GASOLINE

1. Chemical and Physical Data

1.1 Synonyms and trade names

Automotive gasoline

Chem. Abstr. Services Reg. No.: not assigned (8006-61-9 for natural gasoline)
Chem. Abstr. Name: not assigned
IUPAC Systematic Name: –
Synonyms: Benzin; benzine; casinghead (natural gasoline); essence; ethyl; gasohol (with up to 10% ethanol in blend); mogas; motor gasoline; naphtha; petrol; premium leaded; premium low-lead; premium unleaded; regular leaded; regular unleaded; super premium leaded; super premium unleaded

Aviation gasoline

Chem. Abstr. Services Reg. No.: not assigned
Chem. Abstr. Name: not assigned
IUPAC Systematic Name: –
Synonyms: Avgas; Avgas (Grade) 80; Avgas (Grade) 100; Grade 100LL; Avgas (Grade) 115

1.2 Description

'Gasoline' is a generic term used to describe volatile, inflammable petroleum fuels used primarily in internal combustion engines to power passenger cars and other types of vehicle, such as buses, trucks, motorbikes and aircraft. It is a complex mixture of volatile hydrocarbon compounds with a nominal boiling-point range of 50–200°C (USA) or 25–220°C (Europe) for automotive gasoline and 25–170°C for aviation gasoline (CONCAWE, 1985). Hydrocarbons are predominantly in the C_4-C_{12} range (Ladefoged & Prior, 1984; Ward, 1984; CONCAWE, 1986, 1987).

Automotive gasolines are blended from several refinery process streams, including any of the various naphtha streams from direct distillation of crude oil at atmospheric pressure (light straight-run naphtha [3]) by catalytic [22] and thermal [28] cracking processes, by catalytic reforming [15] processes and from alkylation [13] and isomerization [14] of the

lighter distillate streams[1]. They may also contain one or more additional components. The actual composition of gasolines varies widely, depending on the crude oils used, the refinery processes available, the overall balance of product demand, and the product specifications.

Gasoline is marketed as several products, and, within each product line, in various grades. Definitions have been developed for gasolines (American Petroleum Institute, 1981).

(*a*) *Automotive gasoline*

Automotive gasoline is a complex mixture of relatively volatile hydrocarbons, with or without additives, obtained by blending appropriate refinery streams to form a fuel suitable for use in spark ignition engines. Gasoline also includes all refinery products within the gasoline range (American Society for Testing and Materials (ASTM) Specification D 439) that are to be marketed as automotive gasoline without further processing in any refinery operation other than mechanical blending. In Europe and, to a lesser extent, in the USA, oxygenated compounds are also part of automotive gasoline components. Their nature and amounts are regulated. Gasoline includes leaded and unleaded grades, both of which are manufactured from blends of straight-run, cracked, reformed and other naphtha streams. A typical composition of unleaded gasoline is qualitatively similar to premium leaded grade but without lead antiknock additives (Hoffman, 1982). The two common grades of gasoline, premium and regular, differ chiefly in their octane number: regular, 91–93; premium, 96–99 (Ladefoged & Prior, 1984; Langdon, 1986).

(i) *Finished leaded automotive gasoline*

This automotive gasoline is produced by the addition of any lead (see IARC, 1980, 1987a) additive or which contains more than 0.013 g lead/l or more than 0.0013 g phosphorus/l. The differences among US grades are based primarily on the octane rating; these include super premium, premium and regular. Lead compounds are deliberately added to increase octane number and to suppress pre-ignition. In European countries, the amount of lead additive is limited to 0.15 g lead/l (Council of the European Communities, 1987), except in France, Ireland, Italy, Portugal and Spain, where the limit is 0.4 g/l (CONCAWE, 1988). The current grades are premium and regular. Phosphorus additives were used in the past but are now no longer added to gasolines.

(ii) *Finished unleaded automotive gasoline*

This US automotive gasoline contains no more than 0.013 g lead/l and no more than 0.0013 g phosphorus/l (American Petroleum Institute, 1981); lead and phosphorus additives are prohibited by regulation. The same grades as for leaded gasoline are produced. This definition of unleaded automotive gasoline also applies in Europe, except that only premium and regular grades are available. Furthermore, in central Europe and Scandinavia, facilities are installed in service stations which allow blending of leaded and unleaded premium gasoline in a 50:50 ratio, to produce 'intermediate' or 'low lead' grade. Such blends typically contain 0.075 g lead/l and include oxygenated compounds.

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[1]See p. 41 of the monograph on occupational exposures in petroleum refining for characteristics of principal refinery process streams.

(iii) *Gasohol*

Gasohol is a mixture of gasoline with up to 10% volume anhydrous ethanol (Royal Dutch/Shell Group of Companies, 1983).

(*b*) *Aviation gasoline*

This category covers all special grades of gasoline for use in aviation reciprocating engines, as given in ASTM Specification D 910 and Military Specification MIL-G-5572, and includes all refinery products within the gasoline range that are to be marketed straight, or in blends, as aviation gasoline without further processing in any refinery operation other than mechanical blending (American Petroleum Institute, 1981).

1.3 Chemical composition and physical properties of technical products

(*a*) *Automotive gasoline*

Automotive gasoline is a volatile, inflammable, liquid hydrocarbon mixture used almost exclusively to fuel internal combustion engines. It has a typical density of about 0.7–0.8 g/cm^3 (CRCS, 1985) and has a Reid vapour pressure (which is about 10% less than the true vapour pressure at 37.8°C) ranging between 8 and 15 psi [0.4–0.9 atm] (CONCAWE, 1985), depending on the season and geographical location.

The chemical composition of gasoline is highly variable because a product with the desired automotive fuel properties can be formulated in a number of ways. The composition by hydrocarbon type of typical automotive gasolines is given in Table 1. The hydrocarbon components are predominantly in the range C_5–C_{10} with an overall carbon number range of C_4–C_{12}. In Europe, the amount of each component process stream used would normally be

Table 1. Composition by hydrocarbon type of typical automotive gasolines[a]

Composition	Range
Alkanes	4–8 wt %
Alkenes	2–5 wt %
Isoalkanes	25–40 wt %
Cycloalkanes	3–7 wt %
Cycloalkenes	1–4 wt %
Total aromatics	20–50 wt %
Benzene	0.5–2.5 wt %
Paraffins (naphthenes)	30–90 vol. %
Olefins	0–30 vol. %
Aromatics	10–50 vol. %

[a]Adapted from CONCAWE (1985, 1987)

expected to fall within the range indicated in Table 2. A laboratory-blended reference sample of US unleaded gasoline has been reported to contain 44.5% heavy catalytically cracked naphtha [23], 22% light alkylate naphtha [13], 21.3% light reformed naphtha [16], 7.6% light catalytically cracked naphtha [22], 3.8% added butane and 0.8% added benzene (MacFarland *et al.*, 1984; CRCS, 1985). According to CONCAWE, the aromatic fraction of gasoline contains benzene at a normal range of 0–7 vol % and typically at 2–3 vol %.

Table 2. Major component streams in automotive and aviation gasolines[a]

TSCA inventory name and identification number[b]	Refinery process stream (nomenclature used in Europe)	Automotive gasoline (vol. %)	Aviation gasoline (vol. %)
n-Butane [12]	Butanes	0–10	0–2
Light straight-run naphtha [3]	Light straight-run gasoline	0–30	0
Full-range reformed naphtha [15]	Catalytic reformate	30–80	0–40
Catalytically cracked naphthas [22, 23]	Catalytically cracked gasoline	0–60	0
Isomerization naphtha [14]	C_5/C_6 Isomerate	0–30	0–15
Full-range alkylate naphtha [13]	Alkylate	0–5	50–70
Thermally cracked naphthas [28, 29]	Thermally cracked gasoline	0–5	0
Light steam-cracked naphtha [33]	Steam-cracked (pyrolysis) gasoline[c]	0–50	0

[a]From CONCAWE (1985)

[b]See Table 2 and Figure 1 in the monograph on occupational exposures in petroleum refining

[c]Not widely used

A list of specific hydrocarbons detected in US 'midcontinent' gasolines at concentrations of 1 wt % or more is given in Table 3. ASTM specifications for automotive gasolines are provided in Table 4. No European standard is available for leaded automotive gasoline, but in most countries national specifications apply.

Gasoline also contains other additives, used to raise the octane number of leaded gasolines, to keep carburettors clean, to prevent oxidation of gasoline, to prevent corrosion in distribution systems and to differentiate grades of gasoline (Huddle, 1983). A list of typical additives used in automotive gasoline is given in Table 5. A number of contaminants must be removed to provide good quality gasoline, including water, particulate matter, nitrogen compounds, mercaptans and hydrogen sulfide (Huddle, 1983).

(*b*) *Aviation gasoline*

Many of the gasoline requirements of the automotive engine are shared by gasoline-powered aviation engines. However, aeroplane engines have several additional requirements because many involve direct fuel injection into the cylinders and some also have superchargers.

Table 3. Detectable hydrocarbons found in US finished gasolines at a concentration of 1% or more[a]

Chemical	Weight %	
	Estimated range	Weighted average[b]
Toluene	5–22	10
2-Methylpentane + 4-Methyl-*cis*-2-pentene + 3-Methyl-*cis*-2-pentene[c]	4–14	9
n-Butane	3–12	7
iso-Pentane	5–10	7
n-Pentane	1–9	5
Xylene (three isomers)	1–10	3
2,2,4-Trimethylpentane	<1–8	3
n-Hexane	<1–6	2
n-Heptane	<1–5	2
2,3,3-Trimethylpentane	<1–5	2
2,3,4-Trimethylpentane	<1–5	2
3-Methylpentane	<1–5	2
Methylcyclohexane + 1-*cis*-2-Dimethylcyclopentane + 3-Methylhexane[c]	<1–5	1
Benzene	<1–4	2
2,2,3-Trimethylpentane	<1–4	2
Methyl tertiary butyl ether	<1–4	1
Methylcyclopentane	<1–3	2
2,4-Dimethylpentane	<1–3	1
Cyclohexane	<1–3	1
1,2,4-Trimethylbenzene	<1–3	1
2-Methyl-2-butene	<1–2	2
2,3-Dimethylbutane	<1–2	1
trans-2-Pentene	<1–2	1
Methylcyclohexane	<1–2	1
3-Ethyltoluene	<1–2	1
2,3-Dimethylpentane	<1–2	1
2,5-Dimethylpentane	<1–2	1
2-Methyl-1-butene	<1–2	1
Ethyl benzene	<1–2	1

[a]Provided by American Petroleum Institute

[b]The sum of the weighted averages does not equal 100% because numerous components were detected at less than 1%.

[c]These chemicals could not be distinguished by gas chromatography because of similar retention times.

Table 4. Detailed requirements for gasoline (ASTM D439-79)[a]

Volatility class	Distillation temperature (°C) at % evaporated at 101.3 kPa					Distillation residue (vol % max)	Vapour:liquid ratio at 10.3 kPa (V:L)	
	10 Vol % max	50 Vol % min	50 Vol % max	90 Vol % max	End-point max		Test temperature (°C)	V:L max
A	70	77	121	190	225	2	60	20
B	65	77	118	190	225	2	56	20
C	60	77	116	185	225	2	51	20
D	55	77	113	185	225	2	47	20
E	50	77	110	185	225	2	41	20

Volatility class	Reid vapour pressure, max (kPa)	Lead content (max g/l)		Copper strip corrosion max	Existent gum, max (mg/100 ml)	Sulfur max (mass %)		Oxidation stability min (minutes)
		Unleaded[b]	Leaded[c]			Unleaded	Leaded	
A	62	0.013	1.1	No. 1	5	0.10	0.15	240
B	69	0.013	1.1	No. 1	5	0.10	0.15	240
C	79	0.013	1.1	No. 1	5	0.10	0.15	240
D	93	0.013	1.1	No. 1	5	0.10	0.15	240
E	103	0.013	1.1	No. 1	5	0.10	0.15	240

[a]From Hoffman (1982); CRCS (1985); CONCAWE (1988)

[b]The intentional addition of lead or phosphorus compounds is not permitted. US Environmental Protection Agency regulations limit their maximum concentrations to 0.05 g lead per gallon (0.013 g/l) and 0.005 g phosphorus per gallon (0.0013 g/l; by Test Method D 3231), respectively (Huddle, 1983).

[c]The US Environmental Protection Agency in 1986 limited the concentration in leaded gasoline to no more than 0.1 g/gallon (0.026 g/l), averaged for quarterly production of leaded gasoline (CONCAWE, 1988); 1.1 g/l is the maximum amount of lead permitted in leaded gasoline.

Table 5. Typical additives used in automotive gasoline[a]

Purpose	Compound
Antiknock	Tetraethyllead
	Tetramethyllead
	2-Methyl cyclopentadienyl manganese tricarbonyl[b]
Lead scavengers	1,2-Dibromoethane
	1,2-Dichloroethane
Detergents	Amino hydroxy amide
	Amines
	Alkyl ammonium dialkyl phosphate[b]
	Imidazolines
	Succinimides
Antirust	Fatty acid amines
	Sulfonates
	Amine/alkyl phosphates[b]
	Alkyl carboxylates
Antioxidants	Hindered phenols[c]
	para-Phenylenediamine[c]
	Aminophenols
	2,6-Di-*tert*-butyl-*para*-cresol
	ortho-Alkylated phenols combined with phenylenediamine
Dyes	Red: alkyl derivatives of azobenzene-4-azo-2-naphthol
	Orange: benzene-azo-2-naphthol
	Yellow: *para*-diethyl aminoazobenzene
	Blue: 1,4-diisopropylaminoanthraquinone
Anti-icing	Alcohols
	Amides/amines
	Organophosphate ammonium salts[b]
	Glycols
Upper cylinder lubricants	Light mineral oils
	Cycloparaffins
Metal deactivators	*N*,*N*'-Disalicylidene-1,2-diaminopropane
Oxygenates[d]	Ethanol
	Methanol
	Methyl-*tert*-butyl ether (MTBE)
	tert-Butyl alcohol (TBA)
	tert-Amyl methyl ether

[a]From Lane (1980); Huddle (1983); CRCS (1985)

[b]Not used in Europe

[c]Prevalent in Europe

[d]Oxygenates used commonly in Europe are methanol in conjunction with TBA or MTBE. Typical oxygenate contents are 3% methanol + 2% TBA or 5% MTBE. The methanol content in automotive gasolines should not exceed 3%; the MTBE content should not exceed 10%, and total amount of oxygen should not exceed 2.5% (CONCAWE, 1988).

Three grades of fuel are specified for use in aeroplanes: Avgas (Grade) 80 (formerly referred to as 80–87), Avgas (Grade) 100 (formerly called 100–130) and Grade 100LL (a low-lead formulation of Grade 100). A higher octane formulation, Avgas (Grade) 115 (115–145), is no longer in common use (see, e.g., Ward, 1984).

The same types of blending materials as those used in automotive gasolines may be used in aviation gasolines (Table 2), but higher percentages of some stocks (especially alkylates) and additional tetraethyllead (see IARC, 1980, 1987a) are used to meet the higher octane number requirement. The heat of combustion (energy content) is important in aviation fuels — the more energy available per unit of fuel, the less fuel load required for a specific trip. Because aviation gasolines may be subjected to low temperatures in high-altitude flight, the freezing-point of the fuel cannot be above −58°C. Only three additives are permitted in aviation gasoline: dye, tetraethyllead and antioxidant. Each of the three grades of gasoline has a standard colour to ensure that the correct grade is used (Ward, 1984). ASTM specifications for aviation gasoline are provided in Table 6.

Table 6. Detailed requirements for aviation gasoline (ASTM D 910–79)[a]

Requirement	Grade 80	Grade 100	Grade 100LL
Knock value, min, octane number, lean rating[b]	80	100	100
Knock value, min, rich rating[c]	87	100	100
Minimum performance number	87	130	130
Colour	red	green	blue
Dye content:			
Permissible blue dye, max, mg/gallon [mg/l]	0.5 [0.13]	4.7 [1.2]	5.7 [1.5]
Permissible yellow dye, max, mg/gallon [mg/l]	none	5.9 [1.6]	none
Permissible red dye, max, mg/gallon [mg/l]	8.65 [2.3]	none	none
Tetraethyllead, max, ml/gallon [g/l]	0.5 [0.13]	4.0 [1.1]	2.0 [0.5]

Requirement	All grades
Distillation temperature, °C:	
10% evaporated, max	75
40% evaporated, max	75
50% evaporated, max	105
90% evaporated, max	135
Final boiling-point, max °C	170
Sum of 10% and 50% evaporated temperatures, min, °C	135
Distillation recovery, min %	97
Distillation residue, max %	1.5
Distillation loss, max %	1.5
Net heat of combustion, min, Btu/lb [kJ/kg]	18 720 [43 520]
Vapour pressure	
min (kPa) [atm]	38 [0.4][d]
max (kPa) [atm]	48 [0.5]
Copper strip corrosion, max	No. 1

Table 6 (contd)

Requirement	All grades
Potential gum (5-h ageing), max, mg/100 ml	6
Visible lead precipitate, max, mg/100 ml	3
Sulfur, weight max, %	0.05
Freezing-point, max °C	−58
Water reaction	volume change not to exceed ± 2 ml
Permissible antioxidants, max lb/1000 bbl (42 gallons) [g/l]	4.2 [12]

[a]From Hoffman (1982)

[b]For cruising conditions

[c]For takeoff conditions

[d]From CONCAWE (1988)

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(*a*) *Production*

Both automotive gasolines and aviation gasolines are produced primarily by blending component streams from petroleum refinery processing units. Blending of various stocks is a large volume operation. Gasoline components, including alkylates and other high-octane components, are blended with octane-improving additives (such as methyl *tert*-butyl ether), carburettor detergents, antirust agents, anti-icing agents and other additives.

Production volumes of automotive gasoline and aviation gasoline for the period 1970-85 at five-year intervals are shown in Table 7. Production in 1985 is shown for major geographical areas of the world in Table 8 (International Energy Agency, 1987).

(*b*) *Use*

Prior to the early 1900s, gasoline was an undesirable by-product of the manufacture of kerosene. The supply exceeded the demand, so the cut from gasoline to kerosene was processed to produce the minimal amount of gasoline and a maximum of kerosene. Under these conditions, the yield of gasoline was about 10% of crude oil, which was still too great for market needs (Guthrie, 1960). In time, uses were developed for gasoline. Varnish and paint makers used it as a solvent, and special lamps burnt it to illuminate parks and streets (Purdy, 1958).

With the rapid development of the automobile in the early 1900s, gasoline demand began to exceed supply. Over the ensuing decades, many processes were developed to

produce gasoline, and it became the primary product of most petroleum refineries and remains so today (Purdy, 1958; Guthrie, 1960). Consumption volumes for use as automotive and aviation gasolines are presented in Tables 7 and 8.

Table 7. Production and consumption (in thousands of tonnes) of gasoline in the USA and countries of the Organisation for Economic Cooperation and Development (OECD), 1970–85[a]

Area/product	Production/ consumption	1970	1975	1980	1985
USA					
Automotive gasoline	Production	244 495	285 133	284 843	270 562
	Consumption	247 520	286 639	285 052	289 922
Aviation gasoline	Production	2 215	1 561	1 385	969
	Consumption	2 234	1 598	1 459	1 204
OECD					
Automotive gasoline	Production	359 399	429 979	457 053	445 934
	Consumption	362 964	434 325	455 151	459 438
Aviation gasoline	Production	2 919	2 020	2 000	1 453
	Consumption	3 015	2 178	1 934	1 583

[a]From International Energy Agency (1987)

Table 8. Production and consumption (in thousands of tonnes) of automotive gasoline and aviation gasoline by geographical area, 1985[a]

Region/organization	Automotive gasoline		Aviation gasoline	
	Production	Consumption	Production	Consumption
North America	295 241	313 980	1 096	1 329
USA	270 562	289 922	969	1 204
Canada	24 679	24 058	127	125
OECD[b] (Europe)	111 854	105 416	232	150
European Economic Community	99 569	91 081	232	121
Pacific[c]	38 839	40 042	125	104
OECD (All)	445 934	459 438	1 453	1 583

[a]From International Energy Agency (1987)

[b]Organisation for Economic Cooperation and Development

[c]Australia, Japan, New Zealand

(*c*) *Regulatory status and guidelines*

In Sweden, occupational exposure standards of 220 mg/m^3 (8-h time-weighted average (TWA)) and 300 mg/m^3 (15-min TWA) have been established for gasoline with an assumed aromatic content of 46% (CONCAWE, 1987).

In the USA, occupational exposure limits for gasoline have been recommended at 900 mg/m^3 (8-h TWA) and 1500 mg/m^3 (15-min TWA; American Conference of Governmental Industrial Hygienists, 1987). A compilation of national occupational exposure limits for gasoline components has been published (CONCAWE, 1987).

As of 1 January 1986, the US Environmental Protection Agency promulgated as a final rule a low-lead standard of 0.10 g lead per gallon (0.026 g/l) of leaded gasoline (CONCAWE, 1988). An EEC Directive requires Member States to ensure that unleaded gasoline (as defined in section 1.2) is available and evenly distributed throughout their territory from 1 October 1989 onwards (Council of the European Communities, 1987).

2.2 Occurrence

(*a*) *Occupational exposure*

Exposure to gasoline in the work environment has been associated with the following operations or jobs (CONCAWE, 1985, 1987): refinery operations leading to the production of gasoline; tank dipping, pipeline and pump repairs and filter cleaning in refineries, distribution terminals and depots; maintenance, inspection and cleaning of gasoline storage tanks; gasoline distribution via bulk transfer in refineries and terminals; service station attendants; engine and vehicle maintenance; and routine sampling and laboratory analysis of gasoline. Other operations or jobs involving gasoline exposure include: adjustment of gasoline pumps in service stations (Andersson *et al.*, 1984), and the use of gasoline as a metal cleaning solvent (Verwilghen *et al.*, 1975).

Quantitative exposure data typical of various activities are summarized in Table 9 for total hydrocarbons and benzene (see IARC, 1982, 1987b), the two most commonly reported measures of gasoline vapours.

Because of the lower volatility of hydrocarbons with a higher number of carbons, the hydrocarbon composition of gasoline vapours in most occupational situations is different from that of liquid gasoline. Thus, vapours from several European gasolines were found to contain an average of 90% by volume of C_3–C_5 nonaromatic hydrocarbons (compared to 26% by weight in the liquid) and about 2% of C_6–C_8 aromatics (compared to 31% by weight in the liquid; CONCAWE, 1987).

Highest overall 8-h TWA concentrations have been observed for drum filling and marine loading operations, while service station attendants have the lowest exposure levels. High short-term concentrations in air may occur during loading operations on tank trucks with no vapour recovery system; lower levels are observed over the full working day of loader-drivers (Phillips & Jones, 1978).

Table 9. Concentrations (time-weighted average measurements) of airborne gasoline constituents in various operations and occupations

Operation/occupation (region)	Exposure and sampling duration	Concentration (mg/m³)		Reference
		Total hydrocarbons arithmetic mean (range) [no. of samples]	Benzene mean (range) [no. of samples]	
Top loading of road tankers, no vapour recovery (western Europe)	<1 h	451 (6.4–3030) [142]	6.1 (ND[a]–60.5) [142]	CONCAWE (1987)
Top loading of road tankers, no vapour recovery (USA)	8 h	46.4 (9.9–109) [10]	0.9 (0.1–2.3) [43]	Halder *et al.* (1986)
Bottom loading of road tankers, no vapour recovery (western Europe)	<1 h	76 (8.2–234) [59]	1.4 (ND–5.5) [59]	CONCAWE (1987)
Bottom loading of road tankers, no vapour recovery (USA)	8 h	89.8 (21.9–184) [7]	1.1 (0.2–5.9) [38]	Halder *et al.* (1986)
Bottom loading of road tankers, vapour recovery (USA)	8 h	39.6 (9.4–195)[b] [8]	1.0 (0.2–8.9)[b] [56]	Halder *et al.* (1986)
Road tankers during driving (western Europe)	8 h		0.1 (ND–0.3) [20]	Arbetarskyddsstyrelsen (1981)
Marine loading, tanker and barge (USA)	8 h	246 (9.1–1580) [11]	2.3 (0.1–19.5) [11]	Halder *et al.* (1986)
Marine loading deck crews, barges (western Europe)	8 h	263 (1.5–1750) [11]	4.7 (ND–31.5) [11]	CONCAWE (1987)
Railcar top loading (western Europe)	8 h	84.7 (2.0–535) [32]	1.5 (ND–9.5) [32]	CONCAWE (1987)
Drum filling (western Europe)	8 h	858 (61–1748) [9]	27.2 (ND–116) [9]	CONCAWE (1987)
Service station attendants (western Europe)	8 h	29.3 (7.9–101) [13]	0.35 (ND–1.3) [13]	CONCAWE (1987)

Table 9 (contd)

Operation/occupation (region)	Exposure and sampling duration	Concentration (mg/m³)		Reference
		Total hydrocarbons arithmetic mean (range) [no. of samples]	Benzene mean (range) [no. of samples]	
Service station attendants (USA)	8 h	10–67[c] (range of means) [84] from 7 locations	0.06–0.75[c] (range of means) [84] from 7 locations	McDermott & Vos (1979)
Service station attendants (USA)	6–7 h	4.6[d] (1.9–14.3) [8]		Kearney & Dunham (1986)
Service station mechanics (USA)	7 h	2.9[d] (1.1–22.3) [4]		Kearney & Dunham (1986)
Cleaning of gasoline storage tanks (western Europe)	<1 h		(64–1680)[e] [10]	Arbetarskyddsstyrelsen (1981)
Refinery operators, gasoline production (western Europe)	8 h	52.8 (0.7–1820) [62]	0.9 (ND–23.8) [62]	CONCAWE (1987)
Refinery operators, ancillary (western Europe)	8 h	66.0 (3.8–923) [27]	1.0 (ND–14.1) [27]	CONCAWE (1987)
Gasoline truck drivers (USA)	7–8 h	45.8 (19–72.5)[f] [49]	0.45 (0.25–0.65)[f] [47]	Rappaport *et al.* (1987)
Service station attendants (USA)	7–8 h	70 (53–86.8)[f] [49]	0.65 (0.48–0.81)[f] [49]	Rappaport *et al.* (1987)
Rail tanker top loaders (UK)	4 and 5 h		5.1 and 8.0[c] [39] (means for 2 loaders)	Sherwood (1972)
Rail tanker weigher (UK)	6 h		64[c] [23]	Sherwood (1972)

Table 9 (contd)

Operation/occupation (region)	Exposure and sampling duration	Concentration (mg/m³)		Reference
		Total hydrocarbons arithmetic mean (range) [no. of samples]	Benzene mean (range) [no. of samples]	
Loading, rail and road tankers (UK)	35 min–3 h		0.96–21[g] [70]	Parkinson (1971)
Service station attendants (UK)	3.5–14 h		0.96–7.7[c] (range of means) [121] from 9 stations	Parkinson (1971)

[a]ND, not detected

[b]Values for one of three terminals

[c]Converted from ppm

[d]Geometric mean

[e]No mean value given because of highly varying concentration

[f]Approximate 95% confidence interval

[g]Range of means covering 24 operators; converted from ppm

The general trend seen in Table 9 is confirmed in studies focusing on benzene exposure (Irving & Grumbles, 1979; Runion & Scott, 1985). Furthermore, moderate levels of benzene have been measured during the following operations: dismantling of pump filters by pump servicemen (20 mg/m^3) and carburettor and cylinder head demounting in automobile garages (<16 mg/m^3; Holmberg & Lundberg, 1985). Besides benzene, a variety of other gasoline-derived hydrocarbons have been measured in occupational settings. Thus, concentrations of up to 150 hydrocarbons have been reported in 15 job groups involving gasoline exposure (CONCAWE, 1987). Among those, components with independent toxic effects such as *n*-hexane, toluene, the xylenes and trimethylbenzenes were present in concentrations well below their respective established exposure limits. Exposure levels of 1,3-butadiene (see IARC, 1986a, 1987c) for various job groups are summarized in Table 10.

Table 10. Personal exposures (mg/m^3) to 1,3-butadiene associated with gasoline[a]

	Mean	Range	Exposure duration
Production on-site (refining)	0.3	ND[b]–11.4	8–h TWA
Production off-site (refining)	0.1	ND–1.6	8–h TWA
Loading ships (closed system)	6.4	ND–21.0	8–h TWA
Loading ships (open system)	1.1	ND–4.2	8–h TWA
Loading barges	2.6	ND–15.2	8–h TWA
Jettyman	2.6	ND–15.9	8–h TWA
Bulk loading road tankers			
Top loading <1 h	1.4	ND–32.3	<1–h TWA
Top loading >1 h	0.4	ND–4.7	8–h TWA
Bottom loading <1 h	0.2	ND–3.0	<1–h TWA
Bottom loading >1 h	0.4	ND–14.1	8–h TWA
Road tanker delivery (bulk plant to service station)	ND		
Railcar top loading	0.6	ND–6.2	8–h TWA
Drumming	ND		
Service station attendant (dispensing fuel)	0.3	ND–1.1	8–h TWA
Self-service station (filling tank)	1.6	ND–10.6	2-min TWA

[a]From CONCAWE (1987)

[b]ND, not detected

Concentrations of airborne tetraethyllead, tetramethyllead (see IARC, 1980, 1987a), ethylene dichloride (1,2-dichloroethane; see IARC, 1979, 1987d) and ethylene dibromide (1,2-dibromoethane; see IARC, 1977, 1987e), all additives in leaded gasoline, were found to be too low to be detected in the breathing zone of tank truck loaders (McDermott & Killiany, 1978). Additional data on exposure to tetraalkyllead compounds, 1,2-dibromoethane, 1,2-dichloroethane, *tert*-butyl alcohol and methyl-*tert*-butyl ether of gasoline-

exposed workers inside and outside refineries are given in the monograph on occupational exposures in petroleum refining.

Table 11 summarizes various biological exposure measurements made on workers exposed to gasoline.

Table 11. Biological exposure measurements in workers exposed to gasoline

Matrix	Occupation (no. of workers)	Biological indicator	Concentration	Reference
Blood	Tank cleaner (3)	Tetramethyllead	0.01–0.027 μg/ml[a]	Andersson *et al.* (1984)
Blood	Pump attendant (6)	Tetramethyllead	0.005–0.006 μg/ml[a]	Andersson *et al.* (1984)
Blood	Service station attendant (8)	Benzene	<0.003–0.020 μg/ml[b]	Elster *et al.* (1978)
Blood	Service station attendant (8)	Toluene	0.010–0.045 μg/ml[b]	Elster *et al.* (1978)
Urine	Service station attendant (48)	Total thioethers	[c]	Stock & Priestly (1986)
Urine	Service station attendant (51)	Phenol	40 mg/l (mean)[d] >20 mg/l (88% of workers)	Pandya *et al.* (1975)
Urine	Top loading of rail tankers (3)	Phenol	12, 25 (loader) and 83 (weigher) mg/l[b]	Sherwood (1972)
Urine	Service station attendant (5)	Phenol	5–18 mg/l[b]	Parkinson (1971)
Urine	Loading rail tankers (2)	Phenol	ND[e]–10 mg/l[b]	Parkinson (1971)
Urine	Loading and discharging road tankers (7)	Phenol	4–48 mg/l[d,f]	Parkinson (1971)
Exhaled breath	Loading rail tankers (2)	Benzene	0.3–2.8 mg/m³[b]	Parkinson (1971)
Exhaled breath	Top loading of rail tankers (3)	Benzene	0.44, 0.56 and 2.7 (weigher) mg/m³[b]	Sherwood (1972)

[a]Expressed as lead; blood tetramethyllead concentration in reference group, <0.003 μg/ml

[b]Samples taken at end of work

[c]End of working day samples significantly higher than morning samples ($p < 0.001$); pump operators higher than self-service attendants.

[d]Gasoline contained 10–17% of benzene; hot weather conditions

[e]ND, not detected

[f]Gasoline contained 20–33% benzene

(*b*) *Environmental exposure*

Ground water contamination due to leaks from below-ground storage tanks has become a serious environmental problem. In New Jersey, USA, more than 1400 incidents were reported in 1978, resulting in spillage of 1.1 million gallons (4.2 million l) of petroleum compounds. The number of incidents reported has continued to rise and is approaching 2000 per year in New Jersey alone (Kramer, 1982).

Approximately 110 billion gallons (420 billion l) of gasoline are used in the USA each year. Nearly all gasoline used for transportation purposes is stored underground before it is used, but, of the estimated 1.4 million underground gasoline storage tanks in the USA, approximately 85% are made of steel and have no protection against corrosion. Following the rupture of a storage tank, gasoline travels down through the porous material towards the ground water table, adhering to soil particles along the way. If enough gasoline is spilled and the residual saturation requirement is satisfied, free gasoline then enters the water table. Since gasoline hydrocarbons are toxic at concentrations below solubility limits and saturated material can come into contact with fluctuating water tables and/or ground water recharge, saturated soil can pose a long-term threat to ground water supplies due to the relatively soluble aromatic constitutents (Hoag & Marley, 1986).

In a study by Kearney and Dunham (1986; see also Table 9), the concentration of total hydrocarbons measured when customers at a self-service station filled one tank was 3.9–63.5 mg/m^3 (12 samples; average sampling time, 10 min). Concentrations measured in the area of self-service and serviced pump islands and at the perimeter were 3.6–16.1 (three samples; average sampling time, 426 min), 0.9–9.9 (five; 408) and not detected-9.7 mg/m^3 (17; 416), respectively. The concentration of 1,2-dichloroethane during filling of gasoline tanks at self-service stations has been evaluated as 6 μg/m^3 for 2.2 h per year (Gold, 1980).

Accidental releases of gasoline in the recent past include the following. In 1968, a tank leak of 100 000–250 000 gallons (378 500–946 250 l) occurred in Los Angeles-Glendale, CA, USA (McKee *et al.*, 1972). In March 1978, 1900 tonnes of gasoline were released into the waters of Block Island Sound, RI, USA, after the grounding of *Ocean Barge 250* (Dimock *et al.*, 1980). Thirty tonnes of gasoline leaked from a barge near Queen Charlotte Islands, Canada, in March 1984 (McLaren, 1985)

2.3 Analysis

Since gasoline is composed of a complex mixture of hydrocarbons, there are few methods for the environmental analysis of 'gasoline' as an entity, but many methods are reported for the analysis of its component hydrocarbons. These methods are used to identify or 'fingerprint' the origin of a specific gasoline sample on the basis of the proportions of its component hydrocarbons. Selected methods for the quantitative determination of gasoline in air are listed in Table 12.

Four air sampling methods for unleaded gasoline have been tested and compared, two based on charcoal tubes of differing capacity and two on passive organic vapour monitors. The analytical method involves chlorobenzene desorption and capillary or packed column

Table 12. Methods for the determination of gasoline in air

Sample preparation	Assay procedure[a]	Limit of detection[b]	Remarks	Reference
Absorption (porous polymer and charcoal); thermal desorption (one or two stage)	GC/FID capillary column	0.03 mg/m³ THC	Applicable to THC and individual components[c]	CONCAWE (1986)
Absorption (charcoal); desorption (dichloromethane)	GC/FID capillary column	0.5 mg/m³[d] THC	Applicable to THC and individual components[e]	Kearney & Dunham (1986)

[a]GC/FID, gas chromatography/flame ionization detection

[b]THC, total hydrocarbon

[c]Method validated for 22 hydrocarbons (from propane to *n*-decane, including benzene, toluene and *ortho*-xylene); this method also allows the determination of additives such as methanol and methyl-*tert*-butyl ether.

[d]Lower limit of stated working range

[e]24 Aliphatic and aromatic hydrocarbons actually measured in a service station

separation with flame ionization detection. Samples were analysed for total hydrocarbons as well as for eight individual compounds. A dependence on humidity was found at high concentrations of total hydrocarbons (375 mg/m³) for all methods except those involving high-capacity charcoal tubes (American Petroleum Institute, 1984).

Benzene in exhaled air and phenol in urine have been measured by gas chromatographic methods as indices of exposure to gasoline (IARC, 1982; Fishbein & O'Neill, 1988).

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals[1]

Studies on the carcinogenicity in experimental animals of light straight-run naphtha [3] and light catalytically cracked naphtha [22] refinery streams, which are components of automobile gasoline, have been described in the monograph on occupational exposures in petroleum refining.

Inhalation

Mouse: Groups of 100 male and 100 female B6C3F1 mice, six weeks of age, were exposed to 0, 67, 292 or 2056 ppm [0, ~ 200, 870 or 6170 mg/m³] totally volatilized

[1]The Working Group was aware of skin-painting studies in progress in mice using unleaded gasoline (IARC, 1986b).

unleaded gasoline (benzene content, 2%) by inhalation for 6 h per day on five days per week for 103–113 weeks. The sample was blended to conform to US specifications existing in 1976. Ten male and ten female mice from each group were killed at three, six, 12 and 18 months and the remainder at the end of the study. Survival in the groups of exposed female mice was not significantly different from that of controls [rates not reported]. That of the low- and medium-dose male mice was significantly higher than that in controls, although survival of high-dose males was lower than that of controls [rates not reported]. The incidences of hepatocellular adenomas and carcinomas were increased in exposed females. In mice killed at 18–24 months, the percentages of animals with liver tumours were: controls, 14%; low dose, 19%; medium dose, 21%; high dose, 48% [ratio of benign to malignant tumours unspecified]. The incidence of hepatocellular tumours was not increased in treated male mice. A renal adenoma occurred in one high-dose female and a bilateral renal tubular adenocarcinoma in another (MacFarland *et al.*, 1984). [The Working Group noted the inadequate reporting of the experimental data.]

Rat: Groups of 100 male and 100 female Fischer 344 rats, six weeks of age, were exposed to 0, 67, 292 or 2056 ppm [0, ~200, 870 or 6170 mg/ m^3] totally volatilized unleaded gasoline (benzene content, 2%) by inhalation for 6 h per day on five days per week for 107 or 109 weeks. Ten males and ten females from each group were killed at three, six, 12 and 18 months and the remainder at the end of the study. Survival in the groups of exposed female rats was not significantly different from that of controls [rates not reported]. That of control male rats was significantly higher than that of any of the exposed groups after week 80 [rates not reported]. Increased incidences of renal tumours were observed in male rats: renal adenomas — controls, 0; low-dose, 0; medium-dose, 2; high-dose, 1; renal carcinomas — control, 0; low-dose, 1; medium-dose, 2; high-dose, 6. No renal adenoma or carcinoma was observed in female rats. Renal sarcomas occurred in one medium-dose male and in one medium-dose female (MacFarland, 1982; MacFarland *et al.*, 1984). [The Working Group noted the inadequate reporting of the experiment.]

3.2 Other relevant data

(*a*) *Experimental systems*

Absorption, distribution, excretion and metabolism

No data were available to the Working Group.

Toxic effects

Male albino [Wistar] rats given a single dose of 2.0 ml/ kg bw gasoline (Indian Oil Corp.) by intraperitoneal injection showed increased lipid peroxidation in the liver after 24 h (Rao & Pandya, 1978). Female Wistar rats administered 1.0 ml/ kg bw gasoline (Indian Oil Corp.) intraperitoneally had depressed activities of hepatic δ-aminolaevulinic acid synthetase and dehydratase within 20 h (Rao & Pandya, 1980).

Male Porton rats exposed in a chamber to gasoline vapour (50% super:50% standard) at a calculated concentration of 5 mg/l, for 8 h per day for three weeks, showed moderate increases in liver microsomal cytochrome P450 activities (Harman *et al.*, 1981).

In electroencephalographic studies with male Wistar rats given 10 ml/kg bw of either unleaded or leaded (1000 ppm (16.5 mg/kg bw) tetraethyllead) gasoline by intraperitoneal injection, animals given leaded gasoline showed excessive tension and excitement by day 6–7. Both unleaded and leaded gasoline decreased δ, θ and α waves after one to three days, whereas the electrocorticogram of rats given leaded gasoline showed marked α and θ waves after six to seven days (Saito, 1973).

Treatment of male Fischer 344 rats by gavage with 0.04–2.0 ml/kg bw unleaded gasoline daily for nine days markedly increased the number and size of hyaline droplets in cells of the renal proximal convoluted tubules. The renal content of the male rat-specific low molecular protein α_{2u}-globulin was increased up to 4.4 fold (Olson *et al.*, 1987). A series of gavage screening studies using male Fischer 344 rats was conducted on components of gasoline to identify more clearly the major contributors to nephrotoxicity. The alkane components were found to be primarily responsible, and the degree of branching was related to the potency of the nephrotoxic response (Halder *et al.*, 1985). An active nephrotoxic component of gasoline, 2,2,4-trimethylpentane, induced hyaline droplet accumulation, degeneration and necrosis in the renal proximal convoluted tubules after administration of 50–500 mg/kg bw daily by gavage for 21 days. In cell proliferation studies, 2,2,4-trimethylpentane led to a five- to six-fold increase in the labelling index of the P2 segment of the kidney tubule (Short *et al.*, 1986). The extent and localization of cell proliferation elicited by 0.2–50 mg/kg bw 2,2,4-trimethylpentane given by gavage on five days per week for three weeks to male Fischer 344 rats closely paralleled the extent and severity of renal tubular accumulation of crystalloid hyaline droplets and single-cell necrosis. Similar cell proliferation, hyaline droplet accumulation and necrosis were seen in male rats exposed by inhalation to 2–2000 ppm [~6–6000 mg/m^3] unleaded gasoline for 6 h per day on five days per week for three weeks (Short *et al.*, 1987). A metabolite of 2,2,4-trimethylpentane, 2,4,4-trimethyl-2-pentanol, has been shown to accumulate in the male (but not in female) rat kidney and to bind reversibly to kidney α_{2u}-globulin (Charbonneau *et al.*, 1987; Lock *et al.*, 1987).

Female rats [strain unspecified] exposed to 100 ppm [~300 mg/m^3] leaded gasoline vapour (octane rating, 98%; 0.45 g/l tetraethyllead) for 8 h per day, on five days per week up to 12 weeks, exhibited a high incidence of changes in the lung parenchyma characterized by interstitial fibrosis with associated alveolar collapse. Initial changes, appearing after six weeks, included degeneration of endothelium and interstitial fibroblasts followed by hypertrophy of type 2 pneumocytes (Lykke & Stewart, 1978; Lykke *et al.*, 1979). Among female Wistar rats similarly exposed for up to 15 days, reduced levels of pulmonary surfactant, with no qualitative alteration in the phospholipid components, were observed. However, such treatment did not result in changes in RNA or DNA synthesis in lung tissue *in vivo* (Stewart *et al.*, 1979).

Male and female Sprague-Dawley rats exposed to 29, 416 or 3316 ppm (0.11, 1.58 or 12.61 mg/l TWA) unleaded gasoline blend by inhalation for 6 h per day on five days per week for 21 days developed mild renal tubular degenerative and regenerative changes, including increased levels of hyaline droplet formation, necrosis and degeneration of the proximal convoluted tubule of the renal cortex in males only. When exposure was extended

to 90 days at concentrations of 40, 379 or 3866 ppm (0.15, 1.44 or 14.70 mg/l), a concentration-related incidence of tubular dilatation and necrosis at the corticomedullary junction was observed in male rats only (Halder *et al.*, 1984). Similarly, in another study, male Sprague-Dawley rats exposed to 1552 ppm [~4650 mg/m^3] unleaded gasoline vapour for 6 h per day on five days per week for 90 days had regenerative epithelium and dilatation of kidney tubules. These effects were not seen in females and were not seen with leaded gasoline in animals of either sex (Kuna & Ulrich, 1984).

In a long-term study, groups of male and female Fischer 344 rats were exposed to 67, 292 or 2056 ppm [~200, 870 or 6170 mg/m^3] unleaded gasoline vapours for 6 h per day on five days per week for three, six, 12, 18 and 24 months. After three, six and 12 months at the highest doses, the males had increased foci of regenerative epithelium in the renal cortex and dilated tubules. Both exposed and control rats developed spontaneous chronic progressive nephropathy after 18 and 24 months' exposure. However, male rats exposed to 292 and 2056 ppm for 12, 18 and 24 months had linear mineral deposits in the renal medullae (Busey & Cockrell, 1984; MacFarland *et al.*, 1984).

Effects on reproduction and prenatal toxicity

As reported in a review of teratology studies of rats exposed to different fuels by inhalation, exposure of animals on days 6–15 of gestation for 6 h daily to 400 and 1600 ppm [~1200 and 4800 mg/m^3]) of unleaded gasoline resulted in no teratogenic effect (Schreiner, 1984). [The Working Group noted that details were not reported.]

Genetic and related effects

Unleaded gasoline (containing 2% benzene; boiling range, 31–192°C; 39% aromatics) did not induce mutation in *Salmonella typhimurium* TA1535, TA1537, TA1538, TA98 or TA100 in the presence or absence of an exogenous metabolic system from rat liver using either the plate incorporation (0.001–5 μl/plate) or suspension method (3.75–30 μl/ml; Conaway *et al.*, 1984). As reported in an abstract, unleaded gasoline, regular gasoline and two samples of aviation gasoline (one with an additive) did not induce mutation in *S. typhimurium* [strain unspecified] in the presence or absence of an exogenous metabolic system from Aroclor 1254-induced rat liver (Farrow *et al.*, 1983).

A dimethyl sulfoxide extract (5–200 μl/plate) and a residue from evaporation (50–10 000 μg/plate) of unleaded gasoline (American Petroleum Institute reference PS-6) were not mutagenic to *S. typhimurium* TA98 in the presence of an exogenous metabolic system from Aroclor 1254-induced rat and hamster liver, respectively (Dooley *et al.*, 1988).

A commercial leaded gasoline (with a maximum concentration of 0.04% lead and 2–4% v/v benzene) administered by larval feeding of 2.5% in the culture medium induced somatic mutations for eye pigmentation in *Drosophila melanogaster* (Nylander *et al.*, 1978).

Unleaded gasoline (PS-6 with 2% benzene w/w; same lot as used by MacFarland *et al.*, 1984, see p. 176) induced unscheduled DNA synthesis *in vitro* in hepatocytes from male Fischer-344/CrlBR rats (0.05 and 0.10% v/v), in hepatocytes from male B6C3F1/CrlBR mice (0.01% v/v) and in human hepatocytes (0.01% v/v; Loury *et al.*, 1986). Unleaded gasoline (PS-6; same lot as above) did not induce significant unscheduled DNA synthesis

in vitro (0.005–0.010% v/v) in primary cultures of kidney cells from male Fischer-344/CrlBR rats (Loury *et al.*, 1987).

One sample of unleaded gasoline (containing 2% benzene; boiling range, 31–192°C; 39% aromatics) tested at a concentration of 0–1.0 μl/ml in the presence of an exogenous metabolic system from either rat or mouse liver (Conaway *et al.*, 1984) and another sample of unleaded gasoline (PS-6; with 2% benzene w/w) tested either in the presence (0.125–0.175 μl/ml) or absence (0.045–0.070 μl/ml) of an exogenous metabolic system from Aroclor 1254-induced rat liver did not induce mutation in cultured mouse lymphoma L5178Y $TK^{+/-}$ cells. However, mutation was induced in mouse lymphoma L5178Y $TK^{+/-}$ cells in a concentration-dependent manner by both a dimethyl sulfoxide extract of unleaded gasoline (PS-6; with 2% benzene w/w), only in the absence of an exogenous metabolic system from Aroclor 1254-induced rat liver, and a residue from the evaporation of the same unleaded gasoline, only in the presence of an exogenous metabolic system from Aroclor 1254-induced rat liver (Dooley *et al.*, 1988).

As reported in an abstract, unleaded gasoline, regular gasoline and two samples of aviation gasoline (one with an additive) induced mutations in mouse lymphoma L5178Y $TK^{+/-}$ cells but did not increase the frequency of sister chromatid exchange in cultured Chinese hamster ovary cells (Farrow *et al.*, 1983).

Unleaded gasoline (PS-6; with 2% benzene w/w) did not induce mutations at the thymidine kinase locus nor sister chromatid exchange in human lymphoblasts *in vitro* in the presence or absence of an exogenous metabolic system from Aroclor 1254-induced rat liver (Richardson *et al.*, 1986).

Unleaded gasoline (PS-6; with 2% benzene w/w) induced unscheduled DNA synthesis *in vivo* in hepatocytes from male and female B6C3F1/CrlBR mice 12 h after treatment with 2000 mg/kg bw by gavage. The percentage of S-phase cells in the hepatocytes of male, but not female, mice also increased. No increase was observed in unscheduled DNA synthesis *in vivo* in hepatocytes from male Fischer-344/CrlBR rats 2–48 h after gavage treatment at 100–5000 mg/kg bw. However, the percentage of S-phase cells was increased 24–48 h after treatment with 2000 mg/kg bw (Loury *et al.*, 1985, 1986). Unleaded gasoline (PS-6; with 2% benzene w/w) did not induce unscheduled DNA synthesis *in vivo* in kidney cells from male or female Fischer-344/CrlBR rats treated by inhalation at 2000 ppm [~6000 mg/m^3] for four or 18 days (6 h per day) or 2–24 h after treatment by gavage (2000–5000 mg/kg bw single treatment or four daily treatments of 5000 mg/kg bw [male rats only]). The percentage of cells in S-phase increased in kidney cells from male rats exposed for 18 days by inhalation (2000 ppm [~6000 m^3]; 6 h per day) or gavage (2000 mg/kg bw per day; Loury *et al.*, 1987).

Unleaded gasoline (containing 2% benzene; boiling range, 31–192°C; 39% aromatics) did not induce chromosomal aberrations in the bone marrow of male or female Sprague-Dawley CD rats in either of two protocols: 6–48 h after intraperitoneal injections of 0.03, 0.1 or 0.3 ml/rat; or after five daily intraperitoneal injections of 0.013, 0.04 or 0.13 ml/rat per day (Conaway *et al.*, 1984).

Similarly, in another experiment, unleaded gasoline (PS-6) did not induce chromosomal aberrations in the bone marrow of male Sprague-Dawley rats dosed orally with 500, 750 and 1000 mg/kg bw per day for five days (Dooley *et al.*, 1988).

(*b*) *Humans*

Absorption, distribution excretion and metabolism

The more rapid absorption of gasoline via inhalation than by the oral route was suggested in an early review on the basis of experience of poisonings. Conclusive evidence that systemic gasoline poisoning arises solely due to skin absorption has not been documented (Machle, 1941).

After pregnant women working in a chemical industry were exposed to gasoline fumes, gasoline was found in fetal and neonatal tissues; neonatal blood concentrations of gasoline were about double the maternal blood concentrations (Lipovskii *et al.*, 1979).

Urinary thioether excretion was increased in 35 gasoline service station attendants and in 13 workers in self-service stations when samples taken before and after work were compared. The difference between the samples was greater ($p < 0.001$) in persons working in attendant-operated service stations than in those in self-service outlets. Cigarette smokers, in general, excreted higher levels of thioethers in samples taken both before ($p < 0.005$) and after ($p < 0.001$) work (Stock & Priestly, 1986).

Toxic effects

It was stated in an early, extensive review of gasoline intoxications that single oral doses of approximately 7.5 g/kg bw are usually fatal to man; however, death had been caused by ingestion of as little as 10 g. Following inhalation of gasoline, acute intoxication is characterized primarily by severe symptoms in the central nervous system; signs and symptoms may include headache, blurred vision, vertigo, ataxia, tinnitus, nausea, anorexia, weakness, incoordination, restlessness, excitement, mental confusion, disorientation, disturbances of speech and of swallowing, delirium and coma (Machle, 1941).

Several cases of fatal intoxication have been reported. The major pathological findings and symptoms in the nervous system were cerebral oedema and petechial brain haemorrhages. The major pulmonary findings were oedema and haemorrhage. Skin burns and superficial epidermolysis were also reported, in addition to fatty infiltration of the liver (Helbling, 1950; Aidin, 1958; Ainsworth, 1960). Toxic nephrosis was reported in one child (Banner & Walson, 1983).

Eye irritation was the only significant effect reported among volunteers exposed for 30 min to gasoline vapour at concentrations of about 200, 500 and 1000 ppm [~600, 1500 and 3000 mg/m^3] in air; the highest concentrations had the most severe effects (Davis *et al.*, 1960).

Young male volunteers were exposed in a chamber to a range of concentrations of vapour from commercial gasoline. Initial central nervous system symptoms started at concentrations between 700 (0.07%) and 2800 (0.28%) ppm [~2100 and 8400 mg/m^3]; exposure to 1000 ppm (0.1%) [~3000 mg/m^3] gasoline vapour caused serious central

nervous system symptoms; and, at 10 000 ppm (1%) [~30 000 mg/m^3], dizziness and drunkenness started after about 5 min of exposure (Drinker *et al.*, 1943).

Leukocytopenia (13%), thrombocytopenia (7%) and small-diameter erythrocytes were observed among 200 crewmen on gasoline tankers operating mainly in the Black Sea basin. A relationship was seen between length of service of sailors on tankers and the haematological changes (Kirjakov *et al.*, 1966). Haematological changes were also observed in a group of painters who used gasoline diluents for paints (Sterner, 1941).

Among 19 male gasoline station attendants in Australia, aged 16–50 years, all of whom had had more than one year's exposure and none of whom were taking drugs, shorter salivary antipyrine half-lives were observed compared to controls, indicating that occupational exposure to gasoline may result in enhanced microsomal drug metabolism. In these workers, the blood lead level was similar to that of an unexposed population (Harman *et al.*, 1981).

Chronic sniffing of leaded gasoline may cause a range of neurological effects including encephalopathy, ataxia and tremor. In clinical studies of 73 chronic sniffers of leaded gasoline (age range, four to 20 years), 69 showed definite neurological effects and had blood lead levels ranging between 30 and 344 μg/dl (Seshia *et al.*, 1978; Coulehan *et al.*, 1983). In those presenting with encephalopathy, the mean blood level was 95 μg/dl (Coulehan *et al.*, 1983). [The Working Group noted that tetraethyllead may cause hallucinations and behavioural changes, and it is not clear whether the clinical findings are due to the presence of aliphatic and aromatic hydrocarbons in gasoline or to tetraethyllead or to the action of both.]

Cardiac arrest has been suggested as one of the most important causes of sudden death in subjects who sniff gasoline vapour. Death often occurs in association with physical activity, such as running after sniffing or a stressful situation. The mechanism of this sudden death is not fully elucidated, but is likely to be caused by hydrocarbon-induced cardiac arrythmia. No measurement has been made of free norepinephrine at target cells at the time of stress (Bass, 1986).

Effects on reproduction and prenatal toxicity

Sixty-six men with disturbances of sexual function who had been exposed to leaded gasoline for four to eight years were investigated at a district sexological clinic in the USSR. Urological, neurological, endocrinological and psychiatric problems were ruled out as causes of the disturbances in these men. Erection disturbances and early ejaculation were the most common symptoms; investigations of ejaculates revealed low sperm-cell counts, with up to 20% immobile spermatozoa in 44 men. The 24-h urinary excretion of 17 α-ketosteroids was decreased in 16 men. After discontinuation of exposure and subsequent therapy, sexual function was restored or significantly improved in all but two of the men within one to two months; however, no improvement was seen in ejaculates. These effects were attributed to exposure to tetraethyllead (Neshkov, 1971).

Reproductive function and gynaecological disorders were studied in 360 women exposed to gasoline and some chlorinated hydrocarbons, in particular 1,2-dichloroethane and dichloromethane, in a plant manufacturing rubber articles for technical purposes. A

control group of 616 women who had no contact with chemicals was also studied. The majority (78.9%) of exposed women were aged 20–40 years and 60.8% had been employed for three years or more. A higher percentage of exposed women (16.8% *versus* 8.4% of controls) had toxaemia of pregnancy and short gestation period (11.2% *versus* 4.2%), and perinatal mortality was reported to be increased (Mukhametova & Vozovaya, 1972). [The Working Group noted the complex exposure of the women in the rubber plant and the lack of control for potential confounding factors.]

Genetic and related effects

A group of 16 tank cleaners were studied for cytogenetic changes; a subgroup of four men who had cleaned gasoline tanks over the preceding ten months was also included. Micronuclei in bone-marrow cells and chromosomal aberrations in peripheral blood lymphocytes were reported to be significantly more prevalent in the whole group than in the control group (Högstedt *et al.*, 1981). [The Working Group noted that the results were not reported separately for the different subgroups of cleaners and that the workers would have been subjected to mixed exposures.]

3.3 Epidemiological and case report studies of carcinogenicity to humans

The studies considered in this section generally involved mixed exposures. In particular, exposure was often to both gasoline and diesel fuels, and it is not possible from the data to separate the effects of the two types of fuel. In the selection of papers for consideration, emphasis was placed on those which discussed exposure to the fuels themselves and not on those which concerned their combustion products, which are covered in Volume 46 of the *Monographs* series (IARC, 1989).

(*a*) *Cohort studies*

An analysis of the mortality of 23 306 men employed for at least one year between 1950 and 1975 at petroleum distribution centres in the UK was performed by Rushton and Alderson (1983). The dominant job titles were drivers (43%) and operators (20%), according to company records. No detailed exposure data were given. Only 0.2% of the men were not traced in a follow-up of the cohort until 1975. Causes of death (3926) were obtained from central registers; in comparison with male mortality rates for England and Wales, a significant ($p < 0.0001$) deficit in overall mortality (standardized mortality ratio (SMR), 0.85) was observed in the cohort, which was consistent for most malignant and nonmalignant causes of death. Mortality from neoplasms of the lymphatic and haematopoietic tissues was slightly increased overall (77 deaths; SMR, 1.1; $p = 0.3$), reaching significance for myelofibrosis only (SMR, 2.8; $p = 0.04$). Mortality was increased in some subgroups of the population defined primarily by company and job, but no consistent pattern emerged, suggesting that these were chance findings.

In a study of the risks for pancreatic cancer in various occupations, a record linkage was performed between the 1960 Swedish census and the Swedish cancer registry for 1961–79 (Norell *et al.*, 1986). Information on branch of industry was obtained from the census for

about two million male employees aged 20–64 years, and the observed number of pancreatic cancer cases in certain occupational groups was compared with corresponding expected numbers based on cumulative incidence in the total cohort. Particular attention was paid to employment in the wood and paper industry, and to occupations involving potential exposure to metals or petroleum products. The observed number of cases was similar to those expected for the occupational groups studied, although a moderate excess in the incidence of pancreatic cancer was noted among gasoline station workers (SMR, 1.6; 90% confidence interval (CI), 1.1–2.3).

[The Working Group noted the lack of detailed exposure data and lack of control of potentially important confounding factors, which render the interpretation of these studies difficult.]

Information on occupation and cause of death from death records of a total of 429 926 men in Washington State, USA, from 1950–79 were used in a proportionate mortality ratio (PMR) analysis standardized for age and year of death (Milham, 1983). Three occupational groups in which exposure to gasoline may occur were studied: service station and garage owners and attendants; fuel oil dealers/workers and motor vehicle mechanics/repairmen. Considering all age groups during the total observation period, increased PMRs ($p < 0.05$) were found for cancer of the oesophagus, bronchus and lung and for non-Hodgkin's lymphomas in motor vehicle mechanics/repairmen. When specific decades were considered, elevated PMRs were also found for lymphatic leukaemia in motor vehicle mechanics/repairmen (1960–69; 8 cases; PMR, 2.8) and bladder cancer in service station and garage owners and attendants (1950–59; 9 cases; PMR, 2.2; and 1960–69; 11 cases; PMR, 1.9).

A PMR analysis was conducted of all white male deaths (37 426) occurring in the state of New Hampshire, USA, between 1975 and 1985 (Schwartz, 1987). Information on occupation, industry and cause of death was abstracted from death certificates, and expected numbers were calculated from the US general population. Total numbers of 453 and 134 deaths were recorded among motor vehicle mechanics and workers in the gasoline service industry, respectively. No significantly elevated PMR was noted for malignant neoplasms among motor vehicle mechanics, although there was a slight increase for leukaemias and aleukaemias (PMR, 1.8). For workers in service stations, the increase in PMR for leukaemia and aleukaemia was significant (PMR, 3.3; $p < 0.05$). Among nine cases of leukaemia observed, five were myeloid, two were lymphoid and two were unspecified.

[The Working Group noted the limitations inherent in PMR analysis. Furthermore, crude exposure information and lack of control for potentially important confounding factors weaken the possibility of causal interpretations.]

(*b*) *Case-control studies*

(i) *Kidney*

In a population-based case-control study, risk factors for renal-cell carcinoma, including occupational exposures, were investigated (McLaughlin *et al.*, 1984). A total of 506 cases diagnosed between 1974 and 1979 were identified from hospitals in the

Minneapolis/St Paul area of Minnesota, USA. An age- and sex-stratified sample of 714 population controls was taken from the same area. In addition, 495 deceased controls were frequency-matched on age at death and year of death to cases who were either deceased (237) or too ill to be interviewed directly (14). Information on smoking, diet and drug use as well as on medical, occupational and residential history was obtained from interviews of study subjects or next of kin. The response rate was 98%. Positive dose-response relationships were noted for smoking and some other exposures. In men, an elevated odds ratio adjusted for age and smoking was associated with occupational exposure to 'petroleum, tar, and pitch products' (1.7; 95% CI, 1.0–2.9). In a subsequent, more detailed analysis of this material (McLaughlin *et al.*, 1985), no clear association with petroleum-related occupations or with employment as a service station attendant was found, although a nonsignificant upward trend in risk with duration of employment was seen in the latter category.

A study was carried out of 92 white men, aged 30–89, with histologically confirmed renal-cell carcinoma and 1588 controls selected from among patients admitted to the same hospital in Buffalo, NY, USA, from 1957 to 1965 (Domiano *et al.*, 1985). Patients with neoplastic disease or with circulatory, respiratory, mental or urogenital disorders were excluded from the control group. Information on smoking habits, diet, occupational history and other variables had been obtained by interview at the time of admission. The age-adjusted odds ratio for the group exposed to gasoline was 0.53, based on four cases. The age-adjusted odds ratio associated with employment in service stations among men with over 20 pack-years of smoking was 1.6 [95% CI, 0.48–5.3].

A case-control study of cancer at many sites was performed in Montréal, Canada, to generate hypotheses on potential occupational carcinogens (Siemiatycki *et al.*, 1987a,b). Each cancer type constituted a case series. About 20 types of cancer were included and, for each cancer site analysed, controls were selected from among cases with cancer at other sites. Job histories and information on possible confounders were obtained by interview from 3726 men aged 35–70 years with cancer diagnosed at one of 19 participating hospitals between 1979 and 1985. The response rate was 82%. Each job was translated into a series of potential exposures by a team of chemists and hygienists using a check-list of 300 of the most common occupational exposures in Montréal. A separate analysis of risks associated with exposure to different petroleum-derived liquids was performed. Cumulative indices of exposure were estimated for a number of occupational exposures. Exposure below the median was considered to be 'nonsubstantial' and that above the median to be 'substantial'. Among men exposed to aviation gasoline, an increased risk was seen for kidney cancer only (adjusted odds ratio, 3.1; 90% CI, 1.5–6.5). Among subjects classified as having substantial exposure, the odds ratio was 3.9 (1.7–8.8) using a logistic regression analysis taking confounding factors detected in a preliminary analysis into consideration. There was overlap between groups exposed to aviation gasoline and groups exposed to jet fuel resulting from combined exposures (see also monograph on jet fuel).

(ii) *Lower urinary tract*

All residents, aged 20–89 years, of an area in eastern Massachusetts, USA, with newly diagnosed, histologically confirmed transitional- or squamous-cell malignancy of the lower

urinary tract, including the renal pelvis, ureter, bladder or urethra, were ascertained for an 18-month period (Cole *et al.*, 1972). Occupational risk factors were investigated for 461 of the patients with neoplasms and for 485 population controls living in the same area. Of the cases, 94% had a bladder tumour. Data on smoking and occupational histories were obtained by interview. Among men, an age- and smoking-adjusted odds ratio of 1.0 (95% CI, 0.75–1.3) was associated with employment in occupations with suspected exposure to 'petroleum products'; 81% of controls in this exposure category were 'machinists and mechanics'. Specific data on occupations with exposure to gasoline were not provided.

A Danish case-control study of bladder cancer and occupational risk factors consisted of 212 patients (165 men and 47 women), diagnosed in 1977–79 for men and 1979–80 for women at a hospital department serving a predominantly rural area, and 259 population controls (Mommsen *et al.*, 1982, 1983; Mommsen & Aagaard, 1984). Controls were individually matched to cases (men, 1:1; women, 2:1) for sex, age, geographic area and degree of urbanization. Occupational histories were obtained by hospital interviews for cases and by telephone or by mailed questionnaire for controls. The authors compiled a list of occupations thought to involve exposure to oil or gasoline. An odds ratio of 2.7 (95% CI, 1.2–6.2), restricted to men, associated with 'oil or gasoline' work was estimated by logistic regression analysis, without adjustment for potential confounders. Among the exposed men, there were five mechanics, four 'semiskilled workers', three blacksmiths, two printers, two engineers and four workers in other occupations. [An odds ratio of 1.8 was estimated by the Working Group for work as a blacksmith or mechanic, adjusting for smoking habits, nocturia and previous venereal disease. The Working Group noted that information on exposure was obtained differently for cases and controls.]

In a population-based case-control study investigating risk factors for cancers of the renal pelvis, including occupational exposures, a total of 74 cases diagnosed between 1974 and 1979 were identified from hospitals in the Minneapolis/St Paul area of Minnesota, USA (McLaughlin *et al.*, 1983). An age- and sex-stratified sample of 697 population controls was taken from the same area. Information on smoking, diet, drug use and occupational and residential history was obtained by interview with study subjects or next of kin. An age- and smoking-adjusted odds ratio of 2.4 (95% CI, 0.9–6.1) was associated with occupational exposure to 'petroleum, tar, or pitch products'. No further specification was given about exposures or occupations in this group.

As part of the US National Bladder Cancer Study, a population-based case-control study was carried out on occupation and cancer of the lower urinary tract in men in Detroit, MI, USA (Silverman *et al.*, 1983). The cases were diagnosed in 1977–78, and 95% had urinary bladder specified as the primary site. Controls were selected from the general population of the study area in such a way that the age distribution corresponded to that of the case series. Following exclusion of non-whites, of subjects who had never held jobs during at least six months and of refusals, a total of 303 cases and 296 controls remained for analysis. Information on smoking, diet, occupation, residence and other items was obtained by home interviews. Workers in the gasoline service industry had a crude odds ratio of 1.6 (95% CI, 0.8–3.5); after adjustment for smoking, the odds ratio was 1.3. Mechanics and repairmen had an odds ratio of 1.0 (0.6–1.4).

Another part of the US National Bladder Cancer Study was based in New Jersey in 1978 (Schoenberg *et al.*, 1984). The design was similar to that of the study described above and included 658 male incident cases and 1258 population controls. Home interviews with the study subjects provided information on a variety of personal and environmental risk factors. In a logistic regression analysis with adjustment for age and cigarette smoking, the odds ratio was 2.4 (95% CI, 1.5–3.8) for garage and/or service station workers. For motor vehicle mechanics, the odds ratio was 1.3 (0.87–1.8). There was no clear trend in risk in relation to latency since first exposure or duration among the garage and/or gasoline station workers.

A study based partly in New Jersey also used data from the US National Bladder Cancer Study during 1977–78 (Smith *et al.*, 1985). An analysis of some occupational groups among 2108 male bladder cancer cases and 4046 controls frequency matched on age and sex revealed odds ratios for automobile and truck mechanics of 1.3 (95% CI, 0.77–2.3) and 1.2 (0.90-1.6) for nonsmokers and smokers, respectively. The corresponding odds ratios for 'chemically-related exposures' were 1.5 (1.1–2.1) and 0.99 (0.81–1.2). This occupational group included electrical and petroleum engineers, repairmen, mechanics and drivers, as well as garage and service station attendants.

[The Working Group noted that it was not possible to determine the degree of overlap of the two studies carried out in New Jersey.]

(iii) Other sites

Job titles and information on occupational exposure to motor fuels were recorded for all 50 male patients with acute nonlymphocytic leukaemia seen at a department of the University Hospital of Lund, Sweden, from 1969 to 1977 (Brandt *et al.*, 1978). Three clinical groups served as controls: 100 outpatients treated for nonmalignant disorders, 100 treated for allergic diseases and 31 men treated for other types of leukaemias. Eighteen acute nonlymphocytic leukaemia patients, and ten, ten and three patients in the three control groups, respectively, had been occupationally exposed to petroleum products (e.g., as service station attendants and as bus or truck drivers). [The Working Group estimated an unadjusted odds ratio of 5.1 (95% CI, 2.6–9.8).] The authors suggested that benzene present in gasoline was a possible etiological factor, but detailed exposure data were not given. [The Working Group noted the inadequate description of the methodology used in this study.]

Case-control studies on some rare malignant neoplasms, including testicular cancer and cancer of the pancreas, were conducted in five metropolitan areas in the USA between 1972 and 1975 (Lin & Kessler, 1979, 1981). Eligible patients were identified from hospital records, and an equal number of controls was selected from among contemporary admissions to the participating hospitals for nonmalignant diseases and matched to the cases on age, sex, race and marital status. Occupational histories were obtained by interview. The 205 cases of testicular cancer were reported to be 'significantly more likely to be employed as truck drivers, gasoline station attendants, garage workers, firemen, smelter workers and metal heaters or to hold other jobs involving heat exposure'. No quantitative data were given. There seemed to be a positive association between occupational exposure to dry cleaning or

gasoline (e.g., work in service stations and garages) among the 67 male pancreatic cancer cases. For men employed for more than ten years, the odds ratio was 5.1 [95% CI, 1.5–16.9].

A case-control study on occupational risk factors and liver cancer was performed in New Jersey on a total of 355 cases diagnosed from 1975 to 1980, identified from hospital records, the tumour registry and death certificates, and 530 controls selected from hospital records and death certificates and matched to the cases on vital status (Stemhagen *et al.*, 1983). Information on smoking, alcohol consumption and occupation was obtained by home interviews; 96% of the interviews were performed with family members of deceased or incompetent study subjects. Among men, an odds ratio of 2.9 (95% CI, 1.2–6.9) was associated with employment for six months or more at service stations. When the analysis was restricted to hepatocellular carcinomas, the odds ratio increased to 4.2 (1.6–11.4). Other occupations with increased risks for men included farm labourer, wine maker, bartender and employment in laundries and dry-cleaning services.

In the Canadian study described above (p. 185; Siemiatycki *et al.*, 1987b), among men exposed to automotive gasoline, the only significant increase in risk was seen for stomach cancer (odds ratio, 1.5; 90% CI, 1.2–1.9). There was also some evidence of a positive association with duration of exposure. Mechanics and repairmen, who constituted the largest group among those classified as exposed to gasoline, showed an odds ratio of 2.0 (1.1–3.5) in a logistic regression analysis taking into consideration confounding factors detected in a preliminary analysis.

[The Working Group noted that none of the case-control studies provided a detailed description of exposure to gasoline, and it is not clear to what extent exposure to other agents of etiological importance occurred in the occupations of interest. Other types of uncontrolled confounding may also be of relevance.]

(iv) *Childhood cancer*

There have been a number of epidemiological studies on cancer risks in children in relation to the occupations of their parents. Some of the studies have focused on occupations involving exposure to 'hydrocarbons'. As a rule, the classification of exposure to hydrocarbons was based on information on parental occupations; no data were available on exposure to specific compounds. Furthermore, the definitions of occupations involving exposure to hydrocarbons often differed between the studies, which makes it difficult to compare the results. In this section, only studies that provide data on occupations assumed to involve exposure to gasoline, e.g., motor vehicle mechanics and service station attendants, are included.

Fabia and Thuy (1974) conducted a study including children under the age of five years who had died of malignant diseases between 1965 and 1970 in Québec, Canada. The cases were identified from death certificates, hospital insurance data and hospital records. Birth records were found for 386 of the 402 patients ascertained. Two controls per case were selected from birth records matched on date of birth. Information on paternal occupation was obtained from birth certificates. An odds ratio of 2.1 [95% CI, 1.8–2.4] was associated with father's employment as a motor vehicle mechanic or service station attendant. The increased risks for this exposure group were seen for both leukaemias/lymphomas (16

cases) and tumours of the central nervous system (10 cases). [The Working Group could not judge whether the case series was representative of the general population on the basis of the data provided.]

In a similar study, Hakulinen *et al.* (1976) included all cases of childhood (<15 years old) cancer reported to the Finnish Cancer Registry during 1959–68. Controls were matched for date and district of birth. Information on fathers' occupations was obtained from records at maternity clinics. Following exclusions due to lack of exposure data and of twins, a total of 852 pairs remained for analysis. The odds ratio for cancer based on matched analysis was 1.2 (seven pairs) associated with father's employment as a motor vehicle mechanic. For children under five years of age, the odds ratio was 1.0.

Kantor *et al.* (1979) studied the occupations of the fathers of children with Wilms' tumour. All 149 patients with this tumour born in Connecticut, USA, and reported to the state tumour registry between 1935 and 1973 were included. An equal number of controls were individually matched for sex, race and year of birth using birth certificate files. Information on paternal occupation was also obtained from this source. An odds ratio of 2.4 (95% CI, 1.1–5.7) was associated with hydrocarbon-related occupations of the fathers. The excess was contributed largely by occupations involving exposure to gasoline and its combustion products, i.e., driver, motor vehicle mechanic and service station attendant.

A total of 692 children who had died from cancer before the age of 15 in Massachusetts, USA, and had been born during the years 1947–57 and 1963–67 were identified by Kwa and Fine (1980). Two controls were chosen for each case from birth registers, and parental occupations were extracted from birth certificates. The fathers of 5.1% of the cases (and 4.4% of the controls) had worked as motor vehicle mechanics or service station attendants. The percentage of exposed fathers for leukaemia/lymphoma cases was 4.9%, that for neurological tumours 4.5%, for urinary tract carcinomas 11.8%, and for other carcinomas 4.2%. 'Housewife' was listed as the occupation of the mother for 98% of both cases and controls.

Occupations of parents and step-parents were investigated for 296 children with cancer seen at the Texas Children's Hospital Research Hematology Clinic, Houston, TX, USA, in 1976 and 1977 (Zack *et al.*, 1980). One control group included parents of 283 children with other diseases treated at the same clinic; a second control group contained 413 uncles and 425 aunts of the children in the case group. Neighbours with children were selected for a third control group (228 fathers and 237 mothers). Information including occupation, education and residence was obtained by interview. The percentage of fathers with hydrocarbon-related occupations was similar in the different groups. Among fathers of cases, uncles of cases, male neighbours and fathers of clinical controls, 1.0, 1.2, 0.4 and 1.8%, respectively, were motor vehicle mechanics or service station attendants. No association was seen with different types of cancer, for pre- or postnatal paternal occupation or for maternal occupation.

Information on the occupations of parents of children with leukaemia and brain tumours diagnosed in the Baltimore Standard Metropolitan Statistical Area from 1969 and 1965, respectively, to 1974 was obtained by interview of the mothers (Gold *et al.*, 1982). Two control groups providing similar information were also included: one group consisted of

children with no known malignant disease selected from birth certificates and the other of children with malignancies other than leukaemia or brain tumours. Both control groups were matched to the cases by sex, date of birth and race, giving a total of 43 and 70 triplets of cases and controls for leukaemias and brain tumours, respectively. For occupations related to motor vehicles (driver, motor vehicle mechanic, service station attendant and railroad worker/engineer) of the father before birth of the index child, the matched-pair odds ratio for leukaemia was 0.75 with normal controls; for cancer controls, the odds ratio could not be calculated: there were six pairs in which only the case had been exposed, and none in which only the control had been exposed ($p < 0.05$). Corresponding ratios for brain tumour patients were 0.33 and 0.5, respectively. Similar results were obtained when the occupations of the fathers between birth and diagnosis of the index child were considered. No meaningful analysis could be made of maternal occupations since most mothers had not worked outside the home.

Patients with Wilms' tumour diagnosed between 1950 and 1981 were identified through the Columbus Children's Hospital Tumor Registry in Ohio, USA, by Wilkins and Sinks (1984). Two control groups were selected from the Ohio birth certificate files and matched individually to the cases by sex, race and year of birth. One of the control groups was also matched with respect to mother's county of residence when the child was born. Information on paternal occupations could be obtained from the birth certificates for 62 of 105 matched triplets of cases and controls. An odds ratio of 1.4 (95% CI, 0.59–3.1) was associated with hydrocarbon-related occupations of the fathers, i.e., motor vehicle mechanic, service station attendant, driver/heavy equipment operator or metal worker/machinist. Only two fathers of cases and three of controls had worked as motor vehicle mechanics or service station attendants.

A study on possible etiological factors was performed in the Netherlands using cases identified from a nationwide register of childhood leukaemia between 1973 and 1980 (Van Steensel-Moll *et al.*, 1985). Controls were drawn from population registers and individually matched with cases according to age, sex and place of residence. Data on parental occupations, smoking habits, alcohol consumption and viral infections were obtained by a questionnaire mailed to the parents. The response rates were 88% and 66% for the cases and controls, respectively, giving a total of 519 patients with acute lymphocytic leukaemia and 507 controls for analysis. Seven mothers of cases and three mothers of controls reported having had hydrocarbon-related occupations during pregnancy (printer, dyer, service station attendant, pharmacist or chemical analyst), corresponding to an odds ratio of 2.5 (95% CI, 0.7–9.4). For maternal occupation as a petroleum or chemical industry worker, pharmacist or service station attendant one year before diagnosis of the index children, the odds ratio was 1.0 (three cases; 95% CI, 0.2–4.7). For father's occupation at time of pregnancy as a motor vehicle mechanic, machinist, service station attendant or miner, the odds ratio was 0.8 (18 cases; 0.4–1.5), with a corresponding odds ratio for paternal occupation one year before diagnosis of 0.8 (16 cases; 0.4–1.7). Inclusion of some confounding factors in logistic regression models did not materially change the odds ratios.

Occupations of fathers of children who had died from tumours of the nervous system between 1964 and 1980 in Texas, USA, were studied by Johnson *et al.* (1987). Controls were

selected from birth registers and frequency-matched to cases by race, sex and year of birth. Information on paternal occupations was extracted from birth certificates. The final study group consisted of 499 cases with intracranial or spinal cord tumours and 998 controls. There was no consistent increase in risk for hydrocarbon-related occupations as defined in earlier studies. For father's occupation as motor vehicle mechanic or service station attendant, the odds ratio was 0.7 (95% CI, 0.3–1.5).

(*c*) *Correlation studies*

There was an increase in mortality from kidney cancer among US white men, but not women, between 1950 and 1977 which paralleled the increase in production per head of gasoline that had begun some decades earlier (Enterline & Viren, 1985). There was also an association between annual gasoline consumption per head and renal cancer mortality in both men and women in different countries.

(*d*) *Case reports*

Two Indian men developed carcinoma of the tongue or of the tongue and palate within a decade of exposure to petrol, diesel and other machine oils in the repair of agricultural pumps. The carcinomas developed at the site of contact with jet flow during sucking. Both patients were teetotalers, but one was a heavy smoker (Sengupta *et al.*, 1984).

4. Summary of Data Reported and Evaluation[1]

4.1 Exposure data

Gasoline is a complex mixture of volatile hydrocarbons, predominantly in the C_4–C_{12} range, with a boiling range of 50–200°C. Most automotive gasoline is produced by blending naphtha process streams, such as light straight-run [3], reformed [15], alkylate [13], isomerization [14] and thermally [28, 29] and catalytically cracked [22, 23] naphthas. Alkylate naphtha [13] is typically the main component used in the production of aviation gasoline. Saleable gasolines may contain numerous additives, such as alkyllead compounds, 1,2-dibromoethane (ethylene dibromide), 1,2-dichloroethane (ethylene dichloride), alkyl phosphates, phenols, alcohols and methyl-*tert*-butyl ether, in order to meet product specifications. Automotive gasoline may contain 0–7%, and typically contains 2–3%, benzene. Occupational exposure to gasoline vapours occurs during production in petroleum refineries and during transport and distribution to retailers. Exposures to vapours are in most cases principally to lighter hydrocarbons, C_6 or lower. Personal 8-h time-weighted average exposures of bulk and drum gasoline loaders and tank cleaners have been reported as 40–850 mg/m^3 total hydrocarbons and 1–27 mg/m^3 benzene, and for bulk loaders up to 6 mg/m^3 1,3-butadiene. Higher levels of exposure to benzene have been reported for gasoline rail-loading and for some gasoline storage tank cleaning operations. Service station attendants and customers are exposed to lower levels of gasoline vapours.

[1]The numbers in square brackets are those assigned to the major process streams of petroleum refining in Table 2 of the monograph on occupational exposures in petroleum refining (p. 44).

4.2 Experimental data

A sample of totally volatilized unleaded gasoline was tested for carcinogenicity in one strain of mice and in one strain of rats by inhalation, producing an increase in the incidence of hepatocellular adenomas and carcinomas in female mice; no such increase was observed in males. Exposure of male rats resulted in an increased incidence of adenomas and carcinomas of the kidney; no such tumour was found in females.

One sample of light straight-run naphtha [3] and one sample of light catalytically cracked naphtha [22] produced skin tumours in mice. (See the monograph on occupational exposures in petroleum refining.)

4.3 Human data

This section describes studies of occupations in which exposure to gasoline may occur, including service station attendants and motor vehicle mechanics. None of the studies provided detailed data concerning exposure to gasoline. Furthermore, it was not possible to distinguish the effects of the combustion products from those of gasoline itself.

In a large UK cohort study on oil distribution workers, some of whom had presumably had occupational exposure to gasoline, a lower total cancer mortality was found than expected on the basis of national rates, but there was a slightly elevated number of deaths from neoplasms of the lymphatic and haematopoietic tissues. A Swedish register-based cohort study on pancreatic cancer showed moderately increased incidence among service station workers.

Two US proportionate mortality studies showed some consistency regarding elevated risks for some types of lymphopoietic cancers in motor vehicle mechanics, although not all findings were significant. For service station workers, the proportionate mortality ratio for leukaemia and aleukaemia was increased in one study but not in another.

In a US case-control study on kidney cancer, there was some evidence of a positive trend in risk with duration of employment as a service station attendant. Another US study showed a nonsignificant deficit in risk for renal-cell carcinoma among people classified as exposed to gasoline, but an increase in risk was suggested among heavy smokers with employment in service stations. A case-control study of cancer at many sites in Canada revealed an elevated risk for kidney cancer in men exposed to aviation gasoline; there were indications of a dose-response relationship.

Several case-control studies have investigated risks for cancer of the lower urinary tract in different occupations with possible exposure to gasoline. An early study from the USA revealed no excess risk among workers in occupations involving exposure to petroleum products. In a Danish study on bladder cancer, an elevated risk was associated with 'oil or gasoline work'. Nonsignificantly increased risks were found in two US studies on bladder cancer among motor vehicle mechanics, while no increase was seen in a third study. There was a significantly elevated risk for bladder cancer among garage workers and service station attendants in one of these studies, and another showed a nonsignificant elevation in risk for workers in the gasoline service industry. A US study on cancer of the renal pelvis

suggested an elevated risk for workers exposed to unspecified petroleum, tar or pitch products.

A Swedish study, similar in design to a case-control study, indicated an increased risk for acute nonlymphocytic leukaemia in men with occupational exposure to petroleum products. One hospital-based case-control study in the USA revealed an increased risk for testicular cancer in service station attendants and garage workers; another showed an increased risk for pancreatic cancer in men with occupational exposure to dry cleaning agents or gasoline. Another US case-control study demonstrated an increased risk for liver cancer in service station attendants, particularly for hepatocellular carcinoma. A case-control study of cancer at many sites in Canada revealed an elevated risk only for stomach cancer among men exposed to automotive gasoline.

Nine case-control studies from four countries provide data on paternal occupations involving exposure to hydrocarbons and the risk for cancer in children. There was no consistent association between father's occupation and risk for childhood cancer, although significant results appeared in a few of the studies. Only one study gave detailed data on maternal occupations involving exposure to hydrocarbons during pregnancy; this suggested an increased risk for leukaemia in their children. No study specifically assessed exposure to gasoline, but paternal occupations such as motor vehicle mechanic and service station attendant were not consistently associated with an increase in risk.

4.4 Other relevant data

Urinary thioether excretion was increased in samples taken from service station attendants after work. The half-life of antipyrine was reduced in such workers.

No report specifically designed to study genetic and related effects in humans following exposures to gasoline was available to the Working Group.

Male, but not female, rats developed nephropathy after exposure to unleaded gasoline, with hyaline droplet accumulation, necrosis and degeneration of proximal convoluted tubules. The extent and severity of hyaline droplet accumulation paralleled the extent and localization of renal tubular cell proliferation.

Two samples of unleaded gasoline (one described as PS-6, the other as having a boiling range of 31–192°C) were tested in a series of assays for genetic and related effects. Neither sample induced chromosomal aberrations in the bone marrow of rats treated *in vivo*. The PS-6 sample induced unscheduled DNA synthesis *in vivo* in male and female mouse hepatocytes, but not in male rat hepatocytes or in male or female rat kidney cells, nor did it induce sister chromatid exchange or mutation in cultured human lymphocytes. Neither sample induced mutation in cultured mammalian cells; however, an extract of and the residue from the evaporation of the PS-6 sample did induce mutation in cultured mammalian cells. The PS-6 sample induced unscheduled DNA synthesis *in vitro* in mouse, rat and human hepatocytes but not in rat kidney cells. A leaded gasoline induced somatic mutation in insects. The other sample of unleaded gasoline, an extract of the PS-6 sample and the residue from the evaporation of the PS-6 sample did not induce mutation in bacteria (see Appendix 1).

4.5 Evaluation[1]

There is *inadequate evidence* for the carcinogenicity in humans of gasoline.

There is *limited evidence* for the carcinogenicity in experimental animals of unleaded automotive gasoline.

In making the overall evaluation, the Working Group also took note of the following supporting evidence. Unleaded gasoline induces unscheduled DNA synthesis in hepatocytes from male and female mice treated *in vivo* and in cultured mouse, rat and human hepatocytes. There is *limited evidence* for the carcinogenicity in experimental animals of light straight-run naphtha and of light catalytically-cracked naphtha (see the monograph on occupational exposures in petroleum refining). Benzene is carcinogenic to humans (Group 1); for 1,3-butadiene, there is *inadequate evidence* for carcinogenicity in humans and *sufficient evidence* for carcinogenicity in experimental animals (Group 2B) (IARC, 1987).

Overall evaluation

Gasoline *is possibly carcinogenic to humans (Group 2B).*

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[1]For definition of the italicized terms, see Preamble, pp. 25–28.

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