addition to these micro-environments, concentrations in railway trains, London underground, painted rooms, car parks, kitchens while cooking, inside tunnels were also reported in the original papers

Birmingham study (Leung & Harrison, 1998). An important source in indoor air was environmental tobacco smoke, as measured in smoky pubs, where mean concentrations of approximately 79 μg/m^3 (25 ppb) were reported. However, increased levels of benzene from this environment were not reflected in the exposure of those volunteers who wore personal samplers in a pub environment.

Results obtained in these two UK studies are in the range of those reported in other countries (Table 2.4). The largest studies to date are those conducted by US Environmental Protection Agency (EPA), which determined the personal exposure of individuals as part of TEAM studies of benzene and other VOCs. These studies

employed personal air quality monitors to measure exposures of about 800 residents in eight areas of the USA between 1980 and 1987, collecting two 12-hour air samples and one or two tap-water samples during a 24-hour period. Concurrent drinking-water, indoor and outdoor air samples and breath samples were also collected. The results have been published in a number of journals (see for example Wallace, 1989a,b, 1990) and have recently been summarised by Wallace (1996a). They showed that mean personal air concentrations exceed indoor air concentrations, which in turn exceed outdoor air concentrations. Most of the personal exposure to benzene was through air (>99%) with insignificant amounts in water, food and beverages. The average personal exposure was about 15 μg/m^3 (4.7 ppb; see Table 2.4) with a range of 7–29 μg/m^3 (2.2–9.1 ppb). Indoor air levels were in the order of 10 μg/m^3 (3.2 ppb), whilst outdoor air concentrations averaged 6 μg/m^3 (1.9 ppb) with a range of 2–19 μg/m^3 (0.6–5.9 ppb). These results are in agreement with those reported for the two UK studies.

The TEAM study found that the overwhelming source of benzene exposure for smokers was mainstream cigarette smoke; smokers had an average benzene body burden of about 6–10 times that of non-smokers and received about 90% of their benzene exposure from smoking (Wallace, 1996a). For non-smokers, most benzene exposure was ultimately derived from vehicle exhaust or petrol vapour emissions, with a portion of exposure (10%) being due to environmental tobacco smoke.

To summarise, on the basis of the information presented in this section, personal exposure of the general UK population to benzene by inhalation is in the order of 10 μg/m^3 (3.2 ppb). As smoking makes a major contribution to the overall exposure to benzene, whereas for non-smokers exposure will occur primarily from indoor air, and during driving and refuelling at petrol stations, smokers will tend to have higher exposure to benzene than non-smokers.

2.5.10 SUMMARY OF 'TYPICAL' CONCENTRATIONS FOR KEY COMPARTMENTS

A summary of 'typical' concentrations of benzene for the key environment compartments is presented in Table 2.13. In particular, when considering airborne exposure, personal exposure measurements are greater than measured indoor

levels, which are in turn greater than outdoor levels of benzene. The values presented in the table were chosen on the basis of the information in sections 2.5.1–2.5.9, and have been used to assess the average exposure to benzene of the general population in the UK. They are considered to be typical for the purposes of this assessment, which is presented in Section 2.6.

Table 2.13 Summary of typical environmental concentrations for the UK

Media	Concentration	Comment
Air		
Outdoors, rural	1.3 μg/m^3	
Outdoors urban	4 μg/m^3	
Roadside	33 μg/m^3	Adjacent to heavy traffic road
During refuelling	3700 μg/m^3	No evaporative emission control installed
During refuelling	930 μg/m^3	Evaporative emission control installed
In-vehicle[a]	44 μg/m^3	11 times levels of background urban sites
Indoors, rural no smokers[b]	5 μg/m^3	
Indoors, urban no smokers[b]	7 μg/m^3	
Indoors, 1 or more smokers[b]	10 μg/m^3	
Active smoking	800 (400) μg/day	Average daily exposure (and retained dose) assuming that 20 cigarettes are smoked per day, each containing 40 μg of benzene and that 50% of inhaled benzene is absorbed
Personal exposure	10 μg/m^3	
Other compartments		
Drinking-water	0.64 μg/l	
Foodstuffs	2.0 μg/kg	Mean level in TDS food samples
Soil	trace amounts	
Consumer products	trace amounts	
Dermal	trace amounts	

TDS, Total Diet Study

[a] Levels are assumed to be similar while using public and private transport as no information is available for levels in buses. If the main form of transport is by rail, this value is likely to overestimate actual levels; Leung & Harrison (1999) have shown levels in trains to be lower than in-vehicle concentrations.

[b] Owing to lack of monitoring data in other indoor areas, for example offices, schools, etc., it is assumed that exposures in these areas are similar to those reported in the home

2.6 GENERAL POPULATION EXPOSURE TO BENZENE

The health risk associated with human exposure to airborne benzene is a function of its concentration in air and its inherent toxicity, as well as the duration of exposure and inhalation and absorption rates.

Human exposure to benzene is considered to result from ingestion of food and water and from intakes associated with air and, for some people, smoking. The daily intake of a compound is the amount directly taken into the body by inhalation and ingestion. It is possible to determine the daily intake of the average UK individual via ingestion by multiplying the benzene residue level in the food (and water) by the amount of food (and water) consumed. Similarly, the daily exposure through inhalation can be calculated by multiplying the daily amount of air inhaled by the benzene concentration measured in each micro-environment (e.g. concentration in the work-place, in-vehicle, home or outdoors) by the fraction of time spent in that micro-environment. These, in conjunction with appropriate inhalation and absorption rates, can be used to estimate benzene exposure for various sub-populations of the non-occupationally exposed general population.

Sections 2.6.1–2.6.5 provide estimates of the daily dietary and inhalation intakes and time–activity data, consider inhalation and absorption rates and finally provide exposure estimates for both adults and children under different exposure scenarios.

2.6.1 DAILY DIETARY INTAKES

FOODSTUFFS

MAFF conducts yearly surveys (the National Food Survey) to determine the average food consumption of different food products by the UK general population. Domestic food consumption data are collected each year from a representative sample of approximately 7000 households throughout Britain, designed to include differences between regions, income groups, household composition and other socioeconomic factors. The Total Diet Study, carried out on a continual basis, provides, as far as possible, estimates of the average food intakes of the UK population as a whole. As food consumption varies greatly between individuals, the average daily intake of benzene will vary accordingly.

Yearly fresh weight consumption rates of foodstuffs per person were calculated by MAFF (1994) to be as follows: 58 kg of meat and poultry; 104 kg of milk; 20.8 kg of dairy products; 6.6 kg of eggs; 11 kg of vegetable and animal oil; 126.7 kg of vegetables and root crops; 7.3 kg of fish; 75.6 kg of bread and other cereals; 25.2 kg of sugar and preserves; 47.5 kg of fresh fruit and fruit produce; 76.7 kg of beverages; and 0.73 kg of nuts.

By using these consumption rates and the concentrations reported for these food products (see Table 2.11), MAFF (1995) has calculated the total daily intake of benzene from food. Benzene levels in many group food samples were below the detection limit (DL = 1 μg/kg). Dietary intakes were calculated in two ways:

- the chemical was assumed to be present at the DL in any food group sample in which it was undetectable — samples with levels below the DL were assumed to contain benzene at a concentration of 1 μg/kg, thereby giving an overestimate of the actual true concentration; and

- the concentration of the chemical was assumed to be zero if the concentration was below the DL — this value is likely to underestimate the true concentration.

These calculations gave a ‘lower bound’ and ‘upper bound’ estimate of the average UK dietary intake, thereby giving an estimated range of 0.5–2.4 μg/person/day

(see Table 2.11). This estimate was similar to that of 1.2 μg/person/day for the intake of this compound by Canadian adults from food (see MAFF, 1995). Individuals who eat a large proportion of meat and meat products, poultry, fish and/or nuts may be exposed to higher daily intakes of benzene.

WATER

The average daily ingestion of water is generally assumed to be 2 litres per day. By assuming that the average benzene concentration in drinking-water is 0.64 μg/l (see Table 2.13), the daily intake of benzene via this route will be 1.28 μg/person/day.

2.6.2 DAILY INHALATION INTAKES

Based on a pragmatic estimate of exposure that only takes into account outdoor mean rural and urban concentrations (i.e. 1.3–4 $\mu g/m^3$) and assuming that daily inhalation rates by an adult are 20 m^3 of air, benzene levels of 26–80 μg/person/day may be inhaled. These values, however, underestimate the overall daily exposure through inhalation because they do not take into account exposure in other micro-environments such as indoors, in-vehicles, during refuelling or while smoking, which are likely to make a significant contribution. This figure is presented here to illustrate the fact that intake of benzene via inhalation greatly outweighs intakes via food and water consumption, inhalation accounting for at least 95% of the daily exposure to benzene, as numerous studies have demonstrated (e.g. EBS, 1996, Wallace, 1996a). Given the minor contribution that food and water ingestion make to the overall daily intake of benzene in humans, only exposure via inhalation is considered in sections 2.6.3–2.6.5.

2.6.3 TIME–ACTIVITY DATA

In northern European countries, people spend a large proportion of their time indoors (approximately 90–95%), and much of this time is in the home (various

authors, summarised by Mann *et al.*, 1997). The concentration of benzene in non-industrial indoor air exceeds that of outdoor air (see Section 2.5) and exposure in the home can therefore make a substantial contribution to an individual's total exposure to this compound.

Although no in-depth studies have been conducted in the UK to determine time–activity patterns for the general population, there are a few studies that report this type of information for specific population groups. Details of these are presented in Table 2.14 and briefly summarised below.

As indicated in Section 2.5.9, a recent study by Mann *et al.* (1997) on benzene exposure reported time–activity data for four BRE office employees over a period of at least one year. Although this small sample may not be representative of the general population, it provides an in-depth long-term study of activity patterns. These office workers spent an average of 89% of their time indoors, 8% in vehicles (public or private) and the remainder of their time (2%) outdoors.

Another study of 170 homes within the ALSPAC study, mentioned in Section 2.5.2, monitored the number of hours spent in the home each day by each member of the family, using weekly diary sheets (one week per month over a period of 12 months; Farrow *et al.*, 1997). Results indicated that infants (<6 months old) spent a larger proportion of their time in the home (80.4%) than their mothers (76.7%) and fathers (61.3%). However, the mothers covered by this study are less likely to be working outside the home than those with slightly older infants. The study also included a greater proportion of older and better educated mothers than is present in the general population and therefore their time–activity patterns may not be typical. This study highlighted the importance of obtaining data throughout the year to account for seasonal and weekly activity patterns. For example, infants spent longer hours outdoors during the summer months and fathers spent more time at home at week-ends (68%) than on week days (58%) while the reverse pattern was reported for mothers (75% and 80% for week-ends and week days, respectively).

Studies elsewhere (e.g. Roy & Courtay, 1991; Wallace, 1996a) have also reported similar values for time spent indoors, outdoors and in vehicles (Table 2.14). The study by Roy and Courtay (1991) showed that infants (up to 3 years old) spent more hours indoors than adults. However, older children (4–17 years) spent increasing amounts of time outside (Table 2.14). No information has been found regarding the time that infants and children spend in vehicles. For the purpose of this assessment and on the basis of the information presented in Table 2.14, it is

Table 2.14 Selected time–activity data reported (%) for the UK and US

	Indoors				Transport						
	Home	Office*	Other	Total	Private	Public	Total	Outside	Total	Comment	Reference
UK											
Four office workers	52	23	11	86	9	1	10	4	100		Mann *et al.* (1997)
Fathers	61	-	-	-	-	-	-	-	61	170 families in ALSPAC study, 1 year duration starting 6 months before birth of child	Farrow *et al.* (1997)
Mothers	77	-	-	-	-	-	-	-	77		
Infants <6 months	80	-	-	-	-	-	-	-	80		
US											
Infants 0–3 years	79.0	-	17.0	96.0	-	-	-	4.0	100	Indoors other includes office, work-place, school and nursery; outside includes travel, shopping and sports	Roy & Courtay (1991)
Children 4–6 years	74.5	-	12.5	87.0	-	-	-	13.0	100		
Children 7–17 years	74.0	-	13.0	87.0	-	-	-	13.0	100		
Housewives	92.5	-	2.0	94.5	-	-	-	5.5	100		
Employed men	64.5	-	27.5	92.0	-	-	-	8.0	100		
Employed women	74.5	-	18.5	93.0	-	-	-	7.0	100		
Residents	-	-	-	87	7	-	-	6	100	n = 9836 1993–94	Wallace (1996b)

* Includes workplace and school except where specified

assumed that for the general population, 91% of time is spent indoors (home, office or elsewhere), 5% is spent in transport (public or private) to include 2 minutes per week refuelling and the remainder (4%) is spent outdoors. It is also assumed that children and infants will not be exposed to additional benzene during refuelling other than in-vehicle exposure.

2.6.4 INHALATION RATES AND ABSORPTION

A value of 20 m^3 of air/day has been adopted as a standard inhalation rate for humans. This value is widely used to determine the inhaled dose for a given air pollutant for adults. However, breathing rates are affected by numerous individual characteristics, including age, sex, weight, health status and level of physical activity (e.g. running, jogging, etc.). Inhalation rates may be higher among outdoor workers and athletes because levels of activity outdoors may be higher. Therefore these population groups may be more susceptible to air pollutants and are considered to be 'high-risk' groups (Shamoo *et al.,* 1991; Linn *et al.,* 1992).

Approximately 50% of inhaled benzene is absorbed in humans during continuous exposures to 163–326 mg/m^3 (51–102 ppm) for several hours. Results from men and women exposed to 170–202 mg/m^3 (53–63 ppm) for 4 hours showed that 30% of the inhaled dose was retained and that retention decreased with the duration of exposure, reaching a constant level after 2 hours. Women may retain a greater proportion of inhaled benzene than men. Benzene tends to accumulate in tissues containing high amounts of lipids and it crosses the placenta (summarised in WHO, 1993).

Benzene in inhaled air is absorbed into the blood at the alveoli. There is some evidence that the blood:breath ratio increases with decreasing concentrations (Perbellini *et al.*, 1988; Brugnone *et al.*, 1989). For example a benzene blood:breath level ratio of about 20 was observed for nurses exposed only to environmental levels, compared with a ratio of less than half that for chemical workers exposed to higher concentrations (Perbellini *et al.*, 1988). A possible explanation for this phenomenon is the sequestering of a portion of the inhaled chemical by proteins in the blood (Travis & Bowers, 1989). If the capacity of the proteins is relatively small they would become saturated as concentrations

increase, and the laboratory values of the partition coefficient would be approached (Wallace *et al.*, 1996). However, it should be noted that the two population groups used in the experiment conducted by Perbellini and co-workers may not necessarily be comparable (nurses are more likely to be women; chemical workers men, although this information is not provided in their paper).

On the basis of the information presented here, an average daily inhalation rate of 20 m^3/day and an absorption rate of 50% has been assumed for estimating the human absorbed dose of benzene through inhalation. Daily inhalation rates will be higher for specific population groups and absorption rates may also vary with exposure to lower environmental concentrations of benzene. It should be noted, however, that children have much lower inhalation rates; Layton (1993) reported average inhalation rates for infants (<1 year old) and children (aged 1–10 years) of 4.5 and 8.6 m^3 per day, respectively. Similarly, inhalation rates vary according to the level of activity.

2.6.5 HUMAN EXPOSURE ESTIMATES USING DIFFERENT EXPOSURE SCENARIOS

Using information on time–activity patterns (see Section 2.6.3) and inhalation and absorption rates (see Section 2.6.4), in conjunction with measured benzene air concentrations for each micro-environment (see Table 2.13), exposure estimates for the UK general adult population were made for various exposure scenarios:

a) non-smoker who lives in a rural environment;

b) non-smoker who lives in an urban environment;

c) non-smoker who lives in an urban environment in a house where at least one member of the family smokes;

d) smoker who lives in an urban environment; and

e) a smoker who spends 8 hours/day actively working close to heavy traffic (e.g. a road worker on a busy city-centre road).

With the exception of scenario (e), these estimates are based on exposures to average environmental concentrations of benzene and therefore represent best-estimate scenarios. Estimated absorbed daily doses for these five scenarios are presented in Table 2.15. The contribution of each micro-environment for these five scenarios is shown graphically in Figure 2.4.

The estimated mean absorbed dose of benzene to which the general population is exposed via air in non-smoking environments are in the ranges 70–75 μg/day and 89–102 μg/day, for rural and urban residents, respectively (Table 2.15), rural residents being exposed to lower levels owing to the lower indoor air concentrations. These estimates do not take into account differences in commuter times. Similarly, city dwellers may be exposed to higher levels if they live and work in a busy city centre.

Refuelling a car at a petrol station in which evaporative emission control systems have not been installed can lead to an increase in daily benzene doses of 7.4 μg/day. Petrol stations are not currently required to fit vapour recovery equipment (see Section 2.3). However, if a scheme to implement controls to reduce emissions from this source were to be implemented, there should be a gradual reduction of exposure to benzene from this source.

Table 2.15 Estimated absorbed daily doses of benzene (μg/day) for members of the general public under different exposure scenarios[a]

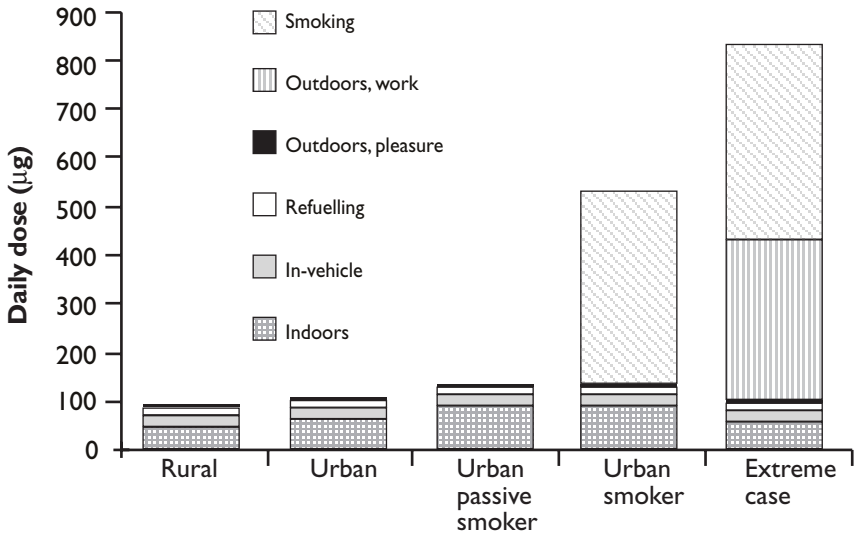
Activity	Rural non-smoker (a)	Urban non-smoker (b)	Urban passive smoker (c)	Urban smoker (d)	Extreme case (e)
Indoors	45.5	63.7	91	91	58
In-vehicle	22	22	22	22	22
Refuelling[b]	1.9–7.4	1.9–7.4	1.9–7.4	1.9–7.4	1.9–7.4
Outdoors, pleasure	0.5	1.6	1.6	1.6	1.6
Outdoors, work[c]	-	-	-	-	330
Smoking	-	-	-	400	400
Total daily dose	70–75	89–95	116–122	516–522	814–819

[a] See text for further details of exposure scenarios (a)–(e); extreme case, an urban smoker who spends 8 hours/day actively working close to heavy traffic

[b] The reported range refers to whether or not vapour recovery equipment has been fitted in filling necks and petrol pump nozzles. As to date these are not required by UK or EU legislation, the higher value will reflect current exposure more accurately and therefore this value is used in Section 5 for evaluating benzene exposure of the general UK population

[c] Breathing rate for heavy activity is 2.5 m^3/hour (Layton, 1993)

Figure 2.4 Estimated daily absorbed doses of benzene for adults under various exposure scenarios



Extreme case: An urban smoker who spends 8 hours a day actively working close to heavy traffic

A similar exercise has been conducted to estimate benzene exposure for infants (<1 year old) and children (aged 11 years) for the following scenarios:

f) an infant who lives in a rural environment;

g) an infant who lives in an urban environment;

h) an infant who lives in an urban environment in a house where at least one member of the family smokes;

i) a child who lives in a rural environment;

j) a child who lives in an urban environment; and

k) a child who lives in an urban environment in a house where at least one member of the family smokes.

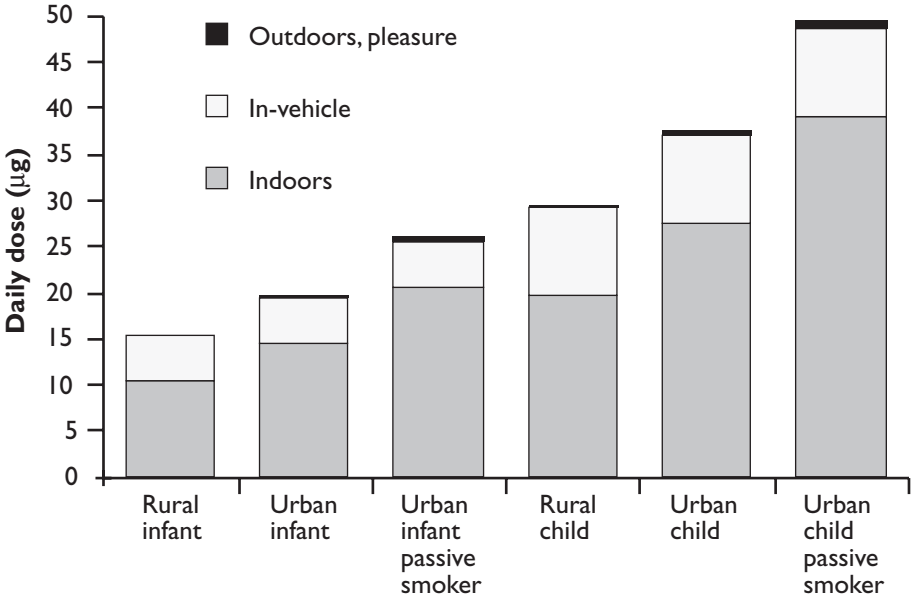
Results are presented in Table 2.16 and shown graphically in Figure 2.5. Exposure during refuelling has not been included in this calculation as infants and children are unlikely to be adjacent to the petrol tank whilst refuelling. Infants and children living in rural areas receive more than half the daily absorbed benzene dose (15.3 μg/day and 29.3 μg/day respectively) of those living in cities (19.7 μg/day and 37.6 μg/day).

Table 2.16 Estimated benzene absorbed daily doses (μg/day) for infants and children under different exposure scenarios[a]

Activity	Rural infant (f)	Urban infant (g)	Urban infant passive smoker (h)	Rural child (i)	Urban child (j)	Urban child passive smoker (k)
Indoors	10.2	14.3	20.5	19.6	27.4	39.1
In-vehicle	5.0	5.0	5.0	9.5	9.5	9.5
Outdoors, pleasure	0.1	0.4	0.4	0.2	0.7	0.7
Total daily dose[b]	15.3	19.7	25.9	29.3	37.6	49.3

[a] See text for further details of exposure scenarios (f)–(k)
[b] Because of rounding total daily dose may not add up to last decimal place

Figure 2.5 Estimated daily absorbed doses of benzene for infants and children under various exposure scenarios



Tobacco smoke is a further important source of benzene exposure for adult smokers and, through passive smoking, for infants and children and non-smoking adults living in households with smokers (Tables 2.15 and 2.16). A recent survey conducted in the Avon area found that 43.2% of households had at least one smoker in the home, and figures published in 1995 showed that 47% of children aged 2–15 years lived in households where at least one person was a current smoker and 66% of children aged 13–15 reported being exposed to other people's smoke (23% of whom claimed to be exposed to cigarette smoke for 15 hours or more a week; Prescott-Clarke & Primatesta, 1997).

On the basis of an estimated benzene exposure of 40 μg/cigarette (see Section 2.5.9 and Table 2.13), smokers may be exposed to average daily benzene doses of 522 μg, with 76% of daily intake being attributed to tobacco (Table 2.15). Passive smoking increases daily benzene considerably in infants and children (to 25.9 μg/day and 49.3 μg/day, respectively for urban dwellers) and daily absorbed doses are likely to be higher for active children (Table 2.16). Benzene exposure may increase to 122 μg/day for non-smoking adults who live in households with one or more smokers. Passive smoking in confined areas (e.g. cars) is likely to increase benzene exposure from this source.

Exposure to benzene may be higher for individuals who spend a large proportion of their day near city centres and congested roads, especially when involved in high levels of activity (as this will increase their inhalation rate and therefore intake of benzene from air). An example of such a situation is presented in scenario (e) where a person who smokes 20 cigarettes/day and works 8 hours/day in an active job (e.g. a labourer) adjacent to a busy city-centre road, may be exposed to an absorbed dose of up to 819 μg/day (Table 2.15).

Levels estimated here are within the same range as those reported in Europe. CONCAWE (1994b), for example, estimated absorbed dose levels of 74 μg/day for non-working, non-smoking, non-driving residents in a rural environment and up to 458 μg/day for office workers who smoke, drive and live in an urban environment. Similarly, EPAQS (1994) estimated daily intakes ranging from 120 μg for a non-smoker living in an unpolluted rural area to 1250 μg/day for a smoker living in a city.

2.6.6 SUMMARY

The UK population is mainly exposed to benzene via inhalation, with food and water ingestion and exposure through dermal contact (of benzene-containing products) being minor contributors to the overall daily intake of benzene. Smokers have the greatest exposure to benzene, this source accounting for nearly 80% of the total daily intake. For non-smokers benzene exposure predominantly occurs from indoor air (as most individuals spend more than 90% of their time indoors), during driving and re-fuelling. Table 2.17 summarises the estimated absorbed daily doses for infants, children and adults. These values are used in Section 5 to evaluate the health risks of benzene exposure to the general UK population.

Table 2.17 Summary of the estimated absorbed daily doses of benzene (µg/day) under different exposure scenarios

Scenario	Daily absorbed dose		
	Infant	Child	Adult
Rural	15.3	29.3	70–75
Urban	19.7	37.6	89–95
Urban passive smoker	25.9	49.3	116–122
Urban smoker	NA	NA	516–522
Extreme case*	NA	NA	814–819

* An urban smoker who spends 8 hours/day actively working close to heavy traffic
NA, not applicable

3 Summary of the health effects of benzene

3.1 INTRODUCTION

This section of the report is concerned with adverse health effects resulting from exposure to low levels of benzene. Numerous reviews over the years have reported adverse health effects associated with exposure to benzene, the more recent of which are ATSDR (1993), Paustenbach *et al.* (1993), Snyder *et al.* (1993), WHO (1993), Hughes *et al.* (1994), Jex & Wyman (1996) and EBS (1996). However, all these effects were associated with occupational exposures (Table 3.1), which involve much higher benzene levels than are encountered in the general environment. Most occupational exposures are presented as 8-hour time-weighted averages (TWAs) and exposures outside the working day are not considered. Furthermore, few of the occupational studies include exposure data for women or for people over the age of 65 years. Studies in children are scarce. Several ecological studies have been conducted that have examined adverse health effects associated with point sources from chemical plants (Blot *et al.,* 1977; Hearey *et al*., 1980; Kaldor *et al.,* 1984; Knox, 1994). However, there are no benzene exposure data in these studies. The general population is exposed to environmental levels of benzene in the order of $\mu g/m^3$ (ppb; Section 2.5.10 and Table 2.13). The lowest observed adverse effect level (LOAEL) from occupational data has been estimated to be 64 mg/m^3 (20 ppm) for acute non-lymphocytic leukaemia (ANLL; EBS, 1996) which is three orders of magnitude higher than environmental levels.

As this report focuses on the health effects associated with environmental levels of benzene, Section 3.2 gives a brief overview of benzene metabolism, followed by a short section reviewing the non-leukaemic adverse effects of benzene (acute toxic, haematological, immunological and mutagenic). The major health risk associated with low-level exposure to benzene is leukaemia and Section 3.4 reviews the epidemiology of this in detail.

Table 3.1 Lowest observed adverse effect levels (LOAELs) observed in humans exposed to benzene

Effect	Description	Exposure	LOAEL	References
Acute toxicity				
Death		Minutes	64 000 mg/m^3 (20 000 ppm)	Thienes & Haley (1972)
Death (oral*)			10 ml (8.8 g)	
CNS	Vertigo, drowsiness, headache, nausea	Hours	800 mg/m^3 (250 ppm)	Clayton & Clayton (1994)
Chronic toxicity				
Haematological	Aplastic anaemia, pancytopenia, MDS	Years	320 mg/m^3 (100 ppm)	Yin *et al.* (1987a) Greenburg *et al.* (1939) Aksoy *et al.* (1972)
	Cytopenia	Years	96–112 mg/m^3 (30–35 ppm)	Fishbeck *et al*. (1978) Kipen *et al.* (1989) Rothman *et al*. (1996)
Mutagenic	Chromosomal aberrations	Years	64–319 mg/m^3 (20–100 ppm)	EBS (1996)
	Adduct formation	Years	40–200 mg/m^3 (12.5–62.6 ppm)	Liu *et al.* (1996)
Carcinogenic	ANLL	Years	32–80 mg/m^3 (10–25 ppm)	Schnatter *et al*. (1996a) Hayes *et al.* (1997)

ANLL, acute non-lymphocytic leukaemia; CNS, central nervous system; MDS myelodysplastic syndrome

* Only effect following oral consumption, all others resulting from inhalation

3.2 METABOLISM

Benzene toxicity is thought to be the result of the interaction between benzene metabolites rather than the effects of a single metabolite acting independently (Eastmond, 1993; Snyder *et al*., 1993; EBS 1996; Jex & Wyman, 1996; Smith, 1996). Benzene metabolism has been discussed in detail in previous reports (EBS 1996; Jex & Wyman, 1996; Park 1996); the process is therefore summarised only briefly here.

After benzene gains access to the body, usually by absorption through the lungs following inhalation, it is metabolised in the liver by the cytochrome P-450 system. Two metabolic pathways appear to be involved, one leading to ring-hydroxylated compounds and one that involves ring opening of benzene. The predominant metabolites that result from prolonged, low-level exposure are phenol, catechol, hydroquinone and 1,2,4-trihydroxybenzene. These are excreted as ethereal sulphates and glucuronides in the urine. The urinary metabolite muconic acid is the only well characterised, ring-opened metabolite formed from benzene *in vivo*.

3.3 ADVERSE HEALTH EFFECTS OTHER THAN LEUKAEMIA

3.3.1 ACUTE TOXIC EFFECTS

Acute toxic effects in the general population have usually been related to poor working conditions, accidents or misuse and abuse of benzene. Inhalation of benzene produces acute toxic effects on the central nervous system (CNS) in humans, which clear rapidly once exposure ceases. Inhalation of 800–1600 mg/m^3 (250–500 ppm) produces vertigo, drowsiness, headache and nausea (Table 3.1), while higher concentrations of 4800 mg/m^3 (1500 ppm) cause euphoria followed by giddiness, headache, nausea, staggered gait and, with continued exposure, unconsciousness (Clayton & Clayton, 1994). Short-term exposures to 9600 mg/m^3 (3000 ppm) can be endured for 0.5–1.0 hours. However, exposure to massive concentrations of 64 000 mg/m^3 (20 000 ppm) or higher can be fatal within 5–10 minutes (Thienes & Haley, 1972; Table 3.1).

Acute oral toxicity of benzene is low. It has been estimated that ingestion of 10 ml (8.8 g) would represent an acute lethal dose in humans (Table 3.1). Gastrointestinal ulceration has also been observed from ingestion of benzene (Appuhn & Goldeck, 1957).

3.3.2 HAEMATOLOGICAL AND IMMUNOLOGICAL EFFECTS

Excessive exposure to benzene (>320 mg/m^3; >100 ppm) results in pancytopenia (reduced number of red and white blood cells) and aplastic anaemia (a more

severe form of pancytopenia). It is generally associated with a marked decrease in the number of cells in the bone marrow, which results in severe clinical manifestations including immunosuppression and myelodysplastic syndrome (MDS; Table 3.1). Lower repeated benzene exposures (96 mg/m^3; 30 ppm) result in cytopenia (a reduction in specific blood cell counts). Affected individuals may display a decrease in white blood cells (leukopenia), potentially resulting in death due to infection, a decrease in platelet count (thrombocytopenia), potentially resulting in death due to haemorrhage, or a decrease in red blood cell count (anaemia; Fishbeck *et al.*, 1978; Kipen *et al.*, 1989; Rothman *et al.*, 1996).

A recent study by Collins *et al.* (1997) investigated the incidence of lymphopenia among workers exposed to low levels of benzene, in the USA. Lymphopenia, defined as fewer than 10 g lymphocytes per litre of blood, was an early and consistent finding in workers in whom benzene toxicity was evident. This study identified 1151 workers (411 exposed to benzene and 740 unexposed) who were employed at a plant from 1986 to 1993, when electronic impedance counting of lymphocytes was made available to the company. The medical industrial hygiene database had information on 940 (82%) of these workers. The primary use of benzene in this company is as a raw material in the manufacture of linear alkyl benzene. Other exposure can occur in the unloading and distribution of benzene in the plant. In total 4213 personal monitoring samples were collected between 1980 and 1993 for workers holding one of the 26 jobs identified as having potential exposure to benzene. The average exposure level was 1.76 mg/m^3 (0.55 ppm; 8-hour TWA), with a range of 0.03–280 mg/m^3 (0.01–87.69 ppm). The authors commented that exposure levels exceeding 6.4 mg/m^3 (2.0 ppm) were rare and primarily related to short-term 'upset' conditions. No increase was found in the prevalence of lymphopenia among benzene-exposed workers (odds ratio (OR), 0.6; 95% confidence interval (CI), 0.2–1.8), taking into account smoking, age and sex. There was also no increase in risk among workers exposed for five or more years (OR, 0.6; 95% CI, 0.2–1.9). It was concluded that there was no increased risk of lymphopenia among workers exposed to low levels of benzene (6.4 mg/m^3; 2 ppm, 8 hours/day).

Toxicological assessments in animals suggest that the immune system may be targeted by benzene (EBS, 1996). Studies in humans have generally been hampered by poor choice of control subject and simultaneous exposure to many chemicals (Snyder *et al.*, 1993; EBS 1996).

3.3.3 MUTAGENIC EFFECTS

Benzene is a known clastogen, causing chromosomal aberrations *in vitro*. Chromosomal aberrations may act as predictors of cancer risk, and their role in subsequent leukaemia is thought to involve chromosome numbers 5 and 7, and may also involve numbers 8 and 12 (EBS, 1996; Irons & Stillman, 1996). Aneuploidy may also be a precursor of leukaemogenesis (EBS, 1996; Irons & Stillman, 1996).

Determination of the likelihood of chromosomal aberrations occurring in humans is hindered by many confounding factors. The data are weakly suggestive that prolonged exposure to long-term average (LTA) concentrations of >64 mg/m^3 (>20 ppm) benzene may be associated with such changes (EBS, 1996). This value has been derived from the studies of Sarto *et al*. (1984), Yardley-Jones *et al*. (1990), Tompa *et al*. (1994), and Karacic *et al*. (1995), which suggest that the LOAEL for chromosomal aberrations in humans lies between 64 and 320 mg/m^3 (20 and 100 ppm; Table 3.1), and concurs with the review by Paustenbach *et al*. (1993), who concluded that benzene exposure at levels sufficient to cause haematotoxicity may also produce clastogenic effects in human lymphocytes.

Other indicators of genetic damage are sister chromatid exchanges (SCEs), DNA crosslinking, DNA adduct formation and DNA repair. However, the results from several studies have been inconsistent (reviewed in Paustenbach *et al*., 1993; Snyder *et al*., 1993; EBS 1996). The development of biomarkers for benzene is currently being explored. Two recent studies have investigated the ability of benzene to induce oxidative DNA damage in occupationally exposed workers by measuring urinary levels of the oxidative DNA adduct, 8-hydroxydeoxyguanosine (8OHdG). It should be noted that the occurrence of 8OHdG in urine, while a measure of oxidative damage, is not specific to benzene. Nilsson *et al*. (1996) found a significant association between the exposure to benzene from petrol during a normal workshift and the increase of 8OHdG over the shift, among exposed workers ($p = 0.02$). The 8-hour TWA exposure to benzene was 0.42 mg/m^3 (0.13 ppm; range 0.01–1.92 mg/m^3, 0.003–0.6 ppm). While these findings suggest that benzene may interact with DNA at relatively low exposure levels, the size of the study population (33 exposed workers and 33 controls) makes interpretation of the data difficult.

A second study, conducted by Liu *et al*. (1996), investigated the ability of benzene to induce 8OHdG formation in four groups of workers exposed to zero (controls), low, medium and high concentrations of benzene. The low exposure group (<40 mg/m^3; <12.5 ppm), consisted of 35 workers employed in a shoe factory, where benzene was used as an industrial solvent and mixed with toluene and xylene. The group with medium exposure (40–200 mg/m^3; 12.5–62.5 ppm) consisted of 24 car painters from the same factory, where benzene was used as a diluent for the paint, and the high exposure group (>200 mg/m^3; >62.5 ppm) was made up of 28 workers employed in another shoe factory with similar conditions. The control group consisted of 30 members of staff from a university in the same city. Both medium (40–200 mg/m^3) and high (>200 mg/m^3; 62.5 ppm) concentrations of benzene resulted in significantly increased levels of 8OHdG compared with controls.

3.4 LEUKAEMOGENESIS

It is now generally accepted that benzene exposure in human populations is causally related to leukaemia and that the link is strongest for ANLL, including acute myelocytic leukaemia (AML). The epidemiological studies to date have been conducted on people occupationally exposed to benzene at higher levels than those to which the general population is exposed. Many studies have not made the distinction between all leukaemia and ANLL, often because of the small number of cases of leukaemia subtypes.

Before describing these occupational studies it is necessary to consider their limitations. Many studies pertain to exposure from before the Second World War, and probably the highest exposures occurred during the 1940s–1960s. However, it was not possible to measure exposures reliably before about 1970. It must also be noted that in most industrial settings workers are exposed to more than one chemical, so that the adverse effects reported could be partially due to some other exposures. Finally, death certificates and cancer registrations, widely used as a source of disease outcome data, are not always completely accurate.

Many studies have looked at adverse health effects due to occupational exposure to benzene, but in order to set in context the evaluation of exposure at environmental levels (See Section 4), the only studies reviewed in detail here are those that have been used to evaluate dose–response.

The most often cited cohort used to assess dose–response relationships for work-place benzene exposures and leukaemia has been the 'Pliofilm' cohort. This cohort consisted of workers employed between 1936–1975 in three US factories manufacturing rubber film, two in Akron, Ohio and one in St Mary's, Ohio. The cohort consisted of 1717 white male workers, of whom 1212 were from the more highly exposed 'wetside' of the operation. Table 3.2 presents the results of several analyses of this cohort, together with results from other studies with quantified benzene exposure estimates.

The Pliofilm cohort has often been used in risk estimation because (i) it contains good information on the duties and exposure histories of the workers and on their

Table 3.2 Studies of occupationally exposed populations with quantified benzene exposure estimates

Exposed population	Exposure		All leukaemia			Leukaemia subtypes			Reference
	mg/m³.years	ppm.years	Cases	Ratios	95% CI	Cases	Ratios	95% CI	
Cohort studies				**SMR/RR**					
Pliofilm	0–16	0–5	1	0.88	0.02–4.89				Paxton *et al.* (1994) using exposure estimates from Crump & Allen (1984)
	16–160	5–50	4	3.25	0.88–8.33				
	160–1600	50–500	6	4.87	1.79–10.6				
	>1600	>500	3	10.3	2.13–30.2				
Pliofilm	0–16	0–5	3	1.97	0.41–5.76				Paxton *et al.*, using exposure estimates from Rinsky *et al.* (1981)
	16–160	5–50	3	2.29	0.47–6.69				
	160–1600	50–500	7	6.93	2.8–14.3				
	>1600	>500	1	20.0	0.5–111.0				
Pliofilm	0–16	0–5	1	1.33	0.03–7.43				Paxton *et al.* (1994) using exposure estimates from Paustenbach *et al.* (1992)
	16–160	5–50	2	1.79	0.22–6.45				
	160–1600	50–500	4	2.80	0.8–7.16				
	>1600	>500	7	11.9	4.8–24.44				
Dow	0–134	0–42	2	1.67	0.14–4.9				Bond *et al.* (1986)
	134–256	42–83	0	0.00	0–3.3				
	>256	>83	1	2.50	0–10.0				
Chemical	0–48	0–15	2	0.97	0.12–3.49				Wong (1987a,b)
Manufacturers'	48–192	15–60	1	0.78	0.02–4.34				
Association	>192	>60	3	2.76	0.57–8.06				
						AMML	**SMR/RR**		
US production	0	0	5	1.1	0.4–2.6	2	1.4	0.2–5.0	Ireland *et al.* (1997)
workers	<3.2	<1	2	2.5	0.3–8.9	1	3.7	0.1–20.6	
	3.2–19.2	1–6	0	0	0	0	0		
	>19.2	>6	3	4.6	0.9–13.4	1	4.5	0.1–25.3	
						ANLL			
Chinese	<128	<40	18	2.2	1.1–4.5	5	1.9	0.5–7	Hayes *et al.*(1997)
production	128–319	40–99	11	2.9	1.3–6.5	5	4.3	1.1–16	
workers	>320	>100	29	2.7	1.4–5.2	11	3.6	1.1–11.6	

Table 3.2 Continued

Exposed population	Exposure mg/m³.years	Exposure ppm.years	All leukaemia Cases	All leukaemia Ratios	All leukaemia 95% CI	Leukaemia subtypes Cases	Leukaemia subtypes Ratios	Leukaemia subtypes 95% CI	Reference
Case–control studies				**OR**					
Canadian petroleum distribution	<1.44	<.0.45	10	1.0					Schnatter *et al.* (1996b)
	1.44–14.4	0.45–4.5	1	0.43	0.01–4.0				
	14.4–144	4.5–45	1	0.16	0.0–1.3				
	>144	>45	2	1.47	0.2–13.1				
						AMML	**OR**		
UK petroleum distribution	<1.44	<0.45	22	1.0		7	1.0		Rushton & Romaniuk (1997)
	1.44–14.4	0.45–4.5	47	1.42	0.8–2.6	15	2.17	0.8–6.1	
	14.4–144	4.5–45	20	2.48	0.7–3.0	9	2.82	0.8–9.4	
	>144	45	1	1.35	0.1–12.8	0	0	0	

AMML, acute myelocytic and monocytic leukaemia; ANLL, acute non-lymphocytic leukaemia; CI, confidence interval; OR, odds ratio; RR, risk ratio; SMR, standardised mortality ratio

medical surveillance; (ii) confounding exposures are less of a problem than in other studies; (iii) detailed individual job histories are available on all workers and the manufacturing process remained largely unchanged over the 40 years; and (iv) relatively large amounts of air sampling data are available to characterise exposure levels for several exposure periods.

Paxton *et al.* (1994) analysed the Pliofilm data using three different estimates of exposure (Rinsky *et al.*, 1981; Crump & Allen, 1984; Paustenbach *et al.* 1992). The lowest exposure estimates were made by Rinsky *et al.* (1981) and the highest by Paustenbach *et al.* (1992). Based on the exposure estimates of Crump and Allen (1984) and Rinsky *et al.* (1981), excess risk for all leukaemia occurred at 160 mg/m^3.years (50 ppm.years), whereas based on the Paustenbach *et al.* (1992) estimates, no risk occurred until a cumulative exposure of greater than 1600 mg/m^3.years (500 ppm.years; Table 3.2).

Schnatter *et al.* (1996a) examined the relationship between specific benzene LTA exposure concentrations (in particular, exposure less than or equal to specific concentrations) and risk of acute myelocytic and monocytic leukaemia (AMML) in the Pliofilm cohort. The three previous exposure estimates (Rinsky *et al.*, 1981; Crump & Allen, 1984; Paustenbach *et al.*, 1992) were ranked and a median exposure estimate was calculated by selecting the middle-ranked estimate for each cell in the job/department/time exposure matrix. The authors then defined the LTA concentration associated with the maximally exposed job (LTA-MEJ) for each worker.

Once the LTA-MEJ had been defined for each worker (and each set of exposure estimates), groups of employees who were only exposed to LTA concentrations below a given concentration (cut-point) were defined; that is, if a worker's LTA-MEJ is 134 mg/m^3 (42 ppm), the entire occupational experience for that worker corresponds to exposures <144 mg/m^3 (<45 ppm). Varying the concentration cutpoints in small increments and calculating standard mortality ratios (SMRs) for each cutpoint enabled empirical thresholds (critical concentrations) not associated with any excess risk to be identified.

Results from this analysis are presented in Table 3.3. Both the median and Crump and Allen (1984) exposure estimates show that LTA concentrations of <160 mg/m^3 (<50 ppm) do not result in increased risk. The Rinsky *et al.* (1981) estimates indicate no risk at levels of <64 mg/m^3 (<20 ppm) but the Paustenbach *et al.* (1992) estimates do not show markedly increased risks until LTA concentrations of 448 mg/m^3 (140 ppm) are reached. This analysis suggests that a critical

Table 3.3 Observed AMMLs, expected cutpoints and SMRs for selected AMMLs and four exposure estimates

Exposure concentration in mg/m^3 (ppm)	Median			Rinsky *et al.*			Crump & Allen			Paustenbach *et al.*		
	Observed AMML	Expected* AMML	SMR	Observed AMML	Expected AMML	SMR	Observed AMML	Expected AMML	SMR	Observed AMML	Expected AMML	SMR
3.2 (1)	0	0.15	0.00	0	0.54	0.00	0	0.18	0.00	0	0.02	0.00
16 (5)	0	0.27	0.00	0	0.60	0.00	0	0.33	0.00	0	0.03	0.00
32 (10)	0	0.30	0.00	0	0.70	0.00	0	0.34	0.00	0	0.03	0.00
48 (15)	0	0.33	0.00	0	0.70	0.00	0	0.43	0.00	0	0.05	0.00
64 (20)	0	0.52	0.00	0	0.81	0.00	1	0.66	1.52	0	0.07	0.00
80 (25)	1	0.66	1.52	4	1.02	3.92	1	0.74	1.35	0	0.28	0.00
96 (30)	1	0.71	1.41	4	1.13	3.54	1	0.83	1.20	0	0.31	0.00
112 (35)	1	0.76	1.32	5	1.34	3.73	1	0.85	1.18	0	0.37	0.00
128 (40)	1	1.00	1.00	5	1.39	3.60	1	0.97	1.03	0	0.47	0.00
144 (45)	1	1.09	0.92	5	1.55	3.23	1	1.06	0.94	0	0.59	0.00
160 (50)	1	1.16	0.86	8	1.64	4.88	1	1.06	0.94	0	0.70	0.00
176 (55)	3	1.24	2.42	8	1.64	4.88	2	1.17	1.71	0	0.70	0.00
192 (60)	4	1.34	2.99	8	1.67	4.79	3	2.80	1.07	0	0.75	0.00
224 (70)	4	1.38	2.90	8	1.67	4.79	3	1.30	2.31	0	0.85	0.00
256 (80)	4	1.45	2.76	8	1.67	4.79	3	1.38	2.17	1	0.33	3.03
288 (90)	4	1.45	2.76	8	1.67	4.79	3	1.38	2.17	1	1.15	0.87
320 (100)	4	1.45	2.76	8	1.67	4.79	3	1.38	2.17	1	1.23	0.81
384 (120)	5	1.57	3.18	8	1.67	4.79	4	1.45	2.76	2	1.34	1.49
448 (140)	8	1.67	4.79	8	1.67	4.79	4	1.45	2.76	5	1.33	3.76
480 (150)	8	1.67	4.79	8	1.67	4.79	4	1.45	2.76	5	1.43	3.50
560 (175)	8	1.67	4.79	8	1.67	4.79	4	1.45	2.76	8	1.58	5.06
640 (200)	8	1.67	4.79	8	1.67	4.79	4	1.45	2.76	8	1.60	5.00
800 (250)	8	1.67	4.79	8	1.67	4.79	4	1.46	2.74	8	1.64	4.88
832 (260)	8	1.67	4.79	8	1.67	4.79	8	1.67	4.79	8	1.67	4.79

From Schnatter *et al.* (1996a)

AMML, acute myelocytic and monocytic leukaemia; SMR, standardised mortality ratio

* for details see text

concentration of 64 mg/m^3 (20 ppm) is required regardless of either the end-point considered (all leukaemia [not shown in this review] or AMML) or exposure estimates used. The median exposure estimates may be a useful compromise in characterising the risk associated with benzene exposure for the Pliofilm workers. However, these indicate a critical LTA concentration of 160 mg/m^3 (50 ppm) when AMML is the end-point. Schnatter *et al.* (1996a) comment that the duration of exposure is inherent in these LTA-MEJ analyses. Using the Rinsky *et al.* (1981) estimates, workers exposed to >60 mg/m^3 (>19 ppm) were exposed for an average of 6 years, while AMML cases were exposed for an average of 13 years. Thus the data suggest that exposures need to occur over a period of years (rather than days or weeks) to result in excess risk of AMML.

Two other US cohorts have been studied by Bond *et al*. (1986) and Wong (1987a,b). The Bond study is a 9-year follow-up of a study by Ott *et al*. (1978) and reports risk estimates among 956 Dow Michigan chemical workers exposed to benzene through processes involving the use of ethylcellulose, chlorobenzene, and alkylbenzenes. Benzene concentrations in the areas where these operations were conducted were estimated on the basis of industrial hygiene monitoring data. Concentrations were in the range 0–2998 mg/m^3 (0–937 ppm), although estimated TWA concentrations were in the range 0.3–14 mg/m^3 (0.1–35.5 ppm) in the various job categories. Three leukaemia deaths were reported compared with the 1.9 expected (Table 3.2); one of the deaths was due to AML. Wong (1987a,b) reported mortality data from 7676 workers from seven different companies; 3536 of the workers were continuously exposed to benzene. As with the Pliofilm cohort, industrial hygiene surveys and a task-based assessment of exposures resulted in the assignment to each worker of a quantitative estimate of benzene exposure over his career. Six leukaemia deaths were reported but none of them were registered as AML on the death certificate (Table 3.2). Thus both Bond *et al*. (1986) and Wong *et al*. (1987a) reported no significant risks at any exposure level and a non-significant excess of total leukaemia in the highest exposure groups.

A subsequent study by Ireland *et al*. (1997) was a follow-up of a group of the population involved in the Wong *et al*. (1987a) study. Follow-up was complete for 4091 of 4172 workers. Benzene was used in five processes involving nitrobenzene, phenol production, chlorobenzene, muriatic acid and alkylbenzenes. However, only chlorobenzene and muriatic acid departments were still operational when the collection of data began in the 1980s, so most exposures had to be estimated using information on process changes and the judgement of an industrial hygienist. Maintenance and production workers were exposed, but LTA concentrations were estimated only for the 666 production workers ever exposed to benzene.

Cumulative exposures were in the range 0.03–2022 mg/m^3.years (0.01–632 ppm.years) in these workers. Unlike the earlier study, cases of AMML were reported separately as well as all leukaemia combined; however, no excess risk was found at any subcategory of exposure level. For all leukaemia types combined there was an excess of three cases observed versus 0.65 expected in the >19.2 mg/m^3.year (>6 ppm.year) category, which approached significance at the 5% level (Table 3.2).

Hayes *et al*. (1997) reported results from a mortality study among 74 828 benzene-exposed workers and 35 805 non-exposed workers in 12 cities in China. The exposed workers were employed between 1972 and 1987 in a variety of occupations including coating applications and rubber, chemical and shoe production. Subjects were identified from initial employment, salary and other factory records. The basic unit for exposure assessment was a factory/work unit/job title combination, which was considered separately during each of seven calendar-year time periods between 1949 and 1987. Person-years were accumulated for the benzene-exposed workers, with a 1.5-year lag, from 1 January 1972 or, if hired later, from the date of first employment in a benzene-exposed job until death, loss to follow-up, or 31 December 1987. Workers exposed to a constant benzene level of 32–77 mg/m^3 (10–24 ppm) had a relative risk (RR) for all leukaemias of 4.0 (95% CI, 1.5–10.7) and for ANLL of 4.9 (95% CI, 1.2–19.8). As shown in Table 3.2, workers with a cumulative exposure to benzene of 128–319 mg/m^3.years (40–99 ppm.years) had a RR for all leukaemias of 2.9 (95% CI, 1.3–6.5) and of 4.3 (95% CI, 1.1–16) for ANLL.

Schnatter *et al*. (1996b) conducted a nested case–control study which identified all fatal cases of lymphohaematopoietic cancer among a previously studied cohort of Canadian petroleum distribution workers (Schnatter *et al*., 1993). The study population consisted of 29 cases (14 of leukaemia, seven of multiple myeloma, and eight of non-Hodgkin lymphoma) and 115 controls. Exposure to benzene occurred mostly in petrol truck drivers, loaders and terminal operators. Exposures over a working career averaged 0.3–19.8 mg/m^3 (0.01–6.2 ppm), although a substantial fraction of cases and controls had experienced LTA concentrations of <3.2 mg/m^3 (<1 ppm) over their career. Cumulative exposure ranged from <3.2–704 mg/m^3.years (<1 to 220 ppm.years; Table 3.2). The OR for all leukaemias was calculated from a logistic regression model as 1.002 for each ppm.year of exposure to benzene.

Rushton and Romaniuk (1997) investigated the risk of leukaemia in workers in the UK petroleum distribution industry who were exposed to low levels of benzene. When a work history was incomplete assumptions were made and when

a work history was largely unavailable a typical work history was used. Of the 90 cases of leukaemia identified (four controls per case), seven were acute lymphatic leukaemia, 31 chronic lymphatic leukaemia, 31 AMML, 11 chronic myeloid leukaemia and 10 other leukaemias (Table 3.2). Cumulative exposures ranged from close to zero to >640 mg/m^3.years (>200 ppm.years), although 81% were <16 mg/m^3.years (<5 ppm.years). No significant risk was found for all leukaemias with higher cumulative exposure to benzene or with intensity of exposure, but risk was consistently doubled in subjects employed in the industry for more than 10 years. The patterns of risk for the lymphatic leukaemia groups were different from those of the AMML group in that duration of employment was the variable most closely related to risk in the former but not the latter. Risk from AMML did not increase with cumulative exposure, maximum intensity or average intensity of exposure analysed as continuous variables. When categorised into discrete ranges, an OR of 2.8 (95% CI, 0.8–9.4) for a cumulative exposure of 14.4–144 mg/m^3.years (4.5–45 ppm.years) as compared with <1.44 mg/m^3.years (<0.45 ppm.years) was obtained for AMML.

To conclude, using the above data, the LOAEL for the development of all leukaemia combined, AMML or ANLL among occupationally exposed workers appears to be in the range of 32–80 mg/m^3 (10–25 ppm; see Table 3.3). However, some studies of workers exposed to lower estimated levels of benzene have found some evidence for increased risk of leukaemia, although it has not been possible to determine clear estimates of risk, partly because of the inadequacy of exposure data and the small number of cases.

It should be noted that to date there are no data relating adverse health effects among women, children or the elderly and quantitative estimates of benzene exposure.

4 Risk to human health from exposure to environmental levels of benzene

The most significant potential adverse health effects from prolonged, low-level benzene exposure are haematotoxicity, genotoxicity and carcinogenicity. Most previous quantitative risk assessments have been conducted using leukaemia as an end-point as this is the most serious health risk associated with prolonged, occupational exposure.

As discussed in the previous section, the LOAEL for leukaemia for workers occupationally exposed to benzene is 32–80 mg/m^3 (10–25 ppm). However, because benzene is considered to be a genotoxic carcinogen, a 'safe' or 'no effect' level cannot be identified. Therefore, many studies have used quantitative risk assessments/modelling to extrapolate from occupational exposures in order to estimate the risk to health from low-level exposure to benzene.

It is important to note that there is a continuing debate regarding the appropriateness of risk assessment using mathematical modelling. In addition,

the underlying mechanism(s) by which benzene causes cancer is not clearly understood nor is it known whether the leukaemogenesis is related to average steady state or intermittent high peak exposure. Quantitative risk assessment using the linearised multistage model often used for carcinogens has recently been seriously challenged as 'unreliable and scientifically unsound' (Lovell & Thomas, 1996), and the UK Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment, for example, does not support the routine use of quantitative risk assessment for chemical carcinogens. In a recent discussion paper, Maynard *et al.* (1995) proposed an alternative approach for the purpose of setting air quality standards and recommended a strategy based on the scientific data, decision points and uncertainty factors. Thus, although this review presents the currently reported risk estimates for benzene-associated leukaemogenesis as the appropriate risk estimates for adverse health effects from low-level exposure to benzene, it is possible that these estimates will change as the mechanism for carcinogenesis is further elucidated and more appropriate models, based on mechanistic considerations, emerge.

The variability between mathematical models and the use of different exposure estimates is clearly illustrated in Table 4.1, which shows that estimates based on the Paustenbach *et al.* (1992) exposure matrix using a non-linear model are 100 000 times smaller than those estimates based on the linear model. The number of estimated additional deaths per million persons continuously exposed to 3.2 μg/m^3 (1 ppb) of benzene ranges from 0.00014–15 deaths.

A summary of the health effects and estimated no observed adverse effect levels (NOAELs) for occupational exposure to benzene based on data from EBS (1996) is presented in Table 4.2. As benzene is considered to be a genotoxic carcinogen a NOAEL for carcinogenicity cannot be assumed. However, for a risk characterisation, a realistic estimate can be made for the concentration below

Table 4.1 Additional deaths per million persons exposed continuously throughout life to 3.2 μg/m^3 (1 ppb) benzene

Exposed population	Leukaemia	Model	
		Linear	Intensity-dependent (NL)
Pliofilm/Crump & Allen (1984)	All leukaemia	24	24
	AMML	21	21
Pliofilm/Paustenbach *et al.* (1992)	All leukaemia	15	0.00017
	AMML	15	0.00014

From Crump (1996)

AMML, acute myelocytic and monocytic leukaemia; NL, non-linear

which adverse health effects are unlikely to be detected. A risk characterisation conducted by EBS (1996), based on extrapolation from occupational studies, concluded that for workers exposed continuously to 3.2 mg/m^3 (1 ppm) or less over a working lifetime there is no detectable increased risk of leukaemia. It further concluded that for those so exposed and for members of the general population exposed continuously to 10.9 µg/m^3 (3.4 ppb) over an average lifetime, there is at present no need for further information and/or testing, or for risk reduction measures, beyond those which are already being applied.

It is always possible that some sectors of the population might be more susceptible to benzene-induced leukaemia. Children may be of particular concern; it could be argued that, as children's blood cells are dividing and maturing more rapidly than those of adults, their susceptibility to an environmental agent capable of causing

Table 4.2 Summary of N(L)OAELs for relevant effects used in the risk characterisation

Effect category	N(L)OAEL	Exposure duration	Basis
Acute toxicity	800 mg/m^3 (250 ppm) LOAEL	Minutes	Human central nervous system effects
Irritation	Irritating	Days/weeks	Animal eye and skin observations
Corrosivity	No effect	No effect	Irritation studies
Sensitisation	No effect expected	No effect	Chemical structure comparison
Reproductive[a]	No functional effect	No effect	Animal data
Developmental[a]	No relevant effect	No effect	Toxic at maternally toxic dose
Mutagenicity	No effect	No effect	*In vitro* studies
Clastogenicity[b]	NA	Days	Animal chromosome aberrations
Repeated dose toxicity, haematopoiesis	64 mg/m^3 (20 ppm) NOAEL	Years	Human cytopenia
Carcinogenicity[b]	NA	Years	Human ANLL

Adapted from EBS (1996)

LOAEL, lowest observed adverse effect level; NA, not applicable; NOAEL, no observed adverse effect level

[a] Effects only seen at doses toxic to the mother, therefore are not considered to be reproductive or developmental effects

[b] Although NOAEL values are not normally accepted for carcinogenic compounds, the EBS (1996) has determined a NOAEL for clastogenicity to be 14 mg/m^3 (4.4 ppm) and carcinogenicity to be 3.2 mg/m^3 (1 ppm) assuming the multiple-step mechanism described by Irons & Stillman (1996)

leukaemia may be enhanced. However, the most prevalent type of leukaemia in children is acute lymphocytic leukaemia (ALL) as opposed to AML, which is the leukaemia most strongly linked to benzene exposure — of the 66 children under 15 who died of leukaemia in 1995, 41 (62 %) died of ALL and 17 (25 %) died of AML (ONS, 1997). Furthermore, leukaemias may also be the result of exposure to radiation or viral infection.

5 Overall evaluation

The risk evaluation conducted for this report has aimed to take into account all sectors of the UK population. This has proved extremely difficult as most exposure data and related health effects in humans have to date, focused on occupational exposure of males of working age.

Tables 5.1 and 5.2 summarise the estimated exposures for a number of non-occupational population groups, and include the contribution of active and passive tobacco smoke, where applicable. Exposures to benzene during refuelling and driving were considered as part of the general population risk characterisation. As acute exposure to benzene for the general population is only likely to occur as a result of accidents or spillages, this scenario is not considered here.

The estimated absorbed doses of benzene for different exposure scenarios for infants, children and adults were estimated in Section 2.6.5 and summarised in Tables 2.15 to 2.17. These values, expressed as daily doses (μg/day), are summarised in Tables 5.1 and 5.2, where they have also been expressed as daily intakes (μg/kg body weight/day). This table also presents the atmospheric concentration to which an individual would have to be exposed every day to achieve the daily dose, that is the 'equivalent atmospheric concentration' (μg/m^3 and ppb). These have been calculated by making various assumptions: values were converted from daily doses to daily intakes by assuming that the average infant (<1 year old) weighs 9.1 kg, the average child (age 11 years old) weighs 41.1 kg and the average male and female adult weigh 70 and 58 kg, respectively. These are obviously average weights and not necessarily representative of the whole UK population, but have been used to give an estimate of exposures in 'typical' individuals. Similarly,

values were converted from daily doses to 'equivalent atmospheric concentration' by assuming that the average infant, child and adult inhales a volume of air of 4.5, 8.7 and 20 m^3/day, respectively. These values were, in turn, converted to ppb by using a conversion factor for benzene of 1 $\mu g/m^3$ = 0.313 ppb. This conversion was necessary to compare exposures to the general population with occupational exposures (which are reported as mg/m^3 or ppm).

Table 5.1 Summary of estimated absorbed doses of benzene for infants and children under different exposure scenarios

	Daily dose (μg/day)	Daily intake (μg/kg bw/day)[a]	Equivalent atmospheric concentration[b] ($\mu g/m^3$)	(ppb)
Rural infant	15.3	1.68	3.40	1.06
Urban infant	19.7	2.16	4.38	1.37
Urban infant, passive smoker	25.9	2.85	5.76	1.80
Rural child	29.3	0.71	3.37	1.05
Urban child	37.6	0.91	4.32	1.35
Urban child, passive smoker	49.3	1.20	5.67	1.77

[a] Values converted from daily doses by assuming that the average infant (<1 year old) weighs 9.1 kg and the average child (11 years old) weighs 41.1 kg; there will be a progression in ranges so that on average a 1–year-old weighs 11.3 kg, a 5-year-old weighs 19.7 kg, an 8-year-old weighs 28.1 kg and so on (Snyder *et al.,* 1975)

[b] Values converted from daily doses by assuming that the average infant and child inhale a volume of air of 4.5 and 8.7 m^3/day respectively; the conversion factor for benzene is 1 $\mu g/m^3$ = 0.313 ppb

Table 5.2 Summary of estimated absorbed doses of benzene for members of the general public under different exposure scenarios

	Daily dose (μg/day)[a]	Daily intake (μg/kg bw/day)[b]		Equivalent atmospheric concentration[c] ($\mu g/m^3$)	(ppb)
		Females	Males		
Rural non-smoker	75	1.29	1.07	3.75	1.17
Urban non-smoker	95	1.64	1.36	4.75	1.49
Urban passive smoker	122	2.10	1.74	6.10	1.91
Urban smoker	522	9.00	7.46	26.10	8.17
Urban smoker who works adjacent to busy road for 8 hrs/day	819	14.12	11.70	40.95	12.82

[a] Upper limits from Table 2.15

[b] Values converted from daily doses by assuming that the average UK female and male weigh 58 and 70 kg, respectively (Snyder *et al.,* 1975)

[c] Values converted from daily doses by assuming that the average individual inhales 20 m^3 of air per day; the conversion factor for benzene is 1 $\mu g/m^3$ = 0.313 ppb

Table 5.1 shows that infants and children receive an average daily dose of 15.3–25.9 and 29.3–49.3 μg/day, respectively, equivalent to an average atmospheric concentration of 3.4–5.76 μg/m^3 (1.06–1.8 ppb) and 3.37–5.67 μg/m^3 (1.05–1.77 ppb). It is worth noting that infants and children exposed to environmental tobacco smoke have benzene exposure levels comparable to those of an adult passive smoker (Tables 5.1 & 5.2). The potential consequences of benzene exposure in infants may be more significant than for children or adults owing to their lower body weight (see Tables 5.1 & 5.2); this is reflected in their higher daily intake (1.68–2.85 μg/kg bw/day) in comparison with children (0.71–1.2 μg/kg bw/day) or non-smoking adults (1.07–2.1 μg/kg bw/day; see Tables 5.1 and 5.2). The worst-case scenario for benzene exposure in the general population is that of an urban smoker who works adjacent to a busy road for 8 hours/day (e.g. a maintenance worker). This individual's average daily exposure would be approximately 41 μg/m^3 (12.8 ppb; Table 5.2). Such a scenario represents a physically active individual whose inhalation rate would be higher than that of a person in a more sedentary occupation.

Most data relevant to an evaluation of exposure of the general population to benzene in the environment and possible adverse effects have come from occupational studies. Occupational exposure usually pertains to an 8-hour day, 5 days a week, for approximately 50 weeks a year, for 40–45 years, while continuous exposure among the general population covers 24 hours a day, 7 days a week, for 52 weeks a year, for approximately 70 years. Nonetheless, even for a worst-case scenario, environmental exposure to benzene is several orders of magnitude lower than the lowest occupational exposures associated with adverse health impacts.

Based on the data presented in this report, the estimated exposure to benzene for the general population (including infants and children; Tables 5.1 and 5.2) is three orders of magnitude less than the lowest exposures (Table 3.1) reported to be associated with observed adverse effects.

6 Conclusions

The major health risk associated with low-level exposure to benzene is leukaemia and the strongest link in humans is with acute non-lymphocytic leukaemia (ANLL). To date, little information has been found relating adverse health effects among women, children or the elderly to benzene exposure, as most studies have involved exposure of male workers. The lowest level of exposure at which an increased incidence of ANLL among occupationally exposed workers has been reliably detected appears to be in the range of 32–80 mg/m^3 (10–25 ppm). Although some studies have suggested that effects may occur at lower levels, clear estimates of risk have not been determined, partly because of the inadequacy of exposure data and the small number of cases. Overall, the evidence from human studies suggests that any risk of leukaemia to adults at general population exposure levels of 3.8 to 41 μg/m^3 (1.19–12.8 ppb), that is at levels three orders of magnitude less than the occupational lowest observed effect level, is likely to be exceeding small and probably not detectable using current methodology. There is no evidence to suggest that continuous exposure to environmental levels of benzene manifests as any other adverse health effect.

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Annex

PHYSICOCHEMICAL PROPERTIES OF BENZENE*

Chemical structure	
Chemical formula	C_6H_6
IUPAC name	Benzene
Common synonyms	Annulene, benzine, benzol, benzole, coal naphtha, cyclo-hexatriene, mineral naphtha, phenyl hydride, pyrobenzol, pyrobenzole
Purity	>99.5% ww — industrial grade. Approximately 70% benzene and 30% toluene and xylene — coal tar benzole
Molecular weight	78.1
Physical form	Liquid at 25 °C
Melting/freezing point	5.5 °C
Boiling point	80.1 °C at 1 atmosphere
Vapour pressure	12.7 kPa at 25 °C
Solubility in water	Slightly soluble: 1.8 g/l at 25 °C
Solubility in non-aqueous solvents	Miscible with acetic acid, acetone, diethyl ether, ethanol and other organic solvents

*From EBS (1996) and WHO (1993) unless otherwise specified

Partition coefficients	Log *n*-octanol water partition coefficient (log K_{ow}) 2.13 (1.56–2.15) at 25 °C Henry's law constant (air–water partition coefficient) 550 Pa.m^3 per mol at 25 °C) Log soil organic carbon sorption coefficient (log K_{oc}): 1.8–1.9
Photo-oxidation	Reaction with OH radicals at 298K: Rate constant (k) = 1.15×10^{-12} to 1.59×10^{-12} cm^3/molecule/s^2; Half-life = 1.5 hours to 2 weeks*
Odour threshold	4.8, 15 and 38.4 mg/m^3 in air have been reported 0.17 mg/l in water
Conversion factor, air concentration	1 ppm = 3.2 mg/m^3 (25 °C and 101 325 Pa) 1 mg/m^3 = 0.313 ppm (25 °C and 101 325 Pa)

*From Nielsen *et al.* (1991)

LIST OF WORKSHOP PARTICIPANTS

WORKSHOP ON BENZENE IN THE ENVIRONMENT: AN EVALUATION OF EXPOSURE OF THE UK GENERAL POPULATION AND POSSIBLE ADVERSE HEALTH EFFECTS

LEICESTER, UK, 6 OCTOBER 1997

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* Now at the Environment Agency, Steel House, 11 Tothill Street, London SW1H 9NF

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Report R3 (1995)

Perinatal Developmental Neurotoxicity
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The Use of Biomarkers in Environmental Exposure Assessment
Report R5 (1996)

Health Effects of Waste Combustion Products
Report R7 (1997)

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Physiologically-based Pharmacokinetic Modelling: A Potential Tool for use in Risk Assessment (1999)

Exposure Assessment in the Evaluation of Risk to Human Health (1999)

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