OCCUPATIONAL EXPOSURES IN PETROLEUM REFINING

1. Historical Perspectives and Description of the Processes

1.1 Historical perspectives

Petroleum oil was used for many centuries in Egypt, China, Mesopotamia and Persia for heating, lighting, roadmaking and building. Small accumulations of oil were reported at Pechelbronn in Alsace in 1498 and in Poland in 1506, and Marco Polo noted 'oil springs' at Baku on the Caspian Sea in the latter part of the thirteenth century. Raleigh, in 1595, reported the existence of the Trinidad Pitch Lake, and there are accounts of Franciscan visits to 'oil springs' in New York in 1632. Similarly, in 1748, a Russian traveller to the Americas commented on sources of oil in Pennsylvania. Oil was produced in Burma from hand-dug wells in substantial quantities by the end of the eighteenth century (Royal Dutch/Shell Group of Companies, 1983).

The modern oil industry began in the USA in 1859 with the successful completion of the Drake well near Titusville, PA (Chiles, 1987). By 1886, Pennsylvania was the leading oil producing state, and total US production was 28 million barrels[1] per year, nearly 60% of the world's total. The principal refined product was kerosene, used mainly for illumination. Because of its smaller supply in relation to coal, petroleum was not used as an industrial or transportation fuel, but continued to be used mainly for lubrication and burning in stoves and lamps (Chiles, 1987).

With the discovery of new oil reserves in the early 1900s, the utilization of oil began to change rapidly as the price of oil dropped significantly. Railroads were the first to take advantage of the oversupply and low prices: between 1899 and 1919, the use of oil by railroads in the USA increased 14 fold. Development of petroleum as a marine fuel took place during the same period. The first vessels to use oil were the tankers transporting crude oil, but conversion of other commercial vessels followed, and the military advantages of oil were soon realized. Industry was also in need of cheap energy, and the switch from coal to oil occurred quickly, beginning with the use of oil as a boiler fuel. In the USA, production tripled from 1900 to 1910 as oil was discovered in Texas, California and the midwest (Chiles, 1987).

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[1] 1 barrel = 0.136 metric tonne of crude oil of specific gravity 0.858 (or °API gravity, 33.5; British Petroleum Co., 1977); see monograph on crude oil

After about 1900, worldwide expansion was much more rapid. Mexico became a producer in 1901, followed by Argentina in 1907 and Trinidad in 1908. By 1910, world production had grown to 900 000 barrels per day, the bulk originating in the USA (560 000) and most of the remainder in Russia (200 000). Oil was found in Persia (Iran) in 1908, and exports there commenced in 1911, leading to the prominence of that region as a source of crude oil. Production in British Borneo and Venezuela began in 1911 and 1914, respectively (Royal Dutch/Shell Group of Companies, 1983).

The development of the internal combustion engine and the rapid growth of the automotive industry after the First World War provided the market needed to support this increased production and assured that the industry would continue to be a major source of transportation and industrial fuels. Gasoline consumption in the USA increased from six million barrels in 1899 — mostly for cleaning, industrial solvents and stove fuel — to 87 million barrels in 1919 (Chiles, 1987). By the mid-1960s, it had already reached 1700 million barrels yearly (Energy Information Administration, 1986). During this period, improvements in automotive engine design necessitated the manufacture of motor fuels of higher quality. Research octane ratings (see glossary) increased from about 70 in 1925 to their present levels of close to 100. The need to increase both the quantity and the quality of motor gasoline in order to meet the demands of the market required the development of new refining processes. The most important of these are shown in Table 1. All are directed towards effecting either a change in the product distribution or product quality or, less often, both.

Table 1. Important process developments in petroleum refining[a]

Year[b]	Process	Operation
1910–15	Thermal cracking	Change gas oil to gasoline
1916	Sweetening	Eliminate mercaptans
1925–29	Vacuum distillation	Produce lubricating oils, change residues to cracking stock and bitumen
1926–29	Alkyllead production	Improve octane number
1930	Thermal reforming	Improve octane number
1932	Hydrogenation	Remove sulfur
1932	Coking	Produce lighter products from residues
1933	Solvent extraction	Improve viscosity index
1935	Solvent dewaxing	Improve pour point
1935	Catalytic polymerization	Increase gasoline yield, improve octane number
1939	Catalytic cracking	Increase gasoline yield, improve octane number
1939	Visbreaking	Reduce quantity of residue
1940–43	Alkylation	Increase gasoline yield, improve octane number
1950	Propane decarbonizing (deasphalting)	Increase cracking stock
1952	Catalytic reforming	Improve octane number
1954	Hydrodesulfurization	Remove sulfur
1956	Inhibitor sweetening	Remove mercaptans
1957	Catalytic isomerization	Improve octane number

Table 1 (contd)

Year[b]	Process	Operation
1960[c]	Fluid catalytic cracking	Increase gasoline yield
1961[c]	Catalytic hydrocracking	Increase gasoline yield
1965[c]	Molecular sieve catalysts	Increase gasoline yield
1974[c]	Catalytic dewaxing	Improve pour point
1975[c]	Residue hydrocracking	Reduce quantity of residue

[a]Adapted and updated from Nelson (1960); for definitions, see glossary

[b]Dates are approximate year of commercialization of the process

[c]From Royal Dutch/Shell Group of Companies (1983)

Today, the world petroleum refining industry produces more than 2500 products, including liquefied petroleum gas, gasoline, kerosene, aviation fuels, diesel fuels, a variety of other fuel oils, lubricating oils and feedstocks for the petrochemical industry. Refineries range from those which simply produce fuels to those which include the manufacture of other products, such as lubricants and bitumens. Processes which are used solely in the manufacture of petrochemicals are specifically excluded from this monograph.

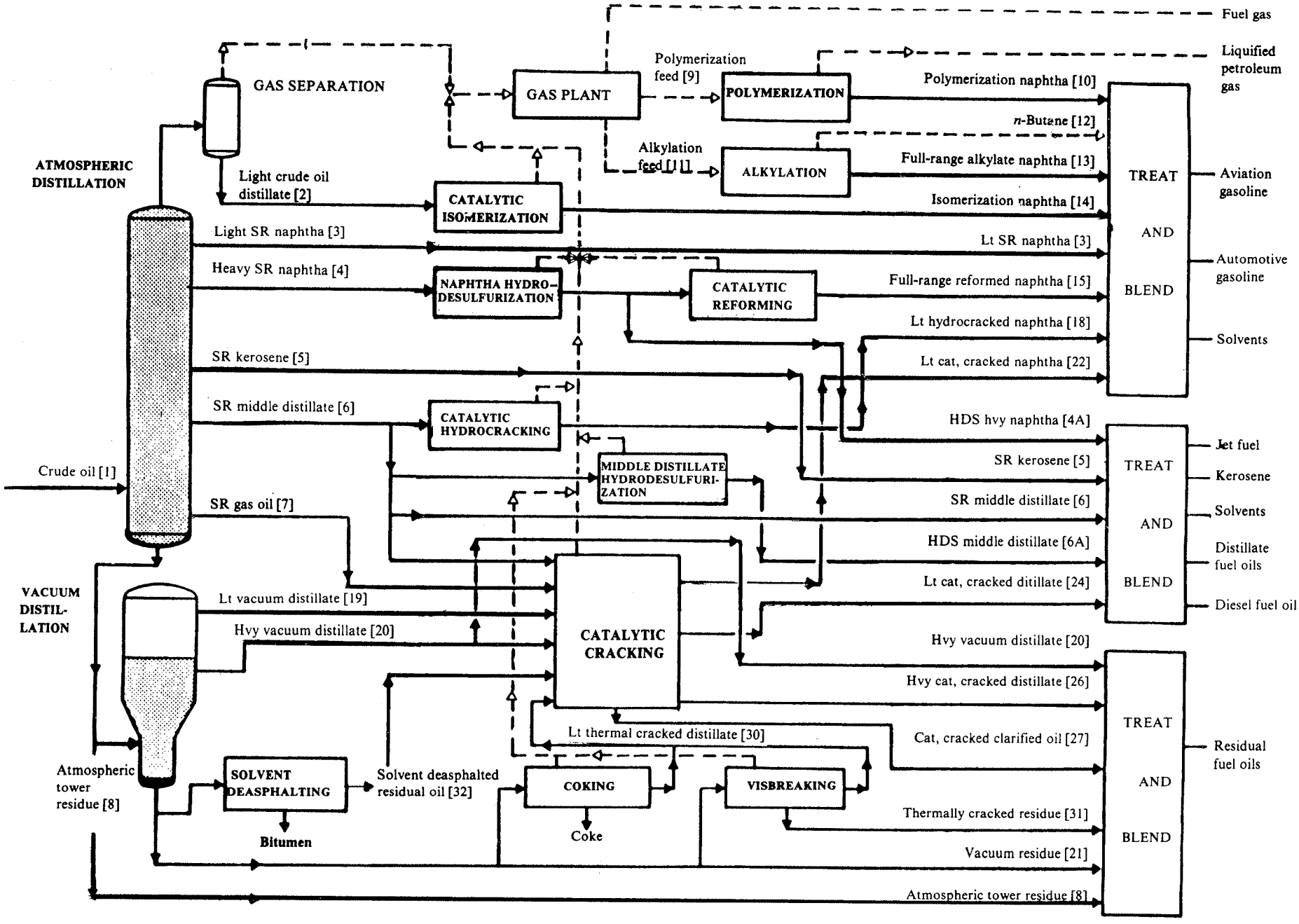
Section 1.2, which describes the major processes used in fuel manufacture, is divided into four parts describing different types of processes: (1) crude separation; (2) light hydrocarbon processing; (3) middle distillate processing; and (4) heavy hydrocarbon processing. Not all of the processes described are used in every refinery. Larger refineries do, however, use most of them. US refineries have generally been designed to maximize automotive gasoline production, while European refineries have generally maximized production of fuel oils. US refineries have therefore typically used more processes and generally produced a minimum of residual oil (Royal Dutch/Shell Group of Companies, 1983).

Most petroleum products are manufactured to specifications of performance, rather than chemistry, and hence may originate from several refinery streams. The composition of the product and the volume produced vary with location, climate and season. For example, in winter, there is a greater demand for fuel oils, and automotive gasoline must contain a larger percentage of volatile products to assure cold-weather starts. Summer weather imposes a reduction in the concentration of volatile components to minimize engine vapour lock and losses due to vaporization. Refinery operations must be sufficiently flexible to accommodate these changing demands.

1.2 Major fuel manufacturing processes

Descriptions of petroleum refining processes are available (Jahnig, 1982; Royal Dutch/Shell Group of Companies, 1983). Processes that lead to lubricant base oils and their derived products and to bitumens have been described in previous volumes of the *Monographs* series (IARC, 1984, 1985). In the present monograph, attention is given principally to processes used in the production of petroleum-based fuels.

Fig. 1. Principal refinery process streams[a]



[a]Provided by the American Petroleum Institute; Cat, catalytic; HDS, hydrodesulfurized; Hvy, heavy; Lt, light; SR, straight-run

Figure 1 summarizes the major fuel manufacturing processes commonly used in petroleum refining and shows the interrelationships that exist between process units in a petroleum refining complex; it is not intended to be a diagram of an actual refinery configuration. Most of the processes discussed in detail are shown, although several that are less common or that are used for a particular type of crude oil are described only in the text. In Figure 1, the process unit feed and product streams are identified by the common designation accepted by the industry. Each name is followed by a number which also appears in Table 2, which gives the Chemical Abstracts designation for the stream, the Chemical Abstracts Service Registry Number and the broad definition of its composition adopted in 1978 under the US Toxic Substances Control Act (US Environmental Protection Agency, 1978, 1979) and, in 1981, under the Commission of the European Communities' Sixth Amendment to the Dangerous Substances Directive — European Inventory of Existing Commercial Chemical Substances (EINECS) (Commission of the European Communities, 1981). Not all of the possible feed and product streams are shown, but those of major importance to the blending of the final fuel products addressed in the monographs on gasoline, jet fuel, diesel fuels and fuel oils (heating oils) are included. The process descriptions that follow are intended to provide an understanding of their purpose and nature, to define the operating conditions and to identify the unit feedstocks and products.

(*a*) *Crude separation*

(i) *Atmospheric distillation*

Distillation at atmospheric pressure physically separates crude oil into fractions of a specific boiling range by distillation and steam stripping. The major processing equipment items include the heat exchanger preheat train, direct-fired furnace, atmospheric fractionator and side-stream product strippers.

Desalted crude oil is preheated in the heat exchanger train by recovering process heat. The preheated crude oil is then charged to a directly fired furnace, where additional heat is supplied to achieve partial vaporization. Both the liquid and vaporized portions are charged to the atmospheric fractionator at a temperature of about 345–370°C.

The crude charge is separated into a number of fractions. The lightest streams are taken from the tower overhead, where they are condensed, and the noncondensible light ends are treated and/or recovered in other refinery units. A number of liquid side-stream fractions are withdrawn from the fractionator at different elevations within the tower. These fractions are charged to strippers where lower-boiling hydrocarbons are removed and returned to the fractionation tower. The stripping medium is either steam, light petroleum gases or reboiler vapours. The atmospheric fractionator also has a zone for stripping bottoms, where lower-boiling hydrocarbons are steam stripped from the atmospheric residue. The fractions from the atmospheric tower are progressively higher boiling as they are withdrawn at successively lower elevations in the tower; however, the final boiling-point of the heaviest side stream generally approximates the temperature at which the crude oil is charged.

Table 2. Characteristics of principal refinery process streams[a]

Process stream[b] (synonym)	CAS No.	Unit from which produced	Unit to which fed	Carbon no. distribution	Boiling range (°C)	Remarks
Crude oil [1] (petroleum)	8002-05-9	–	Atmospheric distillation	C2–>C50	−80 – >600	As a naturally occurring substance, crude oil is not included in the TSCA/EINECS listing
Light crude oil distillate [2]	68410-05-9	Atmospheric distillation	Gas processing, isomerization	C2–C7	−88 – 99	
Light straight-run naphtha [3]	64741-46-4	Atmospheric distillation	–	C4–C10	−20 – 180	Mainly aliphatic hydrocarbons
Heavy straight-run naphtha [4]	64741-41-9	Atmospheric distillation	Naphtha hydro-desulfurization	C6–C12	65–230	
Hydrodesulfurized heavy naphtha [4A]	64742-82-1	Naphtha hydro-desulfurization	Catalytic reforming	C7–C12	90–230	
Straight-run kerosene [5]	8008-20-6	Atmospheric distillation	–	C9–C16	150–290	
Hydrotreated kerosene [5A]	64742-47-8	Kerosene hydrotreatment	–	C9–C16	150–290	
Hydrodesulfurized kerosene [5B]	64742-81-0	Kerosene hydrodesulfu-rization	–	C9–C16	150–290	
Chemically neutralized kerosene [5C]	64742-31-0	Kerosene neutralization	–	C9–C16	150–290	
Straight-run middle distillate [6]	64741-44-2	Atmospheric distillation	Catalytic hydro-cracking, gas oil hydrodesulfuri-zation, catalytic cracking	C11–C20	205–345	

Table 2 (contd)

Process stream[b] (synonym)	CAS No.	Unit from which produced	Unit to which fed	Carbon no. distribution	Boiling range (°C)	Remarks
Hydrodesulfurized middle distillate [6A]	64742-80-9	Middle distillate hydrodesulfurization		C11–C25	205–400	
Straight-run gas oil [7]	64741-43-1	Atmospheric distillation	Catalytic cracking	C11–C25	205–400	
Atmospheric tower residue [8] (reduced crude oil)	64741-45-3	Atmospheric distillation	Vacuum distillation	>C20	>350	Likely to contain 5 wt % or more 4- to 6-ring condensed aromatic hydrocarbons
Polymerization feed [9]	68476-54-0	Gas processing	Polymerization	C3–C5	−45 – 38	Complex mixture of predominantly unsaturated hydrocarbons
Polymerization naphtha	64741-72-6	Polymerization		C6–C12	65–270	Mainly monoolefinic hydrocarbons produced by catalytic polymerization of a mixture rich in propene or butene
Alkylation feed [11]	68477-83-8	Gas processing	Alkylation	C3–C5		Mixture of olefinic and paraffinic hydrocarbons. Ambient temperatures normally exceed the critical temperature for these combinations
n-Butane [12]	106-97-8	Alkylation	C4	−0.5		
Full-range alkylate naphtha [13]	64741-64-6	Alkylation		C7–C12	90–220	Mainly branched-chain saturated hydrocarbons produced by distillation of products of catalytic reaction of isobutane with C3-C5 monoolefins

Table 2 (contd)

Process stream[b] (synonym)	CAS No.	Unit from which produced	Unit to which fed	Carbon no. distribution	Boiling range (°C)	Remarks
Isomerization naphtha [14]	64741-70-4	Catalytic isomerization		C4–C6		Mainly saturated hydrocarbons obtained from catalytic isomerization of straight-chain paraffinic hydrocarbons such as isobutane, isopentane, 2,2-dimethylbutane, 2-methylbutane, 2-methylpentane and 3-methylpentane
Full-range reformed naphtha [15]	68919-37-9	Catalytic reforming		C5–C12	35–230	
Light reformed naphtha [16]	64741-63-5	Catalytic reforming		C5–C11	35–190	May contain 10% or more benzene
Heavy reformed naphtha [17]	64741-68-0	Catalytic reforming		C7–C12	90-230	Contains predominantly aromatic hydrocarbons
Light hydrocracked naphtha [18]	64741-69-1	Catalytic hydrocracking	C4–C10	−20 – 180		
Light vacuum distillate [19] (light vacuum gas oil)	64741-58-8	Vacuum distillation	Catalytic cracking	C13–C30	230–450	
Light paraffinic distillate [19A]	64741-50-0	Vacuum distillation	Lubricant oil manufacture	C15–C30	>350	Contains a relatively large proportion of saturated aliphatic hydrocarbons
Light naphthenic distillate [19B]	64741-52-2	Vacuum distillation	Lubricant oil manufacture	C15–C30	>350	Contains relatively few normal paraffins
Heavy vacuum distillate [20] (heavy vacuum gas oil)	64741-57-7	Vacuum distillation	Catalytic cracking	C20–C50	350–600	Likely to contain 5 wt % or more 4- to 6-ring condensed aromatic hydrocarbons
Heavy paraffinic distillate [20A]	64741-51-1	Vacuum distillation	Lubricant oil manufacture	C20–C50	>350	Contains a relatively low proportion of saturated aliphatic hydrocarbons

Table 2 (contd)

Process stream[b] (synonym)	CAS No.	Unit from which produced	Unit to which fed	Carbon no. distribution	Boiling range (°C)	Remarks
Heavy naphthenic distillate [20B]	64741-53-3	Vacuum distillate	Lubricant oil manufacture	C20–C50	>350	Contains relatively few normal paraffins
Chemically neutralized heavy naphthenic distillate [20C]	64742-34-3	Vacuum distillation	Lubricant oil manufacture	C20–C50	>350	Contains relatively few normal paraffins
Hydrotreated heavy naphthenic distillate [20D]	64742-52-5	Vacuum distillation	Lubricant oil manufacture	C20–C50	>350	Contains relatively few normal paraffins
Vacuum residue [21]	64741-56-6	Vacuum distillation	Solvent deasphalting, coking, visbreaking	>C34	>495	
Light catalytically cracked naphtha [22]	64741-55-5	Catalytic cracking		C4–C11	−20 – 190	Contains a relatively large proportion of unsaturated hydrocarbons
Heavy catalytically cracked naphtha [23]	64741-54-4	Catalytic cracking		C6–C12	65–230	Contains a relatively large proportion of unsaturated hydrocarbons
Light catalytically cracked distillate [24]	64741-59-9	Catalytic cracking		C9–C25	150–400	Contains a relatively large proportion of bicyclic aromatic hydrocarbons
Intermediate catalytically cracked distillate [25]	64741-60-2	Catalytic cracking		C11–C30	205–450	Contains a relatively large proportion of tricyclic aromatic hydrocarbons
Heavy catalytically cracked distillate [26]	64741-61-3	Catalytic cracking		C15–C35	260–500	Likely to contain 5 wt % or more 4- to 6-ring condensed aromatic hydrocarbons

Table 2 (contd)

Process stream[b] (synonym)	CAS No.	Unit from which produced	Unit to which fed	Carbon no. distribution	Boiling range (°C)	Remarks
Catalytically cracked clarified oil [27]	64741-62-4	Catalytic cracking		>C20	>350	Likely to contain 5 wt % or more 4- to 6-ring condensed aromatic hydrocarbons
Light thermally cracked naphtha [28]	64741-74-8	Coking, visbreaking		C4–C8	−10 – 130	Consists predominantly of unsaturated hydrocarbons
Heavy thermally cracked naphtha [29]	64741-83-9	Coking, visbreaking		C6–C12	65–220	Consists predominantly of unsaturated hydrocarbons
Light thermally cracked distillate [30]	64741-82-8	Coking, visbreaking	Catalytic cracking	C10–C22	160–370	
Thermally cracked residue [31]	64741-80-6	Visbreaking		>C20	>350	Likely to contain 5 wt % or more 4- to 6-ring condensed aromatic hydrocarbons
Solvent deasphalted residual oil [32]	64741-95-3	Solvent deasphalting	Catalytic cracking	>C25	>400	Obtained as the solvent-soluble fraction from C3–C4 solvent deasphalting of a residue
Light steam-cracked naphtha [33]	64742-83-2 cracking	Steam		C4–C11	−20 – 190	Consists predominantly of unsaturated hydrocarbons; likely to contain 10% or more benzene
Steam-cracked residue [34]	64742-90-1	Steam cracking		≥C14	>260	Consists predominantly of unsaturated hydrocarbons likely to contain 5% or more of 4- to 6-ring polycyclic aromatic hydrocarbons

[a]From US Environmental Protection Agency (1978); Commission of the European Communities (1981)

[b]Number in brackets is the identifying number for the process stream in Figure 1

Atmospheric tower residue [8] (reduced crude oil) is the highest-boiling fraction and is the charge to the vacuum distillation unit. The products of atmospheric distillation are generally light crude oil distillate [2], light and heavy straight-run naphthas [3 and 4, respectively], straight-run kerosene [5], straight-run middle distillate [6], straight-run gas oil [7] and reduced crude oil. The naphtha streams may be blended into motor fuels or other refinery products or further processed to improve octane rating and reduce sulfur content. The straight-run kerosene [5] may be chemically sweetened or hydrogen-treated and sold directly or sent to blending. The straight-run middle distillate [6] may be sold for diesel or fuel oil, or may be hydrogen-treated, hydrocracked, catalytically cracked or blended. Straight-run gas oil [7] may be sold as fuel oil, or may be hydrogen-treated, hydrocracked, catalytically cracked or blended. Reduced crude oil is usually fed to the vacuum tower, although it may be sold for fuel, blended into fuels, or be hydrogen treated or catalytically cracked. As its name implies, the fractionator operates at atmospheric pressure; temperatures range from 120°C at the top to about 370°C at the bottom.

(ii) *Gas processing*

The purpose of gas processing is to stabilize (i.e., reduce the volatility of) the lightest process stream by removing gaseous hydrocarbons and then to separate the various fractions of hydrocarbon gases. Separation is accomplished by a series of distillation and absorption operations. The particular recovery scheme applied depends primarily on the desired purity. Gas processing can be a simple operation producing fuel gases composed of *n*-butane [12], more volatile hydrocarbons and a light naphtha or a complex one that produces a wide range of individual gaseous and light hydrocarbon products. The feed is a light, sweet gas that comes from various processing units. Units which can directly or indirectly provide the feed gas are: crude distillation, hydrodesulfurization, catalytic cracking, catalytic reforming, thermal cracking and hydrocracking. The operating conditions depend on the products being recovered. Temperatures as low as −73°C are required to obtain an ethane fraction, and high pressures, about 360 psi [24 atm], are used in absorbing propane.

(iii) *Vacuum distillation*

Vacuum distillation separates the residue from the atmospheric fractionator into a vacuum residue [21] and one or more distillate streams. The distillate streams include light and heavy vacuum distillates [19 and 20, respectively] as well as light and heavy distillates of paraffinic or naphthenic crude oils. Light and heavy distillates are used in the production of lubricant oils, the processing of which was described in a previous volume of *Monographs* (IARC, 1984). Vacuum fractionators are maintained at approximately 100 mm Hg [0.13 atm] absolute pressure by either steam ejectors or mechanical vacuum pumps. Distillation temperatures of up to 400°C are not uncommon. Vacuum distillation can be carried out in one or two fractionation stages. Atmospheric tower residue [8] is heated in a directly fired furnace and charged to a preflash tower where a small quantity of distillate is produced as an overhead product. The preflash tower bottoms are charged to the vacuum fractionator for separation of additional distillate. Vacuum residue [21] is recovered as the bottoms product. Steam stripping may or may not be applied to the distillates. The production of well

fractionated distillates, such as lubricant oil stocks, requires steam stripping, whereas the production of heavy catalytic cracking feedstocks, such as vacuum distillate, does not. Depending mainly upon the crude feedstock and the nature of the refinery, the vacuum residue [21] may be converted to bitumen, coked to make gasoline, cracked in a visbreaker to make distillate fuel oils or blended into residual fuel oils. With suitable feedstocks, the vacuum residue [21] may be used to manufacture heavy lubricant oils. Similarly, the heavy distillate from a suitable paraffinic crude oil feed may be used as a charge stock for lubricant oil manufacture. Other distillates are treated much like the gas oil stream from the atmospheric fractionator and are catalytically hydrocracked, catalytically cracked or used as fuel oil.

(*b*) *Light hydrocarbon processing*

(i) *Polymerization*

Polymerization is used to produce high-octane gasoline or a petrochemical feedstock from gaseous olefins. The feedstock may be a relatively pure olefin stream or any combination of olefins, such as ethylene, propylene and butenes. Polymerization naphtha [10] and other liquid products are formed when the olefin gases are passed over an acid catalyst. The most common catalyst used is phosphoric acid, usually dispersed on an inert support. The reaction is exothermic. After reaction, the gaseous product passes through a heat exchanger which heats the incoming feed. The reactor effluent is then fractionated by distillation to produce the product or products required. Reactor temperatures are generally in the range of 135–190°C, at a pressure of about 500 psi [34 atm].

(ii) *Alkylation*

The term alkylation, as commonly used in the petroleum industry, refers to the chemical reaction of a low molecular weight olefin and an isoparaffin to form multiply branched paraffins of high octane rating. Typically, butene and isobutane are reacted to produce the high octane components known as alkylate. The reaction is catalysed by either anhydrous sulfuric or anhydrous hydrofluoric acid. A dry olefinic feed is mixed with excess isobutane and added to the liquid catalyst in the reaction vessel. The reactor effluent is separated into hydrocarbon and acid phases in a settler, and the acid is returned to the reactor. If hydrofluoric acid is used, the alkylate and excess isobutane from the settler are sent to a stripping tower for separation. The stripper yields an isobutane, which is recycled to the feed stream, an *n*-butane side stream and an alkylate bottoms stream which is charged to a fired heater to decompose any organic fluorides. The effluent from the fired heater is the finished alkylate. If sulfuric acid is used as the catalyst, the hydrocarbon liquid from the settler is washed with caustic and water before fractionation. The operating temperature depends upon the catalyst system used. Sulfuric acid alkylation is generally carried out at about 7°C; when hydrofluoric acid is used, the temperature is about 27°C. Pressures are in the range of 100–150 psi [7–10 atm], regardless of the catalyst.

(iii) *Naphtha hydrodesulfurization*

Hydrodesulfurization is used to remove sulfur and nitrogen compounds from the naphtha streams. Both must be reduced to very low levels when naphtha is used as a feed for

reforming or for other processes which are susceptible to catalyst poisoning by sulfur and nitrogen compounds. The naphthas are vaporized, mixed with a hydrogen-rich gas, heated to reaction temperature and passed through a fixed bed of non-noble metal catalyst — generally cobalt-molybdenum. The organic sulfur and nitrogen are converted to hydrogen sulfide and ammonia. Some cracking of hydrocarbons also occurs. The hot effluent from the reactor is cooled and sent to a high-pressure separator, where hydrogen flashes off and is recycled to the feed stream. The liquid from the separator is sent to a fractionator, where hydrogen sulfide, ammonia and any low-boiling hydrocarbons are removed, and the remaining naphtha is distilled into fractions of the desired boiling range. The feed to hydrodesulfurization is a sour naphtha from the crude fractionator with a boiling-point range of about 65–230°C. Operating conditions vary with the composition of the feed, but generally temperatures in the range of 315–430°C and pressures of 300–1000 psi [20–68 atm] are used.

Hydrodesulfurization is applied to other process streams (e.g., kerosene, gas oil, residual oil) under conditions of varying severity.

(iv) *Catalytic isomerization*

Isomerization is used to convert *n*-butane, *n*-pentane and *n*-hexane into their respective isoparaffins. The isobutane is used as a feedstock for alkylation; isopentanes and isohexanes are of sufficiently high octane quality to be used directly as gasoline blending stocks. The feedstock to the isomerization unit must be both dehydrated and desulfurized. Sweet, dry feedstock is mixed with hydrogen, heated to reaction temperature and catalytically hydrogenated to remove any benzene and olefins. It is then mixed with hydrogen chloride (or organic chloride) and passed over a fixed bed of chlorinated platinum-aluminium oxide isomerization catalyst, where straight-chain hydrocarbons are converted to isoparaffins. The effluent product is cooled and passes into a high-pressure separator where recycled hydrogen flashes off. The liquid from the separator is sent to a stripper column where hydrogen chloride is removed. The resulting isoparaffins are neutralized and sent to storage. Isomerization units are operated at temperatures of 240–255°C and at pressures of 300–400 psi [20–27 atm].

(v) *Catalytic reforming*

Catalytic reforming is used to convert low-octane naphthas into high-octane gasoline blending stocks; it may also be done to produce aromatic hydrocarbons such as benzene and toluene for use as solvents and chemical feedstocks. In reforming, cycloparaffins are converted to aromatic compounds by a combination of dehydrogenation and dehydroisomerization. Some paraffins also form aromatic compounds by dehydrocyclization. Hydrogen is a net product of reforming, which can be used in the hydrotreating and hydrodesulfurization units of a refinery. The naphtha feedstock is mixed with hydrogen and heated by exchangers almost to reaction temperatures. The mixture then passes through a series of alternating furnaces and fixed-bed reactors (usually three or four) containing a platinum or platinum-rhenium on alumina catalyst. The furnaces maintain the reaction temperatures between the catalyst beds. The reactor effluent is cooled by heat exchange and sent through a separator where hydrogen is flashed off. The liquid from the separator is

taken to a stripping tower where light ends are removed. The stabilized reformate is sent to storage or is further refractionated in a second tower. Since platinum catalysts are subject to poisoning by sulfur and nitrogen, reforming units require prior hydrodesulfurization of the naphtha feed or contain a pretreater containing a non-noble metal catalyst through which the feedstock and hydrogen pass before entering the main reaction vessels. Reformers are generally operated at temperatures of 427–482°C and at pressures of 100–200 psi [7–14 atm]. The operating conditions depend somewhat upon the boiling range of the feedstock and the activity of the catalyst.

(iv) *Steam cracking*

Steam cracking is used to produce olefinic raw materials which, in turn, are employed in the manufacture of petrochemicals. Although this is essentially a petrochemical operation, the facility is often integrated into larger refinery complexes.

The process involves the thermal cracking of feedstock ranging from ethane to vacuum distillate and utilizes temperatures of around 800–850°C at slightly greater than atmospheric pressure. Heavier feeds produce higher yields of by-products such as naphtha, which, when blended into gasoline, has been called 'pyrolysis gasoline'. Naphtha from steam cracking typically has very high concentrations of benzene (see IARC, 1982, 1987b), and, since approximately the early 1960s, benzene has normally been extracted from naphtha for its commercial value. After mild hydrotreating to saturate olefins and polyolefins that cause instability and gum formation, naphtha from which the benzene has been removed may be blended with other streams to produce gasoline with the required performance specification.

Depending on the nature of the feedstock, the steam cracking process generates residual tars which may sometimes be blended in small quantities into residual heavy fuels.

(*c*) *Middle distillate processing*

(i) *Chemical sweetening*

Chemical sweetening, often referred to as 'doctoring', is used to oxidize low concentrations of mercaptans to disulfides to reduce the odour of products containing mercaptans. This is a frequent practice in refineries that utilize relatively low-sulfur crude oils. With such crude oils, it is more economical to eliminate the odour problem by chemical means than by removing the sulfur in a hydrodesulfurization unit. In all sweetening processes, the stream to be treated is put into contact with an oxidizing agent, with or without a catalyst. Caustics or hypochlorites are commonly used, and a variety of processes can be used to treat mercaptans in virgin streams.

Inhibitor and air–cresylate sweetening are frequently used in combination for catalytically cracked naphthas. In inhibitor sweetening, mercaptans are oxidized in the presence of a phenylenediamine (see IARC, 1978, 1987b) inhibitor, trace amounts of caustic and olefin. The requirement that olefins be present makes the process well suited for the treating of catalytic naphthas; however, the reaction is relatively slow and the process is therefore usually used in combination with air–cresylate sweetening which uses the cresols present in catalytic naphthas as both solvents and oxidation catalysts. Although still in use in many

refineries, this process is gradually being replaced by Merox sweetening. In the liquid–liquid Merox process, the stream to be treated is brought into contact with air and 10% caustic solution containing an oxidation catalyst in a mixing vessel. It then passes to a settler where caustic and excess air are removed and the caustic is recirculated back to the mixer. Any caustic which remains dispersed in the treated product is removed in a sand coalescer. Chemical sweetening is generally carried out at temperatures from ambient to 65°C and at pressures of about 20 psi [1.4 atm].

(ii) *Kerosene hydrodesulfurization*

Hydrodesulfurization can be used to remove sulfur, saturate any olefins and reduce the aromatic content and gum-forming tendency of kerosene. The sour straight-run kerosene [5] feed is mixed with hydrogen, heated in a fired heater and then passed through a fixed-bed reactor containing a nickel- (see IARC, 1976, 1987b) or cobalt-molybdenum catalyst. Organic sulfur is removed as hydrogen sulfide. The reactor effluent is cooled, usually by heat exchange with the feed, and the excess hydrogen is separated and recycled. It is then reheated and steam-stripped to remove dissolved hydrogen sulfide. Operating temperatures are generally in the range of 205–410°C with pressures of 500–800 psi [34–54 atm].

(iii) *Gas oil hydrodesulfurization*

Hydrodesulfurization is used to improve the quality of straight-run gas oil [7] by removing sulfur, nitrogen and metallic contaminants. Any olefins are also saturated. Some cracking into lighter components will occur. The feed to the hydrodesulfurization unit is a sour gas oil from the crude distillation tower. The boiling range varies widely, from 205°C to 400°C. The feed is vaporized, mixed with a hydrogen-rich gas stream, heated to reaction temperature and passed through a fixed-bed reactor containing a non-noble metal catalyst, where nitrogen and sulfur are removed as ammonia and hydrogen sulfide. The hot reactor effluent is cooled and condensed by heat exchange with the feed, and the liquid is sent to a high-pressure separator where the hydrogen flashes off and is recycled. The liquid from the high-pressure separator then flows to a low-pressure separator where the hydrogen sulfide, ammonia and gaseous hydrocarbons are removed. The effluent product is a stabilized, hydrodesulfurized gas oil of improved colour and odour which is sent to storage for later blending or cracking. Operating temperatures are in the range of 260–415°C and pressures 500–800 psi [34–54 atm].

(iv) *Fluid-bed catalytic cracking*

Fluid-bed catalytic cracking is used to convert distillate oil streams into a product commonly described as synthetic crude oil. Synthetic crude oil is a wide boiling-range material from which gaseous hydrocarbons, catalytically cracked naphthas [22, 23] and light and heavy catalytically cracked distillates [24, 26, respectively] are fractionated by distillation. The feed to a fluid-bed catalytic cracker may be any hydrocarbon stock from straight-run kerosene [5] to heavy vacuum distillate [20] or solvent-deasphalted residual oil [32]. It is usually a heavy distillate, with the wide boiling range of 205–400°C. A fluid catalytic cracking unit consists of a catalyst section and a fractionating section which operate together as an integrated processing unit. The catalyst section contains the reactor

and regenerator, which, together with the standpipe and riser, form the catalyst circulation unit. The catalyst moves up the riser to the reactor, down through a stripper to the regenerator, across to the regenerator standpipe and back to the riser. The catalyst is in the form of very small spherical particles which behave like a fluid when aerated with a vapour. Fresh feed and recycling gas oil enter the unit at the base of the riser, where they are vaporized and raised to reaction temperature by the hot catalyst. The mixture of oil vapour and catalyst travels up the riser into the reactor. Cracking commences in the riser and continues until the oil vapours are disengaged from the catalyst in the reactor. The cracked products travel through the reactor vapour line to the fractionator. The spent catalyst flows from the reactor to the regenerator where carbon deposits are burned off. In the fractionation section, the reactor effluent is separated from the catalyst and travels to the fractionation section, where it is separated by distillation into a recycling gas oil which is returned to the riser for further cracking into catalytically cracked clarified oil [27], light catalytically cracked distillate [24], catalytically cracked naphthas [22, 23] and wet gas. Between 50% and 80% of the feed is cracked in a single pass. Typical reactor temperatures and pressures are 475–550°C and 10–30 psi [0.7–2 atm]. A variety of acid-function catalysts are used, including natural clays, silica-aluminas and synthetic zeolites (see IARC, 1987a,b).

(v) *Moving-bed catalytic cracking*

The function of moving-bed catalytic cracking is the same as that of fluidized catalytic cracking. Moving-bed catalytic crackers use the same type of catalyst as fluid units but in the form of extruded pellets about 0.25 [0.6 cm] in diameter by about 0.5 [1.3 cm] in length. They are usually smaller than fluid-bed crackers and generally consist of a catalyst section, contained in a single, tall vessel comprising the reactor and generator, and an associated fractionation section. The catalyst is moved continuously to the top of the unit by bucket elevator or pneumatic lift pipes and flows downwards at a rate of about 4 ft [1.2 m] per min through the surge hopper, which acts as a temporary storage ahead of the reactor, through the reactor where it comes into contact with the feedstocks and into the regenerator where carbon deposits are burned off. The reactor is isolated from the surge hopper and regenerator by steam seals. The products of cracking are separated by distillation into a recycling gas oil, catalytically cracked clarified oil [27], light catalytically cracked distillate [24], catalytically cracked naphthas [22, 23] and wet gas. The feedstocks and operating conditions are essentially the same as those used for fluid-bed catalytic cracking.

(vi) *Catalytic hydrocracking*

Hydrocracking is used to convert heavy feedstocks into lower-boiling, more valuable products. The process employs high pressure, high temperatures, a cobalt- or nickel-molybdenum catalyst and hydrogen. The reaction section is usually divided into two stages: the first is designed to remove sulfur and nitrogen compounds, while actual cracking takes place in the second stage in the presence of excess hydrogen. The effluent from the second-stage reactor is fractionated by distillation into the desired products. The usual feed is a straight-run gas oil [7] or other distillate from the crude fractionator. Temperatures and pressures in the first stage are generally 370°C and 3000 psi [200 atm], and those in the second stage are about 315°C and 1500 psi [100 atm].

(*d*) *Heavy hydrocarbon processing*

(i) *Deasphalting*

Deasphalting is used to separate asphaltic materials from heavy oil fractions. This separation (sometimes referred to as decarbonizing) produces an oil for use as a feed to catalytic cracking or for the manufacture of heavy lubricants, and as a raw bitumen (see IARC, 1985). Deasphalting is usually accomplished by solvent extraction with propane. The feed to a deasphalting unit is usually a vacuum residue [21], reduced crude oil [8] or any other heavy crude fraction containing bitumen. The feed and liquid propane are pumped to an extraction tower in a controlled ratio and at a controlled temperature. The extraction unit is often a rotating-disc contactor. A separation based on the differences in solubility is effected, producing a solution of deasphalted residual oil and one of bitumen. The effluents are processed by evaporation and steam stripping to recover the propane from the oil and the bitumen. Temperatures are usually in the range of 70–105°C and pressures range from 450–600 psi [30–40 atm].

(ii) *Visbreaking*

The purpose of visbreaking (viscosity breaking) is to crack residual oils thermally into lower-boiling and less viscous materials under mild conditions. The charge to the unit, which is typically a waxy reduced crude oil [8], is heated and slightly cracked in the visbreaker furnace. The furnace effluent is quenched with a light gas oil and is fed to the lower or evaporator section of a fractionation tower where it is flashed. A tar, thermally cracked residue [31], accumulates in the base of the tower, while in the upper part the vapours are fractionated into gas, thermally cracked naphthas [28, 29] and thermally cracked distillates [30]. The tower bottoms are withdrawn and vacuum-flashed in a stripping tower and the vacuum distillate returned to the fractionator. Visbreaker furnaces generally operate at temperatures of 450–480°C and at atmospheric pressure.

(iii) *Coking*

Coking is a thermal cracking process in which crude oil residues, catalytically cracked clarified oil [27] and refinery tars are cracked at high temperature and low pressure to produce thermally cracked distillates [30] and petroleum coke. There are two principal coking processes: the fluid coking process and the delayed coking process. Delayed coking is used most widely; in this process, the charge stock is fed to the bottom section of a fractionation tower where material lighter than the desired end-point of the heavy thermal distillate is removed. The remaining material is pumped from the bottom of the fractionator to a coking heater, where its temperature is raised rapidly. The vaporized liquid leaving the coking heater enters a coke drum where coke is formed. The coke is recovered by cutting it out of the drum with a high-pressure water stream. The coker tower is generally operated at a temperature of about 380°C and at pressures of 25–30 psi [1.7–2 atm]. Coking heater temperatures are about 480–580°C.

(iv) *Residual oil hydrodesulfurization*

The function of a residual oil hydrodesulfurization unit is to reduce the sulfur and metal contents of atmospheric tower residues. Reduced crude oil [8] is mixed with hydrogen,

heated in a fired heater and then passed through a fixed bed of catalyst where the reactions occur. The active components of the catalyst are typically chromium (see IARC, 1980, 1987b), molybdenum, iron, cobalt or nickel. Organic sulfur and nitrogen compounds are converted to hydrogen sulfide and ammonia. The products from the reactor are cooled, usually by heat exchange with the feed, the excess hydrogen flashed off in a high-pressure separator and recycled, and the bulk of the ammonia and hydrogen sulfide removed in a low-pressure separator. The products are then reheated and steam stripped to remove any residual hydrogen sulfide or ammonia. The desulfurized residue can be blended into fuel or be processed further to recover gas oil. Residual oil hydrodesulfurization units are generally operated at temperatures of 340–450°C and at pressures of about 1000 psi [68 atm].

1.3 Worldwide distribution of petroleum refinery operations

A general picture of the extent of petroleum refinery operations in various regions of the world can be obtained from data on refinery throughputs (Table 3). Between 1976 and 1986, the total petroleum throughput of refineries in the developed countries of the western world declined, while in other countries refinery throughput has generally increased.

Table 3. Refinery throughputs (thousands of barrels daily)[a], 1976–87

Geographical region	1976[b]	1981[b]	1987[c]		
			Through-put	% of total	Refinery capacity
USA	13 435	12 470	12 855	22.6	15 695
Canada	1 710	1 945	1 605	2.8	2 050
Latin America	5 670	6 575	5 530	9.7	7 420
Western Europe	13 625	11 890	9 795	17.2	14 010
Middle East	2 300	2 205	2 970	5.2	4 120
Africa	1 055	1 525	2 170	3.8	2 630
Japan	4 230	3 630	2 910	5.1	4 505
South-east Asia	1 865	2 480	2 750	4.8	3 745
South Asia	550	795	1 145	2.0	1 295
Australia and New Zealand	655	655	570	1.0	730
Centrally planned economies[d]	11 575	13 420	14 700	25.8	17 880
Total world	56 670	57 590	57 000	–	74 080

[a] 1 barrel = 0.136 metric tonne of crude oil (specific gravity, 0.858)

[b] From British Petroleum Company (1986)

[c] From British Petroleum Company (1988)

[d] Albania, Bulgaria, China, Cuba, Czechoslovakia, Democratic Kampuchea, the Democratic People's Republic of Korea, the German Democratic Republic, Hungary, the Lao People's Democratic Republic, Mongolia, Poland, Romania, the USSR, Viet Nam and Yugoslavia

The importance of the various refinery process streams varies somewhat from region to region and even from season to season for individual refineries. Although detailed data are not available to compare the throughput of various process streams in different geographic regions, regional consumption data for different product groups generally parallel local refinery product distribution, since, historically, refined products are mostly used in the same geographic region in which they are produced. While there are many exceptions to this generalization (e.g., in the Middle East increasing quantities of crude oil are being converted into finished products for export), production and consumption patterns still correlate fairly well at the regional level. Table 4 shows the consumption of gasolines, middle distillates, fuel oils and other petroleum products in several regions of the world from 1976 to 1986. The data reflect the fact that refinery process streams feeding the gasoline pool are most important in the USA, Canada and Australia/New Zealand, whereas middle distillates predominate in European refineries. The most notable trends are the worldwide decline in fuel oil production and consumption and the steady growth in production of all products (except fuel oil) in the lesser developed countries. In Albania, Bulgaria, China, Cuba, Czechoslovakia, Democratic Kampuchea, the Democratic People's Republic of Korea, the German Democratic Republic, Hungary, the Lao People's Democratic Republic, Mongolia, Poland, Romania, the USSR, Viet Nam and Yugoslavia, overall consumption increased from 580.5 million tonnes in 1976 (British Petroleum Co., 1986) to 670.3 million tonnes in 1986 (British Petroleum Co., 1988).

Table 4. Consumption of petroleum products[a] by geographical region (millions of tonnes per year)

Region and product	1976[b]	1981[c]	1987[c]	
			Consumption	% of total
USA				
Gasolines	320.4	297.9	324.1	42.5
Middle distillates	206.3	199.2	216.1	28.3
Fuel oil	146.8	110.6	68.6	9.0
Others	148.9	138.3	154.6	20.2
Total	822.4	746.0	763.4	–
Canada				
Gasolines	29.6	31.3	27.5	39.6
Middle distillates	27.3	25.0	21.8	31.5
Fuel oil	17.1	11.2	6.7	9.6
Others	11.9	14.2	13.4	19.3
Total	85.9	81.7	69.4	–
Western Europe				
Gasolines	131.8	131.1	144.5	24.7
Middle distillates	238.3	220.7	236.3	40.4
Fuel oil	238.3	179.3	111.5	19.1
Others	87.4	87.3	92.9	15.8
Total	695.8	618.4	585.2	–

Table 4 (contd)

Region and product	1976[b]	1981[c]	1987[c]	
			Consumption	% of total
Japan				
Gasolines	43.6	39.8	44.0	21.1
Middle distillates	54.2	60.6	69.0	33.2
Fuel oil	125.7	91.2	57.0	27.4
Others	30.0	32.3	38.1	18.3
Total	253.5	223.9	208.1	–
Australia and New Zealand				
Gasolines	12.2	13.1	13.6	41.5
Middle distillates	9.9	9.8	11.3	34.4
Fuel oil	7.3	5.6	2.4	7.3
Others	4.9	4.7	5.5	16.8
Total	34.3	33.2	32.8	–
Rest of world[d]				
Gasolines	72.7	96.0	110.2	18.3
Middle distillates	139.3	178.1	216.6	35.9
Fuel oil	150.8	190.8	188.0	31.2
Others	59.4	74.5	88.0	14.6
Total	422.2	539.4	602.8	–
Total				
Gasolines	610.3	609.2	663.9	29.4
Middle distillates	675.3	693.4	771.1	34.1
Fuel oil	686.0	588.7	434.2	19.2
Others	342.5	351.3	382.5	17.3
TOTAL	2314.1	2242.6	2260.7	–

[a]'Gasolines' consists of aviation and motor gasolines and light distillate feedstock; 'middle distillates' consists of jet and burning kerosenes, and gas and diesel oils (including marine bunkers); 'fuel oil' includes marine bunkers; 'others' consists of refinery gas, liquified petroleum gases, solvents, petroleum coke, lubricants, bitumen, wax, refinery fuel and loss

[b]From British Petroleum Company (1986)

[c]From British Petroleum Company (1988)

[d]Excluding centrally planned economies (see footnote *d* to Table 3)

2. Exposures in the Workplace

Those compounds that occur in the working environment of petroleum refineries that have been evaluated in previous *IARC Monographs* are listed in Table 1 of the 'General Remarks', p. 32.

2.1 Workers and working conditions

It has been estimated that the world petroleum refining industry employs from 400 000 to 500 000 persons (International Labour Office, 1986) in approximately 700 refineries (American Petroleum Institute, 1987).

A wide range of potential occupational health hazards is present in petroleum refineries. Exposures result from skin contact and the inhalation of gases and vapours, mainly hydrocarbons either naturally present in crude oil and emitted during its refining or formed and emitted during one of the many transformations of the various process streams. Gaseous sulfur compounds such as hydrogen sulfide, sulfur dioxide and mercaptans are emitted during removal and treatment of sulfur. Exposure to dusts and fumes results mostly from maintenance operations such as abrasive blasting, the use of catalysts and the handling of viscous or solid products such as bitumen and coke.

In general, it is considered that exposures to hydrocarbons have not been subject to major reductions over the past two or three decades. Nevertheless, useful reductions have resulted from the gradual introduction of controls over fugitive emissions, increased attention to the control of benzene exposures (CONCAWE, 1986) and greater automation of refinery operations, including sampling and analysis of streams. Over the last 30 years or so, since a large conference in 1951 (Page, 1951) created a much greater awareness of the potential skin hazards from some mineral oil streams, there has been a significant reduction in skin exposure as a result of more effective use of personal protective clothing, improved personal hygiene and safer operating procedures.

The petroleum industry has reached a stage of high automatization, with a concurrent reduction of the work force during the last two decades. It is not known whether such automatization has occurred in all countries to the same extent. Due to the intrinsic risks of fire and explosion from many refinery streams, operations take place in closed systems, and refinery operators spend most of their time in control rooms with little potential exposure to hazardous agents. Ubiquitous exposure exists mainly to hydrocarbon gases and vapours at usually very low levels resulting from constant and fugitive emissions from seals and valves in the complex network of pipes and columns; there is also potential dermal exposure during sampling (Darby *et al.*, 1978). Heavier exposures may be encountered, however, during routine maintenance and turn-round operations (Dynamac Corp., 1985) from episodic or periodic emissions resulting from opening the system or performing specific tasks such as repair, overhaul and construction. Outside contractors are often brought in for major turn-round operations. [The Working Group noted that no data were available on the numbers of outside contractor workers involved in such operations.] During these

operations, cutaneous exposure to a number of chemicals is also a possibility. Other groups with potential heavy exposure to such hazards are those in bulk handling of final products and in laboratories (Clayton Environmental Consultants, Inc., 1982).

The overall distribution of employees in ten US refineries by exposure-based job type has been reported as follows: administration, 21%; maintenance, 36%; operations, 40%; and unknown, 3% (Nelson *et al.*, 1983). A job code classification system for oil refineries has been developed (American Petroleum Institute, 1985) in which workers can be classified using two standardized variables: process and task. This scheme was devised in order to allow better regroupment of workers who share a set of qualitatively common exposures. Other exposure-based work category classifications have been devised for both epidemiological purposes (Nelson *et al.*, 1983; Thomas *et al.*, 1984) and for planning industrial hygiene studies (Futagaki, 1983).

The main substances to which workers may be exposed in petroleum refineries are given in Table 5. The main occupational agents for which airborne exposure levels are available are presented in Tables 6–8. [The Working Group noted the paucity of exposure data available for the period prior to the mid-1970s and for refineries in developing countries, and the lack of any data on skin exposures.]

Table 5. Main substances (and classes of substances) to which workers may be exposed in petroleum refineries[a]

Material	Principal uses or sources of emission
Alumina	Catalyst support, catalyst (sulfur recovery)
Aluminium chloride	Catalyst (isomerization)
Amines, aliphatic (e.g., methylamine) and alkanolamines (e.g. monoethanolamine)	Hydrodesulfurization, acid gas adsorbents
Amines, aromatic (e.g., anisidines* and phenylenediamines*)	Catalytic cracking, residual processing, gasoline antioxidants
Ammonia	Atmospheric distillation, catalytic cracking, sulfur recovery, residual processing, lubricant oil processing, waste waters
Antimony trichloride	Inhibitor (isomerization)
Arsenic compounds*	Crude oil, gas scrubbing
Asbestos*	Pipe insulation, gaskets (formerly), valve seals
Bitumen (asphalt) fumes*	Solvent deasphalting, tanker loading, tank cleaning
tert-Butyl alcohol	Unleaded gasoline blending
Carbon monoxide	Catalyst regeneration (catalytic cracking), use of inert gases, boilers, flares
Chlorine	Rejuvenation of platinum catalyst, cooling water treatment
Chromium and chromium compounds*	Catalyst (catalytic reforming), welding
Clays (e.g., bentonite)	Catalyst supports, grease fillers

Table 5 (contd)

Material	Principal uses or sources of emission
Cobalt and cobalt compounds (including cobalt carbonyl, cobalt molybdate, oxides)	Catalyst (catalytic reforming, hydrocracking, hydrotreating)
Coke	Coking units*
Copper and copper compounds (e.g. copper chloride, copper alloys)	Desulfurization, sweetening operations, catalyst (catalytic reforming)
Crude oil	Crude oil distillation and processing unit
1,2-Dibromoethane (ethylene dibromide)*	Leaded gasoline blending
1,2-Dichloroethane (ethylene dichloride)*	Leaded gasoline blending
Earth, diatomaceous (amorphous silica*)	Crude oil filtration, catalyst support, lubricant oil filtration
Fuels (e.g., gasoline, diesel oil, jet fuel, heating oil)	Fuel blending, storage, loading
Furfural	Oil and grease manufacture, desulfurization
Graphite	Grease filler
Hydrazine*	Boiler-water additive
Hydrocarbons, aliphatic (e.g., propane, *n*-hexane)	Most process units
Hydrocarbons, aromatic (e.g., benzene*, toluene)	Most process units, catalytic cracking and reforming, gasoline blending and loading, wax preparation unit
Hydrocarbons, chlorinated*	Rejuvenation of catalyst (catalytic reforming), solvents
Hydrogen chloride	Isomerization
Hydrogen fluoride (hydrofluoric acid)	Catalyst (alkylation)
Hydrogen sulfide and sulfur compounds (e.g., mercaptans, carbon disulfide)	Atmospheric distillation, catalytic cracking and reforming, hydrocracking, hydrotreating, sulfur recovery, residual processing, lubricant oil processing, waste waters
Iron and iron compounds*	Catalyst (hydrocracking), welding
Ketones (e.g., methyl ethyl ketone)	Lubricant oil solvent dewaxing, atmospheric distillation, residual processing
Lead, inorganic compounds (e.g., lead oxide)*	Desulfurization, removal, sweetening operations
Manganese compounds, organic	Unleaded gasoline blending
Methyl-*tert*-butyl ether	Unleaded gasoline blending
N-Methyl-2-pyrrolidone	Lubricant oil manufacture
Mineral oils (e.g., lubricating oils)*	Oil and grease units
Molybdenum and molybdenum compounds	Catalyst (catalytic reforming, hydrocracking, isomerization, hydrotreating)
Nickel and nickel compounds (e.g., nickel sulfides, nickel carbonyl, nickel oxide)*	Catalyst (isomerization, hydrotreating, hydrocracking, catalytic reforming), welding, cleaning residual fuel oils, combustion products
Nitrogen oxides	Flares, furnaces

Table 5 (contd)

Material	Principal uses or sources of emission
Palladium	Catalyst (catalytic reforming, hydrocracking)
Phenol	Crude distillation, catalytic cracking, residual processing, waste waters, desulfurization, lubricant oil, solvent dewaxing
Phosgene	Catalyst rejuvenation by chlorination (catalytic reforming)
Pitch (petroleum)	Bitumen department, loading operations
Phosphoric acid	Catalyst (polymerization)
Platinum	Catalyst (catalytic reforming, isomerization, hydrotreating)
Polynuclear aromatic compounds*	Atmospheric distillation, catalytic cracking, residual fuel oil, lubricant oil processing, bitumen processing and loading, coking, waste-water treatment
Refined petroleum solvents (e.g., petroleum ether, rubber solvent, varnish makers' and painters' naphtha, Stoddard solvent)	Petroleum solvent manufacturing
Rhenium	Catalyst (catalytic reforming)
Silica, crystalline*	Abrasive blasting, demolition and rebuilding, cracking (catalyst)
Sodium hydroxide	Caustic wash of acid catalysts or acid-treated streams, sweetening operations
Sulfur	Sulfur recovery
Sulfur dioxide	Sulfur recovery, furnaces, flares
Sulfuric acid	Catalyst (alkylation, polymerization), acid treating of lubricant oils
Tetraethyllead and tetramethyllead*	Gasoline blending operations, gasoline storage tank cleaning
Tungsten sulfide	Catalyst (hydrocracking)
Vanadium compounds (e.g., vanadium pentoxide)	Residual fuel oils, cleaning of combustion deposits, flue cleaning

*Compounds marked with an asterisk have been evaluated by the IARC (see IARC, 1987; see also Table 1 of 'General Remarks', p. 32)

[a]From Darby *et al.* (1978); Burgess (1981); Clayton Environmental Consultants, Inc. (1982); Hobson (1982); Futagaki (1983); CONCAWE (1985); Dynamac Corp. (1985); Suess *et al.* (1985)

Table 6. Airborne concentrations of total hydrocarbons and selected aliphatic hydrocarbons in petroleum refineries in mg/m³; 8-h TWA[a] on personal samples (range)

Operation or job description[b] (no. of samples)	Total hydrocarbons	*n*-Butane	*n*-Hexane	Reference
Production on-site (62)	53 (0.7–1820)	10.3 (0–460)	3.0 (0–154)	CONCAWE (1987)
Production off-site (27)	66 (3.7–923)	11.2 (0–221)	2.8 (0–14)	CONCAWE (1987)
Drumming of gasoline (9)	858 (61–1750)	120 (0–301)	52 (2.4–297)	CONCAWE (1987)
Laboratory technician (9)	31 (7–83)	3.7 (0.1–29.5)	4.5 (0.4–8.5)	Viau *et al.* (1987)
Bulk plant operator (4)	66 (13–73)	4.0 (0.5–11.8)	1.4 (0.5–3.2)	Viau *et al.* (1987)
Refinery operator on-site (11)	4 (1–8)	0.4 (ND–1.7)	0.3 (ND–1.8)	Viau *et al.* (1987)
Refinery operator off-site (13)	16 (2–96)	2.8 (0.1–20.5)	0.4 (ND–1.7)	Viau *et al.* (1987)
Refinery, clerical or administration employee (69)	0.2–2.1[c]	–	–	Viau *et al.* (1987)
Process unit operator[d] (56, 54, 54, respect.)	18.9 (10.7–27.2)[e]	3.4 (1.8–5.1)[e]	0.47 (0.32–0.63)[e]	Rappaport *et al.* (1987)

[a]TWA, time-weighted average

[b]On-site involves operators controlling refining process units; operator time is spent in control room, inspection tours of units and specific activities ranging from routine maintenance to collection of samples, opening and closing of valves, etc. Off-site involves operators conducting ancillary operations, such as laboratory technicians, control of bulk storage facilities, tank dipping and sampling, and water-effluent treatment operations.

[c]Range of area samples

[d]Work is primarily outside of the control room, taking readings, obtaining samples, inspecting facilities, etc.

[e]Approximate 95% confidence interval

ND, not detected; –, not measured

Table 7. Airborne concentrations of selected aromatic hydrocarbons in petroleum refineries in mg/m³; 8-h TWA[a] on personal samples (range)

Operation or job description (no. of samples)	Benzene	Toluene	Reference
Production on-site (62)	0.9 (0–23.8)	2.0 (0–67)	CONCAWE (1987)
Production off-site (27)	1.0 (0–14.1)	2.2 (0–19.6)	CONCAWE (1987)
Drumming of gasoline (9)	27.2 (0–116)	41.3 (3.1–195)	CONCAWE (1987)
Maintenance worker (4 studies)	0.3–1.2 (0.03–24)	–	CONCAWE (1986)
Laboratory technician (9)	–	0.8 (ND–3.5)	Viau *et al.* (1987)
Bulk plant operator (4)	–	3.1 (0.7–8.0)	Viau *et al.* (1987)
Refinery operator, on-site (11)	–	0.3 (ND–0.7)	Viau *et al.* (1987)
Refinery operator, off-site (13)	–	0.6 (0.2–2.4)	Viau *et al.* (1987)
Atmospheric distillation of crude oil	0.8	–	Holmberg & Lundberg (1985)
Catalytic reforming	0.2	–	Holmberg & Lundberg (1985)
Laboratory personnel	1.0	–	Holmberg & Lundberg (1985)
Product analysis	0.2	–	Holmberg & Lundberg (1985)
Other refinery workers	0.1	–	Holmberg & Lundberg (1985)
Refining (in general) (14 824)[b]	0.7 ± 2.2 (SD)	– –	Runion & Scott (1985)
Lubricant-dewaxing process (66 and 82)	0.1 ± 0.06 (SD)	3.2 ± 9.7 (SD)	Wen *et al.* (1985)
Lubricant oil extraction	–	<0.1–77 ppm	CONCAWE

[a]TWA, time-weighted average

[b]Estimated TWA >4 h

ND, not detected; –, not measured

Table 8. Airborne concentrations of polynuclear aromatic compounds (PAC)[a] in petroleum refineries

Unit	Job description or process	Sample type[b] (no. of measurements)	Results[c] ($\mu g/m^3$)	Reference
Fluid catalytic cracker units	Supervisor	Personal samples TWA, 7–8 h (4)	GM: 8.8 GSD: 2.6	Futagaki (1983)
	Inside operator	Personal samples TWA, 7–8 h (22)	GM: 11.9 GSD: 3.3	Futagaki (1983)
	Outside operator	Personal samples TWA, 7–8 h (61)	GM: 11.4 GSD: 3.7	Futagaki (1983)
Delayed coker units	Operators	Personal samples TWA, 7–8 h (40)	GM: 7.8 GSD: 8.4	Futagaki (1983)
	Coke handlers	Personal samples TWA, 7–8 h (50)	GM: 14.6 GSD: 4.1	Futagaki (1983)
Bitumen processing units	Bitumen blowing	Area samples TWA, 7–8 h (5)	Range: 1.6–30.6	Futagaki (1983)
	Deasphalting	Area samples TWA, 7–8 h (4)	Range: 1.4–41.2	Futagaki (1983)
	Vacuum distillation	Area samples TWA, 7–8 h (11)	Range of GM: 2.8–18.0	Futagaki (1983)
Bulk handling of bitumen	Road tanker loading	Personal samples[d] TWA, 8 h (4)	Average: 0.033 Range: 0.004–0.095	Brandt & Molyneux (1985)
Turn-round activity on reaction and fractionator towers	Chipping coke	Personal samples[e] TWA, 8 h	120–320	Dynamac Corp. (1985)
	Cutting steel liner	Personal samples TWA, 8 h	210–470	Dynamac Corp. (1985)
	Cutting out distillation trays	Personal samples TWA, 8 h	70	Dynamac Corp. (1985)

[a] 23 individual or groups of PAC and azo heterocyclics with 2–7 rings

[b] TWA, time-weighted average

[c] GM, geometric mean; GSD, geometric standard deviation

[d] 11 individual PAC

[e] Six individual or groups of PAC

2.2 Aliphatic hydrocarbons

Nearly all workers in petroleum refineries are exposed to aliphatic hydrocarbons. The principal individual aliphatic hydrocarbon compounds found in petroleum refinery air samples are butanes, pentanes and hexanes, which account for an overwhelming part of the total hydrocarbons measured. Concentrations of up to 150 hydrocarbons, mostly aliphatic, have been reported in gasoline vapour in gasoline manufacture and distribution operations in Europe (CONCAWE, 1987).

Average exposure levels to hydrocarbons for various categories of workers are summarized in Table 6. These range from fractions of 1 mg/m^3 for administrative or clerical employees to above 1000 mg/m^3 in drumming operations. The latter operation corresponds to a 'worst case' situation, in which operators fill drums with gasoline without good local exhaust ventilation (CONCAWE, 1987). A mean exposure level of 5.4 ppm with a standard deviation of 16.5 ppm, covering a wide number of refinery workers in the USA (1201 full-exposure samples), has been reported (Wen *et al.*, 1984a). In general, gasoline loading operations represent the highest potential for exposure to hydrocarbons. Various short-term and 8-h time-weighted average (TWA) exposure levels for these operations are summarized in the monograph on gasoline. Average exposure of refinery production operators, both on-site and off-site, is well below 100 mg/m^3, with potential short-term extremes above 1000 mg/m^3, which varies according to specific tasks and the relative amount of time spent on the process units and in the control rooms (CONCAWE, 1987). Data on exposure to 1,3-butadiene are given in the monograph on gasoline.

2.3 Aromatic hydrocarbons

In petroleum refineries, exposure to aromatic hydrocarbons originates from their presence in crude oils and the conversion of naphthenes and paraffins during the catalytic reforming process. Exposure levels to benzene and toluene in various work situations are summarized in Table 7.

Group average exposures of production and maintenance workers to benzene vary from about 0.3 to 1 mg/m^3, with higher individual values of above 10 mg/m^3. The highest values have been observed during gasoline drumming operations without good local exhaust ventilation. Gasoline loading operations, in general, give rise to average 8-h levels of about 1–5 mg/m^3, depending on the type of operation (road tanker, railcar, marine) and loading technique. Various short-term and 8-h TWA exposure levels for these operations are summarized in the monograph on gasoline.

Data on exposure to benzene derived from personal sampling of employees of a large refinery in Texas, USA, have been compiled for the period 1973–82 (benzene concentration range in mg/m^3, % of samples): <0.3, 52; 0.3–3, 37; 3–16, 9; 16–30, 1; >30, 0 (727 samples covering 4 h or more). The refinery under investigation included benzene petrochemical units (Tsai *et al.*, 1983). Full-shift personal exposure measurements have also been obtained for 29 work categories in two French refineries, including work in catalytic cracking and reforming units. In only six work categories were the levels of benzene near or above

1 mg/m³; in two work categories (cracker operator and rail car top-loading), maximum concentrations exceeded 10 mg/m³ (Cicolella & Vincent, 1987). In Canada, exposure to benzene in a typical non-benzene producing facility was reported to be usually well below 1 ppm (3 mg/m³). In refineries where pure benzene is produced, exposures can exceed 10 ppm (30 mg/m³) on occasion, with a range of 1–4 ppm (3–13 mg/m³) observed in the laboratory (Petroleum Association for Conservation of the Canadian Environment, 1979). At one US refinery, of 75 samples taken around a catalytic cracking unit, 61 contained less than 0.1 ppm (0.3 mg/m³), 12 had 0.1–0.5 ppm (0.3–1.6 mg/m³) and two exceeded 10 ppm (32 mg/m³; Weaver *et al.*, 1983).

In 1984, the American Petroleum Institute commissioned a study of exposure to benzene in petroleum companies over the period 1978–84 (Spear *et al.*, 1987). Personal exposure data submitted by nine refining companies were analysed in detail to characterize the distribution of exposures within work operations and job categories; the data covered 123 location- and unit-specific job categories. Most 8-h TWA exposures were reported to be below 1.0 ppm (3 mg/m³); however, for some groups, 10% or more of exposures exceeded 1.0 ppm, although only about 5% of measurements reported for maintenance workers exceeded that level. Some short-term exposure data (15-min TWA) were also submitted; most showed levels below 1.0 ppm, although certain groups had very variable exposures with some measurements in excess of 5 ppm (16 mg/m³). These situations frequently involved loading and unloading of barges or tanker trucks.

Several other mononuclear aromatic hydrocarbons were monitored in the CONCAWE (1987) study on gasoline and refineries, including toluene, the xylenes, the trimethylbenzenes and isopropylbenzene (cumene). Mean exposure levels were 6 mg/m³ for toluene, 4.2 mg/³ for the trimethylbenzenes and below 1 mg/m³ for the other hydrocarbons. Worker exposure to aromatic hydrocarbons has also been measured during the performance of various maintenance turn-round activities (Dynamac Corp., 1985). Median 8-h TWA concentrations of benzene, toluene, xylene and cumene were well below 1 mg 34m³ for all jobs. Higher exposure levels (maximum, 7 mg/m³ for benzene) were observed for a pipe fitter and a machinist.

Biological monitoring data on benzene exposure of gasoline-exposed workers are summarized in the monograph on gasoline.

2.4 Polynuclear aromatic compounds

Polynuclear aromatic compounds (PAC) are present in crude oil in various concentrations depending on its source. They are further concentrated in the high-boiling fractions and modified in structure by the various fractionation and cracking operations that yield PAC-containing intermediate or final products, such as gas oils, residual fuel oils, bitumen and coke. PAC are also present in solvent extracts of mineral oils and in waste waters.

Few data have been reported on exposure to PAC in petroleum refineries (Table 8). Three types of processing units have been investigated systematically in nine refineries in the USA (Futagaki, 1983). Personal samples taken in the fluid catalytic cracking unit and in the delayed coker unit both showed total PAC concentrations of 10 μg/m³. Area samples taken

in bitumen processing units indicated levels ranging from about 1 to 40 $\mu g/m^3$. In one refinery where personal samples were taken at the deasphalting unit, total PAC levels varied from 2.5 to 49.8 $\mu g/m^3$. Of the 23 individual or groups of PAC that contributed to the total, including vapour phase and particulate matter, 10 or 11 were found on average in each sample. The average distribution of PAC indicated that at least 85% of the total PAC concentration was constituted by two-ring compounds (naphthalene and its derivatives) and 94% by two- or three-ring compounds. Compounds with five rings or more contributed from less than 0.1% at the catalytic cracker unit and 0.3% at the bitumen processing unit to 1.5% at the delayed coker unit. As an example, the highest concentration of benzo[*a*]pyrene plus benzo[*e*]pyrene was 9.3 $\mu g/m^3$ in a personal sample from a coke cutter. In most samples, however, these two compounds were not detected (<0.01 $\mu g/m^3$).

Loading of road tankers with bitumen in refineries has been associated with levels of <0.1 $\mu g/m^3$ four- to six-ring PAC. Only particulate matter was collected. Concentrations of total particulate matter and benzene-soluble matter were not found to be reliable indices of exposure to these PAC in bitumen fumes (Brandt & Molyneux, 1985).

Personal exposure to several PAC has been evaluated during performance of turn-round operations on reaction and fractionator towers. Potential sources of PAC were residual coke and heavy distillate (Dynamac Corp., 1985). Naphthalene and its methyl derivatives accounted for more than 99% of the total concentration of PAC measured; exposure to anthracene, pyrene, chrysene and benzo[*a*]pyrene was either too low to be detected or $\leqslant 1$ $\mu g/m^3$. Area monitoring for the six PAC during normal activities as well as during shut-down, leak testing and start-up operations following turn-rounds has also been reported. Total concentrations at the various sites monitored (pumps, compressors) ranged up to 400 $\mu g/m^3$, with the majority of measurements below 100 $\mu g/m^3$. The distribution pattern of individual PAC was the same as that reported above.

2.5 Other exposures

(*a*) *Aromatic amines and nitrosamines*

Area samples taken at fluid catalytic cracking units, bitumen processing units and coker units in US refineries contained very low concentrations (<0.1 ppm (0.6 mg/m^3) TWA) of *para*-anisidine in four of 17 samples and of *ortho*-anisidine and aniline in one of the four samples. No *N*,*N*-dimethylaniline, *ortho*-toluidine, 2,4-xylidine or *para*-nitroaniline was detected in any sample, and none of seven *N*-nitrosamines monitored (*N*-nitrosodimethylamine, *N*-nitrosodiethylamine, *N*-nitrosodi-*n*-propylamine, *N*-nitrosodibutylamine, *N*-nitrosopiperidine, *N*-nitrosopyrrolidine and *N*-nitrosomorpholine) was found in any sample at levels above the detection limit of 0.1 $\mu g/m^3$ for a 20–30-l air sample (Futagaki, 1983).

(*b*) *Asbestos*

Asbestos has been used extensively in petroleum refineries, mainly as a thermal insulator and gasket material and for protective screens around welding operations on site. TWA (8 h)

concentrations for employees working with pipe insulation have been estimated to range from 0.1–0.9 fibres less than 5 μm in length per ml of air on the basis of various measurements in one refinery (Darby *et al.*, 1978). Measurements taken during turn-round activities in two refineries involving the removal of lagging, gaskets and insulation indicated 8-h TWA concentrations ranging from 0.01 to 0.15 fibres per ml of air. Lagging from a pipe on a flash tower was found to contain 50–60% amosite asbestos (Dynamac Corp., 1985). CONCAWE reported typical airborne levels of asbestos in the breathing zone of <0.01–0.02 fibres/cm^3 in insulation stripping, valve and joint repacking and overcladding asbestos insulation. Since the mid-to-late 1960s, most refineries have begen to replace asbestos with other materials.

(*c*) tert-*Butyl alcohol and methyl*-tert-*butyl ether*

A few groups of workers involved in the loading of gasoline have been found to be exposed to low average concentrations of these two gasoline additives. Mean 8-h TWA exposure levels, derived from 540 personal measurements of gasoline-exposed workers both inside and outside refineries, were: *tert*-butyl alcohol, 0.26 mg/m^3 (range, 0–30) and methyl-*tert*-butyl ether, 1.8 mg/m^3 (0–170; CONCAWE, 1987).

(*d*) *Coke dust*

Respirable dust concentrations measured while chipping petroleum coke at various locations during turn-round operations in two refineries were found to range from 1.04 to 8.19 mg/m^3 (four personal samples; 8-h TWA), while two measurements of total dust obtained during chipping coke operations inside a regenerator showed a very high level of 166 mg/m^3. Area samples taken during similar operations in one of the two refineries showed that there was potentially substantial worker exposure to coke dust (Dynamac Corp., 1985).

(*e*) *1,2-Dibromoethane (ethylene dibromide) and 1,2-dichloroethane (ethylene dichloride)*

These two substances are used as lead scavengers in leaded gasolines. Concentrations of 1,2-dibromoethane ranging from 0.23 to 1.65 μg/m^3 have been measured at two locations 50–400 ft [15–120 m] down wind of a bulk transfer and a tank truck loading operation. Since service station attendants have an 8-h TWA exposure of about 40 μg/m^3, it may be expected that refinery workers involved in the loading of gasoline are exposed to similar or higher levels (National Institute for Occupational Safety and Health, 1977).

1,2-Dichloroethane, which was used as an extraction solvent, was measured at four locations within one refinery at concentrations ranging from 40 to 800 mg/m^3 (National Institute for Occupational Safety and Health, 1976).

(*f*) *Furfural*

Some refineries utilize furfural to extract lubricant base stocks. According to CONCAWE, the 8-h TWA exposure for maintenance personnel is in the range <0.1–11.4 ppm (0.4–45 mg/m^3).

(*g*) *Hydrazine*

Solutions of hydrazine are sometimes used to scavenge oxygen in boiler feed-water. Normally, these would be handled in a closed system; however, relatively crude systems involving transfer of liquid from drums to the boiler feed-water have been used. According to CONCAWE, breathing-zone concentrations of hydrazine are usually 0.5 mg/m^3 or less for operators wearing respiratory protection. The operation typically lasts only several minutes and is carried out infrequently.

(*h*) *Hydrogen fluoride*

Hydrofluoric acid is used as a catalyst in alkylation units. In such a unit, exposure of plant operators and maintenance men to gaseous hydrogen fluoride has been found to range from below the detection limit of 0.005 mg/m^3 up to 0.18 mg/m^3. Changes in fluoride levels in the urine of workers over a shift were found only in subgroups of workers with higher routine exposures (Brown, 1985). According to CONCAWE, exposure values (8-h TWA) for a press operator are typically 0.1 mg/m^3 or less.

(*i*) *Hydrogen sulfide*

According to CONCAWE, levels of hydrogen sulfide to which workers are exposed are usually 2 ppm (3 mg/m^3) or less during normal operations. Specific tasks may involve a potential for significantly higher exposures.

(*j*) *Ketones*

Lubricating-dewaxing workers were found in one study to be exposed to methylethylketone at 8-h TWA levels of 1.03 ppm (3 mg/m^3; SD, 2.94; 82 personal samples); less than 5% of these samples contained >5 ppm (15 mg/m^3; Wen *et al.*, 1985). Exposures of <0.1–132 ppm (<0.3–400 mg/m^3; 8-h TWA) were measured by CONCAWE in lubricating oil extraction facilities and of 0.1–162 ppm (0.3–480 mg/m^3; 8-h TWA) for maintenance personnel.

(*k*) *Metal welding fumes*

Personal 8-h TWA measurements of iron oxide, chromium, nickel, lead and manganese fumes have been reported covering 15 cutting and welding activities during turn-round operations. In only one location was a high chromium level found, to a maximum of 1.61 mg/m^3 (Dynamac Corp., 1985).

(*l*) *Oil mists*

Airborne concentrations of oil mists in the range of 0.1–0.34 mg/m^3 (8-h TWA) have been reported by CONCAWE in a lubricating oil blending plant, while area concentrations recorded in a crude oil distillation unit ranged from <0.1 to 23 mg/m^3.

(*m*) *Silica*

Measurements of respirable dust containing free crystalline silica were made in one refinery during various turn-round operations, and TWA (8-h) concentrations were compared with permissible exposure limits, taking into account the percentage of free silica. All ratios of TWA concentrations to permissible exposure limits were at one or above: removing firebricks on heater for thermal cracking unit, 1–1.6; installing refractory bricks on same heater, 5.4; sandblasting fractionator, 30–60 (Dynamac Corp., 1985).

(*n*) *Sodium hydroxide and phosphoric acid*

Area samples taken during turn-round operations in the sulfur treating process in one refinery indicated levels of about 0.1 mg/m^3 sodium hydroxide, while none was detected near caustic circulating pumps. Personal samples taken on workers at the polymerization column during removal and replacement of phosphoric acid-containing catalyst indicated 8-h TWA exposures to phosphoric acid of 0.07–0.1 mg/m^3 for loading fresh catalyst (Dynamac Corp., 1985).

(*o*) *Tetraalkyllead*

CONCAWE reported typical airborne concentrations of tetraalkyllead (predominantly tetraethyllead) corresponding to various tasks: handling tanker delivery — 0.03–0.11 mg/m^3 (breathing zone, short-term monitoring); cutting/welding on tanks which had contained leaded gasoline — 0.004–0.11 mg/m^3 (breathing zone, short-term monitoring), 0.003-0.004 mg/m^3 (breathing zone, 8-h TWA). General airborne concentrations (>1 h) of 0.005–5.7 mg/m^3 have been reported in a variety of areas, including operator changing rooms, tank welding/cutting, proximity to tank valves, dip pipes and vacuum pumps.

(*p*) *Vanadium pentoxide and nickel oxides*

The combustion of heavy fuel oils in boilers and furnaces in refinery process units results in the deposition of oxides of vanadium and nickel in furnace boxes, associated ducting and tubes. Cleaning and maintenance of this equipment can result in exposure to the dust from these metal oxides. CONCAWE reported typical breathing-zone concentrations for these tasks as <2 mg/m^3 vanadium oxide and <0.01 mg/m^3 nickel oxides for preparatory work and removal of furnace fire bricks; <0.5 mg/m^3 vanadium oxide and <0.01 mg nickel oxides for furnace inspection; and 0.3–14 mg/m^3 vanadium oxide and 0.1–7.5 mg/m^3 nickel oxides for removal of scaffolding. These values are reported as 8-h TWAs, except for removal of scaffolding. [No data were available to the Working Group regarding exposures to nickel compounds during the loading and unloading of nickel catalyst. However, it is known that this is a short-term operation carried out infrequently.]

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

3.1 Carcinogenicity studies in animals[1]

(a) *Skin application*

(i) *Uncracked distillates and residues of crude oils*

Some studies on the carcinogenicity of untreated vacuum distillates (light or heavy paraffinic or naphthenic distillates [19A, 19B, 20A, 20B] (Bingham & Barkley, 1979; Kane *et al.*, 1984) were reported in a previous volume (IARC, 1984).

Mouse: In a series of experiments, Blackburn *et al.* (1984, 1986) tested a number of undiluted samples derived from the refining of crude oil. In each experiment, groups of 50 male C3H/HeJ mice, six to eight weeks old, were given twice weekly applications of 50 mg of the samples on shaven interscapular skin for 80 weeks or until a papilloma larger than 1 mm^3 appeared. Skin tumour incidence [histologically unspecified] was evaluated in mice surviving at the time at which one-half of the tumour-bearing animals had developed their tumour (or at 60 weeks, whichever came first). The controls consisted of seven groups of 50 mice treated similarly with toluene and four groups of 50 mice that were only shaven. Three skin tumours were seen in the toluene-treated controls and none in the others. The results are shown in Table 9. [The Working Group noted that treatment was suspended in mice that developed a papilloma larger than 1 mm^3 and that details were not given about time of killing or survival of treated and control mice.]

(ii) *Cracked distillates and residues*

Some studies on the carcinogenicity of certain catalytically cracked oils and residues (light and heavy catalytically cracked distillates [24, 26] and catalytically cracked clarified oil [27]; Smith *et al.*, 1951; Shubik & Saffiotti, 1955; Saffiotti & Shubik, 1963; Bingham & Barkley, 1979) were reported in a previous volume (IARC, 1984). Experiments by Blackburn *et al.* (1984, 1986), with the same experimental design as outlined above, are summarized in Table 10.

Mouse: Groups of 30 mice [strain, sex and age unspecified] received thrice weekly skin applications of cracking residues from crude oils (type of cracking unspecified [27 or 31]) of different origins [dose unspecified] for ten months. In one group treated with a cracking residue from Dolinsk crude oil (11.6% paraffins), 12/28 mice developed skin tumours (eight

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[1]The Working Group was aware of several skin-painting studies in progress in mice using various petroleum distillates (straight-run middle distillate [6], light paraffinic distillate [19A], light catalytically cracked distillate [24], hydrotreated heavy naphthenic distillate [20D], hydrotreated light naphthenic distillate [19B], hydrodesulfurized middle distillate [6A]), naphthas (heavy catalytically cracked naphtha [23], alkylate naphtha [13], heavy reformed naphtha [17], straight-run kerosene [5], hydrodesulfurized kerosene [5B], heavy thermally cracked naphtha [29], sweetened naphtha), catalytically cracked clarified oil [27] and vacuum residue [21] (IARC, 1986). Numbers correspond to streams described in Table 2 and Figure 1 of this monograph.

Table 9. Results of experiments by Blackburn *et al.* (1986) on undiluted uncracked distillates and residues of crude oils

No. of groups	Sample	No. of survivors	No. with skin tumours	Average latent period (weeks)
One	Light paraffinic distillate (CAS No. 64741-50-0) [19]	42	27	35
One	Heavy paraffinic distillate (CAS No. 64741-51-1) [20A]	34	31	34
Four	Heavy naphthenic distillate (CAS No. 64741-53-3) [20B]	38	31	50
		34	25	48
		27	16	38
		29	21	42
Two	Straight-run kerosene (CAS No. 8008-20-6) [5]	30	9	70
		27	4	62
One	Hydrotreated kerosene (CAS No. 64742-47-8) [5A]	38	24	79
One	Light straight-run naphtha (CAS No. 64741-46-4) [3]	44	11	85
One	Vacuum residue (CAS No. 64741-56-6) [21]	43	1	70
Two	Hydrotreated heavy naphthenic distillate (CAS No. 64742-52-5) [20D]	41	36	51
		25	21	57
One	Chemically neutralized/hydrotreated heavy naphthenic distillate (CAS No. 64742-34-3/64742-52-5) [20C/20D]	20	12	52

carcinomas). In a further group treated with a cracking residue from Bitkovsk crude oil (14% paraffins), eight papillomas developed in 13 survivors. In another group, no tumour developed after treatment with a cracking residue from Tuimazinsk crude oil (5.9% paraffins) [number of survivors unspecified] (Shapiro & Getmanets, 1962). [The Working Group noted the inadequate reporting of the data and the lack of information on the nature of the cracking process.]

Three groups of albino mice [strain, sex and age unspecified] received thrice weekly skin applications of residues from thermal cracking [31] from two crude oils [dose unspecified] for ten months. One group of 30 mice was treated with fresh residue from Dolinsk crude (11.6% paraffins) and developed 11 skin tumours (five carcinomas). A second group of 30 mice treated with the same residue after it had been stored for three years developed seven skin tumours (one carcinoma). A third group of 60 mice treated with a residue from Grozny crude oil ('low' in paraffins) developed three small papillomas (Getmanets, 1967). [The Working Group noted the inadequate reporting of the data and the lack of controls.]

Table 10. Experiments by Blackburn *et al.* (1984, 1986) on distillates and residues from cracking

No. of groups	Sample	Dose (mg)	No. of survivors	No. with skin tumours	Average latent period (weeks)	Controls
One	Intermediate catalytically cracked distillate (CAS No. 64741-60-2) [25]	50	43	42	16	No skin tumour in 200 sham-treated controls (shaving only)
One	50% mixture of heavy catalytically cracked distillate (CAS No. 64741-61-3) [26] and catalytically cracked clarified oil (CAS No. 64741-62-4) [27] in toluene	25	37	34	21	Three skin tumours in 300 toluene-treated controls

In a series of experiments, Lewis (1983) tested different samples derived from the refining of crude oil. Groups of 10–30 male C3H mice [age unspecified] received weekly, twice weekly or thrice weekly [exact details not given] skin applications of 50 or 100 mg of the samples at a weekly dose of 100–300 mg for 18 months or until a cancer was observed grossly. No control was available. The substances tested were ten samples of higher-boiling fractions from noncatalytic cracking [presumably thermal cracking] residues [31], seven lower-boiling distillate fractions from catalytically cracked oils [24, 26] [sources unspecified] and 19 higher-boiling residual fractions from catalytically cracked oils [27] [sources unspecified]. The samples (characterized by the percentage of distillation yields of <400°C or 400–500°C and benzo[*a*]pyrene content) produced high numbers of skin tumours [proportions of benign and malignant not given]. No correlation between distillation range, benzo[*a*]pyrene content, tumour incidence or time to appearance of the first tumour could be demonstrated for the higher-boiling fractions. A correlation between benzo[*a*]pyrene content and tumour yield was found for the distillates and between benzo[*a*]pyrene content and average tumour latency for the residues. [The Working Group noted that the author was not the original investigator of the study, which was conducted in the 1950s, the inadequate reporting and the lack of controls.]

A group of 120 female white outbred mice, three months old, received thrice weekly skin applications of about 30–40 mg of a heavy catalytic gas oil (heavy catalytically cracked distillate [26]; maximal number of paintings, 105) and were then observed for life. A group of 120 untreated mice from the same colony served as controls. Survival of treated animals was 24–334 days (average, 213 days) and 365 days (average) for controls. The first skin papilloma appeared at 15 days, after six applications; after eight applications, seven mice had papillomas. Treatment was discontinued for 22 days because of episodic disease, during which time all papillomas regressed. On resumption of treatment, the first papillomas

appeared after nine subsequent applications. A total of 97 animals had skin tumours (effective number of mice at time of appearance of the first tumour, 106); of these, 76 had malignant tumours. No skin tumour was observed in controls (effective number, 70). Precancerous lesions, including leukoplakia, dysplasia and papillomas, sometimes in combination, occurred in the oesophagus and forestomach of 55/106 treated animals. Tumours of the oesophagus were found in two treated animals and in none of the controls; forestomach tumours were found in 55 treated animals (51.8%) and in one (1.4%) control. An increased incidence of leukaemia was reported in treated animals (Karimov *et al.*, 1984, 1986). [The Working Group noted the high loss of a number of control animals and the lack of detailed histology, particularly of the leukaemias.]

Three groups of 25 male and 25 female C3H/Bd$_f$ mice, six to eight weeks of age, received thrice weekly applications of 50 μl of a sample of light catalytically cracked naphtha (API-976) [22], either undiluted or diluted 1:1 or 1:3 in acetone, on a 1-cm^2 area of dorsal skin for life or until a tumour persisted for two weeks, at which time the animal was killed. Results for the pooled sexes and three dose levels showed that, of 150 mice, 15 developed skin tumours (11 carcinomas, four papillomas). All but one of the tumours developed between 85 and 115 weeks. No tumour was observed in 100 untreated or in 100 acetone-treated controls of either sex (Witschi *et al.*, 1987). [The Working Group noted that the distribution of tumours among the various groups was not reported.]

A group of 40 C3H/HeJ mice [sex unspecified], seven weeks of age, received skin applications of undiluted samples of 'water-quench' or 'oil-quench' pyrolysis fuel oil (steam-cracked residues [34]) [dose unspecified] thrice weekly for life (19 months). Benzo[*a*]pyrene, the only component measured, was found in the samples at concentrations of 300–500 ppm (mg/l). Two concurrent control groups received skin applications of benzene (solvent controls for other concurrent experiments) or distilled water. In mice treated with water-quench pyrolysis fuel oil, 36 papillomas and 35 squamous-cell carcinomas of the skin developed in 37 effective[1] animals, and, in mice treated with oil-quench pyrolysis fuel oil, 34 papillomas and 34 carcinomas were observed in 39 effective animals. The mean latent period for papilloma development was 10.2–10.3 months and that for carcinoma development was 12.2–12.1 months for both samples. No skin tumour developed among the benzene- or distilled water-treated controls (Weil & Condra, 1977).

Rabbit: Two groups of ten rabbits [strain, sex and age unspecified] received thrice weekly skin applications of residues from thermal cracking [31] of two crude oils [dose unspecified] for 10–17 months. The group treated with fresh residue from Dolinsk crude oil (11.6% paraffins) developed skin tumours [number unspecified]. The group treated with residue from Grozny crude oil ('low' in paraffins) developed 'fewer' tumours than those treated with Dolinsk residue (Shapiro & Getmanets, 1962). [The Working Group noted the inadequate reporting of the data.]

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[1]The 'effective group' was defined by the authors as the number of mice given adequate exposure, calculated from the original number of mice started minus the number that died without a tumour. It is therefore a variable number that decreases by one with each non tumour death and is arbitrarily held constant after the time of the appearance of a tumour in the median tumour-bearing mouse.

(iii) *Effluents*

Mouse: Groups of male C57Bl mice, eight to ten weeks of age, received twice-weekly applications of a drop of test material on a 1-cm^2 area of upper dorsal skin for a total of 17 months, with a one-month interval after the first six months, due to toxicity. Group 1 (40 mice) was treated with undiluted extract of the effluent from a gravity oil separator at an oil refinery [source unspecified], containing 75% aliphatic and 20% aromatic hydrocarbons, collected through carbon for approximately one month in winter. Group 2 (40 mice) was treated for five months with the same sample diluted 1:1 with methyl ethyl ketone, then with undiluted sample as Group 1. The combined results showed an average survival of 13 months, an effective number of 59 mice at the time of the first tumour and a total of four papillomas and one carcinoma in 38 mice examined histologically. A control group of 25 mice was treated with methyl ethyl ketone for four months (treatment was discontinued due to high toxicity) and observed for a further 14 months. Average survival was five months, and no tumour was observed (Hueper & Ruchhoft, 1954). [The Working Group noted that the controls were inadequate and that the test samples were toxic.]

(*b*) *Other routes of administration*

Fish: Soxhlet (particulates) and XAD-2 resin (water) extracts of an oil refinery effluent, dissolved in acetone, were injected into eggs of rainbow trout (*Salmo gairdneri*, Kamloops strain), and trout that hatched from the injected eggs were necropsied at 12 or 24 months of age. Single injections of 6 μg Soxhlet extract or of 4 μg XAD-2 resin extract (equivalent to 200 μl effluent) from a sample taken in 1981, with or without preincubation with rat-liver S9 mix, yielded no tumour at necropsy [time unspecified] in groups of 30 trout; no tumour was found in two groups of 25 trout derived from eggs injected with 4.5 μg of Soxhlet extract from a sample taken in 1982 (Metcalfe & Sonstegard, 1985).

3.2 Other relevant data

(*a*) *Experimental systems*

Absorption, distribution, excretion and metabolism

Dermal absorption studies were performed with clarified slurry oil (catalytically cracked clarified oil [27]) containing radiolabelled surrogates representative of key chemical classes (carbazole, benzo[*a*]pyrene and phenanthrene) at a dose of 20 mg/cm^2 in four female Sprague-Dawley rats. Of the applied radioactivity, 48% of ^{14}C-carbazole, 5% of ^{3}H-benzo-[*a*]pyrene and 21% of ^{14}C-phenanthrene added to the clarified oil were recovered in urine and faeces within four days or remained in the carcass, excluding the pelt (Cruzan *et al.*, 1986).

Toxic effects

In a 13-week dermal toxicity study, groups of ten male and ten female Sprague-Dawley rats received applications of clarified slurry oil (catalytically cracked clarified oil [27]) on their clipped backs on five consecutive days per week at doses of 0, 8, 30, 125, 500 or 2000 mg/kg bw per day. Primary targets of this treatment were found to be the liver, thymus and

bone marrow. Liver enlargement, increases in plasma enzymes and liver-cell degeneration, necrosis and fibrosis were observed; some effects were evident at the lowest dose. The thymus was atrophic, and bone marrow showed erythroid hypoplasia at doses of ≥30 mg/kg bw per day, with accompanying anaemia (Cruzan *et al.*, 1986).

Twenty-one-day inhalation studies were performed with seven petroleum naphtha streams in groups of ten male and ten female or 20 male Sprague-Dawley rats. The treatment groups were exposed to vapours of the test materials for 6 h per day on five days per week for a total of 15 exposures. Three of the naphthas — light straight-run naphtha [3] (1.50, 5.13 or 14.56 mg/l analytical TWA), full-range alkylate naphtha [13] (vapour concentrations, 1.54, 4.92 or 15.31 mg/l) and thermally cracked naphtha [28, 29] (1.13, 3.48 or 9.88 mg/l analytical TWA) — produced severe renal toxicity, degenerative changes and tubular dilatation in male rats, but not in female rats. The lesions consisted of excessive hyaline droplet formation in the epithelium of the proximal convoluted tubules, degenerative changes in the proximal convoluted tubules of the renal cortex and tubular dilatation and necrosis at the cortico-medullary junction. Two of the naphthas — light reformed naphtha [16] (2.00, 5.85 or 20.30 mg/l analytical TWA) and polymerization naphtha [10] (1.04, 3.05 or 9.89 mg/l analytical TWA) — produced a small, dose-related incidence of renal tubular necrosis at the cortico-medullary junction in male rats. Treatment with light catalytically cracked naphtha [22] (0.20, 2.04 or 13.06 mg/l analytical TWA) produced mild nephrotoxicity in males; heavy reformed naphtha [17] (1.03, 2.81 or 10.20 mg/l analytical TWA) did not induce any adverse renal effect (Halder *et al.*, 1984).

Aromatic-rich C_9–C_{10} and C_{11}–C_{12} fractions from reformed naphtha [15] samples were studied in rats, monkeys and mice. Rats exposed by inhalation to 616 ppm of the C_9–C_{10} fraction for 18 h per day on seven days per week for 19 weeks developed cataracts after an additional two months without exposure. Rats exposed to the same concentrations for 18 h on three alternate days and set aside nine months for observation did not develop such ocular changes. Groups of three monkeys were exposed by inhalation to 50 or 200 ppm of the C_9–C_{10} fraction for 7 h per day on five days per week for a total of 90 exposures; no significant gross or microscopic change was observed. [The Working Group noted that details were not given as to which organs and tissues were examined.] Application of 0.10–0.15 g of the C_9–C_{10} fraction on the skin of male C3H mice three times per week for 50 weeks led to skin changes (inflammation, hyperkeratosis, atrophy) and kidney damage (cortical scarring, sclerosis, papillary necrosis). Similar treatment with the C_{11}–C_{12} fraction induced similar skin changes, but microscopic examination revealed no renal change (Nau *et al.*, 1966).

Effects on reproduction and prenatal toxicity

No data were available to the Working Group.

Genetic and related effects

Some studies on the mutagenicity in *Salmonella typhimurium* of vacuum distillates [19, 20] and hydrotreated oil (CAS 64742-57-0) were reported in a previous volume (IARC, 1984).

Dimethyl sulfoxide (DMSO) extracts of six petroleum hydrocarbon samples with boiling-points in the range of 260–538°C were examined for mutagenic activity by preincubation in *S. typhimurium* TA98 in the presence of an exogenous metabolic system from Aroclor 1254-induced rat-liver S9. A mixture of heavy catalytically cracked distillate [26] and catalytically cracked clarified oil [27] produced the highest (280 revertants/μl) response. Mutagenic effects were also seen with five other samples: light paraffinic distillate [19A]; intermediate catalytically cracked distillate [25]; two samples described as a hydrotreated heavy naphthenic distillate [20D]; and a mixture of chemically neutralized heavy naphthenic distillate [20C] and hydrotreated heavy naphthenic distillate [20D] (Blackburn *et al.*, 1984).

Using modified procedures, including DMSO extraction of petroleum oils dissolved in cyclohexane, the activity of 15 petroleum oil samples in *S. typhimurium* TA98 in the presence of an exogenous metabolic system from Aroclor 1254-induced Syrian golden hamster liver S9 was seemingly dependent on the refining process and the boiling range of the mixtures. At 5 μl/plate, the active samples were intermediate catalytically cracked distillate [25] and a mixture of heavy catalytically cracked distillate [26] and catalytically cracked clarified oil [27]. Some activity was also observed at 50 μl/plate of heavy paraffinic distillate [20A]; light paraffinic distillate [19A]; two samples described as hydrotreated heavy naphthenic distillates [20D]; chemically neutralized/hydrotreated heavy naphthenic distillate [20C, 20D], which was used as a positive control; four samples described as heavy naphthenic distillate [20B]; and two samples of straight-run kerosene [5]. No activity was observed with light straight-run naphtha [3], hydrotreated kerosene [5A] or vacuum residue [21] (Blackburn *et al.*, 1986). As reported in an abstract, hydrogenated pyrolysis gasoline [near 33] induced transformed foci in both BALBc/3T3 and C3H/10T1/2 cells (Butala *et al.*, 1985).

Methanol extracts of suspended particulates in effluents from three refineries in Ontario, Canada, were weakly active in *S. typhimurium* TA100 in the presence of an exogenous metabolic system from Aroclor 1254-induced rat-liver S9 but not in *S. typhimurium* TA98 or in either strain in the absence of S9. A methanol extract from one of the three refineries induced sister chromatid exchange in cultured Chinese hamster ovary cells in the presence of an exogenous metabolic system from Aroclor 1254-induced rat-liver S9 (Metcalfe *et al.*, 1985).

Elevated mutation rates were observed in *Zea mays* (waxy system) planted in native soil and in pots of clear artificial soil placed in the vicinity of a petroleum refinery in Illinois, USA (Lower *et al.*, 1983).

(*b*) *Humans*

Absorption, distribution, excretion and metabolism

No data were available to the Working Group.

Toxic effects

In an early study, workers engaged in paraffin refining at the beginning of the century were reported to have an acute acneform, papular skin eruption, often with severely

inflamed nodules and furuncles; a chronic stage with patchy dryness, hyperkeratosis, scaling and fissuring progressing to multiple warty growths was also reported (Davis, 1914). Several other studies have shown adverse skin effects (dermatosis, acne-like changes) among petroleum refinery workers (Žuškin & Žuškin, 1964; Bruevich, 1971; Ruszczak *et al.*, 1981a,b).

Sensitive biochemical and immunological markers of nephrotoxicity were compared in 53 male petroleum refinery workers and 61 age-matched unexposed males. In petroleum refinery workers employed for an average of 11 years (8-h personal TWA hydrocarbon exposure at the time of the study, 1–156 mg/m^3), no change was seen in urinary β-*N*-acetyl-D-glucosaminidase, β_2-microglobulin or retinol-binding protein, in glomerular filtration or in levels of serum circulating immune complexes. There were slight elevations in albuminuria and in mean urinary excretion of a renal antigen (BB-50) in the exposed group and slightly higher titres of antilaminin antibodies in five exposed workers, but no clinically significant renal abnormality was seen (Viau *et al.*, 1987).

Effects on reproduction and prenatal toxicity

Of 408 women employed in petroleum processing plants in the USSR, 27.7% reported disruption of menstrual function, compared to 10.9% of 302 women employed in a garment factory (Sukhanova & Melnikova, 1974). Frequency of menstrual dysfunction increased with increasing duration of employment and was highest among women who worked in the technological laboratories and were continuously exposed to petroleum products at high concentrations. The most common forms of menstrual dysfunction reported by the petroleum processing workers were hypomenorrhoea and premenstrual syndrome. [The Working Group noted that the methods were not well described, and that the ages of all subjects were not given.]

Menstrual and child-bearing functions of 894 women employed in three petroleum processing plants in the USSR were compared with those of 500 women who worked in a machine building plant (Shamsadinskaya *et al.*, 1976). The age distribution was reported to be comparable in the two groups. At the time of interview, 29.7% of the women employed in petroleum processing and 16.7% of the machine factory workers reported gynaecological problems. The most common disturbances reported were 'inflammatory disease' and disturbances of the menstrual cycle. A higher proportion of those employed in petroleum processing were reported to be sterile, and they had a greater rate of spontaneous abortion. [The Working Group noted that the methods were not well described.]

In a study of fetal loss among 89 wives of workers employed in a waste-water treatment plant at a petroleum refinery in Louisiana, USA (Anon., 1985), pregnancy histories were obtained by interviewing the wives, and employment histories for the men were obtained from company records (Morgan *et al.*, 1984). Each pregnancy was classified by the exposure of the father to the waste-water treatment process during the pregnancy (unexposed; E1, any time prior to conception; E2, within four months prior to conception; and E3, three months after conception). The three 'exposed' categories overlapped; thus, a pregnancy could be classified into all three on the basis of the paternal work history. For each category, rates of fetal loss (miscarriage or stillbirth) were calculated. Odds ratios were calculated by dividing

fetal loss rates among the exposed pregnancies by the fetal loss rate for unexposed pregnancies. The odds ratios for E1, E2 and E3 (95% confidence interval) were 2.1 (0.9–4.5), 2.9 (1.3–6.3) and 2.9 (1.4–6.4), respectively. The wives of crafts (maintenance) workers in waste-water treatment experienced a higher risk (odds ratio, 4.9) of fetal loss than did those of production workers (odds ratio, 0.85). [The Working Group noted that caution should be exercised in interpreting the results of this study, since the authors were uncertain about whether their data represented statistical artefact, reporting bias or biological reality.]

A cross-sectional evaluation of sperm concentration and abnormal morphology was conducted among men who had worked in the same waste-water treatment plant described above during the six months prior to the beginning of the study (Rosenberg *et al.*, 1985). A total of 68% of the exposed workers participated in the study (n = 42). Refinery workers who did not work in waste-water treatment were chosen as controls, and the participation rate was 44% (n = 74). A stepwise regression model was used to compare outcomes controlling for age, sexual abstinence, other occupational exposures, use of prescribed drugs, smoking, marijuana use, alcohol consumption and other factors. No significant difference between sperm concentration or the proportion of abnormal morphology was found between the exposed and unexposed workers. [The Working Group noted that slightly over half of the 'unexposed' group (n = 38) were process or mechanical workers in the refinery and could have had other significant occupational exposures that were not taken into account in the analyses.]

Genetic and related effects

As reported in an abstract, an increase in the incidence of sister chromatid exchange was observed in about half of 22 workers with at least ten years of employment in petroleum refining as compared to 18 unexposed individuals controlled for smoking habits and use of medications (Carrano *et al.*, 1980).

In an extensive cytogenetic study in China, both chromosomal aberrations and sister chromatid exchange were examined in peripheral blood lymphocytes of 180 workers in a petrochemical plant and 180 matched controls. Among 30 persons working in a catalytic cracking unit, there was no significant difference in either of the two parameters studied; however, a group of 30 persons working in the sewage-treatment unit of this catalytic cracking unit showed significantly higher mean sister chromatid exchange levels ($p < 0.01$) and increased prevalences of chromatid-type aberrations ($p < 0.001$) and of gaps ($p < 0.001$), as compared to the control group. [The Working Group noted that the increase in the frequency of chromatid-type aberrations was also significant ($p < 0.01$) for workers in the sewage-treatment unit of the phenolacetone plastic unit of the petrochemical plant.] A significant effect on the frequency of sister chromatid exchange was observed among smokers in both the control and worker groups (Zhou *et al.*, 1986). [The Working Group noted that the analysis of chromosomal aberrations was performed in 72-h cultures.]

3.3 Epidemiological studies and case reports of carcinogenicity to humans

(*a*) *Cohort studies*

The cohorts of refinery workers reviewed below had mortality rates for all cancers combined that were consistently lower (10-20%) than those in the general population. It is well recognized that occupational cohorts tend to have below-average mortality, both from all causes and from various major categories of specific causes. These deficits are, typically, manifestations of a health status-related selection process, referred to as the 'healthy worker effect'. The consistent deficit in cancer mortality in refinery workers, when compared with the general population, is compatible with this effect.

In view of this overall deficit in cancer mortality in refinery workers, conventional statistical evaluation of site-specific standardized mortality ratios (SMRs) may be conservative. That is, comparison of the SMR with an 'expected' value of 1.0 derived from the general population — rather than with the underlying SMR for all cancers — may underestimate the true magnitude of any occupation-related increase in risk for specific cancers.

The Working Group also noted the limitations inherent in proportionate mortality analyses in which an over- or underrepresentation of some causes of death influences the magnitude of the proportionate mortality ratio (PMR) for other causes.

The available cohort studies are summarized in Table 11.

(i) *USA*

A series of studies of employees of the Exxon (also known as Humble and Esso) Company in the USA began with a report published in 1940 describing cancer mortality and incidence among male employees of a petroleum refining company who were enrolled in a sickness benefit plan between 1933 and 1938 (Gafafer & Sitgreaves, 1940). A total of 70 cases of cancer were observed among men who contributed about 60 000 person-years of risk during the study period. There were 46 deaths from cancer; 19 were stomach cancer and 13 were cancers of other abdominal organs. The authors noted that the proportion of digestive cancer deaths observed in the study group (69.6%) was higher than that observed in the general US population (57.8%); however, this comparison was not adjusted for age.

Cancer mortality among 15 437 employees of the Humble Oil Company in the Gulf Coast states was examined for a 29-year period ending in 1963 (Baird, 1967). This study included plants previously studied by Gafafer and Sitgreaves (1940), Hendricks *et al.* (1959) and Wade (1963) and consisted of workers in exploration, pipeline, production, refining and sales operations. The proportion of cancer deaths for the period 1935–55 among Humble Oil employees was 12.1% compared with 13.8% for the USA in 1945, unadjusted for age. The proportion of cancer deaths among the 6239 company employees who had worked in petroleum refining was 11.2%. The author concluded that there was no relative excess of cancer deaths among Humble Oil Company employees. [The Working Group noted that there was no adjustment for age, sex or race, and that cancer mortality was not presented by site, length of service or work category (e.g., production, maintenance, office workers).]

Table 11. Cohort studies of petroleum refinery workers

Reference	Study subjects[a]	Comparison population	Period of follow-up	Occupation/ exposure	Cancer site (cause of death)	Number of deaths observed	SMR[b]	Comments
USA[c]								
Hendricks *et al.* (1959)	82 wax pressmen, Exxon, Baton Rouge, LA	US men	1937–56	Wax pressmen	Scrotum (skin)	11		Incidence rate of 806/100 000 observed *vs* 0.15/100 000 expected
Hanis *et al.* (1982)	8666 workers at Exxon, Baton Rouge, LA (refinery and chemical plant)	US general population	1970–77		All causes	1199	0.92*	
					All cancer	249	0.92	
					Pancreas	23	1.5	
					Kidney	9	1.6	
				Operators, mechanics, labourers	Kidney	9	2.1	
				Men hired before 1956	Kidney	9	1.6	
					Pancreas	23	1.5	
Hanis *et al.* (1985a)	15 437 employees of Exxon, Baton Rouge, LA, Bayway/Bayonne, NJ, & Baytown, TX	US general population	1970–77	Refinery and chemical plant workers	All causes	3198	0.91*	Cancer death rates were higher among 'potentially exposed' than 'unexposed' workers (Hanis *et al.*, 1985b)
					All cancer	666	0.94	
					Liver/gallbladder/ bile duct	15	1.3	
					Kidney	22	1.4	
					Brain	15	1.2	
				Baytown, TX	Bone	7	1.6	
					Kidney	6	1.2	
					Brain	6	1.3	
				Bayway/Bayonne, NJ	Stomach	16	1.4	
					Large intestine	32	1.4	
					Lung	77	1.2	
					Kidney	7	1.5	
				Baton Rouge, LA	Pancreas	23	1.5	
					Kidney	9	1.6	

Table 11 (contd)

Reference	Study subjects[a]	Comparison population	Period of follow-up	Occupation/ exposure	Cancer site (cause of death)	Number of deaths observed	SMR[b]	Comments
Thomas *et al.* (1980)	1722 white male OCAW members in TX	US men	1947–77	Petroleum refinery chemical plant workers	All cancer	394	1.3*	Proportionate mortality study including deaths only among active Union members
					Digestive tract	111	1.2*	
					Respiratory tract	134	1.3*	
					Skin	14	1.9*	
					Brain	25	1.8*	
Thomas *et al.* (1982a,b)	2509 male OCAW members employed by 3 TX oil refineries	US men	1943–79		All cancer	553	1.2*	Proportionate mortality study including deaths among active and retired Union members
					Stomach	48	1.5*	
					Pancreas	37	1.4*	
					Lung	157	1.1	
					Skin	13	1.8*	
					Prostate	46	1.4*	
					Kidney	15	1.4	
					Brain	28	2.2*	
					Leukaemia	33	1.8*	
					Multiple myeloma	9	2.0	
Thomas *et al.* (1984)	Male OCAW members employed by 3 TX oil refineries	Internal comparison	1943–79	Intraplant pumping and transport of bulk liquids	Brain	7	2.8	Odds ratios from nested case-control study (Thomas *et al.*, 1982a,b)
				Lubricating oil	Stomach	19	1.7	
				Maintenance work	Stomach	47	4.5	
				Treating	Leukaemia	6	1.6	
				Boiler makers	Leukaemia	5	1.5	
Divine *et al.* (1985)	19 077 white men employed 5+ years by Texaco	US white men	1947–77	Refinery, petro-chemical, research	All causes	4024	0.75*	[Includes workers from refinery A (Thomas *et al.*, 1980, 1982a,b, 1984)]
					All cancer	767	0.75*	
					Pancreas	62	1.1	
					Brain	31	1.1	
					Leukaemia	48	1.2	Significant deficits of cancers of the stomach, large intestine, lung and bladder
					Other lymphatic cancer	25	1.2	
					Benign neoplasms	20	1.5	

Table 11 (contd)

Reference	Study subjects[a]	Comparison population	Period of follow-up	Occupation/ exposure	Cancer site (cause of death)	Number of deaths observed	SMR[b]	Comments
Divine & Barron (1986)	18 798 white men employed 5+ years by Texaco	US white men	1947–77	Refinery operators, >1 year	Brain	19	1.2	Includes all men studied by Divine *et al.* (1985) for whom work histories were available
					Leukaemia	31	1.4	
					Other lymphatic cancer	16	1.3	
					Benign neoplasms	9	1.2	
				Maintenance work, >5 years	Pancreas	30	1.4	
					Kidney	12	1.3	
					Skin	8	1.3	
					Brain	13	1.3	
					Hodgkin's disease	6	1.4	
					Other lymphatic cancer	13	1.6	
					Benign neoplasms	8	1.6	
				Laboratory worker, >5 years	Brain	6	2.2	
					Benign neoplasms	3	2.6	
				Pipe fitters and boiler makers, >5 years	Leukaemia	12	2.9*	
Wen *et al.* (1983)	15 095 men employed at least 1 day at Gulf, Port Arthur, TX	US men	1937–78		All causes	4269	0.84*	[Includes workers from Refinery B (Thomas *et al.*, 1980, 1982a,b, 1984)]
					All cancer	839	0.96	
					Bone	11	2.1*	
					Skin	16	1.2	Significant deficits of cancers of the oesophagus, liver, bladder and rectum and of lymphosarcoma and reticulosarcoma
					Kidney	22	1.1	
					Hodgkin's disease	16	1.5	
					Leukaemia	38	1.1	
					Other lymphatic cancer	20	1.2	

Table 11 (contd)

Reference	Study subjects[a]	Comparison population	Period of follow-up	Occupation/ exposure	Cancer site (cause of death)	Number of deaths observed	SMR[b]	Comments
				White blue-collar workers	Pancreas	37	1.1	
					Lung	185	1.1	
					Skin	13	1.2	
					Prostate	54	1.2	
					Kidney	18	1.2	
					Eye	2	3.4	
					Leukaemia	32	1.3	
					Hodgkin's disease	9	1.1	
					Bone	9	2.3*	
Wen *et al.* (1984b)	12 526 white men employed at least 1 day at Gulf, Port Arthur, TX	US white men	1937–78	Actively employed workers	Bone	3	1.6	Includes white men studied by Wen *et al.* (1983)
					Kidney	8	1.4	
					Leukaemia	14	1.6	
				Terminated workers before retirement	Lung	87	1.2	
					Bone	3	2.2	
					Skin	7	1.6	
					Prostate	16	1.3	
					Hodgkin's disease	6	1.6	
				Retirees	Lung	77	1.2	
					Bone	3	2.5	
					Skin	4	1.2	
					Prostate	37	1.1	
					Kidney	7	1.3	
					Brain	5	1.2	
					Leukaemia	16	1.6	
					Other lymphatic cancer	8	1.6	
Wen *et al.* (1982)	17 251 male and female workers employed at least 1 day at Gulf, Port Arthur, TX	US general population	1935–79	Men employed 20+ years	Brain	20	1.4	Includes all men studied by Wen *et al.* (1983, 1984b)

Table 11 (contd)

Reference	Study subjects[a]	Comparison population	Period of follow-up	Occupation/ exposure	Cancer site (cause of death)	Number of deaths observed	SMR[b]	Comments
Wen *et al.* (1985)	1008 men who worked in the lubricating department of Gulf, Port Arthur TX, refinery	US men	1935–78		Bone	3	10.3*	SMR for prostate cancer increased with duration employed
					Stomach	5	1.2	
					Pancreas	5	1.7	
					Prostate	8	1.8	
					All lymphopoietic cancer	6	1.3	
				Not exposed to solvent dewaxing	Prostate	7	1.9	
Wong & Raabe (1989)	6139 employees of Mobil, Beaumont, TX, refinery	US general population	1945–79		All causes	1582	NR	[Includes workers from refinery C (Thomas *et al.*, 1980, 1982a,b, 1984)]
					All cancer	346	0.96	
					Pancreas	23	1.1	
					Skin	7	1.4	SMR for lymphatic and haematopoietic malignancies increased with duration of employment; significant deficit of digestive tract cancer
					Prostate	36	1.1	
					Brain	9	1.1	
					Lympho- and reticulosarcoma	10	1.5	
					Leukaemia	23	1.7*	
					Other lymphatic cancer	12	1.6	
				Men employed >30 yrs	Leukaemia	NR	2.4*	
				20–39 yrs since first employment	Leukaemia	NR	2.1*	
	4263 employees of Mobil, Paulsboro, NJ, refinery	US general population	1946–79		All causes	1164	NR	SMR for prostate cancer increased with duration employed
					All cancer	243	0.91	
					Prostate	28	1.4	
					Other lymphatic cancer	8	1.4	
				Men employed 20+ yrs	Prostate	NR	1.6*	
	1621 employees of Mobil, Torrance CA, refinery	US general population	1959–78		All causes	250	NR	
					All cancer	56	0.80	

Table 11 (contd)

Reference	Study subjects[a]	Comparison population	Period of follow-up	Occupation/ exposure	Cancer site (cause of death)	Number of deaths observed	SMR[b]	Comments
McCraw *et al.* (1985)	3976 white male employees of Shell Oil, Wood River, IL	US white men	1973–82		All causes	640	0.76*	
					All cancer	161	0.91	
					Leukaemia (acute myeloid)	14(8)	2.1*(3.9*)	
					Other lymphatic cancer	6	1.3	
Wong *et al.* (1986)	14 179 workers at Chevron, Richmond, CA & El Segundo, CA	US general population	1950–80		All causes	2292	0.72*	Significant deficits of cancers of the buccal cavity and pharynx, digestive system (large intestine and pancreas) and lung
					All cancer	462	0.76*	
					Brain	22	1.3	
					Lympho- and reticulosarcoma	17	1.3	
					Other lymphatic cancer	20	1.4	
				Maintenance workers	Brain	14	1.4	
				Operators	Brain	7	1.3	
Nelson *et al.* (1987)	9192 white male Amoco employees	US white men	1970–82		All causes	921	0.73*	Significant deficits of respiratory tract cancer and lymphopoietic cancer
					All cancer	259	0.84*	
					Digestive tract	92	1.2	
					Skin	11	2.0*	
				Operators	Stomach	9	2.1	
					Large intestine	12	1.2	
					Rectum	5	1.8	
				Maintenance workers	Skin	8	3.8*	
					Rectum	5	1.7	
				Routine refinery	Skin	10	2.7*	
Decouflé *et al.* (1983)	259 men employed in a Conoco refinery then petro-chemical plant	US white men	1947–77		All causes	63	0.97	
					All cancer	10	0.81	
					Lymphopoietic system	4	[3.8]*	

Table 11 (contd)

Reference	Study subjects[a]	Comparison population	Period of follow-up	Occupation/ exposure	Cancer site (cause of death)	Number of deaths observed	SMR[b]	Comments
Kaplan (1986)	19 991 men employed in 17 US refineries	US men	1962–80		All causes	3349	0.78*	Study could overlap with any of the other US studies; significant deficits of cancers of buccal cavity and pharynx, lung and bladder
					All cancer	793	0.87*	
					Other lymphatic cancer	30	1.3	
Schottenfeld *et al.* (1981)	55 007 white male employees of 19 US refineries	US white men	1977–79		All causes	393	0.56*	Study could overlap with any of the other US studies
					All cancer	127	0.75*	
					Brain	8	1.6	
					Lymphocytic leukaemia	7	2.7*	
					Larynx	12	1.3	Incidence
					Brain	9	1.3	
					Melanoma	13	1.3	
Canada								
Thériault & Provencher (1987)	1207 men employed 5+ yrs in a Shell Oil refinery in Québec	Québec men	1928–81		All causes	175	0.86*	Significant deficit of lung cancer
					All cancer	39	0.80	
					Brain	4	2.1	
					Stomach	7	1.6	
				<20 years' employment	Brain	4	5.2*	
Hanis *et al.* (1979)	5731 male active and retired refinery employees of Imperial Oil Ltd employed 5+ years	9301 non-refinery workers employed 5+ years	1964–73		Oesophagus and stomach	18	1.2	Standardized mortality ratios
					Intestine and rectum	28	2.0	
					Other digestive tract	21	1.8*	
					Trachea, bronchus and lung	43	1.2	
					Prostate	15	1.3	
					Bladder and kidney	10	1.2	

Table 11 (contd)

Reference	Study subjects[a]	Comparison population	Period of follow-up	Occupation/ exposure	Cancer site (cause of death)	Number of deaths observed	SMR[b]	Comments
	8612 exposed, 2202 moderately exposed to petroleum or its products	4218 unexposed	1964–73	Moderately exposed	Lymphopoietic system	4	1.9	Standardized mortality ratios; age-adjusted mortality rates for cancers of lung and of oesophagus and stomach increased with duration of employment
				Exposed	Oesophagus and stomach	28	3.3*	
				Exposed	Lung	67	1.9*	
UK								
Rushton & Alderson (1980, 1981a); Alderson & Rushton (1982)	34 781 workers at 8 UK petroleum refineries	Men in England, Wales and Scotland	1950–75		All causes	4406	0.84*	Significant deficit overall of lung cancer mortality
					All cancer	1147	0.89*	
					Nasal cavity and sinus	7	2.2*	
					Melanoma	14	2.2*	
				Operators	Oesophagus	13	[1.7]	
				Operators refin. B	Intestine	6	[2.3]	
				Operators refin. F	Rectum	5	[2.2]	
				Labourers	Stomach	56	[1.4]*	
				Labourers refin. F	Stomach	21	[1.7]*	
				Labourers refin. J	Stomach	20	[1.7]*	
				Riggers refin. J	Stomach	7	[3.9]*	
				Fire and safety workers refin. J	Stomach	6	[2.4]*	
				Scientists	Intestine	6	[3.1]*	
				Scientists refin. J	Intestine	3	[4.9]*	
Rushton & Alderson (1981b)	Employees of 8 UK oil refineries who died from leukaemia	Men in England, Wales and Scotland	1950–75		Leukaemia	30	0.95	Leukaemia cases from Rushton & Alderson (1980, 1981a); Alderson & Rushton (1982)
					Lymphatic leukaemia	2	3.0	
					Myeloid leukaemia	5	11.9	
					Acute monocytic leukaemia	4	4.3	

Table 11 (contd)

Reference	Study subjects[a]	Comparison population	Period of follow-up	Occupation/ exposure	Cancer site (cause of death)	Number of deaths observed	SMR[b]	Comments
Alderson & Rattan (1980)	446 men employed in de-waxing plants in 2 refineries	Men in England, Wales and Scotland	1950–75		Buccal cavity and pharynx	2	15.4*	
					Digestive tract	4	1.3	
Sweden								
Malker *et al.* (1986)	Men employed in petroleum refineries from Swedish census	Swedish men	1961–79		Gall-bladder	6	3.8*	Incidence
Norell *et al.*, (1986)	Men employed in petroleum refineries from Swedish census	Swedish men	1961–79		Pancreas	10	1.3	Incidence

[a]OCAW, Oil, Chemical and Atomic Workers' Union

[b]*, statistically significant at the 5% level; NR, not reported

[c]Several studies covered the same US company; Exxon is described by Hendricks *et al.* (1959) and Hanis *et al.* (1982, 1985a,b); Texaco by Divine *et al.* (1985), Divine and Barron (1986) and part of Thomas' studies; Gulf by Wen *et al.* (1982, 1983, 1984a,b, 1985, 1986) and part of Thomas' studies; Mobil (Beaumont) by Wong and Raabe (1989) and part of Thomas' studies; Mobil (Paulsboro) by Wong and Raabe (1989); Mobil (Torrance) by Wong and Raabe (1989); Shell by McCraw *et al.* (1985); Chevron by Wong *et al.* (1986); Amoco by Nelson *et al.* (1987); and Conoco by Decouflé *et al.* (1983)

An elevated risk for cancer of the scrotum was observed among wax pressmen who had been employed for ten years or more during the period 1 January 1937 through 31 December 1956 in an Esso oil refinery (Exxon) in Baton Rouge, LA, where paraffin wax was manufactured (Hendricks *et al.*, 1959; Lione & Denholm, 1959). Cancer incidence among all workers in the refinery was compared with that for the US general white male population at the midpoint of the 20-year study period (Hendricks *et al.*, 1959). Although the overall cancer incidence rate for the refinery workers in general did not exceed that for the USA, wax pressmen who had worked for ten or more years had an overall cancer incidence rate that was more than four times that of US men. Among the 82 pressmen, the rate of scrotal cancer was 806/100 000 (11 cases) compared to a rate of 0.15/100 000 expected on the basis of the experience of US white men. In addition, three cases of stomach cancer and three of cancers at other digestive sites were observed among the wax pressmen; however, expected numbers were not calculated. The scrotal cancer cases occurred only among men who had had skin contact with crude wax saturated with aromatic oils.

A cohort of 8666 workers at the Exxon Baton Rouge, LA, petroleum refinery and chemical plant, some of whom may have been included in the study of Baird (1967), comprised workers who had been employed for at least one month between 1 January 1970 and 31 December 1977 and retirees who were alive on 1 January 1970 (Hanis *et al.*, 1982). About 24% of the employees had begun work at the refinery prior to 1940, and another 24% in 1940-44; however, no information was presented on duration of employment. The mortality experience of the cohort from 1970 to 1977 was compared with that of the total US population, and SMRs adjusted for sex, age, calendar period and race were calculated; 835 employees (9.6%) were lost to follow-up; 85% of those lost were under 40 years of age. There was a significant deficit of all causes of death. The SMRs for pancreatic and renal cancers were elevated, but not significantly so. The renal cancer cases were seen only among employees who had worked as operators, mechanics or labourers and had been hired before 1956. [The Working Group noted the short follow-up period, and that there was no analysis by duration of employment. All of the persons studied are included in the following report.]

A cohort mortality study of employees of three Exxon refineries and chemical plants in Baton Rouge, LA, Bayway/Bayonne, NJ and Baytown, TX, included 15 437 employees who had worked for at least one month during the period 1 January 1970 to 31 December 1977 and followed through 1977, and 6261 retired employees who were alive on 1 January 1970 (Hanis *et al.*, 1985a). More than 50% of the workers had first been employed in 1949 or earlier; 98.7% of workers were followed up. The mortality experience of the Exxon employees was compared with that of the total US population, adjusting for age, sex, race and calendar period. The SMR for all causes of death was significantly less than 1.0. Slight excess mortality was reported for cancers of the liver/gall-bladder/bile ducts, kidney and brain (ICD8 191, 192), primarily among employees hired prior to 1956. At the Baytown, TX, plant, there were elevated SMRs for cancers of the bone, kidney and brain, but none was significant. Among workers at the Bayway/Bayonne, NJ, plant, SMRs were elevated for cancers of the stomach, large intestine, lung and kidney. No analysis was shown by job class (blue-collar, white-collar) or job title. [The Working Group noted the short period of follow-up for many of the employees.]

In further analyses of the Exxon refineries and chemical plants in Baton Rouge, LA, Baytown, TX, and Bayway/Bayonne, NJ, mortality was examined by occupation and work site (Hanis *et al.*, 1985b). Directly adjusted death rates for each subgroup of interest and for the total US population were calculated using the age, sex, race and calendar year distribution of the total cohort as a standard; thus, direct comparisons could be made between mortality rates in cohort subgroups and in the US population by calculating ratios of the directly adjusted rates. Workers were classified as having been 'potentially exposed' or 'unexposed' on the basis of their longest-held job. The 'exposed' category included those who had worked as process operators, mechanical workers and labourers (75% of the study population); while the 'unexposed' category included primarily white-collar office workers (22% of the population). Cause-specific cancer rates were higher among potentially exposed workers than among the unexposed for every cancer site except brain, but none of the site-specific rate ratios was significantly different from 1.0. Directly adjusted death rates were consistently greater than those for the total US population only for renal cancer in each of the three plants. The death rates for pancreatic cancer were higher than the US rates among employees at the Baton Rouge and Baytown plants only, and elevated rates of large intestinal cancer occurred at the Baytown and Bayway/Bayonne plants.

A series of investigations of mortality has been performed among members of the Oil, Chemical and Atomic Workers international union (OCAW) in Texas (Thomas *et al.*, 1980, 1982a,b, 1984). In all of these reports, proportionate mortality among male members of the OCAW was compared with that among US men, adjusting for age, race and calendar period.

The first report concerned 3105 Union members in Texas whose deaths in 1947–77 while actively employed were reported to OCAW and whose death certificates could be located (90%; Thomas *et al.*, 1980). Of the white OCAW members, 1722 had held blue-collar jobs in petroleum refineries and petrochemical plants, primarily in maintenance and production (Thomas *et al.*, 1982a), and had significant excess frequencies of deaths from cancers of the digestive and respiratory systems, skin and brain (ICD8 191, 192).

Subsequent analyses were limited to three petroleum refineries located in the Beaumont/Port Arthur area of the Texas Gulf Coast (Thomas *et al.*, 1982a,b, 1984) and included 1194 retired workers as well as those who had died while actively employed between 1943 and 1979. Among 2509 deceased men who had been employed by the three refineries combined (Thomas *et al.*, 1982a,b), the adjusted PMRs using national rates for all causes of death were significantly elevated for all cancers as well as for cancers of the stomach, pancreas, skin (ICD8 172, 173), prostate and brain (ICD8 191, 192) and for leukaemia. Nine deaths from multiple myeloma were observed and 4.6 were expected, but the PMR was not significant. When national cancer rates were used to calculate proportionate cancer mortality ratios (PCMRs), these ratios were also elevated but significantly so only for brain and leukaemia in whites. When county cancer mortality rates were used, none of the PCMRs was significantly raised. A detailed examination of brain tumour mortality in whites indicated that OCAW members had had elevated frequencies of mortality from benign and unspecified tumours of the brain as well as those specified on death certificates as malignant. [The Working Group noted that, of the 2509 deaths studied,

1161 had also been included in the previous study (Thomas *et al.*, 1980) and that the completeness of records for retired workers is unknown.]

In a nested case-control study, complete work histories of decedents with brain cancer, stomach cancer and leukaemia (31, 52 and 34 cases, respectively) were compared with those of a (1:3) control series of decedents matched by age, sex, date of death, date of first union membership and refinery (Thomas *et al.*, 1984). Cancer-specific relative risks by occupational category were estimated by calculating maximum likelihood estimates of odds ratios using a procedure for matched data. An elevated risk for brain cancer was seen among men who had been involved in intraplant pumping and transport of bulk liquids; however, the median duration of employment in these jobs was shorter for the cases than for the controls. The risk for stomach cancer mortality was elevated among men who had worked in the manufacture of lubricating oils and in refinery maintenance work. Mortality from leukaemia was slightly elevated among men who had worked in operations that involved alkylation, polymerization, the reduction of sulfur constituents of petroleum products and the blending of additives (treating category) and among men who had worked as boiler makers. There was no significant trend by duration of employment for any work category.

In a retrospective cohort study (Divine *et al.*, 1985), standardized mortality among 19 077 white men who had been employed for a minimum of five years by the Texaco company in refinery, petrochemical or research facilities was determined for the period 1 January 1947 to 31 December 1977. Of these, 14 609 (76.6%) were alive on 31 December 1977, and 4024 (21.1%) were dead, and for 444 (2.3%) vital status was unknown. Death certificates were not obtained for 152 (3.8%) of the decedents. Expected mortality was calculated using rates for US white men, adjusting for age and calendar period. There was no significant excess of mortality for any cancer site; however, SMRs were slightly elevated for cancers of the pancreas and brain, leukaemia, cancer of 'other lymphatic tissues' and a category of benign neoplasms which included brain tumours. [The Working Group noted that the cohort included workers in refinery, petrochemical and research facilities; that data were not shown by duration of employment or time since first employment; and that 1008 workers at refinery A in the study of Thomas *et al.* (1980, 1982a,b, 1984) who had died between 1947 and 1977 were included in this study.]

A second investigation of mortality among Texaco employees included 18 798 white men from the earlier analyses for whom complete work histories were available (Divine & Barron, 1986). The cohort was followed for an average of 19 years. Among men who had worked as refinery operators for more than one year, there were nonsignificant excesses of brain cancer, leukaemia, cancer of other lymphatic tissues (ICD7 202, 203, 205) and benign neoplasms; these excesses were smaller in men with five or more years' employment as an operator. Men who had been employed as maintenance workers for at least five years had elevated SMRs for cancer at the following sites: pancreas, kidney, skin (ICD7 190), brain (ICD7 193), Hodgkin's disease, cancer of other lymphatic tissues and benign neoplasms. Among subjects who had worked as laboratory workers for at least five years, there was a slight excess of mortality from brain cancer (ICD7 193) and benign neoplasms (ICD7 210–239). The only significant cancer excess noted in this study was for leukaemia among men employed as pipe fitters and boiler makers for more than five years. No consistent

pattern of increasing mortality was seen by time since first employment or duration of employment for brain tumours among laboratory workers or leukaemia among pipe fitters and boiler makers.

In a cohort study at the Gulf Port Arthur, TX, refinery, all 15 095 men employed for more than one day between 1 January 1937 and 1 January 1978 were followed for vital status on 1 January 1978. Of these, 972 (6.4%) were lost to follow-up; death certificates were not available for 277 (6.5%) of the 4269 male decedents. The average follow-up was 24.7 years. Expected mortality was determined from rates in the US general population, adjusted for age, race and calendar period. Excesses were seen for cancers of the bone, skin, kidney, Hodgkin's disease, leukaemia and cancer of 'other lymphatic tissue'. Only the result for cancer of the bone was significant. When white, blue-collar employees were evaluated separately, SMRs greater than 1 were observed for cancers of the pancreas, lung, bone, skin, prostate, eye and kidney, and for Hodgkin's disease and leukaemia; however, only the SMR for cancer of the bone was significant (Wen *et al.*, 1983). [The Working Group noted that the ICD8 code cited to describe the category 'cancer of other lymphatic tissue' is probably in error and should have been reported as 202–203, 208.]

SMRs for kidney cancer were examined in a separate publication by time since first employment and duration employed; no trend was observed (Wen *et al.*, 1984a).

A separate analysis with regard to employment status (retired, terminated before retirement age, actively employed) was performed on the white men in this cohort. The number of such employees was 12 526; 730 (5.8%) were lost to follow-up, 724 of whom were in the terminated group in which 88% were followed-up successfully (Wen *et al.*, 1984b). Among those who had been actively employed, nonsignificant excess mortality was observed for cancers of bone and kidney and for leukaemia. Among white men who had terminated their employment at the refinery prior to retirement, there was excess mortality from cancers of the lung, bone, skin (ICD8 172, 173) and prostate and from Hodgkin's disease. Mortality among retired men was elevated for cancers of the lung, bone, skin (ICD8 172, 173), prostate, kidney and brain, leukaemia and cancer of 'other lymphatic tissues' (ICD8 202–203, 208). None of the results was significant. Data were not shown by duration of employment, but retirees were assumed to have worked a minimum of 15 years.

In an interim report on 15 698 male and 1823 female workers employed on 15 June 1935 and followed until 31 December 1979 (4766 deaths; 87% follow-up), nonsignificant excess mortality from brain tumours (malignant, benign and unspecified combined) was observed among men who had been employed for 20 or more years (Wen *et al.*, 1982). No variation in SMR was reported for specific cancer sites by calendar period of employment (Wen *et al.*, 1986). [The Working Group noted that the 882 employees at refinery B in the study of Thomas *et al.* (1980, 1982a,b, 1984) who had died between 1947 and 1977 were included in the studies of Wen *et al.*]

Mortality among 1008 men who had worked at any time between 15 June 1935 and 1 January 1978 in the lubricating oil department at the Gulf Port Arthur, TX, refinery was examined separately (Wen *et al.*, 1985). In this department, lubricating oil was manufactured, and wax was separated from the product using a solvent dewaxing process. A mixture

of benzene and methyl ethyl ketone was used in the dewaxing process until 1945, when toluene replaced the benzene. There was a significant excess of bone cancer (SMR, 10.3) based on three deaths; nonsignificant excesses were seen for cancers of the stomach, pancreas and prostate and for all lymphopoietic cancer. Mortality for cancer of the prostate increased with duration employed and was excessive only after 20 years of employment. Seven of the eight prostatic cancer deaths occurred among men who had worked in the lubricating oil department but had not been involved in the solvent dewaxing process.

Refinery C studied by Thomas *et al.* (1980, 1982a,b, 1984) was included in a report by Wong and Raabe (1989). A cohort of all individuals employed at the Mobil Beaumont, TX, petroleum refinery for at least one year between 1 January 1945 and 1 January 1979 was comprised of 6139 employees (1582 deaths; 123 354 person-years). Also included in this report were the Mobil refineries in Paulsboro, NJ (1946-79: number of employees, 4263; number of deaths, 1164) and Torrance, CA (1959-78: number of employees, 1621; number of deaths, 250). Observed mortality in the study cohorts was compared with that expected on the basis of rates for the general US population, adjusted for age, calendar period, sex and race. At the Beaumont, TX, refinery, SMRs were elevated for cancers of the pancreas, skin (ICD8 172, 173), prostate and brain, but were not significant; mortality from lymphatic and haematopoeitic cancer was significantly elevated, due to excess mortality from lymphosarcoma, reticulosarcoma, leukaemia and cancer of 'other lymphatic tissues' (ICD8 202–203, 208). Mortality from lymphatic and haematopoietic cancers increased with duration of employment at the Beaumont, TX, refinery. Mortality from leukaemia was significantly elevated among white men with 30 years' service or more and with 20–39 years' latency. A nonsignificant excess of prostatic cancer was reported at the Paulsboro refinery, and the SMR was significantly elevated among white male employees who had worked for at least 20 years (SMR, 1.6). The SMR for cancer of 'other lymphatic tissues' (ICD8 202–203, 208) was also slightly elevated at the Paulsboro refinery but was not significant. Slight excesses of mortality from stomach and brain cancer were reported at the Torrance refinery.

White male employees (blue-collar and white-collar) of the Shell Oil Wood River refinery in southern Illinois who had worked for at least one day during the period 1 January 1973 to 31 December 1982 and retirees who were alive on 1 January 1973 comprised a cohort of 3976 men, 8% of whom had left employment for reasons other than retirement and were lost to follow-up (McCraw *et al.*, 1985). Using mortality rates for US white men as a comparison, the SMR for all causes of death was 0.76 (640 observed). SMRs were shown separately only for lymphatic and haematopoietic neoplasms; all other cancers were grouped. The SMR for leukaemia was significantly elevated. Mortality from cancer of 'other lymphatic tissues' (ICD8 202–203, 208) was slightly, but not significantly, elevated. There was no excess of other cancers combined. The expected number of deaths from acute myeloid leukaemia was estimated from data on cell-type-specific mortality from US cancer registries, and a significant excess was seen. The authors determined that none of the 14 men who had died from leukaemia were known to have worked in jobs with potentially high exposure to benzene; however, five of the men had been maintenance employees who had worked in numerous plant locations, and their potential exposure to benzene was unknown.

No analysis was shown by duration of employment or job category. A nested case-control study was conducted to evaluate the work histories of the 14 leukaemia deaths observed in this study (Austin *et al.*, 1986), which were compared with those of 50 controls matched on year of birth. Cases did not appear to be clustered in any particular job or work area, and there was no evidence that the cases had had greater opportunity for exposure to benzene than had the controls. [The Working Group noted the short period of follow-up and the small size of the cohort.]

All employees who had worked for at least one year between 1 January 1950 and 31 December 1980 at the Chevron refineries in Richmond and El Segundo, CA, comprised a cohort of 14 179 workers (Wong *et al.*, 1986). In all, 2292 deaths were identified; death certificates were obtained for 98%. Cause-specific SMRs adjusted for age, race, sex and calendar year were calculated using the US general population rates as standard. The SMRs for all causes of death were significantly low for both refineries, individually and combined. The only site-specific cancer excesses noted were for cancer of the brain (ICD8 191, 192), for lymphosarcoma and reticulosarcoma and for cancer of 'other lymphatic tissues' (ICD8 202–203, 208), none of which was significant. SMRs for these cancer sites were elevated among people who had been employees at the Richmond refinery, but not among those at the El Segundo refinery. Employees were classified into three work categories — laboratory, maintenance, operating — on the basis of their first and last jobs. Excess mortality from brain cancer occurred only among employees who had worked in maintenance or as operators. Mortality from cancers of 'other lymphatic tissues' was elevated among cohort members who had worked in any of the three subcategories of blue-collar workers. None of the results by work category was significant. SMRs for cancer of the brain and of 'other lymphatic tissues' were highest ten to 19 years after first employment and decreased after 20 years since first employment. The SMR for brain cancer was highest among workers who had been employed for five to 14 years, but decreased after 15 years of employment. The SMR for lymphosarcoma and reticulosarcoma increased with duration of employment to 1.6 (14 observed) among employees who had worked for 15 or more years.

A cohort mortality study of all Amoco Oil Company employees who had worked for at least six months between 1 January 1970 and 31 December 1980 in any of ten refineries included 9192 white male workers, followed until 31 December 1982 (Nelson *et al.*, 1987). Approximately 2% were lost to follow-up. The mortality experience of refinery workers was compared with that of US white men, adjusting for age and calendar period. The SMR for all causes of death was significantly less than 1. The SMR for all digestive cancers was slightly, but not significantly, elevated. SMRs for cancers at several digestive sites including stomach, large intestine and rectum were elevated among men who had worked as operators; the SMR for rectal cancer was also elevated in maintenance workers. Mortality from skin cancer (ICD8 172, 173) was significantly elevated, and the excess occurred almost exclusively among men who had worked in maintenance jobs. There was also significant excess mortality from skin cancer among men whose exposure to refinery processes was considered to have been routine.

A Conoco plant in the USA which began as a small petroleum refinery in 1915 and was converted to a petrochemical plant between 1947 and 1949 was the subject of a report by

Decouflé *et al.* (1983). During the period that the plant was a petroleum refinery, the products were gasolines, light oils, bunker oils, lubricating oils and wax. After conversion to a petrochemical plant, the primary products were alkyl benzene compounds. The study cohort included 259 men (blue-collar and white-collar) employed between 1 January 1947 and 31 December 1960. The cohort was followed for vital status through 31 December 1977, and observed mortality was compared with the expected rates of US white men, adjusting for age and calendar period. Mortality from lymphatic and haematopoietic cancers among the 194 subjects who had been employed for at least one year at the plant was significantly elevated; one of the cases had multiple myeloma, one had acute monocytic leukaemia, one had chronic lymphocytic leukaemia, and the fourth had multiple myeloma (treated with radiotherapy and melphalan) followed by acute myelomonocytic leukaemia two years later. The first three cases had begun their employment at the plant prior to 1947, and, thus, had worked there during both the refinery and petrochemical phases.

A cohort of 19 991 male workers who had worked for at least one year between 1 January 1962 and 1 December 1980 in one of 17 US refineries (Wong & Raabe, 1988), 51.3% of whom had been hired between 1940 and 1954 and 17.2% before 1940, was followed for vital status through 31 December 1980, and the mortality experience of the cohort was compared with that of US men, adjusting for race, age and calendar period (Kaplan, 1986). Altogether, 3349 deaths were observed; 707 (3.5%) persons were lost to follow-up. The only site-specific cancer for which excess mortality was noted was that of 'other lymphatic tissues' (ICD 202–203, 208), but this was not significant; 16 of the 30 deaths in this category were due to multiple myeloma. [The Working Group noted that no analysis was shown by duration of employment or latency.]

A prospective cohort study conducted by Schottenfeld *et al.* (1981) gave morbidity and mortality among men who had been petroleum industry employees in 19 US companies. A total of 55 007 white male petroleum refinery workers who had been working at any time between 1 January 1977 and 31 December 1979 were included in the analyses; 30 769 were first employed in 1960 or after. Mortality rates during the study period were compared with those of US white men in 1977. Standardized incidence ratios (SIRs) for cancer were calculated using rates for US white men obtained from cancer registry data. Among refinery workers, the SMR for all causes of death was significantly less than 1, and significant deficits were noted for many individual causes of death. There was a slight, nonsignificant excess of mortality from brain tumours. There was a significantly elevated incidence of lymphocytic leukaemia, and incidence was slightly elevated for cancers of the larynx and brain and for melanoma. The authors noted that there was underreporting of deaths. [The Working Group noted the short follow-up period (average, 1.6 years), which can result in either higher or lower figures. No analysis by duration of employment was shown.]

[The Working Group noted that the populations in many of the US studies overlapped (see footnote *c* to Table 11). The two industry-wide studies (Schottenfeld *et al.*, 1981; Kaplan, 1986) included many of the same refineries studied individually.]

(ii) *Canada*

A cohort of workers in a Shell Oil refinery located in east Montréal, Québec, consisting of men who had been employed for more than five years between the start of operations in 1928 and 31 December 1975 was studied twice, at a five-year interval (Thériault & Goulet, 1979; Thériault & Provencher, 1987). Of the 1207 men in the cohort, 175 had died by 31 December 1981 and 78 (6.5%) were lost to follow-up. Cause-specific observed mortality in the cohort was compared with that expected on the basis of mortality rates for men in the province of Québec, adjusting for age and calendar period. The SMRs for all causes and for all cancer were low (0.86 and 0.80, respectively). Site-specific excess mortality was noted for stomach cancer and brain cancer, but neither of the SMRs was significantly greater than 1. The deaths from brain cancer were clustered among workers with fewer than 20 years' employment since their date of hire (four observed; SMR, 5.2), and this SMR was significant. A fifth case of brain cancer, still alive at the end of the study, was also reported. Three of the cases had worked as operators (two in light oils, one in heavy oils). One was a boiler maker working in maintenance, and one was a stationary engineer in the thermal station. SMRs for digestive system cancers increased with time since first employment, but the numbers were small. The SMR for lung cancer showed a significant deficit.

Mortality during the period 1964–73 among 15 032 male current and past employees of Imperial Oil Limited, who had had at least five years of employment, was examined using age-adjusted direct standardization techniques (Hanis *et al.*, 1979). Cause-specific mortality rates among the 5731 refinery workers (821 deaths; 2.2% lost to follow-up) in the cohort were compared with those among the 9301 non-refinery company employees (690 deaths; 7.9% lost to follow-up). The total study cohort was also divided into 'exposed' (8612), 'moderately exposed' (2202) and 'unexposed' (4218) on the basis of their likelihood of daily contact with petroleum or its products at some time during the follow-up period. Workers classified as exposed had mortality rate ratios that were significantly elevated for cancers of the oesophagus and stomach and of the trachea, bronchus and lung. Among moderately exposed workers, there was nonsignificant excess mortality from lymphatic and haematopoietic system malignancies when they were compared to unexposed workers. Mortality rates among refinery workers were higher than those for non-refinery employees for cancers of the oesophagus and stomach, intestine and rectum, other digestive organs, trachea, bronchus and lung, prostate and bladder and kidney. Excess mortality from digestive cancer occurred primarily among men who had been employed in services, maintenance, refinery operation and garage work. There was no significantly elevated rate ratio associated with any particular job. The lung cancer rate ratios were highest among men who had worked in office jobs, plant clerk jobs and building trades. Age-adjusted mortality rates for cancers of the oesophagus and stomach and trachea, bronchus and lung increased with duration of employment among 'exposed' workers.

(iii) *UK*

A cohort of 34 781 workers at eight oil refineries in the UK included all men who had worked continuously for one year between 1 January 1950 and 31 December 1975 (Rushton & Alderson, 1980, 1981a; Alderson & Rushton, 1982). Observed mortality (4406 deaths) in

the study group was compared with that expected on the basis of mortality rates among men in England and Wales for the English and Welsh refineries and among men in Scotland for the Scottish refineries, adjusted for age and calendar period; 73 men (0.2%) could not be traced. The SMR for all causes of death was significantly less than 1. The only significant excesses of site-specific cancer mortality noted were for cancer of the nasal cavities and sinuses and for melanoma (Rushton & Alderson, 1980). Among the 9589 men who had worked as operators, excess mortality was seen for oesophageal cancer when results for all the refineries were combined, for intestinal cancer at refinery B and for rectal cancer at refinery F. Labourers experienced elevated mortality from stomach cancer at all refineries combined, at refinery F and at refinery J; riggers and fire and safety workers at refinery J also had elevated risks for stomach cancer. Scientists experienced higher than expected mortality from intestinal cancer at all refineries combined and at refinery J. Stomach cancer mortality decreased with duration of employment overall and at refinery J, but increased with duration of employment at refinery F. Intestinal cancer mortality increased with duration of employment overall and at refineries B and F (Rushton & Alderson, 1981a).

Men who had been employed in methyl ethyl ketone dewaxing plants in two of the refineries included in the study described above were the subject of a separate report (Alderson & Rattan, 1980). Among the 446 men who had worked in these plants, site-specific excess mortality was noted for cancers of the buccal cavity and pharynx and of the digestive tract.

In a nested case-control study, Rushton and Alderson (1981b) compared exposure to benzene among men who had died from leukaemia and among controls selected from the study population of the eight UK oil refineries described above. Two control groups were used: one matched by refinery and year of birth, and a second matched by refinery, year of birth and length of service. There was no excess of leukaemia overall when observed mortality in the refinery population was compared with national rates; however, there were excesses for specific categories: unspecified lymphatic leukaemia, unspecified myeloid leukaemia and acute monocytic leukaemia. The SMRs for all lymphatic leukaemia combined and for all myeloid leukaemia combined were not significantly elevated. A nested case-control analysis suggested a relationship between elevated risk for leukaemia and exposure to benzene, which the authors suggested was confounded by length of service. The odds ratio for leukaemia among men with medium or high exposure to benzene relative to those with low exposure was 2.0, and risk increased with duration of service in the refinery. None of these results was significant.

(iv) *Sweden*

An investigation of occupational risk factors for histologically confirmed biliary tract cancer in Sweden was conducted by linking 1960 census information on occupation with cancer incidence data from the National Swedish Cancer Registry for 1961–79 (Malker *et al.*, 1986). SIRs among workers in specific industries and occupations were calculated by dividing the observed number of cases in each occupational group by the number expected on the basis of national rates among all employed persons, adjusting for birth cohort and sex. Men employed in petroleum refining had significantly elevated SIRs for gall-bladder and other biliary tract cancer.

In a similar analysis of the same cohort, a nonsignificant increase in SIR was noted for cancer of the pancreas (Norell *et al.*, 1986).

[The Working Group noted that these two studies were primarily of an exploratory nature to investigate occupational hazards.]

(b) Case-control studies

The case-control studies reviewed in this section were conducted within the general population setting and examined relationships between the specific cancer at issue and occupational history — either by industry or by broad categories of jobs. Often, no specific hypothesis was being tested. The Working Group presumes that, in addition to the studies reviewed here, in which positive relationships were found, there will have been an indeterminate number of other case-control studies in which no such relationship with a history of working in the petroleum refining industry was found but for which the findings were not reported.

It is unlikely that an equivalent problem exists for the other category of case-control study, conducted ('nested') within a population of petroleum refinery workers and examining the relationship of a specific cancer to specific jobs or exposures within the industry. Such nested case-control studies are included in the preceding section.

(i) *Urinary tract*

A population-based case-control study of bladder cancer conducted in three provinces of Canada included 480 male and 152 female adult case-control pairs (Howe *et al.*, 1980). Newly-diagnosed cases identified from cancer registries between April 1974 and June 1976 were matched by age and sex to neighbourhood controls. Lifetime occupational histories were obtained from personal interviews. Men who had ever worked in the petroleum industry had a significantly elevated risk for bladder cancer (odds ratio, 5.3; 95% confidence interval (CI), 1.5–28.6), which was unchanged after controlling for cigarette smoking. [The Working Group noted that no information on duration of employment was given.]

Histologically confirmed cases of bladder cancer were ascertained among white persons treated in two community hospitals in northern New Jersey, USA, in 1978 and were matched on age, sex, place of birth, hospital and census tract of current residence with patients treated for other conditions in the same hospitals, excluding those with a history of neoplasm or of tobacco-related heart disease (Najem *et al.*, 1982). The relative risk for bladder cancer was estimated by calculating odds ratios stratified by potential confounders. Lifetime occupational histories were obtained for the 75 cases and 142 controls. There was a significantly elevated risk for bladder cancer among study subjects who reported having worked in the petroleum industry (22 cases; odds ratio, 2.5; 95% CI, 1.2–5.4). Risk was highest among subjects who had never smoked (six cases; odds ratio, 5.6) and among current smokers (eight cases; odds ratio, 2.6) and was only slightly elevated among ex-smokers (eight cases; odds ratio, 1.4). [The Working Group noted that no analysis was shown by duration of employment.]

Data from the Detroit, MI, component of the population-based US National Bladder Cancer Study included 420 histologically confirmed, newly diagnosed cases of carcinoma (or papilloma not specified as benign) of the bladder, renal pelvis, ureter and urethra among adult men between 1 December 1977 and 30 November 1978; 95% were carcinoma of the urinary bladder (Silverman *et al.*, 1983). These analyses were limited to the 303 white male cases and 296 white male, randomly-selected adult population controls, matched for age and sex, who were interviewed. Using lifetime occupational histories, crude odds ratios were calculated for ever having worked in each occupation and industry listed. There was an excess risk for cancer of the lower urinary tract among men who had ever been employed in the petroleum extracting and refining industries (six cases; relative risk, 6.0; 95% CI, 0.7–49.8), which was not significant. [The Working Group noted that no data were given by duration of employment.]

A death certificate-based case-control study in 19 southern Louisiana parishes included 347 residents who had died between 1960 and 1975 and whose underlying cause of death was attributed to bladder cancer (Gottlieb & Pickle, 1981). An equal number of controls was selected from persons who had died from causes other than cancer, matched on age, sex, race and parish of residence. Usual industry and occupation listed on the death certificates of study subjects were compared, and a logistic regression model was used to calculate maximum likelihood estimates of the odds ratios for particular variables, adjusting for potential confounding factors. The odds ratio for bladder cancer among white men (176 case-control pairs) whose usual industry of employment was listed as petroleum refining was 4.5 (six cases). Cases who had lived near petroleum refineries also had slightly elevated odds ratios for bladder cancer (whites: 31 cases, odds ratio, 1.1; blacks: three cases, odds ratio, 1.4; based on 238 case-control pairs of whites and 109 of blacks).

In a hospital-based case-control study in La Plata, Argentina, the relationship of bladder cancer to occupational history was examined (Iscovich *et al.*, 1987). An incident series of 117 cases of carcinoma confirmed histologically between March 1983 and December 1985, from ten hospitals, was compared with 117 hospital controls and 117 neighbourhood controls, both groups matched with cases for sex and age. As part of a standardized, interviewer-based questionnaire, a detailed occupational history was obtained for the three occupations of longest duration and the most recent one; job titles were coded according to the ILO classification (International Labour Office, 1970). After pooling the two controls groups and controlling for age and level of cigarette smoking, the only significant increases in occupation-associated risk for bladder cancer were found for lorry or railway drivers (20 cases; odds ratio, 4.3) and for petroleum refinery workers (seven cases; [crude odds ratio calculated by the Working Group, 3.7; 95% CI, 1.1–11.6]); adjusted for age and tobacco use, 6.2). [The Working Group noted that the method of selecting neighbourhood controls, while described unclearly, could have entailed selection bias.]

(ii) *Lung*

Deaths from cancer of the trachea, bronchus and lung among men in two Canadian cities (London and Sarnia) between 1969 and 1973 (348 cases) were ascertained from vital statistics records, and usual industry and occupation were recorded from death certificates

(Wigle, 1977). An equal number of controls who had died from other causes were matched on city, calendar period of death and age. Fifty-seven study subjects were residents of Sarnia, where 28% of the male work force was employed in petroleum refining or the chemical industry; while 291 were from London, where 1% of the men were so employed. Five cases and 12 controls were employed in petroleum refining [odds ratio calculated by the Working Group, 0.42; 95% CI, 0.2–1.0]. [The Working Group noted that no information was available on smoking habits.]

Usual occupation and type of industry listed on the death certificates of residents of 19 southern Louisiana, USA, parishes were obtained for all lung cancer deaths (3327) that occurred between 1960 and 1975 and for an identical number of adults who had died from causes other than cancer, matched on sex, race, age and parish of usual residence (Gottlieb *et al.*, 1979). A logistic model was used to calculate odds ratios (adjusted for age, marital status, year of death, birthplace and parish of residence) by sex and race to estimate the risk for lung cancer of specific occupational and industrial categories. Among men who had been employed in petroleum refining, the race-adjusted odds ratio for lung cancer was 1.3 (95% CI, 0.93–1.9). The sex-adjusted odds ratio for lung cancer among whites who had been employed in petroleum refining was 1.3 (95% CI, 0.88–1.8) and that among blacks was 2.2 (95% CI, 0.59–7.9). Odds ratios for lung cancer among subjects whose usual residence had been in a town in which there was a petroleum refinery were elevated in each sex-race group (white men: 306 cases; odds ratio, 1.2 (95% CI, 0.97–1.4); black men: 28 cases; odds ratio, 1.9 (0.99–3.6); white women: 58 cases; odds ratio, 1.3 (0.86–2.0); black women: ten cases; odds ratio, 1.7 (0.60–4.6)). However, none of the results was significant. Further analyses of specific occupations within the petroleum industry indicated a significantly elevated odds ratio for lung cancer among men who had been employed in skilled maintenance trades or operator jobs in petroleum refining and who had died at age 60 or older (25 cases; odds ratio, 2.4; 95% CI, 1.0–5.9; Gottlieb, 1980). When the study group was restricted to subjects whose length of residence at the location listed on the death certificate could be verified from public records, subjects who had lived within a mile of a petroleum industry work site for at least ten years had an elevated lung cancer risk (work site with <100 employees: 11 cases; odds ratio, 1.5; work sites with $\geqslant 100$ employees: 32 cases; odds ratio, 1.7). Among subjects who had lived near a petroleum industry work site and whose usual occupation had been in the petroleum industry, there was a significantly elevated risk for lung cancer (36 cases; odds ratio, 2.3), controlling for year of death, age, race, years of residence and industry size (Gottlieb *et al.*, 1982). [No information on smoking habits or on exposure to asbestos was available.]

(iii) *Other sites*

A preliminary study of risk factors for pancreatic cancer in the same Louisiana parishes included 876 case-control pairs identified from death certificates for the years 1960–75, using the same methods as for the studies on bladder and lung cancer (Pickle & Gottlieb, 1980). There was a two-fold excess risk for pancreatic cancer among white men whose usual industry of employment had been petroleum refining (15 cases; odds ratio, 2.1; 95% CI, 0.86–5.2), but this was not significant. Pancreatic cancer risk was elevated among white men

(40 cases; odds ratio, 1.2), white women (36 cases; odds ratio, 1.2) and black women (three cases, odds ratio, 1.4) whose usual residence had been near a petroleum refinery, but not among black men (three cases; odds ratio, 1.0).

Usual industry and occupation on the death certificates of 718 white men aged 30 and over who had died from malignancies or unspecified tumours of the brain were compared with those of 738 white men who had died of other causes, excluding epilepsy and stroke, and were frequency matched for age and study area (Thomas *et al.*, 1986). All study subjects were residents of three geographical areas of the USA with a heavy concentration of petroleum and chemical industries (southern New Jersey, Philadelphia area and Gulf Coast of Louisiana), who had died between 1979 and 1981, and for whom a death certificate was found (99.7%). Risk for brain tumours in each usual occupation and industry listed was estimated by calculating a maximum likelihood estimate of the odds ratio, adjusting for age, marital status and occupation status (blue-collar, white-collar). The odds ratio for petroleum refining was 1.2 (95% CI, 0.6–2.6).

In a further analysis, lifetime occupational histories were obtained through interviews with next-of-kin (Thomas *et al.*, 1987); 483 cases and 386 controls agreed to be interviewed. The analysis was performed on 300 white men who had had confirmed astrocytic tumour of the brain (astrocytoma, glioblastoma multiforme or mixed glioma with astrocytic cells). Astrocytic tumour risk associated with ever having been employed in specific industries was estimated by maximum likelihood techniques. Among men who had ever been employed in petroleum refining, the odds ratio for astrocytic tumours was 1.5 (18 cases; 95% CI, 0.7–3.2). The elevated risk among men ever employed in petroleum refining was limited to those who had worked in production and maintenance jobs (15 cases; odds ratio, 1.7; 95% CI, 0.7–4.2); however, among those whose duration of employment was known, risk decreased with increasing duration of employment in the industry (<5 years: five cases, odds ratio, 6.7; 5–9 years: two cases, odds ratio, 1.3; ≥20 years: four cases, odds ratio, 0.8). [The Working Group calculated that this trend was statistically significant.]

A death certificate-based case-control study was conducted in the counties of Cleveland, Humberside and Cheshire and the Wirral district of Merseyside in the UK to examine the relationship between occupation and risk for five cancers — of the oesophagus, pancreas, kidney and brain and melanoma (Magnani *et al.*, 1987). Cases had been male residents of the study areas who had died from one of the five cancers between the ages of 18 and 54 during the periods 1959–63 and 1965–79 (data for 1964 were not available). One set of controls who had died from other causes was matched to each case on county of residence and another set on 'local authority area' of residence; both sets were matched on sex and age at death. Occupation and industry listed on the death certificates were used to classify subjects into occupational and exposure categories. There were 244 cases of oesophageal cancer with 935 controls, 343 of pancreatic cancer with 1315 controls, 99 of melanoma with 361 controls, 147 of kidney cancer with 556 controls, and 432 of brain cancer with 1603 controls. Significantly elevated odds ratios were not reported for oesophageal, pancreatic or kidney cancer in association with petroleum refining occupations; there were significantly elevated odds ratios for melanoma (odds ratio, 8.0; 95% CI, 1.5–43.7) and brain cancer (odds ratio, 3.5; 1.5–8.1) associated with occupational exposure to coal and petroleum products. Both

results were due to clusters of workers employed in petroleum refining. The four melanoma cases so employed had the following occupations reported on their death certificates: process worker/blender, engineer, security officer and clerk of works. The odds ratio for brain cancer was significantly elevated among men employed in petroleum refining (odds ratio, 2.9; 95% CI, 1.2–7.0), and four of the seven cases had worked as process operators.

Several studies on parental occupation involving exposure to hydrocarbons and cancer risks in children are reviewed in the monograph on gasoline. One of the studies, described more fully in that monograph, looked specifically at petrochemical occupations and industries and included 499 Texas children who had died from intracranial and spinal cord tumours and 998 controls (Johnson *et al.*, 1987). On the basis of information on paternal occupation extracted from the birth certificate, an odds ratio of 2.0 (95% CI, 0.6–6.2) for children of petroleum refinery workers was observed.

(*c*) *Correlation studies*

A survey by county of the average annual age-adjusted lung cancer mortality rates for the years 1950–69 among white men in the USA indicated higher than expected lung cancer rates (1.32 per 100 000), when compared with total US rates, in counties where at least 1% of the population was employed in the petroleum industry (Blot & Fraumeni, 1976). A second survey examined cancer mortality rates in 39 US counties where at least 100 persons were employed in the petroleum industry and the estimated number of workers comprised at least 1% of the county population (Blot *et al.*, 1977). White male residents of the petroleum industry counties had significantly higher average age-adjusted mortality rates for cancers of the lung (rate ratio, 1.15), nasal cavity and sinuses (rate ratio, 1.48), stomach (rate ratio, 1.09), rectum (rate ratio, 1.07), testis (rate ratio, 1.10) and skin (rate ratio, 1.10) than those of control counties with similar demographic characteristics.

Average annual age-adjusted cancer incidence rates for the period 1971–77 among Kaiser Health Foundation plan members living near petroleum and chemical plants in the San Francisco Bay area of the USA were compared with those among other San Francisco Bay area residents who did not live near the plants (Hearey *et al.*, 1980). Site-specific rates for cancer were not elevated for members living near the petroleum and chemical plants.

Average annual age-adjusted cancer incidence rates for the period 1969–77 in Contra Costa County, CA, USA, were examined to determine whether there was any correlation with levels of air emissions from petroleum and chemical plants (Kaldor *et al.*, 1984). The county was divided into four exposure areas, from low to high, based on air levels of sulfur dioxide, hydrocarbons and nitrogen oxides. Among men, significantly increasing incidence rates by level of exposure were found for cancers of the buccal cavity and pharynx, of the stomach, trachea, bronchus and lung, of the prostate and of the kidney. For all cancer sites combined, rates increased by exposure level, and the trend was significant. Among women, significantly increasing trends were noted only for cancers of the buccal cavity and pharynx.

Average annual age-adjusted mortality rates for multiple myeloma by state economic area in the USA were calculated for the period 1950-75 for each sex and race (Blattner *et al.*, 1981). A multiple regression model was used to examine the relationship between the

magnitude of the rates for multiple myeloma and various social, demographic and employment characteristics of the state economic areas. Rates for multiple myeloma among white men were elevated in areas where more than 1% of the population was employed in the petroleum industry, and the regression coefficient was significantly different from 0.

(d) Case reports

An employee of a petroleum refinery near Chicago, IL, USA, treated for an epithelioma [squamous-cell carcinoma] of the skin of the arm, was the subject of an early case report (Davis, 1914). The employee had worked for more than 20 years in a refinery department where crude paraffin was pressed to remove the petroleum oil distillate. The crude wax residue remaining in the presses was removed by a manual scraping process, and workers' bare arms were exposed to the oil-containing wax. Investigation at the plant indicated that most of the workers in the department had developed skin lesions in the form of 'wax boils', pigmented spots, wart-like growths and epithelioma.

A review of ten cases of cancer of the scrotum among wax pressmen at the Esso Baton Rouge, LA, USA, petroleum refinery was conducted by Lione and Denholm (1959). All of the men had been exposed to crude wax containing 20–40% petroleum oil distillate for a minimum of 15 years, the longest exposure period being 38 years. During the process of separating wax from crude distillate, the workers' clothing became contaminated with the crude wax, particularly in the lower abdominal and genital areas. Pathological diagnoses indicated that all ten of the cases were squamous-cell carcinomas. [The Working Group noted that these cases were included in the study by Hendricks *et al.* (1959), p. 91.]

Cases of leukaemia that occurred during the period 1962–71 among employees of eight Esso affiliates in Europe were studied to determine whether leukaemia had occurred more often than expected in association with exposure to benzene in petroleum refining (Thorpe, 1974). Eighteen cases were reported during the study period among employees of only four of the affiliates; the other four companies reported no case of leukaemia. Eight of the cases were considered to have been exposed to benzene in their jobs; these were two tank truck drivers, two refinery mechanics, two refinery operators, one marketing repair mechanic and one marketing superintendent. Expected mortality from leukaemia was estimated by applying the mortality data of the World Health Organization for 1966 to the estimates of person-years at risk for the eight companies; the ratio of observed to expected mortality from leukaemia among the benzene-exposed workers was 1.2, which was not significant.

4. Summary of Data Reported and Evaluation

4.1 Exposure data

Approximately 3000 million tonnes of petroleum fuels, solvents, lubricants, bitumens and other products are produced annually from crude oil. World-wide, the petroleum refining industry employs about 500 000 persons in more than 700 plants. Process operators and maintenance workers may be exposed to a large number of substances which occur in

crude oil, process streams, intermediates, catalysts, additives and final products. Aliphatic and aromatic hydrocarbons and hydrogen sulfide have commonly been measured in the air of working environments. Less commonly, polycyclic aromatic compounds have been detected at specific process units. In general, the concentrations of benzene in modern refineries have been reported to be less than 3 mg/m^3, with higher levels in some operations. Exposure *via* the skin to high-boiling materials may also occur.

The major process streams are listed in Table 2, p. 44; the numbers given in square brackets below are those assigned to the streams.

4.2 Experimental data

Several refinery streams used in the manufacture of (or sold directly as) mineral lubricating oils and processing oils were evaluated in Volume 33 of the *IARC Monographs*. The Working Group that prepared that monograph concluded that there was *sufficient evidence* for the carcinogenicity in experimental animals of untreated vacuum distillates [19, 20], of hydrotreated vacuum distillates [based on 19 and 20] and of the high-boiling fraction of catalytically cracked oils [26, 27]. A more recent working group which met to re-evaluate all agents considered in volumes 1–42 of the *IARC Monographs*, resulting in Supplement 7, concluded that there was *sufficient evidence* for the carcinogenicity of untreated and mildly treated mineral oils in experimental animals. The following summary covers experiments on refinery streams that were not considered previously or which have been published since Supplement 7 was prepared. In most of these experiments, no distinction was made in the published reports between benign and malignant skin tumours.

Uncracked distillates and residues[1]

In a series of experiments of similar design, several atmospheric and vacuum distillates were tested by repeated skin application to mice. One sample of a light straight-run naphtha [3], one sample of light paraffinic vacuum distillate [19A], one sample of heavy paraffinic vacuum distillate [20A] and four samples of heavy naphthenic vacuum distillates [20B] produced a marked increase in the incidence of skin tumours. Two samples of straight-run kerosene [5] and one sample of hydrotreated kerosene [5A] also produced skin tumours.

Two samples of hydrotreated heavy naphthenic distillate [20D] and one sample of a chemically neutralized/hydrotreated heavy naphthenic distillate [20C/20D] tested in mice by skin application produced a marked increase in the incidence of skin tumours.

One sample of vacuum residue [21] was tested by skin application in mice; no significant skin tumour response was observed.

Cracked distillates and residues

One sample of light catalytically cracked naphtha [22], three light catalytically cracked

[1]Subsequent to the meeting, the Secretariat became aware of one study in which skin tumours were reported in mice after application to the skin of petroleum naphtha (boiling range, 53–213°C) [near 4] (Clark *et al.*, 1988) and of another study in which it was reported that skin tumours developed in mice after skin application of a virgin heating oil blending base (boiling range, 142–307°C) [probably 5] (Biles *et al.*, 1988).

distillates [24] and one intermediate catalytically cracked distillate [25] were tested in mice by skin application and induced skin tumours.

Several high-boiling distillates [26] and residues [27] of catalytically cracked oils and several thermally cracked residues [31] were tested in experiments in mice by skin application, producing high incidences of benign and malignant skin tumours.

Thermally-cracked residues [31] originating from two different sources were tested by skin application in rabbits, producing some skin tumours, but the study was considered inadequate for evaluation. In one study in mice, skin application of water-quench pyrolysis fuel oil or oil-quench pyrolysis fuel oil (steam-cracked residues [34]) produced carcinomas and papillomas of the skin.

Effluents

Two studies on petroleum refinery effluents were inadequate for evaluation.

4.3 Human data

Taking into consideration the overlap in cohort studies conducted in the USA, ten separate, company-specific cohorts were studied. Two industry-wide study cohorts from the USA comprised various combinations of these cohorts. The cohorts mentioned hereafter refer to the ten separate US cohorts, two from Canada and one from the UK.

Information on specific jobs or exposures was available in only a few of the epidemiological studies of petroleum refinery workers. Some caution should be applied in interpreting the relative risks for cancer in cohort studies of petroleum refinery workers. As for most cohorts of actively employed persons, the overall risk for cancer in all of the cohort studies reviewed here was lower than that in the general population. Yet, it is the cancer experience of the general population that has been conventionally used, in published papers, in evaluating the rates of specific cancers in refinery workers. Significant deficits were reported for cancers at some sites in certain studies; such findings are mentioned in this summary only when a consistent pattern emerged. Caution should also be applied in interpreting the findings from those case-control studies conducted within the general population setting. Most of the studies reported had positive findings, and are likely to be an incomplete selection of case-control studies in which occupational exposures have been investigated.

One case report and one case series describe clusters of skin cancer cases (squamous-cell carcinoma) among wax pressmen who had been exposed to crude paraffin wax saturated with aromatic oils. Significant excess mortality from skin cancer was reported among three refinery cohorts, one of which included the wax pressmen from the case series. In a second cohort, the overall excess was due to an elevated risk for malignant melanoma. In the third, excess skin cancer risk was experienced primarily by maintenance workers. Skin cancer mortality was elevated in three additional cohorts, but the increase was not significant. A case-control study showed a significantly elevated risk for malignant melanoma among men employed in the coal and petroleum products industry, with a cluster of cases employed in petroleum refineries.

Mortality from leukaemia was significantly elevated in two refinery cohorts; in one of these, mortality increased with duration employed and also with time since first employment. Nonsignificant excess mortality from leukaemia was reported among two additional cohorts; in one of these, the excess was significant for boiler makers and pipe fitters. Elevated mortality from unspecified lymphatic leukaemia, unspecified myeloid leukaemia and acute monocytic leukaemia, but not other cell types, was reported in a subset of workers in the British cohort whose exposures included benzene. A significantly elevated incidence of lymphocytic leukaemia was reported in a large cohort study which included many of the refineries in the USA. Excess mortality from 'cancer of other lymphatic tissues' (multiple myeloma, polycythaemia vera and non-Hodgkin's lymphoma, excluding lymphosarcoma and reticulum-cell sarcoma), which was not significant, was reported in five refinery cohorts. One report indicated significant excess mortality from leukaemia and 'cancer of other lymphatic tissues' combined.

Mortality from malignant neoplasms of the brain was elevated in six of the refinery cohorts, but this was significant in only one of the studies and only for workers with short duration of employment. The elevated mortality was seen in operators and in maintenance and laboratory workers. A case-control study of astrocytic brain tumours showed a decreasing trend in risk with duration employed among men who had ever worked in petroleum refining during their lifetime. Another case-control study showed a significantly elevated risk for malignant neoplasms of the brain among men employed in petroleum refining.

Stomach cancer mortality was elevated among six refinery cohorts, significantly so in only one, among labourers, riggers and fire and safety workers; it was associated with lubricating oil production in one refinery and with solvent dewaxing in another. Mortality increased with increasing duration of employment in one of the studies.

Kidney cancer mortality was elevated, but not significantly so, among three petroleum refinery cohorts, particularly among operators, labourers and maintenance workers. Kidney and bladder cancer mortality combined was elevated in one refinery cohort. Five case-control studies of bladder cancer showed excess risk associated with employment in petroleum refining; the results were significant in two of these.

Pancreatic cancer mortality was reported to be elevated in four petroleum refining cohorts, and was associated with employment in the petroleum refining industry in one case-control study; however, none of these results was significant.

Excess mortality from cancer of the prostate, which increased with duration of employment, was reported in two refinery cohorts, and an overall excess was reported in two others. The only result that attained significance was found for men employed for 20 years or more in one of the refineries.

Lung cancer mortality was elevated in two refinery cohorts but not significantly so. There was a significant excess of lung cancer among workers with daily exposure to petroleum and its products in one of these cohorts. In five cohort studies, significant deficits in mortality from lung cancer were seen. In a case-control study, refinery maintenance workers and operators had a significantly elevated risk for lung cancer.

Mortality from malignant neoplasms of bone was elevated in two cohorts; the excess was significant in one of them, and specifically in association with employment in lubricating oil manufacture.

4.4 Other relevant data

It was reported in one study that wives of maintenance (crafts) workers employed in the waste-water treatment area of a petroleum refinery experienced an excess risk of fetal loss. In one study, an increased prevalence of chromosomal aberrations and of sister chromatid exchange was found in a group of workers in the sewage-treatment unit of a petroleum refinery, but no such effect was observed among a group of workers in a catalytic cracking unit.

Light straight-run [3], full-range alkylate [13] and thermally cracked naphtha [28, 29] produced severe renal toxicity in male but not in female rats.

Previous working groups have reported that vacuum distillates from petroleum refining [19, 20] and hydrotreated oils induced mutation in bacteria (IARC, 1984, 1987).

Extracts of light paraffinic distillate [19A], heavy paraffinic distillate [20A], heavy naphthenic distillate [20B], straight-run kerosene [5], hydrotreated heavy naphthenic distillate [20D] and chemically neutralized/hydrotreated heavy naphthenic distillate [20C/20D] induced mutation in bacteria. Extracts of hydrotreated kerosene [5A], light straight-run naphtha [3] and vacuum residue [21] did not induce mutation in bacteria.

Extracts of an intermediate catalytically cracked distillate [25] and of a mixture of a heavy catalytically cracked distillate [26] and a catalytically cracked clarified oil [27] induced mutation in bacteria. (See Appendix 1.)

4.5 Evaluation[1]

There is *limited evidence* that working in petroleum refineries entails a carcinogenic risk. This limited evidence applies to skin cancer and leukaemia; for all other cancer sites on which information was available, the evidence is inadequate.

There is *sufficient evidence* for the carcinogenicity in experimental animals of light and heavy vacuum distillates, of light and heavy catalytically cracked distillates and of cracked residues derived from the refining of crude oil.

There is *limited evidence* for the carcinogenicity in experimental animals of light straight-run naphtha, of straight-run kerosene, of hydrotreated kerosene and of light catalytically cracked naphtha.

In formulating the overall evaluation, the Working Group also took note of the following supporting evidence reported in Supplement 7: benzene and untreated and mildly

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

treated mineral oils are carcinogenic to humans (Group 1). There is *sufficient evidence* for the carcinogenicity in experimental animals of several polycyclic aromatic hydrocarbons[1].

Overall evaluation

Occupational exposures in petroleum refining *are probably carcinogenic to humans (Group 2A).*

5. References

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