This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the United Nations Environment Programme, the International Labour Organisation, or the World Health Organization.

Environmental Health Criteria 20

SELECTED PETROLEUM PRODUCTS

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The International Programme on Chemical Safety (IPCS) is a joint venture of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. The main objective of the IPCS is to carry out and disseminate evaluations of the effects of chemicals on human health and the quality of the environment. Supporting activities include the development of epidemiological, experimental laboratory, and risk-assessment methods that could produce internationally comparable results, and the development of manpower in the field of toxicology. Other activities carried out by IPCS include the development of know-how for coping with chemical accidents, coordination of laboratory testing and epidemiological studies, and promotion of research on the mechanisms of the biological action of chemicals.

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NOTE TO READERS OF THE CRITERIA DOCUMENTS

While every effort has been made to present information in the criteria documents as accurately as possible without unduly delaying their publication, mistakes might have occurred and are likely to occur in the future. In the interest of all users of the environmental health criteria documents, readers are kindly requested to communicate any errors found to the Division of Environmental Health, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda which will appear in subsequent volumes.

In addition, experts in any particular field dealt with in the criteria documents are kindly requested to make available to the WHO Secretariat any important published information that may have inadvertently been omitted and which may change the evaluation of health risks from exposure to the environmental agent under examination, so that the information may be considered in the event of updating and re-evaluation of the conclusions contained in tbe criteria documents.

WHO TASK GROUP ON ENVIRONMENTAL HEALTH CRITERIA FOR SELECTED PETROLEUM PRODUCTS

Members

Dr D. A. Akintonwa, Department of Biochemistry, Faculty of Medicine, University of Calabar, Calabar, Nigeria
Dr L. Boniforti, Department of Contaminants, Laboratory of Toxicology, Institute of Health, Rome, Italy
Dr K. W. Jager, Shell Internationale Research, Maatschappij B.V., The Hague, Netherlands *(Rapporteur)*
Professor L. Jirásek, 1st Dermatological Clinic, Charles University, Prague, Czechoslovakia
Professor A. A. Kasparov, Institute of Industrial Hygiene and Occupational Diseases, Academy of Medical Sciences, Moscow, USSR *(Vice-Chairman)*
Professor W. O. Phoon, Department of Social Medicine and Public Health, Faculty of Medicine, University of Singapore, Singapore *(Chairman)*
Dr M. Rouhani, Institute of Occupational Safety and Health, Ministry of Labour and Social Affairs, Teheran, Iran (Present address: Nice, France)
Dr E. Schmidt, Directorate of Malariology and Environmental Sanitation, Ministry of Health and Welfare, Caracas, Venezuela
Dr N. K. Weaver, American Petroleum Institute, Washington DC, USA

Representatives of other organizations

Dr P. V. C. Pinnagoda, International Labour Organisation, Geneva, Switzerland
Professor L. Parmeggiani, Permanent Commission and International Association on Occupational Health
Dr J. W. Huismans, International Register of Potentially Toxic Chemicals, United Nations Environment Programme, Geneva, Switzerland
Mr J. Wilbourn, International Agency for Research on Cancer, Lyons, France

Secretariat

Dr A. David, Medical Officer, Office of Occupational Health, World Health Organization, Geneva, Switzerland *(Co-Secretary)*
Dr M. A. El Batawi, Chief Medical Officer, Office of Occupational Health, World Health Organization, Geneva, Switzerland
Mrs B. Goelzer, Scientist, Office of Occupational Health, World Health Organization, Geneva, Switzerland *(Co-Secretary)*
Dr Y. Hasegawa, Medical Officer, Environmental Health Criteria and Standards, World Health Organization, Geneva, Switzerland
Dr M. Sharratt, Senior Toxicologist, BP Group Occupational Health Centre, Middlesex, England *(Temporary Adviser)*

Further to the recommendations of the Stockholm United Nations Conference on the Human Environment in 1972, and in response to a number of World Health Assembly Resolutions and the recommendation of the Governing Council of the United Nations Environment Programme, a programme on the integrated assessment of the health effects of environmental pollution was initiated in 1973. The programme, known as the WHO Environmental Health Criteria Programme, has been implemented with the support of the Environment Fund of the United Nations Environment Programme. In 1980, the Environmental Health Criteria Programme was incorporated into the International Programme on Chemical Safety. The result of the Environmental Health Criteria Programme is a series of criteria documents.

The Office of Occupational Health, WHO, was the unit responsible for the development of the Environmental Health Criteria document on Selected Petroleum Products.

The Task Group for this document met in Geneva from 15–19 October 1979. The meeting was opened by Dr M. A. El Batawi, Chief, Office of Occupational Health, who welcomed the participants and the representatives of other international organizations on behalf of the Director-General.

The Task Group reviewed and revised the second draft criteria document and made an evaluation of the health risks of exposure to selected petroleum products.

The first and second drafts were prepared by Dr K. W. Jager, Shell Internationale Research, Maatschappij B. V., The Hague, Netherlands. Comments on the second draft, which have been incorporated in this report, were received from the national focal points for the WHO Environmental Health Criteria Programme in Australia, the Federal Republic of Germany, Mexico, the United Kingdom, and the USA, and from the WHO Collaborating Centres of Occupational Health in: Chile, Finland, Indonesia, Netherlands, Singapore, Sweden, Switzerland, the United Kingdom, and the USSR. Additional comments were received from Dr. R. E. Eckardt (USA), Dr M. Rouhani (Iran), from the International Petroleum Industry Environmental Conservation Association, and from the American Petroleum Institute.

The collaboration of these national institutions, international organizations, and individual experts is gratefully acknowledged. The Secretariat also wishes to thank Dr K. W. Jager and Dr M.

Sharratt for their invaluable assistance in the final stages of the preparation of the document.

As the final text of the evaluation could not be distributed at the meeting, it was circulated to all participants in November 1978. The comments received were then considered by the Rapporteur and some members of the Secretariat, and suggested alterations were included. Later, section 2.1.2, Methods of sampling and analysis, was completely rewritten by Mr. T. P. C. M. van Dongen of the Shell Laboratory (Amsterdam) and Dr K. W. Jager, the Rapporteur.

The document has been based, primarily, on original publications listed in the reference section. However, several recent reviews of health aspects of petroleum products have also been used, including: Petroleum Handbook (1966); API Toxicology Reviews (API, 1965, 1967, 1969); US DHEW (1970); and Lazarev & Levina (1976).

The purpose of this document is to review and evaluate available information on the biological effects of some petroleum products, and to provide a scientific basis for decisions aimed at the protection of human health from the adverse consequences of exposure to these substances in both the occupational and general environments.

It was only feasible to discuss several groups of related products, and to select priorities among them. Thus, non-fuel products derived from crude oils are considered in three broad groups, i.e., petroleum solvents, lubricating base-oils, and bitumens. These have been selected as priorities, because of their widespread use and because large sub-groups of the population may come into close contact with them through occupational or domestic use. Moreover, adverse health effects are known to occur from occupational exposure to some of these products.

Base chemicals derived from the cracking of crude oil fractions, such as ethylene, propylene, and other olefins, and fuels derived from crude oils ranging from gasoline to heavy fuel oil, are not discussed in this document. As fuels and non-fuels of a similar boiling range may have similar effects, e.g., on the skin or, after aspiration, on the respiratory tract, most toxicological data discussed in this review are more or less relevant to crude oil-derived fuels of a similar boiling range. In fact, it is impossible to make a strict division between data relating to fuels and non-fuels and they have been considered together, whenever relevant.

The published literature and other available information have been critically evaluated and where possible, an attempt has been made to establish whether or not, under certain conditions, a potential risk to man exists. Suggestions for avoiding established risks and for further studies have also been made.

The environmental impact, if any, of the products has only been considered where it is directly related to the health of man.

Details of the WHO Environmental Health Criteria Programme including some terms frequently used in the document may be found in the general introduction to the Environmental Health Criteria Programme published together with the environmental health criteria document on mercury (Environmental Health Criteria 1, Mercury, Geneva, World Health Organization, 1976), now also available as a reprint.

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Financial support for the publication of this criteria document was kindly provided by the United States Department of Health and Human Services through a contract from the National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA – a WHO Collaborating Centre for Environmental Health Effects.

The following conversion factors have been used in the present document:

benzene	1 ppm = 3.0 mg/m^3
gasoline	1 ppm = 4.5 mg/m^3[a]
heptane	1 ppm = 4.0 mg/m^3
hexane	1 ppm = 3.6 mg/m^3
octane	1 ppm = 4.85 mg/m^3
pentane	1 ppm = 3.0 mg/m^3
toluene	1 ppm = 3.75 mg/m^3
xylene	1 ppm = 4.35 mg/m^3

[a] A conversion factor for gasoline of 1 ppm = 4.5 mg/m^3 has been used throughout the document, though this factor normally varies according to the composition of the gasoline.

1. SUMMARY AND RECOMMENDATIONS FOR FURTHER STUDIES

1.1 Summary

1.1.1 Properties and analytical methods

1.1.1.1 *Properties*

(a) Crude oils are a complex mixture of straight and branched chain paraffinic, cycloparaffinic, aromatic and polynuclear aromatic hydrocarbons together with small amounts of sulfur and nitrogen compounds. The composition of crude oils varies considerably with geographical origin. They can be broadly divided into paraffinic, asphaltic, and mixed crude oils. Paraffinic crude oils provide large amounts of paraffinic hydrocarbons, paraffin wax, and high grade oils, while asphaltic crude oils province more cycloparaffins and high viscosity lubricating oils.

(b) Petroleum solvents, produced by the distillation of crude oils, are also complex mixtures of hydrocarbons. They are generally classified on the basis of distillation ranges. Special boiling-point solvents, such as petroleum ether and rubber solvent, are mixtures of C-5 to C-9 normal- and branched-chain paraffins and cycloparaffins with a boiling-range of 30–160 °C. With solvents such as Stoddard solvent, mineral spirits, and low aromatic white spirits, the chain lengths are longer (C-7 to C-12) and the boiling-range higher (150–220 °C) and they contain various amounts of aromatic compounds. Higher boiling-point solvents (B.P. 160–300 °C) containing more than 9 carbon atoms per molecule are also produced.

(c) Lubricant base oils, greases, and waxes are products with boiling-points in the range of 300–700 °C that are normally produced by high-vacuum distillation of the residues of the initial distillation.

(d) Bitumen, the solid and semi-solid residue of the distillation process, varies from a highly viscous liquid to a brittle solid, at ambient temperatures, and consists of a mixture of asphaltenes (high relative molecular mass aromatic and heterocyclic hydrocarbons), resins (polymers formed from unsaturated hydrocarbons during processing), together with saturated hydrocarbons and aromatic hydrocarbons containing one or more benzene rings per molecule (including polynuclear aromatic hydrocarbons).

1.1.1.2 *Analytical methods*

A vast and specialized literature on sampling methods and analytical techniques is available for petroleum products. Many techniques have proved useful, e.g., infrared spectroscopy, thin-layer

chromatography, ultraviolet fluorescent spectrometry, capillary gas-chromatography, and chromatography combined with mass spectrometry.

1.1.2 Sources of environmental pollution

(a) Crude oil is normally transported in large volumes in tankers and pipelines. Breakdown or leakage of these may cause a major and sudden environmental hazard. Less significant degrees of pollution have resulted from the cleaning out of oil tankers. Certain volatile components, especially hydrogen sulfide but also other sulfur compounds, acids, and hydrocarbons may contaminate the atmosphere near oilfields and refineries.

(b) As a rule, petroleum solvents do not present serious pollution problems for the general population, since they are mainly used in industry and seldom domestically. Spillage or use in poorly ventilated rooms or without proper control measures may cause serious work-place pollution. Solvents containing *n*-hexane or benzene may present particular hazards with respect to health.

(c) Because of their nature and uses, lubricating base oils, greases, and waxes rarely present problems for the general population though spillage may create localized environmental problems. However, in industry, some of these products, especially the metal working oils, may produce marked contamination of the workplace and equipment.

(d) From the available evidence, it appears that bitumen is not a significant source of environmental pollution but, under certain conditions, occupational exposure may occur.

1.1.3 Environmental concentrations and levels of exposure

1.1.3.1 *General population exposure*

Little information is available concerning the concentrations of petroleum products in air, water, or food. Most of the crude oils are produced from deep wells, but natural seepage occurs on land and on the sea-bed. Natural bitumen and asphalt deposits occur in several parts of the world. There are not sufficient data available to estimate the total environmental exposure of human beings to these petroleum products. On occasions, the general population may be exposed for short periods to fumes from heated bitumen used in road building or roofing. Small amounts of hydrocarbons, probably derived from petroleum hydrocarbons, have been found in shell fish. Volatile petroleum components may contribute to atmospheric pollution near refineries, and storage and pumping areas.

1.1.3.2 *Occupational exposure*

(a) Crude oil is usually handled in closed systems from oil well to refinery, so that workers are not exposed to it, unless a serious breakdown or leakage occurs. However, volatile components can escape at well heads, pump glands, or through vents in storage tanks and tanks on ships.

(b) Petroleum solvents are extensively manufactured and are widely used in many occupations. Because of their volatility, industrial exposure to "special-boiling-point" spirits can sometimes be high. Excessive exposure has occurred and has caused ill health in workshops where ventilation was insufficient. With white spirits, skin contact is usually of greater importance than inhalation, at least at ambient temperatures. Skin contact is particularly important in relation to high aromatic solvents, since the aromatic moieties tend to penetrate skin readily. Both skin contact and exposure to fumes or mists of high boiling-point aromatic solvents can occur occupationally.

(c) The extent of occupational exposure to lubricating oils, greases, and waxes depends on the occupation and on the precautions adopted. Some lubricants and transformer oils are handled only occasionally, while work with automatic lathes of old design can result not only in direct contamination of clothes and exposed skin, but also in the inhalation of oil mist that may be produced by the machine and will further contaminate the skin and clothing. Moreover, other equipment, floors, and even roofs may become contaminated.

(d) Extensive exposure to bitumen may occur in such occupations as roadbuilding and repairing, roofing, and flooring.

1.1.4 Effects on experimental animals

(a) Crude oil

Toxicological studies on mice and rabbits have shown that, in general, the tumorogenicity of crude oils is lower than that of some distilled fractions.

(b) Petroleum solvents

The few data available suggest that solvents are readily absorbed when inhaled or ingested and that excretion is also rapid. The metabolic products of benzene and *n*-hexane are well established but the metabolism of other petroleum solvents is not well documented.

Animal studies have been complicated by the fact that mixtures

have generally been studied and that the composition of superficially similar products can vary greatly. However, studies on representative samples have demonstrated that solvents present a low oral and percutaneous hazard for rats. Skin is severely damaged only on prolonged, repeated contact; "short-chain" solvents mainly have a defatting action, while dermatotoxic effects are found with "longer-chain" solvents. In general, the higher the aromatic content of the solvents, the more intense the effects, whatever the route of exposure. In short-term exposure (4–8 h) of rats, atmospheric concentrations causing the death of 50 % of animals (LC_{50}) ranged mainly from approximately 1000–15 000 ppm. The main signs of poisoning were respiratory tract irritation, depression of the central nervous system (CNS), and coma, followed rapidly by death.

The presence of small volumes of solvent in the respiratory tract led to chemical pneumonitis in all species tested. The degree of injury depended on the viscosity rather than on the chemical nature of the materials; the higher the viscosity, the lower the possibility of aspiration into the deeper parts of the lungs.

Repeated exposure of rats, cats, and dogs to the vapours of a wide range of petroleum solvents showed that the toxicity was consistently low. However, exposure to *n*-hexane resulted in pathological changes similar to those associated with peripheral neuropathy in man. The maximum no-observed-adverse-effect level for *n*-hexane is not yet certain. Results of teratogenicity studies on a wide range of hydrocarbon solvents have been essentially negative.

Benzene and the aromatic extracts are the only well-defined petroleum solvents for which carcinogenicity has been reported.

(c) Lubricating base oils, greases, and waxes

These substances are of low acute oral and dermal toxicity, though high oral doses have a laxative effect.

In long-term studies on mice, rats, guineapigs, and rabbits, it has been demonstrated that the carcinogenic activity of these products resides in the polynuclear aromatic hydrocarbon fraction. By suitable refining, oils, greases, and waxes can be obtained that consistently give negative results in skin-painting tests. The most potentially carcinogenic substances have been found among the 4,5, and 6 condensed ring polynuclear compounds with relative molecular masses ranging from 230 to 330. Experimental evidence suggests that some long-chain aliphatic, alicyclic, and alkylaromatic hydrocarbons may act as co-carcinogens, when applied to the skin together with the carcinogenic fraction.

It has been shown that washing the skin of animals after application of carcinogenic oils decreases both the number and rate of appearance of tumours. The degree of reduction is related to the

time between application and washing. A lowering of the frequency of application of the oils also reduces the rate of tumour development.

Carcinogenic activity has been demonstrated in certain metal-working and textile oil formulations and there is evidence that carcinogenic polynuclear aromatic compounds may be produced, when oil products are subjected to high temperatures.

Aspiration of oils has been shown to induce a foreign body reaction in animal lungs as well as lipid pneumonia. However, when animals were exposed to oil mist, very little was retained in the lungs, and lipid pneumonia did not occur, even at high exposure levels. From studies on the mouse, rat, hamster, rabbit, and dog, it would appear that atmospheric exposure to 5 mg/m^3 of oil mist is without risk.

Oral administration of food-grade mineral oils and waxes to rats did not result in any carcinogenic or chronic toxic effects.

(d) Bitumens

Although some bitumens applied to the skin of mice exhibit carcinogenic activity, it is low compared with that of coal tar, and it is generally accepted that the toxicity of bitumens is low.

1.1.5 Clinical and epidemiological studies in man

(a) Crude oils

Many cases of keratotic changes and epithelioma on exposed parts of the skin have been reported in workers exposed to crude oils. The relative roles of the oil and of other factors, e.g., sunlight, is uncertain.

(b) Petroleum solvents

Petroleum solvents with boiling-ranges up to 230 °C are primary irritants, though their irritant and defatting actions decrease as the boiling-range increases. Solvents of naphthenic origin or with a high aromatic content tend to be the most irritant. On repeated contact, the keratin layer of the skin is damaged, making the skin more susceptible to other irritants, sensitizing agents, and bacteria.

Acute occupational poisoning by gasoline vapour has usually been the result of entering unpurged gasoline tanks or other premises, where high concentrations of gasoline vapour have accumulated. With increasing concentrations of gasoline vapour, exposed subjects may experience drowsiness, dullness, numbness, and headache followed by dizziness, ataxia, and nausea. Exposure to higher

concentrations of vapour, or for a longer period, may lead to loss of consciousness followed by death, which may be preceded by convulsions.

In the last 15 years, an increasing number of cases of polyneuropathy have been reported in workers exposed to high concentrations of volatile petroleum solvents, mainly consisting of technical hexane. Though *n*-hexane seems to play a major role, the possibility that other components of the solvents may have a similar or synergistic action cannot be ruled out.

Ingestion of large volumes of solvent is usually well tolerated, unless aspiration occurs. Small volumes (1–2 ml) of kerosene will, if aspirated, cause acute chemical pneumonitis, which is often fatal. The prognosis of chemical aspiration pneumonitis has improved over the past years with improved methods of treatment. Where no aspiration occurs, the symptoms are similar to those following overexposure to vapour.

Long-term exposure to low vapour concentrations has been reported to produce non-specific symptoms such as nervousness, loss of appetite, and nausea. Other symptoms referable to the peripheral and central nervous systems, the gastrointestinal tract, the lungs, eyes, and reproductive system have also been described. No dose-concentration effect relationships can be derived from present knowledge either for short-term or long-term exposures. It is considered probable that blood abnormalities, previously reported following exposure to solvents, were, in fact, due to the presence of benzene in the solvents.

(c) Lubricating oils, greases, and waxes

Exposure of the skin to these products can induce several types of disorder including primary irritation, oil acne, hyperkeratosis, and photosensitivity. The degree of severity of these disorders depends on the nature of the oil, the integrity of skin, the frequency and length of contact, and individual susceptibility. In general, lower-boiling-point materials have a more pronounced defatting effect, while the higher-boiling-point materials induce the formation of acne. In many cases, additives or contaminants in the oils are responsible for the disorders, rather than the oil itself.

Prolonged exposure to non-solvent, refined mineral oils has been associated with the induction of cancer of the scrotum, e.g., in machine operators and those involved in spinning operations. Less frequently, cancer at other sites, including the hand and forearm, lung, and bronchus have been associated with exposure to oils containing significant concentrations of polynuclear aromatic compounds. Results of epidemiological studies have suggested an association between exposure to oil mist and an increased incidence

of pulmonary cancer. However, the exact levels of exposure to the oils and polynuclear aromatic compounds in these studies is not known. Very rarely, cases have been reported of lipid pneumonia associated with prolonged exposure to high concentrations of oil mist. Whether there was a causal relationship is uncertain.

(d) Bitumen

Evidence from epidemiological studies on workers in oil refineries, highway construction, roofing industries, and bitumen transport firms strongly suggests that petroleum-based bitumens do not present a significant health hazard.

The possibility that bitumen and the vapours emanating from it might contribute to the overall incidence of cancer of the skin and of the respiratory tract has to be considered in view of their content of polynuclear aromatic compounds, but there are no data to substantiate this.

1.1.6 Evaluation of health risks

Available information indicates that the health risks for the general population from the production of crude oil and the manufacture and use of petroleum products are very low. Under normal circumstances, there is, at the most, a nuisance because of pollution of the air and/or water.

The major risks are related to the health of workers involved in the manufacture or handling of these products.

Exposure to high concentrations of the vapour of petroleum solvents can produce narcotic effects. Long-term exposures to low concentrations have been reported to produce non-specific symptoms. The no-observed-adverse-effect level of exposure has not been established for these products. Prolonged exposure to *n*-hexane has resulted in the development of polyneuropathies most of which have proved reversible on cessation of exposure. In the case of solvents containing benzene, the possibility of bone marrow depression and leukaemogenesis must be borne in mind. Prolonged skin contact with petroleum solvents can lead to contact irritative dermatitis, but only rarely to contact allergic dermatitis.

Both types of skin disease occur more frequently in professions using products derived from base oils, especially metal-working oils. Such diseases may cause considerable distress, they affect the general well-being and reduce the capacity to work. Skin cancer has been described in workers after prolonged and intensive exposure to less refined base oil derivatives, e.g., the metal-working oils formerly in use. Practically all these skin diseases appeared

in occupations where hygiene and working conditions were poor. These factors were as important as the intrinsic toxicity of the oils.

Exposure to low concentrations of mists of highly refined oils appears to be without serious health hazards; this is not necessarily the case with less refined oils, which have been reported to cause an increased incidence of cancer of the respiratory tract, after prolonged high-level exposure.

There is no evidence to suggest that the production and use of bitumens presents a health hazard for the general population and for workers (other than burns from splashes of hot bitumen).

1.1.7 Control measures

Every effort should be made to avoid the contamination of workers, the workplace, or the general environment with petroleum products. This can be achieved by appropriate technological measures and good work practice.

As far as possible, products containing highly toxic compounds should be avoided and alternatives sought.

Where contact is unavoidable, suitable protective equipment should be used. Health education of employers and workers should be promoted emphasizing the necessity for maintaining high standards of personal hygiene. When necessary, pre-employement, and regular periodic medical examinations should be carried out on exposed workers.

Adequate control programmes should be implemented, including the disposal of many types of waste oil products.

1.2 Recommendations for further studies

1.2.1 Analytical aspects

A major problem in assessing the health hazards of petroleum products is that the majority have been developed and specified according to their physical properties such as the boiling-point and viscosity rather than their chemical composition. Products with the same physical properties may vary considerably in chemical composition (e.g., different proportions of isomers) and, hence, biological properties. It is, therefore, important for future experimental animal and human studies that analytical methods should be available to establish the chemical structure of the products to which subjects are exposed, and research into suitable methods should continue. Analytical methods suitable for determining low con-

centrations of solvents and oil products and their individual components in the environment should continue to be developed and some consideration should be given to the development of simple control techniques at the work-site level.

1.2.2 Sources and levels in the environment

In some cases, the use of aromatic extracts and highly aromatic base oils should be reconsidered and alternatives sought, where there might be a risk of carcinogenic effects on the skin and respiratory tract.

More information is needed on the concentrations of petroleum products and their constituents in the work-place and the general environment, especially in the neighbourhood of refineries and petrochemical plants. Such data would result in more meaningful epidemiological studies and would be of use in the development of suitable measures to control pollution and the exposure of the general population.

There is a need to understand more fully the factors responsible for the production of oil mists and the importance to health of inhalation of particles of various sizes. Most oil mists contain chemical additives and the possible effects of these, when inhaled by man, must be considered.

Improved methods for quantifying human exposure to petroleum products in the working environment are required. While inhalation exposure can be estimated from atmospheric monitoring, the extent of exposure through skin contact has rarely, if ever, been examined.

International cooperation is needed in the elaboration and clarification of exposure limits for petroleum products and their components in water, air, and the working environment. These should be based on adequate evaluation of their risks.

1.2.3 Studies on experimental animals

More studies are needed of the mechanisms by which petroleum products produce injury in experimental animals. Little information is available on the metabolism and pharmacokinetics of the components of oils. In particular, elucidation of the dose/time/effect relationships of exposure of animals to *n*-hexane would be of value in assessing acceptable human exposure levels. Information on the neurotoxicity of other components of petroleum solvents and on their ability to act synergistically with *n*-hexane should also be sought. The possible effects of petroleum solvents on aspects of

the reproductive processes, not already studied in depth, should be examined. A quick and reliable analytical method for determining 4, 5, and 6 condensed ring polynuclear aromatic compounds needs to be developed and its predictive value in assessing carcinogenic potential examined. Similarly, a short-term biological test for carcinogenicity, applicable to oil products, would be of great value in providing a method for the rapid assessment of the potential carcinogenicity of oils.

1.2.4 Human studies

Further studies to determine the dose-effect relationships of exposure to a wide range of petroleum oil and solvent products would be of value, particularly in relation to long-term exposure. In such studies, the possibility that any adverse effect produced by exposure might be influenced by working conditions (e.g., general work environment, heat, stress, and noise) should be considered and, if necessary, investigated. As well as studying general health, possible specific actions on the cardiovascular, gastrointestinal, and central and peripheral nervous systems should be considered. Possible susceptible groups, and factors such as age, sex, state of health, and genetic background should also be taken into consideration. There is a need to assess the extent of health problems caused by the use of petroleum products in the developing countries, where exposure conditions may be less well controlled; relatively few studies relating to these problems have been carried out.

Efforts should be made to develop common criteria for the detection and definition of health effects in order to allow comparison of findings between different research workers and institutes throughout the world.

2. CRUDE OILS

2.1 Properties and Analytical Methods

2.1.1 Chemical composition and properties

Crude oils originate from the decomposition and transformation of aquatic, mainly marine, animals and plants that became buried under successive layers of mud and silt some 15–500 million years ago; they are essentially very complex mixtures of many thousands of different hydrocarbons. Depending on the source, the oils contain various proportions of straight and branched-chain paraffins, cycloparaffins, and naphthenic, aromatic, and polynuclear aromatic hydrocarbons. The younger oils are characterized by their more asphaltic nature. As many "paraffins" of high relative molecular mass may contain naphthenic and/or aromatic rings, this should not be understood as a sharp division between defined chemical entities.

The hydrocarbons may be gaseous, liquid, or solid, under normal conditions of temperature and pressure, depending on the number and arrangement of carbon atoms in the molecules. As a general rule, at ambient temperatures, compounds with molecules containing up to 4 carbon atoms are gaseous; those with 5–20 carbon atoms, liquid; and those with more than 20 carbon atoms, solid. In crude oil, gaseous and solid compounds occur dissolved in the liquid fraction. Solidification of crude oils is caused by the presence of waxy normal paraffins of high relative molecular mass. Unsaturated hydrocarbons such as olefins and alkynes do not occur in crude oils.

Crude oils are similar to coal in that they are greatly enriched in carbon and hydrogen compared with the average composition of the earth's crust. Both are excellent sources of carbon for chemical synthesis.

The sulfur content of crude oil ranges from less than 2 to 60 g/kg, depending on the origin of the oil. The sulfur is present not only as sulfide but also as mercaptans, thiophenes, and more complex organic sulfur compounds. The level of organic nitrogen compounds in most crude oils is less than 1 g/kg, but some may occasionally contain as much as 20 g/kg. Nitrogen compounds in crude oil are complex and mostly unidentified structures, which, through thermal decomposition during the distillation process of crude oil, are converted to simpler structures. Crude oils may also contain some naphthenic acids and phenolic compounds (Petroleum Handbook, 1966).

As crude oils are the decomposition products of former aquatic animal and plant organisms, it is not surprising that they contain

most, if not all, of the known elements. These are mainly present in very small quantities, i.e., only in mg/kg or small fractions of mg/kg. However, nickel, molybdenum, and mercury levels are sometimes as high as 10 mg/kg and vanadium levels, 50 mg/kg (Mason, 1966; Bertine & Goldberg, 1971). More complete coverage of crude oil trace elements can be found in BP (1975).

Crude oils vary widely in appearance and consistency from country to country and from field to field. They range from yellowish brown, mobile liquids to black, viscous semi-solids. The differences are due to the different proportions of the various molecular types and sizes of hydrocarbons. One crude oil may contain mostly paraffins, another mostly naphthenes. Whether paraffinic or naphthenic, one may contain a large quantity of lower hydrocarbons and be mobile or contain a lot of dissolved gas; another may consist mainly of higher hydrocarbons and be highly viscous, with little or no dissolved gas. The nature of the crude oil governs, to a certain extent, the nature of the products that can be manufactured from it and their suitability for special applications. A naphthenic crude oil will be more suitable for the production of asphaltic bitumen, a paraffinic crude oil for wax. A naphthenic crude oil, and even more so an aromatic one, will yield lubricating oils with viscosities that are sensitive to temperature. However, with modern refining methods there is greater flexibility in the use of crude oils to produce any desired type of product. Crude oils are usually classified into three groups, according to the nature of the hydrocarbons they contain:

(a) Paraffin base crude oils

These contain paraffin wax, but little or no asphaltic matter. They consist mainly of paraffinic hydrocarbons and usually give good yields of paraffin wax and high-grade lubricating oils.

(b) Asphaltic base crude oils

These contain little or no paraffin wax, but asphaltic matter is usually present in large proportions. They consist mainly of naphthenes and yield lubricating oils that are more viscosity sensitive to temperature than those from paraffin base crude oils. These crude oils are now often referred to as naphthene base crude oils.

(c) Mixed base crude oils

These contain substantial amounts of both paraffin wax and asphaltic matter. Both paraffins and naphthenes are present together with a certain proportion of aromatic hydrocarbons.

This classification is a rough-and-ready division into types and

should not be used too strictly. Most crude oils exhibit considerable overlapping of the types described and by far the majority are of the mixed base type (Petroleum Handbook, 1966).

A useful compilation of the various characteristics and approximate composition of most relevant crude oils is given in Anon (1973).

2.1.2 Methods of sampling and analysis

As the methods of sampling and analysis are the same for crude oils, petroleum solvents, and lubricant base oils, a general discussion follows.

The petroleum products dealt with in this document are mostly complex mixtures of closely related chemical compounds, identified as a product on the basis of certain physical and chemical characteristics related to their intended use. Because of the complex nature of these products, only some of the relatively simple, low-boiling components can be determined individually, and even these cannot be selectively monitored in the working area without appreciable expense. Thus monitoring for groups of compounds such as "total hydrocarbons", etc. is often unavoidable.

The objective of the analysis will, in general, be to determine the concentration of any particular suspected component class rather than to identify the product. Moreover, because of differences in the volatility, solubility, etc. of the components, the product will lose its "identity" the moment is escapes from its original confinement and enters the environment.

Potential health hazards associated with handling petroleum products mainly arise from skin contact and inhalation. By proper precautionary measures, the risk of skin contact can easily be controlled. The occurrence of air contaminants, however, quite often escapes human perception and this section will be devoted to ways of assessing levels of contaminants in air.

Based on their different toxicological behaviour, 3 classes of air contaminants can be distinguished, namely: gases and vapours (from, e.g., solvents, petrol); mists (from, e.g., higher-boiling refined oils); and fumes (from, e.g., high-boiling aromatic extracts, bitumens).

Sampling and analysis for these 3 classes will be discussed separately and particular attention will be given to single components at present considered to be the most hazardous, such as benzene, *n*-hexane, and polycyclic hydrocarbons.

Though, in the context of this Environmental Health Criteria document, methods for the monitoring of both the air in the workplace and the ambient air are relevant, only methods for work-

place monitoring will be briefly reviewed. The most sensitive methods for monitoring work-place air could also be used for monitoring the generally much lower levels in the ambient air.

The most frequent reason for sampling the air in the work-place is to measure the concentration of hazardous agents to which the worker may be exposed. The preferred way of assessing the exposure level is to determine the time-weighted average (TWA) concentration for a normal 8-h working day in the breathing zone of an individual worker. For area monitoring, fixed station or portable monitors are used. Data obtained in this way are independent of the presence and movement pattern of the worker.

A detailed description of sampling strategy is given, for instance, in NIOSH (1977a).

An alternative method for the determination of the amount absorbed by a worker is biological monitoring, i.e., assessment of the absorbed substance or its metabolites in biological material (urine, blood, expired air). Such methods are available for many substances, but unfortunately not for petroleum products, with the exception of benzene and its homologues and, to a certain extent, *n*-hexane. The principles of biological monitoring have been reviewed by many authors, e.g., Piotrowski (1977).

The types of pollutants that occur in the work-place can be divided into 2 broad categories, based on their physical state, namely: gaseous pollutants and aerosols. Methods for sampling gaseous pollutants are different from those for aerosols.

2.1.2.1 *Gases and vapours*

For personal monitoring, sampling and analysis are usually performed in 2 separate steps. Samples are collected, mostly over a prolonged period of time, from the breathing zone of the worker by passing the contaminated air at a flow rate of 50–200 ml per min (using a personal sampling pump carried by the worker) through a small tube containing a suitable adsorbent (NIOSH, 1973; Clayton & Clayton, 1978; Voborsky, 1980). For hydrocarbon vapours, activated charcoal is one of the best adsorbents.

Recently, passive dosimeters, based on diffusion of the substance into an adsorbing layer, have been developed and marketed. Though laboratory studies have shown these dosimeters to be as accurate as adsorbent tubes using sampling pumps, more field data are needed to prove their validity.

For grab samples, the contaminated air may also be collected in Tedlar, Mylar, or Saran bags or in gas pipettes. Such samples must be analysed as soon as possible, because of possible sample losses.

The techniques used for personal monitoring can also be used for area monitoring. In many instances, however, the high specificity

and accuracy that can be obtained by the sophisticated methods used for the analysis of personal monitoring samples is not required and relatively simple, direct reading instruments can often be used when searching for leakages, when monitoring areas with only a single substance as a contaminant, or when monitoring areas where the total hydrocarbon level is generally below the exposure limit for any of the individual substances of concern.

The most simple direct reading instrument is the colorimetric indicator tube, usually used with a hand pump, a wide variety of which are available. However, while it is true that colorimetric indicator tubes are of low initial cost and simple and convenient to use, there are distinct limitations and potential errors inherent in this method. A manual describing the applications and limitations of these devices is available (AIHA, 1976). Other, commercially available, direct reading instruments include portable infrared instruments, portable gas chromatographs, and non-specific analysers, such as total hydrocarbon analysers (ACGIH, 1978b).

An analytical procedure may, however, include several of the following steps: sample recovery, concentration, pre-separation, derivatization, and analysis.

The sample can be recovered from solid collection media by solvent extraction or by thermal desorption. When a liquid absorbent is used, a concentration step may be required.

Very many analytical techniques are available. However, as the quantities of organic material to be determined are generally minute and concealed in a matrix of many other substances, some analytical techniques are especially suitable, such as gas chromatography (GC), gas chromatography and mass spectrometry (GC/MS), and high-pressure liquid chromatography (HPLC) with ultraviolet or fluorescence detection.

Criteria for the choice of analytical technique include: specificity required; quantities involved; ease of operation; suitability for automation; and cost per analysis.

The principles of the analytical techniques mentioned are described extensively in many monographs. For example a short description of all relevant analytical techniques is given in NIOSH (1973). Thus, only those for total hydrocarbons, *n*-hexane, and benzene will be discussed here.

(a) Total hydrocarbons

Colorimetric indicator tubes are available from most manufacturers for the determination of total hydrocarbons in the work-place air. These tubes normally cover the range from about 100 ppm to several thousand ppm (corresponding to gasoline levels ranging from 450 mg/m^3 to several grams per m^3, if a conversion factor of

4.5 is applied). Many commercial instruments are also available (ACGIH, 1978), the most reliable being those based on flame ionization detection. These methods are generic in nature and the instruments have to be calibrated, e.g., against methane or *n*-octane. The read-out is not absolute, as the detector response differs according to the composition of the hydrocarbons.

(b) n-Hexane

Depending on the situation, one of the 2 following approaches can be applied in analysing specifically for *n*-hexane:

(i) *n*-Hexane as the main contaminant: direct area monitoring can be performed using either a flame ionizing detector, without previous separation (total hydrocarbon detector), or the total hydrocarbon or low range *n*-hexane colorimetric indicator tubes (*n*-hexane tubes are non-specific and react to all hydrocarbons; the range is from about 20 mg/m^3 upwards).

The NIOSH method S-90 (NIOSH, 1977–79), using the charcoal tube/carbon disulfide desorption method with GC-analysis on packed columns is suitable for personal monitoring.

(ii) *n*-Hexane present as one of the constituents of a hydrocarbon mixture: In this case the matrix is very complicated. It is more or less a prerequisite to use capillary GC to obtain a satisfactory separation. Sample recovery is preferably carried out with a 2-step thermal desorption, though solvent desorption using a solvent with a longer retention time on the GC column (e.g., decane) could be used.

Recently, it has been suggested that the urinary excretion of hexane metabolites could be used for monitoring occupational exposure to *n*-hexane and its isomers (Perbellini et al., 1981).

(c) Benzene

If benzene is the main pollutant, total hydrocarbon analysers, or, even better, the benzene colorimetric indicator tubes can be used (ranges available: from 0.15 to 150 mg/m^3, sensitive to other aromatic compounds, somewhat sensitive to hydrocarbons).

In all cases, the personal monitoring charcoal-tube/carbon-disulfide-desorption/GC-analysis method can be used, i.e., NIOSH method S-311 (NIOSH, 1977–79).

A detailed description of the determination of benzene in work environments can be found in CONCAWE (1981a).

Biological monitoring for benzene exposure is carried out by measuring the elimination of phenol (metabolite of benzene) in urine. Several colorimetric methods (using 2,6-dibromo-*N*-chloro-*p*-benzoquinoneimine-Gibbs reagent, 2,6-dibromoquinone-4-chlorimide, diazo-*p*-nitroaniline or 4-dimethylamino-2,3-dimethyl-1-phe-

nyl-3-pyrazolin-5-one (4-aminopyrine)) or gas chromatographic methods are available. A concentration of phenol in urine of more than 25 mg/litre indicates some exposure to benzene (Truhaut & Murray, 1978).

2.1.2.2 *Aerosols*

The sampling of aerosols is performed by drawing a measured volume of air through a filter, an impaction or impingement device, or an electrostatic or thermal precipitator. The most common method, especially for personal monitoring, consists of drawing air, at a well-defined rate, through a filter. For personal monitoring, a portable pump and a suitable filter in a filter-holder, located in the worker's breathing zone, is used.

For area monitoring, some direct reading instruments for grab sampling are also available based on, e.g., light-scattering, attenuation of beta radiation, and changes in the resonant frequency of a piezoelectric quartz crystal (ACGIH, 1978).

In some cases, size-selective sampling is necessary. This can be accomplished by placing a cyclone or elutriator in front of the sampler, or by the use of special-size selective sampling devices. When, however, the aerosol also presents a hazard through absorption via the gastrointestinal tract, total particulate matter should be sampled.

In many instances, the total particulate concentration in air is the only information needed, in which case, a gravimetric determination of the material collected is all that is required.

On the other hand, if it is necessary to determine the benzene-soluble matter present in the total particulate matter collected, the collected matter must first be extracted with benzene. The extract must then be evaporated to dryness and the residue weighed (NIOSH, 1977–79). When more detail is required concerning the composition of the aerosol collected, the benzene extract should be analysed for the substances of concern.

Mists

Aerosols generated from refined oils and oils with a relatively low aromatic content are often referred to as mists. The methods of analysis most frequently used for mists consist of drawing air, at a well-defined rate, through a preweighed and preconditioned glass-fibre filter and recording the weight gain. If the weight gain indicates that the total particulate concentration in the work atmosphere is well below the appropriate exposure limits, no further analytical action is required for the air sample. However, when concentrations in excess of such levels are found, investigators invariably require determination of the oil content of the filter.

For this purpose, the filter is extracted with a suitable solvent and the oil content of the extract determined, either gravimetrically (after evaporation of the solvent) or spectrophotometrically, using ultraviolet or infrared adsorption or fluorescence spectrophotometry (CONCAWE, 1981b; NIOSH, 1977–79).

The exposure limits for mists are mainly established as total particulate oil mist and, for general investigations and control work, it is recommended that sampling should be designed to take this into account. Nevertheless, there may be some occasions when the investigator feels it necessary to assess the concentration of respirable particles in the mist, and special sampling techniques, e.g., using a cyclone, will need to be employed. Experience, however, does suggest that, in general, the equivalent diameter of particles in oil mists in engineering workshops is well below 5 μm and hence they may be regarded as respirable. Thus, it is common industrial practice to sample for total particulate matter.

For area monitoring, one of the direct reading devices mentioned earlier could also be used.

Fumes

Aerosols generated from high-boiling aromatic extract oils and bitumens are called fumes.

Where exposure to fumes from materials containing significant concentrations of polycyclic aromatic hydrocarbons, such as aromatic extract oils, is likely to occur, some guidance can be gained from the AGGIH TLV-TWA of 0.2 mg/m^3 for particulate polycyclic aromatic hydrocarbons (as benzene-soluble material BSM). Coal tar pitch volatiles include the fused polycyclic hydrocarbons that volatilize from the distillation residues of coal, petroleum, wood, and other organic matter. In the case of aromatic extract oils, the fact that a major part of the BSM consists of non-polycyclic aromatic compounds should be taken into account (NIOSH, 1977b).

With regard to the present standard for BSM, the analytical method is as follows: total particulate matter suspended in air is collected on a glass-fibre filter, with a silver membrane back-up filter. The filter is extracted with benzene, using ultrasonic agitation. An aliquot of the extract is evaporated to dryness and the residue is weighed (NIOSH, 1977–79).

If it is felt necessary to characterize more fully the polycyclic aromatic hydrocarbons (PAHs) present in the benzene extract of the fume samples, further analysis of these extracts can be performed as follows:

(a) GC method (Grimmer & Böhnke, 1972; Grimmer, 1979): The filter extract is treated in several steps to isolate a fraction, enriched in PAHS. This fraction is then analysed by capillary GC/MS. For very complex products, the aerosol composition

might be too complicated to obtain a reasonable chromatogram, even after all the pre-separation steps.

(b) HPLC separation with fluorescence detection (Das & Thomas, 1978; Belinky, 1980).

The filter extract is evaporated and dissolved in 0.5–1 ml of benzene. This extract is directly injected into the HPLC instrument. As the fluorescence detector only records the highly unsaturated molecules, the larger part of the matrix does not give any signal at all on the detector. Only the alkyl-substituted and unsubstituted polycyclic aromatic compounds give rise to a detector signal.

Specificity for selected substances can be increased substantially by a proper choice of excitation and emission wavelengths.

For the more volatile polycyclic aromatic hydrocarbons, like pyrene, some losses may occur during sampling, due to volatilization. If these more volatile polycyclic aromatic hydrocarbons are also of interest, the filter collector could be backed up by a silicagel tube. The silicagel from this tube is then treated in the same way as the filter.

2.2 Sources of Environmental Pollution

2.2.1 Natural occurrence

Crude oils are exclusively natural products, most of which are produced from artificial wells. Natural seepage of crude oils occurs in various parts of the world, not only on land, but also on the seabed; however, this represents only a minor source of environmental pollution in comparison with man-made sources.

2.2.2 Man-made sources

2.2.2.1 *Production*

Taking world-wide figures, total crude oil production for 1973 was about 2900 million tonnes, i.e., approximately 10 times the crude oil production in 1938. The rate of growth of production has declined since 1973 (the 1979 level was just over 3200 million tonnes), and very little overall increase, if any, is expected in the near future.

2.2.2.2 *Uses*

In some areas, e.g., Japan, certain unrefined crude oils are used as fuels.

Negligible amounts of unrefined oils are used for such applications as road construction and malaria control.

In some areas, where crude oils come to the surface in natural seepage, they have been used by the local population, since prehistoric times, for a number of purposes, but mainly for heating and lighting.

Nearly all the crude oil produced is processed in refineries into various fuel and non-fuel fractions.

An example of an integrated flow scheme for the processing of crude oil is shown in Fig. 1. The crude oil distillation (a straightforward distillation process) and subsequent vacuum-distillation (distillation under high vacuum) of the residues of the first process splits crude oil into its basic fractions which, after further treatment, purification, and sometimes blending with additives, are used as commercial products. The major petroleum fractions are listed in Table 1 in broad categories according to increasing boiling-point.

Certain petroleum fractions, such as naphtha or wax can be submitted to various thermal or catalytic cracking processes and to other refinery processes such as alkylation, and isomerization. In the course of these processes, long-chain paraffinic hydrocarbon molecules are broken down into smaller molecules including unsaturated (olefinic) compounds. Some of these olefins may stay in the end-product of the cracking process, others, especially if under the influence of high temperatures and catalysts, will react among each other and form more complex structures ranging from isooctanes to polynuclear aromatic hydrocarbons (Badger, 1962).

The products obtained from cracking processes can be distilled into various fractions in a similar way to crude oils, though obviously the composition of the fractions is different. For instance, they contain a certain percentage of olefins that are highly valued as base materials for the chemical industry. By suitable choice of cracking procedures, the yield of special compounds such as gasoline components or olefins can be boosted. On the other hand, fractions

TABLE 1. Range of major petroleum fractions

Fuels	Boiling range (approximate)	Non fuels
natural gas refinery gas liquefied petroleum gas (LPG)	<10 C	
gasolines kerosenes gas oils	35 C 300 C	petroleum solvents naphtha
heavy fuel oils	300 C 700 C	base oils also used for lubricating, metal working and textile oils petrolatum petroleum waxes
	>700 C	bitumens, coke

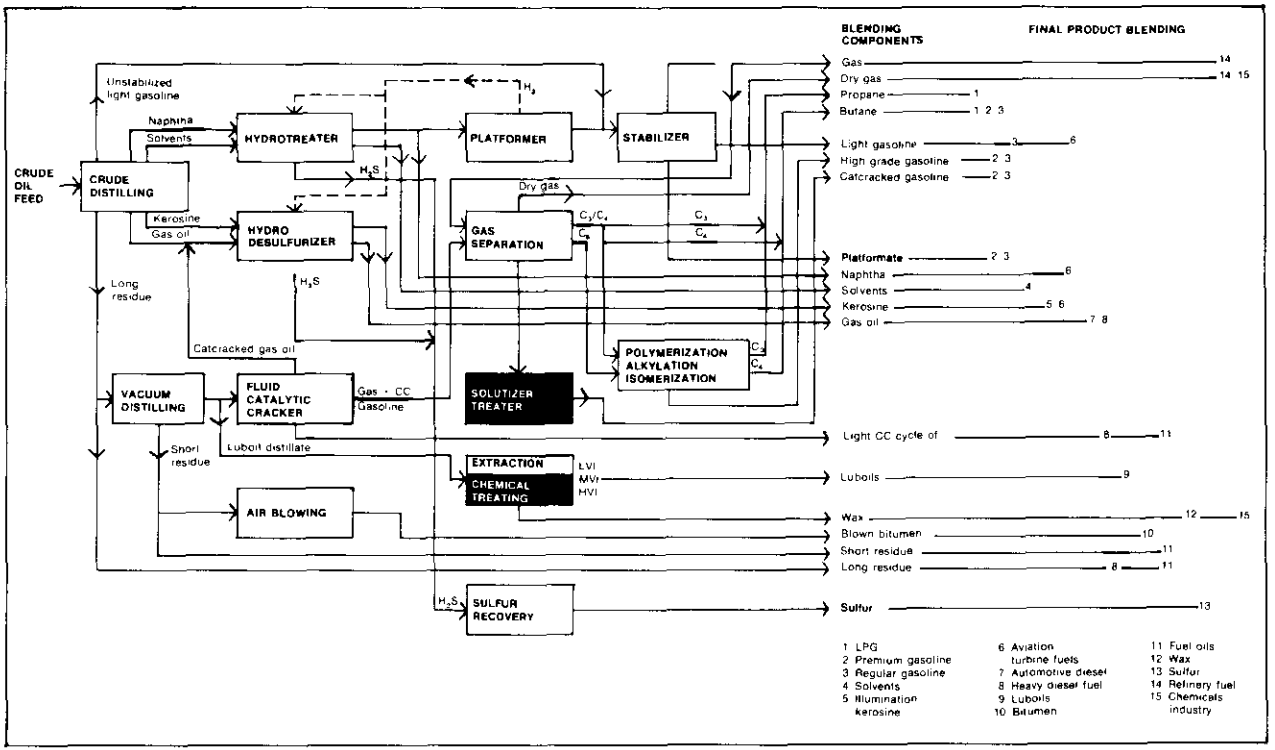

Fig. 1. Integrated flow system for processing crude oil (Adapted from: Petroleum Handbook, 1966).

derived from the cracking of petroleum products contain a higher percentage of polynuclear aromatic hydrocarbons than corresponding straight-run crude oil fractions. The implications of this will be discussed later.

Examples of olefinic base chemicals derived from cracking processes are: ethylene, acetylene, propylene, butylenes, pentenes, and higher aliphatic olefins, such as butadiene, isoprene.

It is outside the scope of this review to give further details and other refining processes.

2.2.2.3 *Disposal of waste*

In a refining process, the release of oil into refinery effluents is practically negligible and of a lower order of magnitude than tanker washings in tankers that do not use the "load-on-top" system. Waste gas in production fields is generally burnt on the spot. In refineries and chemical plants, it may be necessary to burn some gas at a flare for reasons of safety, and some oil and gas is consumed as refinery fuel. Atmospheric pollutants in and around refineries basically consist of saturated and unsaturated hydrocarbons, carbon monoxide, hydrogen sulfide, and sulfur dioxide (Poliansky & Musserskaja, 1971; Krasovitskaja, 1976). Sulfur dioxide, hydrogen sulfide, and mercaptan emissions are not discussed in this review and emissions of hydrocarbon vapours into the atmosphere from storage terminals, filling stations, and cars will be covered in another document.

2.3 Toxicological Effects of Crude Oils

As, in this document, crude oils are discussed only to provide background information for the petroleum solvents, lubricating base oils, and bitumens derived from them, no detailed discussion will follow concerning environmental exposure levels, environmental distribution and transport, physiological factors relating to mammalian uptake, dose-response relationships, and maximum permissible levels. Most of the relevant aspects will, however, be covered in the sections on fractions derived from the crude oils. This also applies to toxicological effects on experimental animals and man, with the exception of a very few studies that are related to crude oil exposure only.

The toxicological and nuisance aspects of hydrogen sulfide and mercaptans have been reviewed in detail by Miner (1969) and Sullivan (1969). A review on hydrogen sulfide has been prepared by NIOSH (1977c) and an Environmental Health Criteria document on hydrogen sulfide has recently been published (WHO, 1982).

2.3.1 Effects on experimental animals

Leitch (1924) examined 16 untreated crude oils from various parts of the world for their carcinogenicity by applying them 3 times a week to the skin of mice and found significant differences in tumorigenicity among these oils. Similar results were reported by Hieger & Woodhouse (1952) in skin tests on mice and rabbits. The tumorigenicity of the crude oils they examined was low in comparison with that of some of the distilled fractions. Skin tests were also carried out on mice and rabbits by Antonov & Lints (1960), who found that Saratov oil possessed weak carcinogenic properties. The main causes of death in these tests, however, were pneumonia and general intoxication, probably from absorption of oil components through the skin. The authors found that rabbits were more sensitive than mice, as did Hieger & Woodhouse (1952).

Batt-Neal & Wolman (1977) demonstrated skin tumorigenicity and amyloid deposition following skin exposure of mice to saturated acetone extracts of various oils collected from beaches.

2.3.2 Effects on man

Examination of 743 oilfield workers exposed to California crude oil and excessive sunlight revealed that 7 of them had epitheliomas on exposed parts of the body and that nearly 20 % had keratotic changes on the hands, forearms, face, and neck. Five of the 7 subjects, who developed epitheliomas, were blonds, though blonds were in the minority in this group of workers (Schwartz et al., 1947).

During 1938–39, Schwartz saw 189 cases of carcinomas on exposed parts of the skin; 128 were in males, 71 of whom were oilfield workers 20 others being workers exposed to excessive sunlight only. Emmett (1975) mentions the strong potentiating effect of UV radiation on other potentially carcinogenic exposures. In southern Texas, however, the incidence of skin carcinomas in 330 oilfield workers was low, which underlines the fact that Texas and Pennsylvania oils are known to be less carcinogenic than California oil (Twort & Ing, 1928).

In a study on 50 volunteer operators, who had not previously been in contact with oil and petroleum products, crude oil was applied to the skin of the inner surface of the forearm, for periods of 3–6 h. An inflammatory reaction of the skin developed with moderate erythema, oedema, and slight burning. Changes in the thermosensitive threshold were noted, as well as an increase in the permeability of the epidermis (Gusein-Zade, 1975).

3. PETROLEUM SOLVENTS

3.1 Properties and Analytical Methods

3.1.1 Chemical composition and properties

Only solvents consisting of hydrogen and carbon alone and produced from petroleum will be considered in this review. It should be noted, however, that similar solvents are also produced from coal.

Petroleum solvents consist of complex mixtures of hydrocarbons reflecting the hydrocarbon constituents of the crude oil or, more usually, the intermediate refinery streams from which they are distilled. Because of their complex nature, classification is a problem and no standard, worldwide-accepted nomenclature exists. However, providing that it is recognized that considerable overlapping and many exceptions occur, they can be classified into 3 broad subdivisions, based on distillation ranges:

(a) special-boiling-point solvents (SBPs) – grades with narrow or wide distillation ranges within the main limits of 30–160°C;

(b) white spirits – grades distilling within the main range 150–220 °C, the boiling-points of individual grades usually ranging over more than 20 °C;

(c) high-boiling aromatic solvents – grades distilling in the range 160–300 °C with final boiling-points above 220 °C.

Benzene, toluene, and the xylene isomers occur as components of petroleum solvents, but as they fall more naturally into the category of chemical intermediates, they will be referred to here only in so far as they are important as components of the mixtures being discussed.

Two further clarifications can be made. Firstly, it is common industrial practice to ascribe the name of the predominant isomer present to the petroleum solvent; thus the descriptions pentane, isopentane, hexane, isohexane, and heptane are commonly met. However, in almost all cases, the amount of the named isomer present in an industrial scale product will not exceed 95 % v/v of the solvent and may be as small as 30 % v/v.

Second, most petroleum solvents are marketed on the basis of typical physical properties rather than on chemical specifications, because of the limitations during refining of controlling the complex mixtures of isomers that make up the petroleum solvents. As production techniques become more sophisticated, greater control is possible and more properties can be specified within narrower limits. However, even when such narrow limits are met, the mixture of components present may vary, because of variations in the types of crude oil being processed and alterations in conditions in processing units.

To meet the wide range of properties required by the market, several different processes are used. Distillation is the common process setting the volatility range. Chemical conversion techniques, including reforming, alkylation, and hydrogenation, alter the chemical composition and hence the solvency, as do physical conversion techniques such as solvent extraction and molecular sieve separation. Specific treatments such as caustic soda and sulfuric acid washing and clay percolation are frequently applied to remove odourous substances, chiefly sulfur compounds.

The reader is referred to Boenheim & Pearson (1973) for detailed discussions of the chemical and physical composition and uses of petroleum solvents.

3.1.1.1 *Special-boiling-point solvents (SBPs)*

These are highly purified naphtha fractions with specially selected boiling ranges. The boiling range may be narrow or wide, and generally falls within the limits of 30–160 °C. SBPs are classified according to their boiling range, e.g., SBP 62/82. Petroleum ether, lighter fluid, spot remover, and rubber solvent are consumer products in this range. Generally, SBPs consist of a mixture of hydrocarbons in the C-5 to C-9 range: normal and branched paraffins, cycloparaffins, and aromatic compounds. They contain only traces of olefins. An example of the composition of a typical sample of straight run (i.e., non-dearomatized) SBP 80/110 is given in Table 2.

3.1.1.2 *White spirits*

The boiling-range of this group of solvents falls within the limits 150–220 °C (intermediate between gasoline and kerosene). These solvents can be classified into low-aromatic grades (approximately 15–20 % aromatic hydrocarbons) and high-aromatic grades (45 % or more aromatic hydrocarbons). They generally consist of hydrocarbons in the C-7 to C-12 range, again including normal and branched paraffins as well as naphthenic (cycloparaffins) and aromatic compounds. Olefins are present in trace amounts only. Stoddard solvent, mineral spirits, low-aromatic white spirits (LAWS) and turpentine-substitute are well-known examples from this range.

3.1.1.3 *High-boiling aromatic solvents*

Aromatic hydrocarbons occur naturally in certain crude oils in widely varying concentrations. They are also formed during secondary processes such as thermal and catalytic reforming. They can be concentrated and extracted by solvent extraction.

Apart from benzene, toluene, and xylene, which will not be

TABLE 2. Composition of typical sample of SBP 80/110[a]

Hydrocarbon type	Hydrocarbon	% mass present in sample[b]	Boiling point °C
normal paraffins	*n*-pentane	0.2	36.2
	n-hexane	8.2	69.0
	n-heptane	17.2	98.4
branched paraffins	2 methyl butane T[c]	0.1	27.9
	2,2 dimethyl butane T	trace	49.7
	2,3 dimethyl butane T	0.3	58.0
	2 methyl pentane	1.5	60.3
	3 methyl pentane	1.6	63.3
	2,2 dimethyl pentane	1.0	79.2
	2,4 dimethyl pentane	1.3	80.5
	2,2,3 trimethyl butane T	0.3	80.9
	2,3 dimethyl pentane	9.7	89.8
	3 methyl hexane	9.2	91.9
	3 ethyl pentane	3.1	93.5
	2,2,4 trimethyl pentane	trace	99.2
	2,2 dimethyl hexane	trace	106.8
	2,5 dimethyl hexane	0.6	109.1
	3,3 dimethyl hexane T	trace	112.0
	2,3 dimethyl hexane	0.8	115.66
	3,4 dimethyl hexane	trace	117.7
	3 methyl heptane	0.5	118.9
cyclo C-6 paraffins	cyclohexane	8.4	80.7
	methyl cyclohexane	14.2	100.9
cyclo C-5 paraffins	cyclopentane T	trace	49.3
	methyl cyclopentane	4.7	71.8
	1,1 dimethyl cyclopentane T	2.9	87.9
	1-cis-3-dimethyl cyclopentane T	1.9	90.8
	1-trans-3-dimethyl cyclopentane T	2.7	91.7
	1-trans-2-dimethyl cyclopentane T	0.5	91.9
	1-cis-2-dimethyl cyclopentane T	0.5	99.5
	ethyl cyclopentane	0.6	103.5
	1,1,3 trimethyl cyclopentane T	0.8	104.9
	1-trans-2-cis-4-trimethyl cyclopentane T	0.4	109.3
	1-trans-2-cis-3-trimethyl cyclopentane T	0.4	110.2
	1,1,2 trimethyl cyclopentane T	0.3	113.7
unidentified paraffins		1.1	Probably 110.0
aromatic compounds	benzene	0.7	80.1
	toluene	3.9	110.6
olefins		0.4	

[a] From: Shell International Petroleum Co., London (unpublished data).
[b] Average of duplicate analyses.
[c] T = tentative identification.

discussed separately in this review, this group includes solvents with an aromatic content of 80–100 %, and a wide boiling-range from 160 to 300 °C. High-boiling aromatic solvents are obtained by distillation or solvent extraction from refinery fractions such as kerosene and lubricating base oils, and consist of very complex mixtures of hydrocarbons with more than 9 carbon atoms per molecule. The composition of a typical sample of one of these aromatic hydrocarbons from the middle range (distillation range approximately 192–203 °C) is given in Table 3.

TABLE 3. Composition of typical sample of Solvesso 150[a]

Hydrocarbon		% v/v of solvent
n-butylbenzene		2.47
sec-butylbenzene		0.08
tert-butylbenzene		0.05
m-cymene		0.13
o-cymene		0.01
p-cymene		0.52
1.2-diethylbenzene		1.72
1.3-diethylbenzene		1.10
1.4-diethylbenzene		0.56
1.2-dimethyl-3-ethylbenzene		2.86
1.2-dimethyl-4-ethylbenzene		6.64
1.3-dimethyl-2-ethylbenzene		0.71
1.3-dimethyl-4-ethylbenzene		4.17
1.3-dimethyl-5-ethylbenzene		2.80
1.4-dimethyl-2-ethylbenzene		3.26
m-ethyltoluene		0.37
o-ethyltoluene		0.02
p-ethyltoluene		0.01
indane		0.46
isobutylbenzene		0.32
isopropylbenzene		0.01
1-methyl-3-*t*-butylbenzene		0.76
1-methyl-2-*n*-propylbenzene		1.26
1-methyl-3-*n*-propylbenzene		2.08
1-methyl-4-*n*-propylbenzene		1.93
1-methylindane		0.91
2-methylindane		2.43
4-methylindane		9.28
5-methylindane		2.02
naphthalene		4.03
n-propylbenzene		0.00
1.2.3.4-tetramethylbenzene		3.66
1.2.3.5-tetramethylbenzene		8.84
1.2.4.5-tetramethylbenzene		5.53
toluene		0.02
1.2.3-trimethylbenzene		0.10
1.2.4-trimethylbenzene		0.05
1.3.5-trimethylbenzene		0.01
m-xylene		0.05
o-xylene		0.03
p-xylene		0.03
C-11-naphthalenes		0.31
C-11-indanes		3.58
C-11-alkylbenzene		18.27
C-12-alkylbenzene		0.73
C-12-indanes		0.08
C-13-alkylbenzene		0.02
C-10-indenes		0.10
C-11-indenes		0.07
C-12-naphthalenes		trace
C-13-naphthalenes		
C-12-indenes		0.10
aromatic compounds	Total	94.55

[a] Courtesy Esso Standard Oil Company, New York, N.Y., USA (From: Gerarde, 1960).

Most aromatic solvents are highly purified "white" solvents. Those in the higher boiling range, derived from lubricating base oil stocks by solvent extraction, may be less pure and coloured. They are often by-products and are used as solvents for various technical purposes. In many cases, they are referred to as "processing oils" instead of solvents, and considered under lubricating oils.

3.1.2 Purity of petroleum solvents

In these complex mixtures, impurity is, of course, a matter of definition. Components that are taken out in the course of the various refining and treating processes used to obtain the more pure solvents could be regarded as such. The major impurities would then be sulfur compounds such as hydrogen sulfide, mercaptans, and thiophens, as well as, olefins and other reactive unsaturated hydrocarbons.

A second category of impurities includes the hydrocarbons that have been demonstrated to be carcinogenic in animals and man, such as benzene, the polynuclear hydrocarbons and related heterocyclic compounds containing nitrogen or sulfur.

Generally, the total sulfur content, the olefin content, and the total aromatic content are specified for commercial petroleum solvents. Where special products such as food-grade materials are concerned, the benzene content is specified as well as the UV absorption limits at certain wavelengths, as a measure of the polynuclear aromatic hydrocarbon content.

3.1.3 Methods of sampling and analysis

See section 2.1.2.

3.2 Sources of Environmental Pollution

3.2.1 Natural occurrence

Petroleum solvents do not occur in nature as such, but only as components of the crude oils from which they are derived. Environmental pollution is always man-made and related to the use of the solvents.

3.2.2 Man-made sources

3.2.2.1 *Production*

Because there is no uniform system of definition and classification of petroleum solvents, firm statistics concerning the magnitude of production of this group of materials do not exist. The best estimate of the world-wide production of the group of solvents would be 9 million tonnes for the year 1979.

3.2.2.2 *Uses*

It is not feasible to give more than a general outline of the uses of the range of petroleum solvents.

(a) Special-boiling-point solvents (SBPs)

SBPs are mainly used as: solvents and thinners in lacquers and paints; extraction solvents for perfumes, for vegetable oils and oil and fats of animal origin; quick-drying solvents in printing-ink, coatings, and adhesives; lighter fuel; and for dry-cleaning and degreasing purposes.

(b) White spirits

White spirits are mainly used as: solvents and thinners for lacquers, paints, resins, and printing-ink; solvents in formulations of chemical products, e.g., pesticides; and for metal degreasing, wool degreasing, and dry-cleaning.

(c) Aromatic extracts

The higher-boiling and less-purified aromatic extracts have very good solvent properties for many polymers and are used as extender-oils in rubber, plastics, and bitumens, and also as solvents in printing-ink and pesticide formulations. Furthermore, they can be used as base-materials in the manufacture of carbon black.

3.3 Environmental Exposure Levels

Specific data are not available concerning levels of petroleum solvents in air, water, food, or other environmental media. However, low concentrations of hydrocarbons found in mussels have probably been derived from petroleum hydrocarbons present in the environment (Ehrhardt & Heineman, 1975).

Because of the relatively low boiling-range of these solvents, industrial exposure to vapour may sometimes be high. This is known to occur, especially in small workshops with insufficient ventilation, where, for example, adhesives are used routinely. Although a lot of consumer products may contain these solvents, excessive domestic exposure would not normally be expected unless neat solvent were used for cleaning purposes, indoors. Very limited, indirect exposure of the general population is possible following the use of these solvents as extractants in the production of food-grade vegetable oils.

Exposure to the higher-boiling and less-purified aromatic extracts is mainly confined to occupational situations, where excessive skin-contact may occur, or exposure to vapour in processes carried out at elevated temperatures or with high-speed machines that could give rise to fumes or mists. This will be considered in detail under lubricating base oils.

3.4 Environmental Distribution and Transformation

Data on the distribution between media, environmental transformation and degradation, interaction with physical, chemical, or biological factors and bioconcentration, are not available for petroleum solvents.

However some information exists concerning the behaviour and degradation of crude oil in water (Floodgate, 1972, Hellmann & Zehle, 1972), and of hydrocarbons in general (Walker et al., 1975), and there is much information on the microbial degradation of individual petroleum hydrocarbons (Van der Linden & Thysse, 1965; Haines & Alexander, 1974).

From these publications it can be seen that the subject is highly complex and many factors have to be taken into account, such as the composition of the oil product, the extent of dispersion into the medium, and climatic conditions.

3.5 Metabolism

3.5.1 Absorption

The kinetics are determined by diffusion rates, solubility in fat, and the concentration gradients in the individual compartments of the body.

The highly volatile C-5, C-6, and C-7 paraffins, cycloparaffins, and aromatic hydrocarbons readily pass across the alveolar membrane into the bloodstream and are transported within minutes to the central nervous system. Longer-chain homologues can, to a certain extent, also pass the alveolar membrane, but their principal effect is local. This was shown by Gerarde (1963) in studies on rats.

The alveolar air and blood concentrations of white spirit have been measured in man following inhalation (Åstrand et al., 1975). Aromatic hydrocarbons were absorbed to a greater extent into the bloodstream than aliphatic hydrocarbons (approximate values being 62 % and 50 %, respectively). Similar uptake values in man were shown for the aromatic hydrocarbons, benzene and toluene, by

Nomiyama & Nomiyama (1974), for xylene by Šedivec & Flek (1976), Åstrand et al. (1978), and Riihimäki et al. (1979), and for ethylbenzene by Bardoděj & Bardodějová (1970). Nomiyama & Nomiyama (1974) demonstrated a much lower pulmonary absorption for *n*-hexane, the only aliphatic compound that they tested; it was also rapidly excreted.

The skin is only permeable to hydrocarbons of a certain size. With paraffinic substances, the maximum chain length appeared to be up to 14 C-atoms (Scheuplein & Blank, 1971). Aromatic compounds have a more compact structure and, in studies on guineapigs, Hoekstra & Phillips (1967) showed that compounds from this group with a higher number of C atoms could still pass the skin barrier.

The absorption of vapours through the skin is of minor importance. For example, in man, whole body skin exposure to 2250 mg/m^3 (600 ppm) of toluene was equivalent to an inhalation exposure of less than 37.5 mg/m^3 (10 ppm) (Riihimäki & Pfäffli, 1978). However, absorption during immersion in liquid solvents may be considerable. Percutaneous absorption during immersion of both hands in pure xylene was equal to an inhalation exposure of 435 mg/m^3 (100 ppm) (Engström et al., 1977). The permeation of xylene is thus about 20 nmol/min per cm^2 (Engström et al., 1977; Riihimäki, 1979) and that for toluene, 3 µmol/min per cm^2 (Cohr & Stockholm, 1979). Cutaneous exposure was probably a major route of absorption in 2 cases of acute renal failure with oliguria, caused by exposure to diesel oil (Barrientos et al., 1977; Crisp et al., 1979).

Data for absorption in the intestinal tract are not available, but it is presumed that it would resemble absorption in the alveoli rather than that through the skin.

3.5.2 Distribution in the body

Tissue hexane levels in rats, following inhalation of anaesthetic concentrations, were measured by Böhlen et al. (1973). The tissue distribution generally depended on exposure time and was proportional to the lipid content of an organ until saturation occurred. The liver was a special case for, as its lipid level changed rapidly, the saturation level varied. Hexane was also apparently bound to some blood components.

Women working at conveyor belts gluing parts of rubber footwear had concentrations of petroleum solvents (no details on physicochemical properties given) in the blood ranging from $2 \cdot 35 \pm 0.4$ up to 4.6 ± 0.6 mg/litre at concentrations in the air of 100–300 mg/m^3. The solvent concentration in the blood increased with increasing length of the working period from 1.6 mg/litre in the first year to 2.5 mg/litre after 3.5 years and 3.4 mg/litre after 7–8 years of service.

Wistar rats were exposed to the solvents used in the factory at concentrations in air of 300–1000 mg/m³ for 30–45 days, 4 h/day. The concentration of solvent in the blood amounted to 0.45 ± 0.05 – 1.2 ± 0.01 mg/litre (Lipovskij et al., 1977a).

Transfer of petroleum solvents through the placenta was studied in 85 pregnant women workers in the rubber industry, who came into contact with petroleum solvents during work (physicochemical properties of the solvents not defined, concentration in the air of the operating premises 300 ± 10 mg/m³). The average level of solvents in the blood of 46 pregnant women, on whom abortion was performed, was 1.27 ± 0.3 mg/litre. A level of 3.29 ± 0.6 mg/kg was found in the tissue of the embryo. Women giving birth to a child (39 women) had a level of solvents in the blood of 2.5 ± 0.3 g/litre, while the content in the blood of the umbilical cord was 3.5 ± 0.3 g/litre. The concentration of solvents in the blood of the newborn infants was twice that of the mothers.

Pregnant Wistar rats were exposed to the same solvent at a concentration of 300 ± 10 mg/m³, for 48 days, 4 h per day. The solvent was present in the blood, brain, liver, placenta, uterus, and fetal tissues (Lipovskij et al., 1979).

3.5.3 Biotransformation

In both man and animals, the aliphatic hydrocarbons are generally considered to be biochemically inert and excreted in the same form (Williams, 1959). However, it has been shown that some normal alkanes will, at least in part, be oxidized by the mammalian organism. For example, Ichihara et al. (1969) demonstrated the oxidation of decane in animals such as mice and rats, and the oxidative pathway of *n*-hexane to hexane-2,5-dione and hexane-2,5-diol via methyl-*n*-butylketone has been well established (see for example Spencer et al., 1978).

As far as the metabolism of the cycloparaffins and aromatic hydrocarbons is concerned, the half-life, form, and rate of excretion of each component of the solvent has to be considered. It should be mentioned, however, that the metabolism of individual compounds will not be discussed in this document and readers are referred to the reviews by Williams (1959) and Gerarde (1960).

The carcinogenicity of the solvents is thought to be due to the presence of benzene and some of the polynuclear aromatic compounds.

3.5.4 Elimination

The elimination of the lower-boiling solvents (SBP type) in both

animals and man is usually rapid and mainly occurs via the respiratory tract. However, in the case of ingestion of the heavier solvents (white spirits), elimination mainly takes place with the faeces (Browning, 1965).

3.6 Effects on Experimental Animals

It has been mentioned in section 3.1.1, that the petroleum solvents under discussion in this document are more or less complex mixtures of a range of hydrocarbons. For the commercial products, the specification given generally includes the specific gravity, boiling-range, and total content of aromatic hydrocarbons. The concentrations of individual components vary, within certain limits, with the source of the crude oil from which the solvent is derived, and with the processes by which it is produced. These facts should be kept in mind because:

(a) the toxicity data developed for a certain solvent-specification indicate the order of magnitude of the toxicity of this type of product;

(b) in practice it would be impossible and impracticable to carry out complete toxicity testing on every single solvent on the market. It is only sensible to develop toxicity data for typical representative samples of a certain boiling range and within a certain specification of aromatic content. In the evaluation of the results, however, the analytical composition of the material – especially its contents of *n*-hexane, benzene, and polynuclear aromatic hydrocarbons should be taken into account.

3.6.1 Short-term exposure

Hine & Zuidema (1970) examined various aspects of the acute toxicity of 10 samples of petroleum solvents that contained components representative of the range of hydrocarbons found in commercial petroleum solvents. Four were aromatic solvents containing at least 98 % aromatic hydrocarbons (coded A) and 6 were non-aromatic solvents containing less than 1 % aromatic hydrocarbons (coded S). The boiling ranges and principal components of the samples examined are given in Table 4.

Acute oral, inhalation, and percutaneous toxicity and skin and eye irritancy were examined for all samples. Intratracheal aspiration was simulated with 2 samples and repeated skin irritation tests were carried out using 5 of the samples. Undiluted samples were used for the investigations, all of which were carried out on rats with the

TABLE 4. The boiling-range and principal components of solvents examined for acute toxicity[a]

Sample	Boiling-range	Principal components
A-1	281–286 °F (138–141 °C)	C-8 aromatic compounds (ortho, meta, and paraxylene; ethyl benzene)
A-2	362–398 °F (163–203 °C)	C-9, C-10 and C-11 aromatic compounds
A-3	364–408 °F (188–209 °C)	C-10 and C-11 aromatic compounds
A-4	384–507 °F (196–264 °C)	C-11 to C-14 aromatic compounds
S-1	149–166 °F (65–75 °C)	C-6 normal and isoparaffins (hexanes) and naphthenes (cyclohexane, methylcyclopentane)
S-2	196–220 °F (91–104 °C)	C-7 normal and isoparaffins (heptanes) and naphthenes (methylcyclohexane, dimethylcyclopentane)
S-3	313–356 °F (156–180 °C)	C-9 and C-10 normal and isoparaffins and naphthenes
S-4	368–395 °F (187–212 °C)	C-11 and C-12 normal and isoparaffins and naphthenes
S-5	345–402 °F (174–216 °C)	C-12 isoparaffins
S-6	384–500 °F (195–260 °C)	C-13 to C-16 normal and isoparaffins and naphthenes

[a] From: Hine & Zuidema (1970)

exception of skin and eye irritancy and skin toxicity rests in which rabbits were used.

The findings of Hine & Zuidema (1970) which are summarized in Table 5, showed that all the solvents tested could be considered of low hazard to health unless aspirated or inhaled in extremely high concentrations. Aromatic solvents were more toxic than non-aromatic materials, the dose of solvent required to kill 50 % of rats, when administered orally or percutaneously, being lower for aromatic than for non-aromatic solvents. Skin and eye irritancy were also greater with aromatic solvents. The toxicity of the vapours could not be compared, because the volatility of samples varied greatly. All solvents induced similar toxic effects, whatever the route of administration, including central nervous system depression (characterized by incoordination, prostration, and coma) followed by death. Convulsions sometimes occurred. All solvents caused skin and eye irritation though, in general, as the chain length of the non-aromatic solvents increased their irritant properties decreased. Repeated skin exposure led to skin irritation and necrosis with all solvents.

Hoekstra & Phillips (1963) found that light mineral oils, when applied topically to the skin of guineapigs, caused epidermal hypertrophy, hyperplasia, hyperkeratosis, and depilation. Examination of the effects of various oil fractions demonstrated that the main effect of the short-chain volatile paraffins was to defat the skin, while longer-chain and aromatic hydrocarbons had a dermatoxic effect that was related to the permeability of the skin to these compounds. The maximum dermatoxic effect was seen with hydrocarbons containing 14–19 carbon atoms, while a transition to non-dermatoxicity occurred around 21–23 carbon atoms. This was confirmed with pure *n*-paraffins, but variations may exist with other types of hydrocarbons. Simultaneous application of innocuous

TABLE 5. Toxicity of solvents. Summary of results[a]

Test	Sample	Result	Classification
Oral	A-1	10.0(7.5 – 13.3)	practically non-toxic
LD_{50}	A-2	4.5(3.0 – 6.8)	slightly toxic
(ml/kg)	A-3	13.3(7.5 – 23.7)	practically non-toxic
	A-4	12.3(8.1 – 18.7)	practically non-toxic
	S-1	>25.0[b]	relatively harmless
	S-2	>25.0[b]	relatively harmless
	S-3	>25.0[b]	relatively harmless
	S-4	>25.0[b]	relatively harmless
	S-5	>25.0[b]	relatively harmless
	S-6	>25.0[b]	relatively harmless
Vapour	A-1	6 350(4 670 – 8 640)	slightly toxic
exposure	A-2	>2 450[c]	SVNTART[d]
LC_{50} in ppm	A-3	>580[c]	SVNTART
for 4 h	A-4	>553[c]	SVNTART
	S-1	73 680(66 310 – 79 940)	practically non-toxic
	S-2	14 000 – 16 000	practically non-toxic
	S-3	2 000 – 2 600	slightly toxic
	S-4	>710	SVNTART
	S-5	>792	SVNTART
	S-6	>263	SVNTART
Aspiration	A-4	5/10	hazardous
(mortality)	S-6	5/10	hazardous
Primary	A-1	2.21	moderately irritating
skin	A-2	2.04	moderately irritating
irritation	A-3	2.17	moderately irritating
	A-4	2.79	moderately irritating
	S-1	1.92	slightly irritating
	S-2	1.13	slightly irritating
	S-3	2.38	moderately irritating
	S-4	1.04	slightly irritating
	S-5	1.29	slightly irritating
	S-6	0.75	minimally irritating
Eye[e]	A-1	6.33	moderately irritating
irritation	A-2	6.0	moderately irritating
	A-3	4.33	moderately irritating
	A-4	3.67	slightly irritating
	S-1	0.33	minimally irritating
	S-2	1.0	minimally irritating
	S-3	2.0	minimally irritating
	S-4	0	minimally irritating
	S-5	0	minimally irritating
	S-6	0	minimally irritating
4-h	A-1	approx. 5.0	practically non-toxic
percutaneous	A-2	approx. 5.0	practically non-toxic
LD_{50} rangefind	A-3	approx. 5.0	practically non-toxic
(ml/kg)	A-4	approx. 5.0	practically non-toxic
	S-1	>5.0	practically non-toxic
	S-2	>5.0	practically non-toxic[f]
	S-3	>5.0	practically non-toxic[f]
	S-4	approx. 5.0	practically non-toxic[f]
	S-5	5.0	practically non-toxic[f]
	S-6	5.0	practically non-toxic[f]
Repeated	benzene	3.6	
skin	toluene	3.5	
irritation[e]	A-1	3.3	

[a] From: Hine & Zuidema (1970).
[b] Doses above this amount not practical for testing.
[c] Maximum concentration obtainable at 25 °C.
[d] SVNTART = Saturated vapours not toxic at room temperature.
[e] Lowest toxicity classification may be "relatively harmless".
[f] Scored according to the method of Draize.

long-chain substances together with irritant short-chain substances greatly reduced their toxicity, though this effect was less marked with aromatic solvents.

In further studies on the effects of inhaling the vapours of hydrocarbon solvents (Carpenter et al. 1977a, b, c), the acute (4-h exposure) LC_{50} and no-observed-adverse-effect concentrations were studied in rats cats, and dogs. Results are summarized in Table 6.

These studies confirmed the occurrence of central nervous system depression and there was also evidence of respiratory tract irritancy. There were no marked or consistent differences between the species examined. The major factor determining the acute inhalation hazard was the volatility of the solvent, those containing 9 or more carbon atoms tending to be insufficiently volatile to produce concentrations high enough to be lethal over a short period of exposure. One exception was a "high naphthenic" solvent, which was peculiar also in that depression was not preceded by signs of irritation of the respiratory tract, so that there was no warning of overexposure. Increased aromatic content did not consistently result in increased inhalation toxicity, though earlier work (Lazarew, 1929) suggested that the acute inhalation toxicity of gasoline vapours increased with increasing contents of cycloparaffins and aromatic hydrocarbons. The narcotic action was also found to increase in each step by a factor of 3 in the series – pentane, hexane, heptane, and octane (Fühner, 1921). Swann et al (1974) found that anaesthesia occurred with these compounds at concentrations of 32 000 ppm or more and that respiratory tract irritation increased with chain length. Full anaesthesia can be produced with gasoline (Haggard, 1921), but anaesthetic concentrations are little lower than those that cause convulsions and death (Browning, 1965).

The greatest health hazard arises when hydrocarbon solvents are aspirated into the lungs. This rapidly induces acute chemical pneumonitis, which is characterized by pulmonary oedema and haemorrhage, and is generally fatal (Waring, 1933; Lesser et al., 1943; Gerarde, 1959). Gerarde (1959) demonstrated that the ratio of the oral and intratracheal LD_{50}s was 140:1 for kerosene, the intratracheal LD_{50} being 0.2 ml for rats. This and other evidence demonstrated that pulmonary injury was caused by direct contact with the solvent and not by solvent present in the blood, following its absorption through the gastrointestinal tract.

The same author found that viscosity appeared to be the property that determined the aspiration hazard of liquid hydrocarbons. Lower-boiling-point solvents (B.P. up to 100 °C) evaporated so rapidly in the mouth of anaesthetized rats that death was due to CNS depression following absorption of the vapours. Higher-boiling-point solvents tended to induce chemical aspiration pneumonitis. With alkanes, the aspiration hazard decreased sharply with solvents containing 16 or more carbon atoms, probably because the viscosity of such solvents prevented aspiration into the alveoli. In the aromatic series, side-chains containing more than 6 carbon

TABLE 6. Toxicity of solvents[a]

Coined name	Boiling range °C	Composition[b] (%)			Major Constituents carbon number	4 - 8 h LC_{50} mg/litre (ppm)			13-wk Inhalation NEL mg/litre (ppm)		Human data		Recommended hygiene limit mg/litre (ppm)
		P	N	A		rat	dog	cat	rat	dog	Odour threshold mg/m³ (ppm)	Sensory threshold mg/litre (ppm)	
V.M. & P. Naphtha	118 - 151	55.4	32.7	11.9	C-7 to C-10	16 (3400)	>8 (>1700)	>19 (>4100)	2.8 (600)	2.8 (800)	0.7 - 7 (0.15 - 1.5)	2.1 (450)	2.0 (430)
Stoddard solvent	153 – 194	47.7	37.6	14.7	C-8 to C-12	>8.2 (>1400)	>2.9 (>510)	>10 (>1700)	1.1 (190)	1.9 (330)	0.5 - 5 (0.9 - 9)	7.85 (>150)	1.15 (200)
Rubber solvent	75 - 112	41.4	53.6	4.9	C-6 to C-7	61 (15000)	>5.9 (>1500)	>49 (>12000)	7.9 (2000)	7.9 (2000)	40 (10)	1.7 (430)	1.7 (430)
Mixed xylenes	138 – 141	–		100	C-8	29 (6700)	>5.4 (>1200)	<41 (<9500)	3.5 (810)	3.5 (180)	0.6 – 6 (.14 – 1.4	>0.46 (>110)	0.46 (110)
'60' Solvent	128 - 159	c28.8	c21.4	c49.5	C-8 to C-9	24 (4900)	>9.5 (>1900)	<20 (<4100)	0.44 (90)	1.4 (280)	10 (2)	C. 1.3 (260)	0.44 (90)
'70' Solvent	157 – 211	16.5	15.7	67.8	C-9 to C-11	>4.4 (>810)	>2.4 (>440)	>2 (>370)	1.1 (200)	1.1 (200)	4 (0.7)	0.32 (59)	0.32 (59)
'140 Flash aliphatic solvent'	184 - 205	60.8	35.7	3.4	C-5 to C-12 (sic)	>0.27 (>43)	>0.21 (>33)	> saturated vapour	>0.23 (>37)	>0.23 (>37)	4 (0.6)	0.31 (49)	0.23 (37)
'80' Thinner	96 – 142	9.7	18.9	71.4	C-6 to C-8	27 (6200)	>2.1 (>480)	>24 (>5500)	>1.7 (>390)	>1.7 (>390)	4 (0.9)	0.45 (100)	0.45 (100)
'50' Thinner	98 - 105	66.3	0.6	33.1	C-7	33 (8300)	>3.4 (>600)	>30 (>7600)	2.4 (600)	2.4 (600)	10 (2.5)	1.7 (430)	1.7 (430)
Deodorised kerosene	208 – 272	55.2	40.9	3.9	not stated probably C 12 to C-15	>0.1 (14)	This value applies for all toxicity evaluation and is a saturated atmosphere at room temperature.						0.1 (14)
'40' Thinner	187 - 231	35.4	32.9	31.5	C-9 to C-13	>0.2 (>33)	>0.25 (>41)	>7 (aerosol)	0.22 (36)	0.22 (36)	1 (0.17)	0.21 (35)	0.15 (25)
Toluene concentrate	95 – 110	38.7	15.4	45.9	C-6 to C-7	35 (8800)	>3 (>760)	>31 (>7800)	3.9 (980)	3.9 (980)	10 (2.5)	1.9 (480)	1.9 (480)
'High aromatic solvent'	184 – 206	0.3	0.8	98.9	C-9 to C-12	>0.38 (>66)	This value applies for all animal toxicity evaluations and is a saturated atmosphere at room temperature				0.4 (0.07)	0.15 (26)	0.15 (26)
'High naphthenic solvent'	157 183	29.0	69.9	1.1	not stated probably C-9 to C-11	5.3 (960)	3.8 (>690)	--	2.1 (380)	--	--	--	2.1 (380)
'Naphthenic aromatic solvent'	151 200	24.7	37.2	38.1	C-9 to C-11	>10 (some aerosol present)	–	–	2.2 (380)		–	–	2.2 (380)

[a] Summary of data from Carpenter et al. (1977a,b,c).
[b] P = paraffins, N = naphthenes, A = aromatic compounds.
[c] For details of actual length of LC_{50} exposure, see original papers.
[d] NEL/No-ill effect/exposures 6th/day, 5 days/week for 13 weeks

atoms also tended to diminish the aspiration hazard, as did blending with more viscous lubricants (Gerarde, 1963).

3.6.2 Long-term exposure

The repeated skin tests of Hoekstra & Phillips (1963) and Hine & Zuidema (1970) have already been mentioned in section 3.6.1.

Smyth & Smyth (1928) exposed guineapigs for 4 h/day, 6 days/week, for a total of 65 exposures to a gasoline-type solvent (boiling-range 145–183 °C) at a concentration of 6750 mg/m³. During the earlier exposures, the animals appeared to be restless. This was followed by slight narcotic effects. Diarrhoea and albuminuria developed temporarily, but blood, lung, and other changes were absent.

In a recent series of inhalation studies on various hydrocarbon fractions, Carpenter et al. (1977a, b, c) provided much new information on the toxicity of a wide range of solvents. Physical properties and the general chemical constitution are detailed in the papers and the approximate compositions are given in Table 6. The no-observed-adverse-effect levels of individual solvents following inhalation studies over 13 weeks in rats and dogs is also tabulated, together with the human sensory response (section 3.7.1.2). In general, these studies were remarkable in the lack of toxicity that they indicated. The few toxic effects that did occur, were usually kidney damage in rats and minor haematological variations.

Other long-term animal studies have been carried out with the lower-boiling fractions and more specifically with technical hexane and technical heptane, because of their possible neurotoxic effects and to establish a safe level of industrial exposure (TLV).

Mature female Wistar rats were exposed to petroleum solvent vapour (physicochemical properties not given) at a concentration of 300 ± 8.2 mg/m³ for 30–45 days, for 4 h/day. The serotonin content of the myometrium in exposed rats equalled 75.7 ± 2.6 µg/kg compared with 68.47 ± 2.5 µg/kg in the control group. Uterine contractions were more numerous and stronger in exposed animals. The level of solvent in the venous blood was 2.0 ± 0.4 mg/litre. In the uterine tissues it was almost twice as high (3.8 ± 0.6 mg/kg). The increase in serotonin content in the organism could cause disturbances in the transport of the fertilized egg cell and the nidation, and subsequently, early abortion (Lipovskij, 1978).

Miyagaki (1967) exposed 5 groups of 10 male mice to vapour concentrations of technical hexane of 360, 900, 1800, 3600, and 7200 mg/m³. There was a sixth control group. The exposures lasted 24 h/day, 6 days/week, over a period of one year. The composition of the hexane used is uncertain. The measured vapour concentrations correlated well with those calculated. Electromyographical studies

were carried out and strength-duration curves, electrical reaction time, flexor/extensor ratios, and gait-posture were observed. The muscular atrophy of the hind legs was measured and in some of the animals, histological examination of the distal mucles of the hind legs was carried out. Evidence of neurogenic muscular atrophy was only seen in the group receiving the highest exposure. At the lowest exposure level (360 mg/m^3), no changes were found in any of the variables studied. At the other levels, changes were found related to the severity and duration of exposure. Based on their results, the authors proposed a reduction in the TLV to 360 mg/m^3.

In a different study, which included a group of 5 rats (sex and age not stated) exposed to a hexane concentration of 3060 mg/m^3, over a period of 143 days (no other details given) and a control group, no significant differences were found in average body weights and blood values (haematocrit, total serum protein, and protein fractions) between treated and control animals. Histological examination of "many" organs revealed only a "slight reaction of the RES in the spleen" in the exposed animals. In the sciatic nerve and its ramifications, injuries such as degeneration of myelin and axon cylinders were seen. The myoneural junction remained unaffected. The exposed group manifested some decrease in nocturnal activity (Kurita, 1967).

Truhaut et al. (1973) published the results of electrophysiological studies on rats exposed to technical hexane or technical heptane. The air concentration of hexane was 7200 ± 720 mg/m^3 and that of heptane, 6000 ± 600 mg/m^3 (calculated and expressed as *n*-hexane and *n*-heptane). The duration of exposure was 5 h/day, 5 days/week for 1–6 months. The initial weight of the male and female rats was 150g. No data on the growth-weight curves were included. The composition of technical hexane was given as:

n-pentane	0.3 %
methyl-2-pentane and cyclopentane	25.1 %
methyl-3-pentane	18.4 %
n-hexane	45.8 %
methylcyclopentane	8 %
methylhexanes	1.2 %
benzene	1.2 %

and that of technical heptane as:

methyl-2-hexane plus dimethyl 2,3 pentane plus cyclohexane	9.8 %
methyl-3-hexane	16.2 %
n-heptane	52.4 %
dimethyl 2,4 hexane plus methylcyclohexane	15.4 %
methylheptane	3.3 %
benzene	0.1 %
toluene	2.8 %

Electrophysiological studies were carried out on isolated sciatic and saphenous nerves taken from anaesthetized rats. During the first 2 months of exposure, no changes were found in any of the treatments but, in the succeeding months, symptoms of neural involvement were detected, in general, increasing with the duration of exposure. The signs were: decrease in conduction-velocity, increase in refractory period, and decrease in excitability. Histopathological examination did not reveal clear-cut demyelination, but early indications of this type of change were certainly found. Truhaut has recently cast doubt on these findings, stating that his experimental method was not sufficiently rigorous to allow his earlier conclusions to be made (Truhaut, 1978).

Numerous studies on the neuropathological effects of *n*-hexane have been published including a review by Schaumburg & Spencer (1976). Rats exposed for 24 h/day to an *n*-hexane concentration of 1440–2160 mg/m^3 for about 20 weeks developed peripheral neuropathy. Toxicity data on the presumptive *in vivo* neurotoxic oxidation products of *n*-hexane have also been published (Spencer et al., 1978). It should be mentioned that many authors have used the term "*n*-hexane" loosely; the tested material often really consisted of various C-6 hydrocarbons.

Some other hydrocarbon solvents have been implicated as possibly causing neuropathy, following prolonged exposure to high concentrations. As these reports are generally related to human exposure, they will be considered in section 3.7.2.1. Of relevance is the observation that toluene inhaled by rats over a period of one year induced electrophysiological changes at concentrations of 7500 mg/m^3 and 750 mg/m^3 but not at 375 mg/m^3 (Matsumoto, 1971). Fournas & Hine (1958) exposed rats to high concentrations of various alkyl aromatic hydrocarbons and found some clinical evidence of neurotoxicity with most of the compounds tested; *p*-*t*-butyltoluene was shown to induce CNS damage in rats by Ungar et al. (1955).

3.6.3 Mutagenicity, teratogenicity, and carcinogenicity

3.6.3.1 *Mutagenicity*

The potential mutagenic activity of selected petroleum products was assessed using a battery of *in vivo* and *in vitro* bioassays, including the dominant lethal test, the Ames' test (with and without activation), the mouse lymphoma cell transformation test, and observations on cytogenicity. The following products elicited

negative responses in one or more tests: UM&P Naphtha, Stoddard Solvent, mixed xylenes, "60 Solvent", "70 Solvent", 140° Flash Aliphatic Solvent, "50 Thinner", kerosene, toluene, high solvency naphtha- unleaded petrol, and No. 2 heating oil (40 % aromatic compounds). Positive mouse lumphoma cell transformation tests were elicited by benzene, diesel fuel, No. 2 heating oil, and jet A fuel; positive results in cytogenetic tests (clastogenic responses) were obtained with rubber solvents, "60 Solvent", high aromatic solvent, No. 2 heating oil, and jet A fuel. For each of these products the Ames bacterial bioassay was negative (API, 1974, 1975b, c, 1977a, 1978a, d, f, 1979d).

3.6.3.2 *Teratogenicity*

Tests for teratogenicity induced by inhalation of high and low doses of benzene, Stoddard Solvent, toluene, mixed xylenes, unleaded petrol, high aromatic solvent, *n*-hexane, diesel fuel, VM&P naphtha, kerosene, rubber solvent, jet fuel A, and No. 2 heating oil were all negative. However, benzene exposure at 120 mg/m^3 induced a statistically significant increase in fetal resorptions in rats (API, 1974, 1975a, b, c, 1977 a, b, 1978a–f, 1979a–d).

3.6.3.3 *Carcinogenicity*

Carcinogenicity tests have only been conducted on the group of high-boiling aromatic extracts derived from the solvent refining of lubricating base oils. These studies will be considered together with long-term studies on lubricating base oils, but, in short, practically the whole of the carcinogenic polynuclear aromatic hydrocarbons were found in the extracts from the base oils. However, the carcinogenic activity of the extracts was considerably less than that of coal-tar-derived products.

Similar carcinogenicity studies have not been carried out with the lower boiling aromatic solvents (white spirits). Such studies would be indicated, though the content of potentially carcinogenic 4, 5 and 6 condensed ring polynuclear aromatic hydrocarbons in these aromatic solvents is probably much lower than in high boiling aromatic solvents, because of the lower boiling range. Lijinsky & Raha (1961) mention, however, that no commercial distillation procedure will completely remove all traces of polynuclear aromatic hydrocarbons from petroleum solvents and that special treatment is necessary to achieve this. Though, in most cases, the authors found very low concentrations (in the µg/m^3-range), they are of the opinion that these levels should be investigated, particularly in food-grade material.

3.7 Effects on Man

3.7.1 Controlled exposures

3.7.1.1 *Effects of dermal exposure*

Klauder & Brille (1947) patch-tested petroleum solvents of various boiling ranges on the skin of human volunteers. They found a correlation between the boiling ranges of the petroleum products of paraffinic origin and their irritant and defatting action on the skin. Both effects decreased, the higher the boiling range. Petroleum solvents with boiling ranges up to and including that of kerosene (approximately 230 °C) were found to be primary irritants. Petroleum solvents of naphthenic origin or with a high aromatic content were more irritant than solvents of paraffinic origin of the same boiling range. The skin of Negroes showed a higher tolerance than that of Caucasians.

Pre-existing skin disease may increase the susceptibility of the skin to the effects of contact with petroleum solvents and will also facilitate uptake by this route (Klauder & Brille, 1947; Riihimäki & Pfäffli, 1978).

The effects of various solvents on the horny layer of the skin were examined by Malten et al. (1968) and Spruit et al. (1970). They found that petroleum ether (SBP 40/65) caused serious irritation of human forearm skin, when applied for periods of 10–30 min. When applied for 15 min on 6 successive days, injury occurred in the horny layer. Recovery – as measured by water vapour loss – could take up to 6 weeks. The skin irritation and the changes in the composition of the horny layer were independent phenomena.

Tagami & Ogino (1973) applied undiluted refined kerosene to the arm of a volunteer in an occluded patch-test. After 1 h, a burning sensation developed, slight erythema appeared after 2 h, and after 7 h, the skin was tender and very red, even beyond the patch-test site. After 12 h, the burning sensation had subsided but a large tense bulla had appeared surrounded by small scattered vesicles. This changed into a large flaccid purulent bulla 24 h later, which easily broke, leaving a raw surface. The main differences between the test situations just described were: (*a*) a marked difference in boiling range (volatility and skin penetration) of the products tested; and (*b*) the length of exposure, the effect increasing with increasing duration of exposure.

The same authors then applied 85 %, 70 %, 55 %, and 40 % dilutions of the kerosene in mineral oil in covered skin test on 34-adult male Negro and Caucasian volunteers. The skin of all the subjects reacted to 85 % kerosene solution, the 70 % solution caused skin irritation in 29 subjects, the 55 % solution in 8, and the

40 % solution was completely without effect. The skin of Negroes appeared to be less irritated by kerosene than that of Caucasians; the influence of age was not clear. No definite correlation was found between individual response to kerosene and the permeability of the horny layer of the skin (Tagami & Ogino, 1973).

3.7.1.2 *Effects of inhalation*

Inhalation of air containing petrol at concentrations of 1350–3150 mg/m³ for 18 min by human volunteers did not cause any symptoms; a 14-min exposure to 12 600–31 500 mg/m³ induced dizziness (Fieldner et al., 1921). Davis et al. (1960) exposed human volunteers for 30 min to concentrations of petrol of 900, 2250, or 4500 mg/m³ in air. Very few symptoms were noted. Itching and burning of the eyes was apparent in most subjects in the highest exposure group.

The human odour- and sensory irritation thresholds were measured as part of the toxicity evaluation of solvents carried out by Carpenter et al. (1977a) (Table 6). It can be seen that vapours of hydrocarbon solvents can be detected at rather low concentrations, but that unpleasant odour and irritation only become apparent at much higher concentrations. Nevertheless, in establishing an exposure limit for each solvent, human sensory data were often limiting factors.

In volunteer studies, psychological functions were affected by a 50-min exposure to a concentration of white spirit of 4000 mg/m³ resulting in a prolonged reaction time and impaired short-term memory. Lower concentrations did not have any effect (Gamberale et al., 1975).

3.7.2 Epidemiological studies

A distinction between epidemiological and clinical studies has always been difficult in view of the inadequacy of reporting. The various aspects will therefore be discussed under headings relevant to the information available.

3.7.2.1 *Occupational exposure*

(a) Haematological effects

Benzene is unquestionably the most dangerous hydrocarbon used in industry and the benzene content of some petroleum solvents presents a major long-term hazard for man. In particular, special boiling solvents in the lower-boiling range may contain a considerable percentage of benzene (Gerarde, 1960). In this review,

it is impossible to consider in detail the effects of benzene, which basically causes bone-marrow depression and has a leukaemogenic action. Excellent reports on all aspects of benzene toxicity can be found in: ILO (1968); Deutsche Forschungsgemeinschaft (1970); IARC (1974); and Laskin & Goldstein (1977).

In the past, benzene-like effects have also been ascribed to other low-boiling petroleum solvents. However, there now seems to be general agreement that these effects only occur, when benzene is present in the mixture (Browning, 1959, 1965).

(b) Neuropathological effects

The neuropathological effects of inhalation of petroleum solvents in man have been discussed in a number of reviews including those of Cavanagh (1973), Allen (1975), Seppäläinen (1975), Comstock (1977), and Savolainen (1977). The reviews include discussions of methods used to evaluate human neuropathy.

Over the past 15 years, an increasing number of cases of polyneuropathy and other neurotoxic effects have been described in workers exposed to hydrocarbon solvents. Many of these cases have been associated with prolonged and repeated exposure to high concentrations of *n*-hexane. Frequently, such exposure has resulted from poor ventilation in a workroom in which solvents containing high concentrations of hexane have been used. Miyagaki (1967) reported hexane concentrations in air of 1800–3600 mg/m^3 in the workroom and 7200 mg/m^3 near the source in a work-place where 17 cases of peripheral neuropathy occurred. Yamamura (1967) and Inoue et al. (1970) found concentrations ranging from 1800–9000 mg/m^3 in a work place where, over a 9-year period, 93 out of the 1662 workers suffered from polyneuritis. These workers used glue in the manufacture of vinyl sandals for 8–14 h daily, probably for more than 5 days each week, over long periods, in poorly ventilated rooms. The presence of hexane in glues is reported to have caused similar incidents in Italy and Iran (Capellini et al., 1968; Scrima & de Rosa, 1973; Ghazai, 1974). In most cases, the extent of exposure to hexane was uncertain, either because air concentrations were not measured or because excessive skin contamination occurred; workers frequently handled the glues and washed residues off the skin with hexane-containing solvents. In other cases, air concentrations were measured. Hexane concentrations of approximately 2340 mg/m^3 (but at times up to 4680 mg/m^3) were found in a small, poorly ventilated workroom in which 3 women, who developed polyneuropathy, had worked; again excessive skin contact took place (Herskowitz et al., 1971; Ishii et al., 1972). Glue was also the source of hexane concentrations of 1000–4000 mg/m^3 found by Paulson & Waylonis (1976) in the air of a work-place where 8 out of 50 employees developed mild neuropathy.

The main clinical manifestation in these cases was polyneuropathy of the glove-and-stocking type with sensations of numbness and cold. This was accompanied by muscular weakness and headaches. Gradual recovery was usual, when exposure ceased, with the exception of some subjects who had severe muscular atrophy. Peripheral nerve biopsy showed demyelination with relative preservation of the axon. Iida et al. (1969) reported that in 44 cases there was a reasonable, but not exact, correlation between clinical findings and electromyography and nerve conduction velocity data.

Optic involvement was observed by Inoue et al. (1970). The neuro-ophthalmological function was studied by Raitta et al. (1978) in 15 workers who had been exposed at work over periods of 5–21 years to hexane concentrations of 1800–3600 mg/m^3, with occasional levels of 10 800 mg/m^3. Defective colour discrimination was found in 12 of the workers and slight macular changes in 11 out of 15. The visually evoked potentials and electroretinograms were interpreted by Seppäläinen et al. (1979) as indicating cerebral dysfunction, probably a conduction block in intracerebral axons.

Polyneuropathy attributable to the inhalation of hexane has also been observed in "glue sniffers" – subjects who inhale solvent vapours to induce elation or other states of mind. Cases including very rare cases following medicinal use, were described by Schwarz (1933), Browning (1965), Karani (1966), Gonzales & Downey (1972), Matsumura et al. (1972), Taher et al. (1974) and Korobkin et al. (1975). Other incidents have been reported or reviewed by Shirabe et al. (1974), and Poklis & Burkett (1977). While hexane appears to have played a major role, a direct or synergistic action of other components cannot be ruled out.

Some cases have been described that were thought to arise from the long-term, continuous domestic use of kerosene stoves in poorly ventilated rooms (Contamin et al., 1960). Under simulated conditions, hexane concentrations of about 1440 mg/m^3 were produced in experimental rooms by Lièvre et al. (1967).

The possibility of the production of peripheral neuropathy by components other than hexane, or the intensification of the activity of hexane, is suggested by some clinical reports. Cargill (1972) (cited by Gaultier et al., 1973) described peripheral neuritis in workers using glue containing cyclohexane, gasoline "c", and methyl ketone, and Franco et al. (1979) reported sensory and peripheral motor conduction disturbances, where exposure to cyclohexane had occurred. The condition was described by Gaultier et al. (1973) in subjects who had been in prolonged contact with a glue solvent containing 80 % pentane, 5 % hexane, and 14 % heptane. Gasoline concentrations of 2250 mg/m^3 were found in the workshop atmosphere. Atmospheric gasoline concentrations of up to 5625 mg/m^3 (mainly *n*-pentane, *n*-hexane, and *n*-heptane) were

found in workshops where workers had developed polyneuropathy and had complained of insomnia, irritability, and other non-specific CNS symptoms. White spirit has also been implicated as a cause of peripheral neuropathy (Gaultier et al., 1973). Heavy exposure to jet fuel vapours was reported in workers who experienced dizziness, palpitations, nausea, and headaches, later followed by signs and symptoms of polyneuropathy; higher vibration thresholds, compared with unexposed controls were also found. (Knave et al., 1976).

Other symptoms besides those of polyneuropathy have been described in subjects exposed to hydrocarbon solvents. Sterner (1941) reported headaches, nausea, mental depression, anorexia, inability to concentrate and sustain activity, and slight anaemia, in workers exposed to gasoline vapours (used to dilute spray paint) containing 5–10 % aromatic hydrocarbons and producing concentrations of total aromatic hydrocarbons in air of 300–800 ppm.[a] Knave et al. (1978) compared 30 workers, occupationally exposed to jet fuel, with unexposed controls. The average period of exposure was 17 years and the estimated TWA exposure was 300 mg/m³. Significant differences were found between exposed and unexposed groups in the incidence and prevalence of psychiatric symptoms, psychological test results, especially attention and sensorimotor speed, and in electroencephalograms. Exposure of car painters, over many years, to low concentrations (31.8 % of the Finnish TLV on average) of solvent mixtures containing toluene, xylene, butyl acetate, and "white spirit", was found to be associated with an increased incidence of sleep disturbance, absentmindedness, falling asleep while watching the television, and headaches. Lower peripheral nerve conduction velocities, psychomotor impairment, and personality changes were more common in exposed than in control subjects. Further studies are needed to elucidate the significance of such findings (Hänninen et al., 1976; Seppäläinen et al., 1978).

In summary, the most serious adverse neurological effect of hydrocarbon solvents in man is the production of peripheral neuropathy. Observations in man and studies on experimental animals support the view that exposure to *n*-hexane is the principal cause. However, the synergistic activity of other hydrocarbons is possible, such a phenomenon has been reported following the sniffing of a glue thinner containing both the neuropathic solvent, methyl-*n*-butyl ketone, and the non-neuropathic solvent, methyl ethyl ketone (Altenkirch et al., 1977). At present, the possibility that other hydrocarbons also have some neurotoxic activity cannot be ruled out.

Peripheral neuropathy has occurred only in conditions of prolonged and repeated exposure to high concentrations of hydro-

[a] Since the composition is not given, it is not possible to transform this concentration into mg/m³, the adopted SI unit.

carbon solvent vapour in air; in many cases, there was also excessive skin contact. Atmospheric exposure levels in excess of 2 g/m^3 are usually encountered where peripheral neuropathy is seen, but more studies are required to clarify the situation, and until this is done, close supervision is needed to ensure that the TLV for solvents is not exceeded. Further studies are also necessary to determine the significance of psychological disturbances and of neurophysiological findings in workers exposed to lower levels of the hydrocarbons.

(c) Effects on reproductive functions

Examination of 408 female workers in petroleum refineries, who had been subjected to long-term exposure to hydrocarbons, hydrogen sulfide, and other products related to the treatment of sulfurous crude, revealed disturbances in the menstrual function, mainly in the form of hypomenstruation and pre-menstrual syndromes. According to Suhanova & Melnikova (1974), such disturbance of the menstrual function in female workers in refineries and in persons suffering from chronic intoxication from petroleum products (36 persons in the age bracket 30 - 39 years) is caused by the hypofunctioning of the ovaries.

Beskrovnaja et al. (1979) studied the gynaecological disease rate in more than 5000 female operators in plants producing rubber articles (petroleum solvent vapour concentration in the air of 250–350 mg/m^3). They observed disturbances in the menstrual cycle in workers with more than 5 years' service and a high frequency of metrorrhagia. As the period of service increased, a reduction in the frequency of miscarriages was noticed, which was interpreted by the authors as possible adaptation. A disturbance of the ovarian function was noted in 24.4 % of the workers examined, mostly in the form of a functional deficiency of corpus luteum.

Investigations of vaginal smears of 184 female gluers in the rubber industry in the age bracket 18–38 years revealed a disturbance of the ovarian function with reduced estrogen stimulation in 21.7 % of the women (10.4 % in the control group). This figure was related to the period of service. After 10 years service, the percentage was twice as high as after 5 years' service.

Women who had been in contact with petroleum solvents were found to have a reduced estrogen level in the blood (22.2 µg/day compared with 29.6 µg/day in the control group). Essentially, no changes were observed in the excretion of the follicle-stimulating and luteinizing hormone pregnanediol. The authors of this study assumed that the sensitivity of the ovaries towards the stimulating effect of the gonadotrophins was reduced (Hrustaleva et al., 1979).

Novikov et al. (1979) studied lactation in 332 nursing mothers

288 of whom worked in the rubber industry (vulcanizers, pressers, gluers). The concentration of petroleum solvents (the physicochemical properties of which are not described) in the air of the operating premises was predominantly 300 mg/m^3. Hypolactation, found in 23.8 % of the women compared with 6.7 % in the control group was related to length of service. Hydrocarbon solvents were found in the milk of all the persons examined (71) in concentrations of 0.50 ± 0.05 mg to 0.60 ± 0.09 mg/litre. The serotonin content of the blood of these women was significantly lower than in the control group. It is assumed that hypolactation was the result of the effect of solvents on the lactation control mechanism via the hypothalamus and the serotoninergic system.

(d) Effects on the skin

Skin can also be affected by exposure to solvents. In a study on skin conditions and other diseases in 54 gasoline and diesel station workers, skin conditions related to exposure to gasoline and diesel fuel were minimal and did not interfere with capacity to work. Only dryness, chapping, and reddening of the skin were found. The dark skin of Indonesians seemed to be more resistant to these effects. The gasoline vapour in the working environment caused some non-specific symptoms in addition to those resulting from heavy out-door work (Suma'mur & Susianti Wenas, 1979).

3.7.2.2 *General population exposure*

Data are not available concerning the exposure of the general population to petroleum solvents with the exception of that of "sniffers" and addicts already mentioned in section 3.7.2.1.

3.7.3 Clinical studies

It should be noted that literature surveys of clinical studies and clinical effects have been published by Gerarde (1960), Browning (1965), and Levina (1976).

3.7.3.1 *Effects of dermal exposure*

In general, petroleum solvents have a defatting action on the skin and, on repeated contact, cause injury to the horny layer (section 3.7.1.1). This makes the skin more susceptible to other irritants, sensitizing agents, and bacteria. It may also result in progressive dermatitis, characterized successively by dryness, redness, chapping and scaling, which could lead, by sensitization,

to eczema. These stages of dermatitis may be seen in workers in garages or automobile repair shops, who wash their hands with solvents, petrol or kerosene (Tagami & Ogino 1973). The more aromatic solvents, in particular, can cause a significant degree of primary skin irritation. The defatting action and primary irritation caused by petroleum solvents decrease, the higher the boiling range (section 3.6.1).

Cases in which gasoline or kerosene remains in contact with the skin for prolonged periods mainly occur in children or in unconscious accident-cases, when clothing has become soaked with the solvent. In such cases, the lesions start with a burning sensation and erythema, followed by the formation of small or large vesicles, blisters, or even extensive epidermolysis. The vesicles and blisters may become mucopurulent in a few days. The acute picture is that of a chemical burn, (Helbling, 1950; Aidin, 1958; Ainsworth, 1960; Stewart, 1960; Browning, 1965; Hunter, 1968; Tagami & Ogino 1973).

Gasoline may occasionally be absorbed through the skin in toxic quantities if large areas of skin such as the hands and forearms are regularly exposed (Hayhurst, 1936), or in cases of extensive epidermolysis in contact with gasoline-soaked clothing. However inhalation of vapour plays a significant additional role in all these cases and generally is the main route of absorption (Browning, 1965).

3.7.3.2 *Effects of inhalation*

The acute effect of massive overexposure to gasoline vapour is mainly narcosis with loss of consciousness and possibly convulsions, which may be fatal (Browning, 1965). Octane causes rapid and deep narcosis, pentane and hexane are less powerful narcotics, but they and heptane exert a paralytic effect on the central nervous system and its respiratory centre.

In more gradual overexposure, the symptoms just described may be preceded by eye irritation, irritation of the respiratory tract, dizziness, headache, and a sense of drunkenness.

A gasoline concentration of 9000 mg/m^3 can be breathed without significant ill-effects by most people but susceptible subjects may show symptoms after exposure to 1350–2250 mg/m^3 (Ainsworth, 1960). At 31 500 mg/m^3, dizziness and symptoms of drunkenness may appear. Exposures in excess of 45 000 mg/m^3 soon become intolerable and may rapidly prove fatal (Machle, 1941, Aidin, 1958). Lower and higher values have been quoted, obviously depending on the composition of the gasoline (Browning, 1965). The margin of safety between narcosis and respiratory arrest is very narrow in exposures to high concentrations of gasoline (Wang, 1961).

Absorption of gasoline vapour by inhalation may be very rapid

if the concentration is high, especially with the lower members of the paraffinic range, and symptoms can appear within a few minutes. Excretion, probably of unchanged vapours, takes place mainly via the lungs (Browning, 1965).

Acute occupational poisoning by gasoline vapour is mostly caused by entering unpurged gasoline tanks or other premises where high concentrations of gasoline may have accumulated. Exposure to high concentrations may also occur in car accidents, when victims are trapped and/or unconcious.

Histopathological changes found in subjects who have died after exposure to high concentrations of gasoline vapour include: hyperaemia and petechial haemorrhages in the lungs, and, sometimes, necrosis of the alveolar walls. There may be haemorrhages or effusions in internal organs and serous cavities (Helbling, 1950; Ainsworth, 1960; Browning, 1965). Liver and kidney may show fatty degeneration. Hyperaemia and oedema of the brain are common in this condition and myelin swelling may occur (Machle, 1941).

Long-term exposure to low (unspecified) vapour concentrations may cause nonspecific symptoms of the nervous system and digestive tract (Zielhuis, 1961; Browning, 1965; Muhametova & Podrez, 1975; Sehtman et al., 1979), including changes in liver function and in the visual organ. In women, the reproductive organs may be affected (Muhametova & Podrez, 1975; Sehtman et al., 1979). Neurological disturbances, as described in section 3.7.2.1 may develop (Hayhurst, 1936; Machle, 1941; Browning, 1965). Browning (1965) considered that significant changes observed in the blood count were caused by the presence of benzene in the solvent.

This chronic form of toxicity may be found in small, insufficiently ventilated workshops where solvents, or products containing them, are handled in an unsatisfactory way (section 3.7.2.1) and when these materials are used in substantial amounts in enclosed spaces, particularly for cleaning or degreasing (Anon., 1974).

3.7.3.3 *Effects of ingestion*

Accidental ingestion of petroleum distillates in the range of petroleum solvents is an important cause of poisoning in children (Waring, 1933; Nunn & Martin, 1934; Lesser et al., 1943; Carithers, 1955; Daeschner et al., 1957; Gerarde, 1959, 1963). Most cases, however, are caused by gasoline and kerosene and fewer by petroleum solvents. The symptomatology is the same in all cases.

Coughing, choking, and gagging are often noted at the time of ingestion of these substances. Respiratory embarrassment may be present early, indicating that aspiration has taken place. Epigastric discomfort may develop, followed by vomiting with a further risk

of aspiration. Aspiration by one mechanism or another is reported to occur in up to 95 % of cases in children, but this depends on the situation and on the type (boiling-range) of the solvent involved. Aspiration is less common in adults, but may occur when trying to siphon gasoline from a tank. Small amounts of kerosene of the order of 1 – 2 ml, if aspirated, can cause severe and even fatal pulmonary changes. On the other hand, if aspiration does not occur, much larger quantities can be tolerated (Daeschner et al., 1957; Hensen, 1959; Browning, 1965). Browning (1965) quotes a value of 7.5 g/kg body weight, but this may depend on the type of solvent. Children appear to be more susceptible to the toxic effects than adults (Siwe, 1932). In cases where aspiration does not take place, and especially with the lower-boiling solvents, central nervous system symptoms may develop such as lethargy, convulsions, and coma. With smaller doses, the symptoms include vertigo, headache, and signs of drunkenness. Nausea, vomiting, and diarrhoea may occur and the stools may be blood-tainted.

In uncomplicated cases, the gastrointestinal symptoms will disappear within 48 h. Pulmonary symptomatology will not develop, if aspiration has not occurred and if there was no massive exposure to vapours.

The syndrome of acute chemical aspiration pneumonitis will be described in a wider context in section 4.8. Human experience is in accordance with the results of experimental animal studies (section 3.6.1). Chemical pneumonitis with pulmonary oedema and haemorrhagic frothy sputum may develop extremely rapidly following aspiration of petroleum solvents. Roentgenographic changes may be seen within a few hours, especially at the lung bases. Later, bacterial pneumonia can complicate the situation (Daeschner et al., 1957; Gerarde, 1963).

The prognosis of aspiration of hydrocarbon solvents appears to have improved with better treatment in the course of time. Siwe (1932) reported that 50 % of the cases he reported were fatal, Nunn & Martin (1934) reported 28 % mortality following the ingestion of gasoline and 9.2 % following kerosene-ingestion, and Blattner (1951) reported that death resulted in 10–14 % of cases of kerosene poisoning. Recently, 3 cases have been described, where exposure to diesel oil seemed to cause acute renal failure with oliguria (Reidenberg et al., 1964; Barrientos et al., 1977; Crisp et al., 1979). However, in 2 cases, absorption seemed to have been mainly through the skin (section 3.5.1).

4. LUBRICATING BASE OILS AND RELATED OILS, GREASES, AND WAXES

4.1 Properties and Analytical Methods

4.1.1 Chemical and physical properties

Base oils are a limited group of petroleum products in the boiling-range of 300–700 °C, normally derived from the high-vacuum distillation of the residues of the crude-distilling process. These oils undergo a further refining process before being used.

Lubricating oils, metal-working oils, and related products are produced by blending base oils in order to obtain the desired physical properties. Chemical additives are frequently added, usually in small amounts (a few mg to a few g/kg) to improve the performance of the lubricant. In some special cases, higher concentrations are necessary. Additives belong to the following general categories: viscosity-index improver, emulsifiers, wetting agents, antioxidants, dispersants, antiwear additives, extreme pressure additives, rust-inhibitors, antifoam agents, pourpoint depressants, and germicides.

Greases based on mineral oil consist of solid or semisolid dispersions of metallic soaps and other thickeners in a mineral oil base.

Petroleum waxes are crystalline solids at normal temperature. "Slack wax", a soft, impure paraffin-wax is obtained in the manufacture of lubricating base oils from paraffinic crude oils by a dewaxing process. Slack wax can be refined into 2 types of commercial wax: paraffin wax and microcrystalline wax.

Base oils are very complex mixtures of hundreds to thousands of different hydrocarbons, containing straight-chain and branched paraffins, cycloparaffins, naphthenic, aromatic, and polynuclear aromatic hydrocarbons in the range of C-17 and higher. The separate molecules are so large, that any molecule may, for instance, contain one or more aromatic rings with one or more long side-chains.

The actual composition depends on the source of the crude oil, from which the product is derived, and the manufacturing and treating processes used. They range from thin, easily flowing "spindle oils" to thick "cylinder oils". A limited number of base oils are used for blending to obtain the commercial products. As the relation between viscosity and temperature is an important factor in this field, base oil grades are characterized by their viscosity and viscosity index (VI). The higher the viscosity index, the less the change in viscosity with temperature.

Low viscosity index (LVI) oils are used whenever the viscosity temperature characteristics and oxidation stability are of less importance. In general, they are derived from naphthenic oils and

undergo treatment with sulfuric acid and clay or are given a hydro-finishing treatment.

Medium viscosity index (MVI) oils, can be used as a base for general-purpose lubricants. They can be derived from naphthenic (MVIN) or paraffinic (MVIP) feedstocks. MVIP has to be dewaxed and can also be solvent refined, acid- and clay-treated or hydro-treated.

High viscosity index (HVI) oils, are prepared by both solvent refining and dewaxing of paraffinic feedstocks. They are used for gasoline and diesel engine oils and for turbine lubricants, because they are, in general, more oxidation-stable than other base oils and have appropariate viscosity/temperature characteristics.

White oils are generally produced by more drastic refining of MVI oils, in order to remove unsaturated compounds, aromatic compounds, and other constituents that influence colour, odour, taste, and acceptability as food-grade material. Solvent extraction followed by repeated treatment with oleum and alkali is used. Hydrogenation is another means of producing such oils.

Medicinal oil is the highest purified grade, which complies with the requirements of the various national pharmacopoeias and regulations on food-grade material. As liquid paraffin, the same grade is used as a lubricant for food-handling machines and as an ingredient in pharmaceutical preparations and cosmetics.

Technical white oils, less rigidly purified than medicinal oil, are non-carcinogenic oils that can be used for the lubrication of textile machinery, spinning mules, etc., but are mainly used in the cosmetic industry in the manufacture of hair-oils, creams, etc.

Aromatic extracts, which are obtained in the solvent-refining process, have already been discussed in section 3.1.1.

Petroleum waxes consist essentially of high relative molecular mass paraffinic hydrocarbons with approximately 20–40 carbon atoms per molecule. Paraffin waxes consist mainly of normal paraffins together with some iso and cycloparaffins. They are macrocrystalline with a melting-point of 43–71 °C.

Microcrystalline waxes on the other hand, consist mainly of iso and cycloparaffins with some alkylated aromatic hydrocarbons. They are mostly soft materials, but may sometimes be a hard brittle solid.

When highly purified, the colour may be white, however, it is usually yellow or amber, sometimes even black. The melting-point is 60–90 °C. The paraffin oil content ranges from 5 to 50 g/kg.

Petrolatum is also known as petroleum jelly and is a micro-crystalline wax with a high oil content.

4.1.1.1 *Purity of Product*

As these oils and waxes are complex mixtures, the nature and

proportion of potentially undesirable "impurities" depends to a large extent on the definition of the term and on the degree of refining. In the range from the highest refined oil – for example, white medicinal oil – to the least refined oil, "impurities" could include polynuclear aromatic hydrocarbons and unsaturated hydrocarbon compounds.

It is clear that highly purified products can be obtained at the cost of extra refining and treating processes. Paraffin waxes are an example of progressive refining: fully refined paraffin wax is a white solid material containing an oil concentration of less than 5 g/kg. It is odourless and tasteless and has a melting-point of 50–70 °C. Candle waxes range from fully refined paraffin wax to less refined waxes containing oil levels of up to 15 g/kg. This type of wax is not completely colourless and odourless. Scale wax and match wax contain an oil residue of up to 30 g/kg.

4.1.2 Methods of sampling and analysis

See section 2.1.2.

4.2 Sources of Environmental Pollution

4.2.1 Natural occurrence

Base oils occur in nature only as components of the crude oils from which they are derived.

4.2.2 Man-made sources

4.2.2.1 *Production*

As mentioned earlier, lubricating base oils are a group of petroleum distillates and residues in the boiling-range 300–700 °C, derived by high-vacuum distillation of the residues obtained in crude oil distillation (section 4.1.1). In order to obtain base oils with the qualities and specifications needed for various applications, further refining and treatment of the various distillate fractions is needed. The main processes used are:

(a) Solvent extraction

This is a process by which aromatic hydrocarbons can be extracted from oil fractions, thus obtaining a low aromatic or aromatic-free raffinate, and a high aromatic extract. Liquid sulfur

dioxide, sulfolane, benzene, phenol, or furfural can be used as solvents for this purpose. The raffinate can be used for producing a lubricating base oil, the extract can be used as a solvent (see under petroleum solvents).

(b) Dewaxing process

In this process, "slack wax" is separated (crystallized) from base oil fractions obtained from paraffinic crude oil residues. This is done by cooling, followed by filter-pressing. The separation of wax and oil under chilled conditions is facilitated by the addition of solvent. The resulting wax may still have an oil content of up to 100 - 400 g/kg.

(c) Acid treatment

The oil is mixed with 98 % sulfuric acid and the acid sludge is centrifuged off. This is usually followed by clay treatment in which the oil is mixed with absorbent clay, followed by filtration. This neutralizes the oil and improves colour, odour, and stability.

(d) Hydrofinishing

This is a catalytic hydrogen treatment at elevated temperature and pressure. Improved stability and colour of the oil is obtained by the hydrogenation of unstable compounds, which removes sulfur and saturated olefins, diolefins, and aromatic components.

As the definition and classification of lubricating base oils are not clear, it is difficult to give precise production data for this group of products. The best current estimate is 35–38 million tonnes per year. Though there was a decrease in the annual production after 1973, lubricant production has subsequently increased, but at a lower rate.

4.2.2.2 *Uses*

In general, the main functions of lubricating oils and metal-working oils are: to reduce friction, to remove generated heat, to remove debris from the contact area, and to protect against corrosion. In addition, mineral oils are used as hydraulic media in a wide variety of applications. Very general remarks have already been made concerning the composition of, and the various additives in, lubrication oils, metal-working oils, and greases. The following is a list of the most important categories of products on the market, from which it is clear that the great majority are handled in industrial situations, and that the general population has regular contact with only a few such products:

(a) Industrial lubricating oils, which can vary from thin spindle-oil to the very viscous oils used in steam engines;

(b) Lubricants for internal combustion engines of various types;
(c) Crankcase, compressor, gear, and turbine oils;
(d) Greases for bearings and other purposes;
(e) Hydraulic, transformer, insulating, heat-transmission oils;
(f) Cooling, quenching, anticorrosion, and mould oils;
(g) Metal-working oils: cutting, grinding, rolling, drilling, drawing-oil, a multitude of products for specific purposes. They consist in general of complex mixtures with various additives, for use in the neat state and also as water extendible fluids or emulsions;
(h) Textile oils: spindle, hatching, technical white lubricating oil;
(i) Process oils: used in printing-inks, as rubber extenders, and as technical white oils in cosmetics, etc;
(j) Waxes of various grades and purity;
(k) Medicinal white oil used for medicinal and food-grade applications.

The manufacturing, treating, and purification processes used in the preparation of the base oils vary according to the future application of the commercial product.

Many of the products can undergo considerable changes during use. This should be borne in mind in extrapolating from used oils to the original product in the case of adverse health effects, e.g., in the case of skin sensitization. The following are a few examples of changes that may occur:

(a) During use, the chemical and physical characteristics of lubricating oils change, mainly because of contamination, oxidation, and polymerization. Metal particles, airborne dust, water, and, in the case of internal combustion engine oils, small quantities of fuel, acids, and soot, are the main contaminants. All this can result in the formation of sludge.

(b) Metal-working oils become contaminated in use with a wide variety of foreign matter, in particular metal particles (and ions). Water-based metal-working emulsions can also be affected by bacteria, yeasts, and fungi. Oxidation and heat cracking may occur at the application point, causing smoke, steam, and oil mist to be emitted into the working environment. Nitrite may be added to most water-based cutting oils, thus these sometimes contain carcinogenic nitrosamines (Zingmark & Rappe, 1977).

Cutting oils, lubricating oils, and greases can also contain diethanolamine, which may react with nitrites and nitrogen oxides in the air to form nitrosamines.

(c) Quenching oils are used for hardening steel. Oxidation and cracking of the oil can occur because of the high temperatures involved. The amount of benzo (a) pyrene in lubricating oils increases considerably when they are exposed to heat during use,

as in motor-car engines, metal quenching, and other processes (Thony et al., 1975).

4.2.2.3 *Disposal of waste*

Without a proper method for the disposal of used lubricating and other oils, severe environmental contamination and hazards may occur.

There is a vast literature on methods for the disposal, reuse, and recovery of industrial lubricants and much research is being done in this field. It would be out of context in this document to go into a detailed discussion of the various aspects. For this, the reader is referred to Concawe Report 9/73 (Concawe Task Force, 1973) and API publication No. 4036 (API, 1969), which contain discussions on the situations in Western Europe and the USA, respectively, as well as on more general aspects.

At present, the main ways of disposal are:

(a) dumping in sewage systems, waterways, etc; this is illegal in many countries and ecologically undesirable;
(b) dumping into the ground, in garbage dumps, in dry wells, if approved by local authorities;
(c) using as road oils, etc;
(d) controlled incineration or burning for heat value;
(e) re-refining and other recycling methods.

4.3 Environmental Exposure Levels

Specific data are not available concerning levels of this group of products in air, water, food, or other environmental media, levels of possible contamination, and uptake by man.

Depending on occupation and on the hygiene precautions adopted, skin exposure in workers can vary from minimal to very high. No systematic measurements have been carried out in this field. Exposure to oil mists occurs in certain manufacturing processes and applications, such as the operation of automatic lathes. This type of exposure has been measured by various authors and will be discussed in section 4.7.1.2. Secondary oral intake of unknown quantities of mineral oil can take place under these conditions.

When "sulphofrezol" (approximate composition: 50–60 % "goudron" (?flux oil), 40–50 % spindle oil distillate, and 1.7 % sulfur) was used as a lubricating and cooling liquid on metal-working lathes, the air of the operating premises was found to contain an oily aerosol in concentrations of 1–50 mg/m^3, hydro-

carbons at 26–150 mg/m³, carbon monoxide at 8–12 mg/m³, formaldehyde at 0.05–1.2 mg/m³, sulfur dioxide at 2–20 mg/m³, and benzo(α)pyrene at 0.01–0.2 mg/m³. When multicomponent lubricating-cooling liquids containing chlorine and fluorine compounds are used as additives, hydrogen chloride and other substances may also find their way into the workroom air. It is therefore essential to provide the metal-working lathes with vapour-extracting facilities (Medved' et al., 1976).

4.4 Environmental Distribution and Transformation

Data on lubricating base oils concerned with distribution among media, environmental transformation and degradation, interaction with physical, chemical, or biological factors, and bioconcentration are not available. However, as mentioned in section 3.4, there is a lot of information concerning the microbial degradation of individual petroleum hydrocarbons. For example, it has been shown that certain polynuclear aromatic hydrocarbons in lubricating oils can be oxidized by bacteria; benzo(*a*)pyrene and benzo(*a*)anthracene have been shown to be oxidized to cis-dihydrodiols. The oxidation is not thought to reach the stage of carcinogenic activation found in mammals, as this would result in a trans-configuration (Gibson et al., 1975).

4.5 Metabolism

Because of the complex and variable composition of compounds in this group, only a few factual data relating to their metabolism can be given.

The skin barrier is permeable only to hydrocarbons of a certain relative molecular mass and structure. For paraffinic substances this appears to be up to 20 carbon atoms. However, from their studies on guineapigs, Hoekstra & Phillips (1963) reported that, because aromatic compounds have a more compact structure, compounds in this group with a higher number of carbon atoms might still pass through the skin barrier.

In studies on mice, rats, hamsters, rabbits, and dogs, mineral oil droplets were phagocytosed in the lungs and clinical observations in man have shown that deposition takes place in the hilar nodes, from where they may be transported to other organs such as the spleen (Sante, 1949; Proudfit et al., 1950; Shoshkes et al., 1950; Wagner et al., 1964). Almost all (95–99 %) of ingested food-grade mineral oil

leaves the body unchanged in the faeces, 1–5 % being absorbed as such via the intestinal mucosa. Phagocytosis may play a part in this. The ingested part of the oil is transported throughout the body via the lymphatics and the bloodstream. Storage takes place in adipose tissue or in the fat in organs. After excessive exposure, mineral oil droplets have been identified in mesenteric and portal lymph nodes, and also in liver, spleen, and adipose tissue in man (Stryker, 1941; Ebert et al., 1966; Boitnott & Margolis, 1966b).

Data relating to food-grade mineral oil have been reviewed in WHO (1974). Very few data are available on the biotransformation and rate of elimination of this group of products but data concerning some of the components are referred to in section 3.5.

Injections of 0.5 ml of various mineral oils were made in the peritoneal cavity of mice and the oil recovered after 7 24 days (Twort et al., 1937). Both the refractive index and density of the oil had decreased proportionally, probably as the result of chemical transformation in the body. Treatment of mineral oil with sulfuric acid and clay, or solvent extraction had a similar effect. The solvent extracts, however, showed increased refractive indices and densities. The authors suggested that both parameters might be useful indicators of the carcinogenicity of the mineral oil.

4.6 Effects on Experimental Animals

4.6.1 Short-term exposure

Data are not available concerning the LD_{50}s of base oils but the oral and dermal LD_{50} data available for commercial lubricating oils indicate that, in general, these products are only moderately or slightly toxic.

Acute no-observed-adverse-effect levels have not been determined. Oral studies with food-grade mineral oils show that these are laxatives. The same applies to non-food-grade commercial mineral oils, though it is impossible to predict whether in a certain case a toxic or laxative effect will prevail.

4.6.1.1 *Effects of dermal exposure*

More factual information is available on the acute or short-term effects of mineral base oils on the skin. In a very thorough study Hoekstra & Phillips (1963) examined the effects of mineral oils and their fractions on the skin of guineapigs. It appeared that very short-chain paraffins had a mainly defatting action on the skin and that the effects of longer-chain and aromatic hydrocarbons were

closely related to the permeability of the skin to these compounds. We can do no better than cite the summary of this work:

"A number of light mineral oils applied topically to the skin of guinea-pigs caused a marked epidermal hypertrophy, hyperplasia, hyperkeratosis, and subsequent depilation. This dermatoxic effect could not be closely related to source of the crude oil or its viscosity, degree of refinement, or the acid used in refinement.

"*n*-Paraffin, isoparaffin, naphthene and aromatic fractions separated from light mineral oil each produced the dermatoxic effect as did highly purified individual paraffins from C-12 to C-18. Oleic acid caused only a slight dermatoxic effect. Fractional distillation of an aromatic-free mineral oil demonstrated that while all lower-boiling fractions were dermatoxic, a distillation range was reached at which the fractions were innocuous to the skin. This was also true for *n*-paraffin-, isoparaffin-, monocyclic naphthene-, and polycyclic naphthene-rich fractions derived from a mineral oil. Fractional distillation of the aromatic hydrocarbons from mineral oil representing the same distillation range did not yield fractions without skin-damaging effect. Crude estimates of the molecular size of the *n*-paraffins, isoparaffins, monocyclic naphthenes, and polycyclic naphthenes by comparison with the boiling-temperatures of known, homologous series of hydrocarbons indicated that the maximum skin damage resulted from hydrocarbons of about 14 to 19 carbon atoms. The transition point to non-dermatoxic hydrocarbons occurred at about 21–23 carbon atoms. This was verified with purified *n*-paraffins. Variations may exist for the different types of hydrocarbons.

"Simultaneous application of the innocuous 'higher-boiling" mineral oil fractions with dermatoxic "lower-boiling" fractions or with hexadecane greatly reduced or eliminated the skin-damaging effects. The alleviation of the skin damage from aromatic fractions by simultaneous application of the "higher-boiling", non-aromatic fractions was much less pronounced.

"The hyperkeratotic reaction of the skin to petroleum hydrocarbons appears to be a very general response to lipid solvents and is not related to any specific reactive group or type of structure. Molecular size seems to be very important in determining the dermatoxic properties of hydrocarbons, the larger molecules being innocuous. Under the conditions of the experiments the very low-molecular weight hydrocarbons also had little or no dermatoxic properties, presumably because of their volatility. It is postulated that the skin barrier is permeable only to hydrocarbons of a certain maximal effective size and that penetration into or through the barrier is essential for the initiation of the hyperkeratotic response. The alleviation of the dermatoxic effect of hydrocarbons by admixture with innocuous, higher molecular weight hydrocarbons, is likewise explained by a reduction in penetration of the dermatoxic component through the skin barrier" (Hoekstra & Phillips, 1963)

4.6.2 Long-term exposure

Most long-term studies with mineral oils have been concerned with the carcinogenicity of the compounds. Data concerning mutagenicity, embryotoxicity, and teratogenicity are lacking.

4.6.2.1 *Carcinogenic effects*

The carcinogenic activity of certain polynuclear aromatic hydro-

carbons is attributed to electronic structural features of the molecule. The various theories on these mechanisms are discussed in detail by Arcos & Argus (1974), Bergel (1974), and Jerina & Daly (1974). Carcinogenic polynuclear aromatic hydrocarbons have regions of high-electron density in their molecules, the so-called K-regions that are readily epoxidized by tissue mixed-function oxidases and more specifically by the enzyme aryl hydrocarhon hydroxylase.

Polynuclear aromatic hydrocarbons are in fact precarcinogens, which, though harmless in themselves, are metabolized in the body, by the combined action of mixed function oxidase and epoxide hydratase (4.2.1.63), to biologically reactive intermediates that constitute the ultimate carcinogens (Sims et al., 1974). The enzymes responsible are active in the liver, and in other organs such as the skin, lungs, and intestines.

Whether, in fact this metabolism leads to detoxication or to "lethal synthesis" may differ with various polynuclear aromatic hydrocarbons and may depend on many other factors (Anon., 1975). The short-lived epoxides resulting from the metabolism of at least some of the polynuclear aromatic hydrocarbons are probably the activated metabolites with the real carcinogenic effects.

Evidence is now accumulating that it is the 7,8 dihydroxybenzpyrene – 9,10 oxide of 3,4 benzo(*a*)pyrene that is the ultimate carcinogen and, consequently, this has now superseded the K-region epoxide in biological importance with regard to carcinogenicity (Yang et al., 1976; Thakker et al., 1977; Yagi et al., 1977; Koreeda et al., 1978). The enzyme aryl hydrocarbon monooxygenase (according to recent international rules of nomenclature) in the case of 3,4 benzo(*a*)pyrene, is referred to as benzopyrene 3-monooxygenase (EC1.14.14.2) (de Pierre & Ernster, 1978).

There are indications that the tissue concentrations of the enzyme aryl hydrocarbon hydroxylase vary considerably with the age, sex, species, strain, and environment of the animal (Nebert & Gelboin, 1969). Outside agents, such as polynuclear aromatic hydrocarbons, can induce the activity of this enzyme (Wattenberg, 1972). It seems that the inducibility depends on genetic factors in both mice and human subjects (Nebert et al., 1972; Kellerman et al., 1973). In mice, it seems to depend on a single dominant autosomal gene (Nebert et al., 1972).

4.6.2.2 *Effects of dermal exposure and subcutaneous administration*

Leitch (1922) repeatedly painted crude shale oil on the skin of mice. He obtained skin tumours in a substantial percentage of the mice. Similar tests were carried out by Twort & Ing (1928) and Twort

& Twort (1931) using a range of crude oil as well as more refined products of both shale oil and petroleum oil. They found that petroleum oils had a lower and sometimes negligible carcinogenic activity compared with shale oils. Naphthenic oils were less active than oils with a high aromatic content. The more potent fractions could be extracted with solvents from the oils.

Acid treatment of the oils decreased the carcinogenic activity and heavier-grade oils were less potent than spindle oils.

Oils with a boiling-point above 370 °C, derived from fluid catalytic cracking, appeared to be carcinogenic to the skin of mice. The most potent fraction distilled between 430 and 550 °C, and the carcinogenic activity was contained in the aromatic components of these oils.

Woodhouse (1934) compared the carcinogenicity of sulfur-dioxide-solvent-extracts of spindle distillates, derived from crude oils from different parts of the world, with that of the unrefined spindle oils and coal-tar, using a mouse-skin-painting technique. He found that in all cases, the carcinogenic activity, which was more or less characterized by its UV-fluorescence spectrum, was concentrated in the solvent extract. Potency varied according to the source of the crude oil. The potency of the most active extract, however, was lower than the activity of coal-tar. By thorough sulfur-dioxide-solvent refining, the carcinogenicity of the spindle oil was almost completely removed. The same author (Woodhouse, 1950) reported studies on the carcinogenic activity of various petroleum fractions and extracts. Results were in line with his previous findings and with those of other workers. Three white oils including medicinal liquid paraffin gave negative results.

More recent studies have been aimed at identifying the carcinogenic substances.

Dilution of carcinogenic oils with non-carcinogenic oils more than proportionally reduced the carcinogenic activity, which at times disappeared completely. Mild hydrogenation or treatment with active absorbents reduced, but did not abolish carcinogenicity. Mild acid treatment, on the other hand, did not have such an effect (Smith et al., 1951). Eight samples of unrefined "slack waxes" obtained from pressing operations – still containing 12–29 % of oil – were painted 3 times a week on the skin of white mice (Smith et al., 1951). Aromatic extracts, obtained by the solvent refining of these waxes, were examined in the same way. After skin-painting for almost the life span of the animals, some benign tumours were found with all samples and in a few cases, skin carcinomas developed. The aromatic extracts, however, were much more active. The authors concluded that the aromatic components, which were removed by further refining of the waxes, were the cause of the carcinogenic activity of "slack waxes".

Fischer et al. (1951) described methods for the determination of polynuclear aromatic hydrocarbons: the ultraviolet absorption method, the caffein extraction method, the chromatographic refractometric method, and the maleic anhydride method. Levels, determined by any of these methods, were fairly well correlated with the tumorigenic potency of these oils as established in animal experiments. These analytical techniques are relatively simple and much more rapid than long-term animal experiments. They are considered to have some predictive value. A further development is the DMSO extraction/refractive index method.

The correlation between the analytical data and the carcinogenic activity in skin-painting studies on mice is now under investigation (Shell Toxicology Laboratory – private communication) and encouraging results have been obtained with the lower- and higher-range polynuclear hydrocarbons. The compounds in the middle range are still under investigation.

Auld (1940) considered that it was not the general UV-fluorescence that was characteristic of carcinogenicity but the pattern of the spectrum and its classification. However, in a report by the Analytical Subcommittee of the Institute of Petroleum (Catchpole et al., 1971a), it was concluded that, at the time of the report, there was no suitable, easy and quick method for determining either the total polynuclear aromatic hydrocarbons or individual carcinogens in them.

The tumorigenic activity of various concentrations of a large number of pure aromatic hydrocarbons was examined in different strains and species of animals by Hartwell (1951), who found that the potent substances contained 4,5, or 6 condensed aromatic rings with relative molecular masses ranging from 230 to 320.

Cook et al. (1958) tried to isolate individual carcinogens from 3 Kuwait crude oils by fractional distillation and various treatment processes. They tested the fractions obtained on the skin of mice and rabbits and found that more of the carcinogenic activity was contained in the fraction distilling between 350 and 400 °C and that this activity was associated with the aromatic constituents. Solvent extraction with aqueous acetone or furfural removed the activity, which passed into the extract (20 % of the original fraction). Several polynuclear aromatic hydrocarbons such as di-, tri-, and tetramethylphenanthrenes, tetramethylfluorene, 1-methylpyrene, 1,2-benzofluorene and 8-methyl-1,2-benzofluorene could be identified in these extracts as well as some complex organic sulfur compounds such as dibenzothiophen derivatives and polycyclic thiophens, a number of which are known to have carcinogenic activity. Pentamethylcarbazole was identified as an example of a complex organic nitrogen compound. Similar findings were obtained by Bogovsky et al. (1960) on fractionating Estonian shale oil.

Approximately 100 fractions were separated from a catalytically cracked oil by various techniques (Tye et al., 1966). Selected fractions were chemically analysed and assayed for carcinogenicity by repeated application to the skin of C3H mice. In the highest-boiling fractions (438–455 °C), the major carcinogens were 4 and 5 ringed polynuclear aromatic hydrocarbons, benzo(*a*)pyrene as a characteristic carcinogen was present at a concentration of 0.4 %. In the intermediate boiling range (404–438 °C), unsubstituted and methyl-substituted 4-ringed polynuclear aromatic hydrocarbons formed the major carcinogens, benz(*a*)anthracene and its alkyl homologues being present at a concentration of 0.4 %. In the low-boiling fraction (339–404 °C), assorted smaller molecules including alkyl-3-ringed polynuclear aromatic hydrocarbons were present. Benzo(*c*)-phenanthrenes, the most dominant carcinogens in this fraction, were present at a concentration of 0.01 %. The carcinogenic potency in the bioassay was found in the intermediate- and high-boiling fraction (boiling-range 404–455 °C); fractions boiling at under 349 °C did not appear to be carcinogenic.

Generally, where the alkyl-substituted 4–6 condensed-ring polynuclear aromatic hydrocarbons were concerned, the longer the side-chain, the lower the carcinogenic activity (Auld, 1950).

These findings were confirmed by the United Kingdom Medical Research Council (1968), who reported similar studies. Uncracked crude oil fractions boiling at above 350 ° C, which had the highest carcinogenic activity in skin tests on mice and rabbits, contained the same or similar polynuclear aromatic hydrocarbons; no other new carcinogens were found. After solvent extraction, the carcinogenic activity of the extract was much higher than that of the raffinate, which was very low.

The carcinogenicity of individual polynuclear aromatic hydrocarbons will not be discussed in this document. For this, the reader should refer to IARC (1973).

The fact that various cracking processes considerably increase the contents of polynuclear aromatic hydrocarbons in mineral oils has been demonstrated by Kennaway (1925), Twort & Fulton (1930), Twort & Twort (1935), Pates (1952), and Dietz et al. (1952). Kennaway (1925) discovered that skin cancer of mice could be produced with synthetic tars obtained by pyrolising substances like acetylene, isoprene, yeast, human skin, and a non-carcinogenic petroleum. Badger (1962) pyrolysed a whole range of aliphatic and simple aromatic hydrocarbons at 700 °C. It was concluded from an analysis of the resulting tars that, at high temperatures, polycyclic aromatic hydrocarbons were formed from simpler hydrocarbons via primary radicals formed by carbon-hydrogen and carbon-carbon fission. The same process occurred at 550 °C, but to a much lesser extent.

Skin tests on C3H-mice using 15 base oils with known content

of polynuclear aromatic hydrocarbons, which, in some cases, only differed in their refining history, revealed that solvent-refining removed the carcinogenic components to such an extent that none of the oils treated in this manner induced carcinomas (Bingham et al., 1965). Solvent extraction was carried out with the usual solvents including phenol, cresol, and furfural. Conventional acid and clay treatment only removed certain of the polynuclear aromatic hydrocarbons and all oils treated in this way still retained some carcinogenic activity. In these tests, a general correlation was again found between the content of 4 and 5 ring polynuclear aromatic hydrocarbons and the carcinogenicity of the base oils examined.

Catchpole et al. (1971b) compared mass spectrometry analysis of an untreated distillate with its solvent-treated and its hydrogenated derivatives. The decrease in polynuclear aromatic hydrocarbons thiophenes, and sulfur in both treated samples compared with the untreated sample was quite marked. Smaller differences were found between the levels in the two refined samples.

In studies by Boehme & Huehnermann (1966), the relative amounts of aromatic compounds present in some of the more purified mineral oil products were determined from their UV absorption spectra. The relative concentrations were:

medicinal white oil	1
paraffin waxes	100
microcrystalline waxes	300
white petrolatum	1000
yellow petrolatum	10 000

The carcinogenicity of a sample of amber petrolatum was tested on the skin of mice. A 15 % solution of the petrolatum in iso-octane, did not show any significant carcinogenicity. The solvent-extracted aromatic fraction (1.2 % of the original material) tested in iso-octane solution at 50 times its concentration in the petrolatum did not produce any carcinogenic effects on mouse skin (Lijinski et al., 1966). Studies are reported by Oser et al. (1965) in which 3 kinds of pharmaceutical and food-grade petrolatum were administered to mice in the form of a single subcutaneous injection of 100 mg of petrolatum per mouse. Observations over 18 months did not reveal any carcinogenic or other toxic effects.

Liquid paraffin was found to be non-carcinogenic in long-term skin testing on mice by Twort & Twort (1931) and Woodhouse (1934). White mineral oil was also found to be non-carcinogenic in mice after long-term skin application (WHO, 1974).

Shubik et al. (1962) examined 36 samples of petroleum wax. Eight samples contained identifiable polynuclear aromatic hydrocarbons; the highest concentration was 0.64 mg/kg. The results of skin and subcutaneous testing follow in the author's words:

"Five petroleum waxes were tested by repeated skin application

in benzene solution to mice and rabbits. In addition one of the test waxes was fractionated and its aromatic and non-aromatic components were tested separately on mice, also by repeated skin applications. Solvent-treated controls were kept. No carcinogenic effects were detected. Five petroleum waxes were tested in mice by subcutaneous implantation in disc form. Fibrosarcomas developed around the implants with incidences correlated to the melting points of the waxes. In addition, one of the test waxes was fractionated and its aromatic and non-aromatic components tested separately, the same wax was also tested subcutaneously in powdered form The findings indicate that the subcutaneous sarcomas occurred as a result of the physical rather than the chemical properties of the materials."

From the various studies, it would seen that there is no relation between the carcinogenicity of a lubricating base oil and its potential to cause dermatitis.

In all the previously mentioned studies and others by Horton et al. (1963) and Bingham & Horton (1966), there is general agreement that the carcinogenicity of a mineral oil is largely related to the aromatic fraction with a boiling-point above 370 °C, and more particularly to the polynuclear aromatic hydrocarbons containing 4 6 condensed benzene rings. However, some long-chain, aliphatic, alicyclic, and alkyl-aromatic hydrocarbons from a lower boiling-range with 10–20 carbon atoms, such as *n*-dodecane, cyclohexyl-decane, and dodecyl-benzene may act as accelerators or co-carcinogens. Though completely non-carcinogenic themselves, they were found to increase tumour incidence and reduce the time of appearance, when carcinogenic fractions dissolved in them were applied, to the skin of mice (Horton et al., 1963; Bingham & Horton, 1966). However, in order to act as a cocarcinogen, *n*-dodecane must be present in a concentration of 20–30 % or more. Such solutions in accelerating solvents show an unusual capacity to spread upon the skin (Horton et al., 1957, 1965).

In a further study on the effects of co-carcinogenic compounds on the carcinogenic action of benzo(*a*)pyrene and benz(*a*)anthracene on the skin of mice (Bingham & Falk, 1969), the co-carcinogenicity of *n*-dodecane was confirmed. However, when the authors claim "that there is a 1000-fold increase in the enhancement of potency of low concentrations of benzo(*a*)pyrene and benz(*a*)anthracene when dodecane is the diluent", this statement may not be fully justified by the results obtained in relatively small numbers of animals per test group. Nevertheless 50 % *n*-dodecane in the solvent decaline doubled or trebled the tumour incidence in the highest dose-group, and tumours were found at much higher dilutions than when decaline alone was used as a solvent. When 2-dodecanol and 2-phenyldodecane were used in various concentrations in the sol-

vent of benzo(*a*)pyrene, higher concentrations of these 2 substances shortened the interval of appearance of tumours rather than increasing the total incidence of tumours.

From this it would appear that these acccelerators would not have any effect, when present in an intrinsically non-carcinogenic oil, and that they would only have an effect in other oils, when present in appreciable concentrations. This effect seems to be due, at least in part, to the spreading power of the solvent causing more intimate contact with a greater skin area. On the other hand, a more plausible explanation could be an increase in P-450 enzyme induced by dodecane, which possibly does not occur with 2-dodecanol and 2-phenyldodecane. 3,4 Benzo(*a*)pyrene can induce P-450 microsomal mixed function oxidase and this can also catalyse arylhydrocarbon (AH) monooxygenase activity (de Pierre & Ernster, 1978). The increase in P-450 induced by dodecane will accelerate and increase the formation of the ultimate carcinogen 3,4 benzo(*a*)pyrene and thus increase the total incidence of tumours. However, these substances will not normally he present in base oils and related products, because they fall into a different boiling range.

Apart from this, some frequently used additives – which in themselves are non-carcinogenic – such as elemental sulfur and some sulfur-containing compounds such as benzyldisulfide, ditertiary butylpolysulfide and ditertiary octylpolysulfide (Horton et al., 1965; Bingham et al., 1965; Bingham & Horton 1966) as well as certain phenols (Boutwell & Bosch 1959) have also been shown to enhance the carcinogenic activity of polynuclear aromatic hydrocarbons on the mouse skin. Addition of sulfur to a non-carcinogenic oil did not, of course, have any effect on the carcinogenicity (Bingham et al., 1965). Baldwin et al. (1964) reported that additives such as lead naphthenate did not have an enhancing effect and there are indications that other components of complex mineral oils with a boiling-range above 370 °C act as inhibitors of the carcinogenic effect of polynuclear aromatic hydrocarbons, e.g., the saturated (probably cyclic) hydrocarbons (Bingham & Horton, 1966).

Sunderland et al. (1951) reported skin tests of mineral oil fractions on mice, under various conditions. They found that washing the skin with soap and water, after the application of the oil, reduced both the numher of tumours and the rate of appearance. The reduction was related to the length of the interval between oil application and washing. Painting once, instead of twice, weekly greatly reduced the rate of tumour appearance.

From human experience (section 4.7.1.1), it is known that the ultraviolet radiation of sunshine has a potentiating effect on the carcinogenicity of mineral oils. Similar indications exist from animal studies (Emmett, 1975). It has also been demonstrated that certain co-carcinogenic *n*-alkanes may increase the carcinogenic

potential of certain wavelengths of UV light on mouse skin (Bingham & Word, 1977).

In comparative studies with various mineral oil fractions on the skin of mice and rabbits, it became apparent that the rabbit skin was more sensitive than the mouse skin according to the type, number, and growth rate of tumours (Cruickshank & Squire 1950; Hieger & Woodhouse 1952; Antonov & Lints 1960; UK Medical Research Council, 1968). In some instances, mineral oil fractions were non-carcinogenic to mouse skin, but positive on the skin of rabbits (Shubik & Saffiotti), 1954). While, rats and guineapigs are apparently less sensitive than mice (Sugiura et al., 1949; Desoille et al., 1973) Rhesus monkeys appear to be fairly sensitive (Sugiura et al., 1949).

As to the suspected causes of intra- and inter-species differences in susceptibility to polynuclear aromatic hydrocarbons, the levels of the enzymes forming and detoxifying the biological reactive intermediates, the ultimate carcinogens, in the tissue of the various strains and species might be one of the important factors (section 4.6.2.1). Clear intra-species differences in tumorigenic response have been reported by, for example, Smith & Sunderland (1951) and Gilman & Vesselinovitch (1955).

In addition to these studies on "pure" mineral oil fractions and various additives, some studies with metal working oils and textile oils have been published.

Two cutting oils based on sulfurized mineral oils, were diluted with water and were tested in various concentrations on the skin of 3 strains of mice. Both were found to be carcinogenic. A marked reduction in incidence and an increase in induction time of tumours was found at a dilution of 1:8 compared with 1:4 (Gilman & Vesselinovitch, 1955). The same authors (Gilman & Vesselinovitch, 1956) compared a straight cutting oil and a water-soluble cutting fluid in 2 different strains of mice. They found a consistent, comparable but low incidence of skin tumours in 3 separate trials.

In a later study, 3 commercial additive-containing cutting oils, one of which was an emulsifiable oil, were repeatedly applied to mouse skin for up to 31 weeks. Carcinogenic skin changes were observed with all these oils but were, possibly, less marked with the emulsifiable oil. In addition to these carcinogenic effects, focal necrosis of the liver associated with amyloid deposition and amyloidosis of the skin, spleen, and kidneys were observed. The additives may have had a contributory effect in some of the pathological changes observed (Jepson et al., 1977).

In the case of cutting oils, the temperatures to which the oils are exposed at the cutting edges of the tools are such that cracking of the oil might conceivably occur and theoretically a non-carcinogenic cutting oil might become carcinogenic during use. An unspecified

used cutting oil from the sump of a machine was tested on the skin of mice and rabbits. It induced benign tumours in rabbits only (Cruickshank & Squire, 1950). As the fresh oil was not examined, no conclusion can be drawn concerning the previously-mentioned assumption.

Unused cutting oil, used cutting oil, and residue from the sump were compared in skin tests on 2 strains of mice by Dargent et al. (1967). Both used and unused cutting oil caused a high incidence of skin ulceration. Hyperkeratosis and papillomas were more frequent in the case of used oils and a single case of skin cancer occurred in the groups of mice treated with used oil and sump residue.

Cutting and quenching oils, fresh and used, were tested on the skin of rats, guineapigs, and mice. All tests on rats and guineapigs were negative. In mice, skin tumours were more numerous and more malignant with used oils than with fresh oil. Only used oils produced tumours in organs distant from the site of application. The unused quenching oil was found to contain a benzo*(a)*pyrene level of 0.6–0.8 mg/kg (ppm); in the used oil, this fraction had increased to 20 mg/kg, which is in agreement with the finding of its increased carcinogenicity. The increase in carcinogenic polynuclear aromatic hydrocarbons may be the result of thermal cracking due to the heat of the process (Desoille et al., 1973). The studies of Thony et al. (1975) indicated that the increase in polynuclear aromatic hydrocarbons in cutting oils was very small and considerably less than for quenching oils and engine oils. The benzo*(a)*pyrene content of new cutting oils ranged from 0 to 150 mg/kg, compared with 0 to 250 mg/kg for used cutting oils.

A sample of commercial jute batching oil of unspecified origin and composition, containing a concentration of 3,4-benzopyrene of less than 1 mg/kg, was tested for carcinogenic activity on the skin of mice. The oil in question induced malignant skin tumours in 6 out of 24 test animals and proved to be a potent tumour promotor in mice pre-treated with 7,12-dimethylbenz*(a)*anthracene (DMBA) (Roe et al., 1967).

To summarize, it may be concluded that: *(a)* the carcinogenic activity of mineral oils seems to be related mainly to the presence and concentration of certain polynuclear aromatic hydrocarbons, containing 4,5, or 6 condensed rings; and *(b)* cracking processes tend to increase the polynuclear aromatic hydrocarbon contents in petroleum products. For example such compounds may accumulate in a metal working oil in contact with the host cutting edge of a tool.

The polynuclear aromatic hydrocarbon content of mineral oils can be decreased by solvent extraction and/or by hydrogenation. Acid treatment is less effective for this purpose.

Analytical methods for the determination of total polynuclear aromatic hydrocarbons should provide a useful, quick, and cheap

tool for predictive screening of mineral oils for carcinogenicity. These methods should be biologically validated. The correlation will not always be good, because the carcinogenicity of polynuclear aromatic hydrocarbons varies considerably and because of the unpredictable effects of cocarcinogens, inhibitors, and accelerators.

Various substances that are used as additives such as sulfur compounds, as well as substances that may normally be present in mineral oils, such as *n*-dodecane, may act as cocarcinogens. Other saturated hydrocarbons, normally present, may act as inhibitors of the same effect.

It is clear from animal studies that washing with soap and water substantially reduces the hazard to the skin of repeated and long contact with potentially carcinogenic oils.

4.6.2.3 *Effects of inhalation and intratracheal exposures*

The aspiration hazard and toxicity for animals of a number of hydrocarbons and hydrocarbon mixtures was determined by Gerarde (1963). This study has been discussed in more detail in section 3.6.1. He found that the aspiration hazard decreased with increased viscosity of the product and with mixtures containing low viscosity products.

Mice were exposed to mists of various mineral and vegetable oils with an average droplet size of 2.5 μm, 80 % of the particles retained in all areas of the lungs were 2.5 μm or less in diameter. The highest concentration of retained particles was found around the terminal bronchioles and alveolar ducts in all parts of both lungs. Oil particles were immediately phagocytosed, a process that was essentially completed within 48 h, unless prolonged exposures (2–4 weeks) had been given. The initial concentration of retained oil droplets was similar for all types of oil mists. During a 90-h follow-up, however, the concentration of vegetable oil droplets decreased progressively, whereas the concentration of mineral oil droplets remained practically unchanged. After 2–4 weeks of exposure, mineral oil droplet retention gave rise to localized slight foreign-body reactions as well as to a few patches of lipoid pneumonia. Of the other oils, only cod liver oil caused a moderate foreign-body reaction (Shoshkes et al., 1950).

The effects of prolonged inhalation of oil mists (mineral oil levels in air of 63–132 mg/m^3) were observed in mice, rats, rabbits, and monkeys. Ordinary automobile lubricating oil and a smoke-screening oil, were tested for periods varying from 100 to 365 consecutive days (Lushbaugh et al., 1950) The authors found that surprisingly little oil accumulated in the lungs and that whatever was retained was rapidly phagocytosed and transferred to the pulmonary connective tissue and the hilar lymph nodes. Lipoid pneu-

monia was not found to be a hazard at these dosages, though the incidence of infectious pneumonia in the exposed monkeys greatly increased. Many exposed monkeys died of a hyperplastic gastritis, probably because much of the inhaled oil was initially deposited in the nasal passages and subsequently swallowed. Hyperplastic gastritis was especially evident with the shale oil (which is different from petroleum oil) used as smoke screening oil (Lushbaugh, 1947). No significant increase in tumour incidence or reduction in the latent period of tumour production was found in the mouse study.

Hueper & Payne (1960) compared the carcinogenicity of various petroleum products and coal-tar in long-term tests on mice, rats, and guineapigs. Rats and guineapigs were exposed for 6 h/day, 4 days a week, for up to 2 years, to a cutting oil mist consisting of a 10:1 mixture of neutral paraffin and prime lard oil. In some cases, this caused multi-focal adenomatosis in the lungs of the animals. A carcinoma of the lung was found in only 1 of 105 exposed rats and not in any of 65 guineapigs.

In tests on mice, Wagner et al. (1961) found that inhalation of either mineral or motor oil mist reduced the acute lethal effects of respired oxidants such as ozone and nitrogen dioxide. The effect was demonstrable only after a latent period of up to 8–9 days following oil mist exposure and was thought to result from the formation of a thin film of oil on the alveolar surfaces.

Long-term inhalation toxicity studies using a highly purified white mineral oil, composed of naphthene-based saturated hydrocarbons, were reported by Wagner et al. (1964). Five species of laboratory animals (dog, rabbit, rat, hamster, mouse) were exposed daily, for periods from one year to 26 months, to a petroleum-base mineral oil mist at concentrations of 5 mg/m^3, the current USA threshold limit value, and 100 mg/m^3. Histological evaluation of tissues of the dogs and rats exposed to 100 mg/m^3 showed significant pulmonary alveolar and hilar lymph node oil deposition and/or lipid granuloma formation after 12 months of exposure. In addition, these animals showed significant increases in the activities of basic and magnesium-activated phosphatases.

Body-weight gain, haematological variables, and respiratory function values did not deviate significantly from the control data at any of the exposure levels. Studies with a spontaneous pulmonary-tumour-susceptible strain of mouse presented equivocal evidence of an increased rate of tumour formation at the 100 mg/m^3 concentration. These findings suggest that prolonged exposure to a mineral oil mist concentration of 5 mg/m^3 would not present any toxic hazard. It would appear, however, that protracted exposure at approximately 100 mg/m^3 would, in time, produce harmful physiological effects.

The toxicity of aerosols of various petroleum oils (industrial, transformer, and compressor distillates) differed only slightly in a long-term experiment by Lutov (1974). White rats were exposed to concentrations of 13, 30, and 60 mg/m³ for 5 h/day, for 6 months. Changes in the electrocardiogram, and reductions in arterial pressure, respiratory frequency, and immunological reactivity were seen even at 12–13 mg/m³, which was considered to be just above the threshold level. A concentration of 5 mg/m³ is recommended as a maximum permissible concentration for petroleum oil aerosols without additives.

In a further long-term study on white rats, Lutov et al. (1976) studied the toxicity of petroleum oil aerosols in concentrations ranging from 11.4 ± 1.5 to 61.4 ± 5.2 mg/m³ in combination with products obtained by thermo-decomposition, i.e., hydrocarbons in concentrations ranging from 200.0 ± 5.8 to 410.0 ± 12.8 mg/m³ and carbon monoxide in concentrations ranging from 11.2 ± 1.5 to 35.4 ± 4.6 mg/m³. White female rats were exposed for, 5 h/day over a 6-month period. The combined exposure was found to produce more marked effects on the parameters tested in the earlier experiment.

The minimum concentrations of oil aerosol that caused functional changes in the respiratory system with a single inhalation were in the range of 860–1200 mg/m³. When concentrations of 53 and 60 mg/m³ were used in the long-term experiment, physical growth was impaired and the functional condition of the nervous system and the liver changed. There were morphological changes in the lungs including a catarrhal-desquamative bronchitis, a swelling of the alveolar membranes, formation of oleogranules, and the presence of a large quantity of oleophages and oil droplets in the lymphatic vessels and the peribronchial and bronchopulmonary lymphatic nodules. At concentrations of 10–17 mg/m³, the changes were slight and reversible. A maximum admissible concentration in the air of a work place of 5 mg/m³ is the official USSR exposure limit (Ivanov et al., 1978).

In tests on rabbits, Laughlen (1925) demonstrated that mineral oil given by mouth or nose can enter the trachea. Corper & Freed (1922), injected olive oil and medicinal mineral oil intratracheally into rabbits in amounts of 0.5–1.0 ml. The oil was readily aspirated into the finest pulmonary divisions and into the alveoli. It was retained for months and caused a mild proliferative reaction typical of a foreign body reaction. In studies by Pinkerton (1928), rabbits and puppies were injected intratracheally with animal, vegetable, and medicinal oil. Complete removal of the oil from the lungs took several months in all cases. Neutral vegetable oil produced practically no reaction, animal oils caused giant cell formation and rapid and marked pulmonary fibrosis. Mineral oil was rapidly phago-

cytosed, giant cell formation and slight fibrosis were apparent after 2–3 months, and storage of the oil took place in the bronchial lymph nodes.

4.6.2.4 *Dietary studies*

Long-term oral studies have not been conducted with lubricating base oils.

Lushbaugh & Hackett (1948/1949) carried out a study in which rats received an average of 0.2 ml/rat per day of a highly refined diesel-engine lubricating oil, used as smoke screening oil, in their diet for a period of 14 months. In this group of 40 rats, 2 developed foci of colonic mucosal hyperplasia and one developed colonic adenocarcinoma.

Results of various dietary studies using food-grade and pharmaceutical-grade materials, such as medicinal and food-grade mineral oil, and food-grade paraffin waxes are included in the following summary, though these studies with highly purified material are not representative for the less purified grades.

Schmahl & Reiter (1933) fed 2 % (w/v) mineral oil in the diet of rats for 500 days without adverse effects. In studies by Daniel et al. (1953), rats were kept for 15 months on diets supplemented with 10 % liquid paraffin, without adverse effects. Five kinds of petroleum waxes were tested by feeding rats a diet containing 10 % of the wax for 2 years. The rats were then observed until natural death. No toxic or carcinogenic effects were found (Shubik et al., 1962). In the studies by Oser et al. (1965), already reported in section 4.6.2.2, 3 kinds of petrolatum were also administered to rats in the diet at 50 mg/kg diet. Observations over 2 years did not reveal any carcinogenic or other toxic effects.

4.7 Effects on Man

The general population does not have any contact with base oils; contact with the commercial products derived from them will, at most, be occasional and of a lower order of magnitude than occupational exposure. Cases of accidental ingestion are exceptions.

However, pharmaceutical grade liquid paraffin in the form of medicinal oil is widely used as a laxative (faecal softener).

Occupational exposure to base oils is restricted to the small group of workers who manufacture them in oil refineries and to workers in blending units, who mix and blend them with additives in order to produce commercial products such as lubricating oils, greases, metal-working oils, and textile oils. These activities are

normally carried out in closed systems in which case occupational contact is minimal and discontinuous, usually accidental. This also applies, when the finished product is put into containers.

4.7.1 Occupational exposure

Epidemiological and clinical data concerning base oils are almost non-existent. Thus, in this section, it is only possible to analyse epidemiological studies of workers exposed to products containing base oils, such as lubricating oils, metal-working oils, and textile oils.

From the list of lubricating oil products given in section 4.2.2, it is clear that various groups of workers are occupationally exposed to these products, the most widely-used being the metal-working oils and textile oils.

The magnitude of occupational exposure varies considerably. In the case of some lubricants and transformer oils, handling is only occasional, and, even then, exposure is minimal. In other situations, such as in the earlier years of mule spinning and in work with automatic lathes of old design, extremely high exposure did – and sometimes still does occur. Not only is there continuous direct contamination of clothes and exposed parts of the skin, but the rapid movement of the machinery may turn the oil into an aerosol and thus generate an oil mist that can be inhaled and further contaminate skin and clothing. Equipment and floors may become covered with an oil-film and situations have been described where oil even dripped from the roof.

A certain degree of oil mist generation may also occur in the printing and rubber industries and with pneumatic equipment (e.g., drills), especially under conditions of limited ventilation such as are found underground.

Even under the best technical conditions, it may sometimes be difficult to completely avoid contamination. For example, in the case of toolsetters, the wearing of protective clothing impedes easy movement, and clothing, including underwear, may become soaked with oil.

Henry (1946/1947) gave an excellent insight into the types and magnitude of occupational exposure up to the time of the report. It is known that some of these conditions had continued for a period of about 20 years. However, in many countries, great improvements have been made since then. An understanding of the range of such exposures is needed to put epidemiological studies of later years into perspective, especially in view of the long latency of carcinogenic effects. In the evaluation of such studies, it has to be kept in mind that today's findings may reflect the industrial hygiene situation of 20–30 years ago.

4.7.1.1 *Skin disorders*

A great variety of skin disorders attributed to working with mineral oil or with products based on mineral oils, such as metal working fluids, are mentioned in the medical literature. This is not surprising considering the many factors that influence their development (van Raalte, 1963; Key et al., 1966; Kipling, 1968; Hodgson, 1970, 1973).

The main factors include: *(a)* the degree of intrinsic potential of a mineral oil product to damage the skin; *(b)* the integrity of the skin; *(c)* the degree and continuity of contact between oil and skin; and *(d)* individual predisposition.

The situation, however, is more complex than this, for, in actual practice, a multitude of other factors may influence the main conditions to such an extent and in such a complex way, that a cause-and-effect relationship may become obscured. Most authors agree that practically all skin disorders attributed to exposure to mineral oil products can be prevented entirely by adequate industrial and personal hygiene practices, and that the majority of cases have occurred in workshops where inadequate conditions prevailed.

Some of the more important factors in the complex interplay are:

(a) Factors related to the mineral oil product used:

(i) Base oil:

the lower the boiling-point of the oil, the more pronounced the solvent action of the product; this causes defatting of the skin and leads to dryness, chapping, scaling, and cracking;

the higher the boiling-point, the more blocking of skin pores occurs, giving rise to acne formation;

some mineral oils are more irritant than others; the lower-boiling fractions are sometimes, but not always, more irritant than higher-boiling fractions (section 4.6.1);

mineral oils themselves do not appear to be sensitizers.

(ii) Additives:

these may be primary irritants or sensitizers in their own right (e.g., chromium salts), though manufacturers try to avoid the use of such additives;

solvents and detergents increase the defatting effect of the lower boiling-range oils;

some chlorinated additives, such as chlorinated naphthalenes, may cause chloracne. The use of chlorinated naphthalenes was discontinued in most countries, many years ago.

(iii) Changes in the composition of the oil that may occur during its use:

cracking of oil fractions may occur due to heat;

reactions may occur between components of the mixture

or between them and materials that are added at a later stage;

metal salts or ions may be formed in the mixture or solution in the case of metal-working oils; in the case of, for example, chromium and nickel, this can cause skin reactions in sensitized workers.

(iv) Impurities of all kinds may accumulate in, for instance, metal-working oil baths in which the oil is not regularly changed. Important among these impurities are: metal particles, which may cause microtraumata of the skin; and microorganisms, which may cause inflammation of the skin by way of infection or exotoxins; bacteria, yeasts, or fungi may be present in mono- or mixed culture, and some of these organisms can degrade an oil and form potentially irritating compounds.

(b) Factors related to the work situation:

(i) design of workshop and equipment determine to a large extent the magnitude and duration of exposure to the oil, and whether this exposure is continuous or intermittent;

(ii) availability of general and exhaust ventilation of sufficient design and capacity may determine whether there is exposure to oil mist or not;

(iii) use of protective clothing such as gloves, will diminish duration and intensity of skin contact;

(iv) general hygienic facilities such as wash basins near the work-place, shower facilities, frequent changing and laundering of work clothing, all of which help in limiting the extent and duration of exposure;

(v) hands and contaminated parts of the body should be washed with fatty toilet soap and, after washing the skin should be treated with a suitable emollient cream; use of solvents, and alkaline or abrasive soaps for washing can damage the skin and contribute to the occurrence of skin diseases.

(c) Individual factors:

(i) general and hereditary conditions of the skin may predispose to adverse skin effects from all sorts of chemicals;

(ii) work discipline and safety-mindedness can influence the duration and intensity of the exposure;

(iii) proper use of safety equipment and general hygiene facilities, as well as personal hygiene in the form of frequent bathing and changing of underwear, will help to avoid over- and prolonged exposure.

Contamination of the skin may often occur despite all precautions taken, particularly in the case of metal-working oils. Wiping with oil-soaked rags is an additional source of contamination and

may cause skin lesions. Continuous wearing of oil-contaminated clothing is an important factor in the etiology of scrotal cancer. Rapidly rotating machinery may generate oil foams and mists.

The most common form of skin disorder is acute or chronic contact irritative (toxic) dermatitis caused by the irritative action of various components, additives, and/or impurities in mineral oils. Dermatitis may be preceded by defatting and/or maceration of the skin. Mechanical irritation, microtraumata, and skin cuts may play a role in its origin. Clinical signs of contact irritative dermatitis are, in order of severity, erythema, oedema, bullae or necrosis, and sharp demarcation of the affected areas from unaffected ones.

The other type of dermatitis is contact allergic dermatitis (synonym: contact eczema) caused by allergic sensitization to various allergens. Additives or impurities are the most allergenic components of oil formulations. The signs of eczema are more variable then those of toxic dermatitis and include erythema, papulae, vesiculae, bullae, scales, hyperkeratoses, and rhagades. These lesions have a tendency to spread into areas that have not been in direct contact with the allergen. Eczema may be preceded by contact irritative dermatitis, from which it develops by secondary sensitization.

Oil folliculitis, or oil acne is characterized by the triad comedones, folliculitis, and follicular scars. The lesions are found on the parts of the body with the greatest exposure. Friction from clothing and machinery rubbing the oil into the exposed parts of the skin, is an important additional factor. First there is plugging of the hair follicles and pores of the skin by follicular hyperkeratosis, cell debris, and oil with its impurities, followed by blackheads and secondary infection. Poor personal hygiene is the main cause. Oil acne occurs more often in the earlier years of exposure to oil. Later, there appears to be a gradual change in the reaction of the skin to the oil (Kinnear et al., 1954). Chlorinated naphthalenes and related compounds have given rise to chloracne.

Photosensitivity is an abnormal sensitivity of the skin to sunlight caused by certain constituents of coal-tar, but also sometimes by mineral oil constituents. Related to this is melanosis, the general darkening of the skin that may follow acute photodermatitis, as well as toxic melanoderma, which develop after long-term exposure to oils containing certain anthracene fractions. Both photosensitivity and melanosis rarely result from exposure to mineral oil.

Hyperkeratosis may occur either together with dermatitis and oil acne of long standing, or in isolation – mostly on the forearms or other heavily exposed parts of the body. Two forms of hyperkeratosis can be distinguished: *(a)* circular, white and flat hyperkeratotic areas of a few mm in diameter, sometimes in the form of smooth plaques; these may occur in small clusters and are slightly

raised above the level of the surrounding skin; and *(b)* a second form, which may occur at the same time, and consists of rugose, pigmented warts that are considerably raised above the surrounding tissue level. The pattern is generally irregular, but may be round or oval.

Precarcinogenic changes may be present in the hyperkeratotic plaques in the form of rough, slightly raised patches, which sometimes may take the form of horns or warts. In themselves these forms are still harmless, but they have a tendency to become malignant. As soon as these forms contain some malignant cells they are called keratoacanthomata. After growing for a certain period, they may be shed from the skin. Another form of precarcinogenic change that may be encountered is the shark- or shagreen-skin, a pigmented, atrophic skin, beset with small horns and warts.

A basal cell carcinoma (basalioma) is a very slowly enlarging tumour of the skin. It may ulcerate, or invade the area round it, but, in general, it does not metastasize. The most common form of malignant tumour is the squamous cell carcinoma (spinalioma), starting as a small tumour, that may arise from a keratosis or in apparently healthy skin. It continues to grow, starts ulcerating, invades surrounding tissues and eventually may metastasize. None of these conditions is limited to mineral oil exposure. Similar changes may occur as a result of UV-light exposure, excessive doses of X-rays, exposure to pitch coal-tar, or ingestion of arsenic. A specific localization, however, is the epithelium of the scrotum. In this case "it is reasonable to assume that it could be caused by occupational exposure to soot, tar, pitch, or oil" (Kipling, 1968).

A combination of various potentiating factors, such as mineral oil contact and exposure to sunlight (UV-radiation) increases the tendency to develop skin cancer (Schwartz et al., 1947; Smiley, 1951; Kinnear et al., 1954; Emmett, 1975). This is especially pronounced in persons with fair hair.

4.7.1.2 *Skin carcinogenicity*

The history of the development of skin cancer as a result of exposure to mineral oil, as well as the major epidemiological literature related to the subject have been reviewed by the International Agency for Research on Cancer (IARC, 1973). To quote their findings:

> "Volkmann (1875) described scrotal cancers among workers producing paraffin by the distillation of coal-tar. Subsequently, Liebe (1892) noted the absence of such hazard among workers exposed to pure paraffin. Several investigators have since shown that cancers among paraffin workers are not due to the paraffin but to impurities in oils produced during processing (Leitch, 1922; Hendricks et al., 1959). Refined paraffin is free of PAH and does not induce skin cancer in mice (Shubik et al., 1962).

"Bell (1876) first described cancer of the scrotum in a Scottish shale oil worker. In a 23-year period, 49 Scottish paraffin workers developed skin cancer of which 13 were scrotal (Henry, 1946).

"The cotton mule spinning industry in Great Britain originally used shale oil for the lubrication of the spindles (Henry, 1946). The first case of death from scrotal cancer in a worker who used shale oil in mule spinning occurred in 1923 (Bridge & Henry, 1928). In the years 1920 to 1943, there were 1303 legally notified cases of skin cancer in the British mule spinning industry, including 824 of the scrotum. There were 575 fatal cases of scrotal cancer recorded between 1911 and 1938 (Henry, 1946).

"In Great Britain, the Mule Spinning Regulations have ensured that since 1953 only oil drastically refined with sulphuric acid shall be used in mule spinning and that mule spinners shall be medically examined every six months. These measures, together with the marked decline of the process of mule spinning, have produced a sustained fall in the incidence of cancer of the scrotum in Great Britain.

"Cutting oils used by workers to cut metals were found to increase the risk of skin cancer in Birmingham, England (Cruickshank & Squire, 1950; Cruickshank & Gourevitch, 1952), particularly among workers in automatic machine shops. Between 1950 and 1967, 187 cases of scrotal cancer occurred in this region, of which at least two-thirds could be attributed to oil (Waterhouse, 1971).

"At the present time toolsetters and setter operators in automatic shops who use neat cutting oil have an increased risk of cancer. The work requires constant contact with the machines and consequent contamination with the oil. In the Birmingham area of England, a high frequency of skin and scrotal cancer from oil has occurred, particularly among bar automatic machine workers; but other engineering practices also present a cancer hazard, e.g., metal rolling, tube drawing, metal hardening and machine operating. Although the major risk is from exposure to undiluted oils, emulsions have been incriminated occasionally. The industries most affected are those with automatic shops, such as nut and bolt manufacturers. Workers have also been affected after exposure during the changing of transformer oil in electrical sub-stations and during the painting or spraying of mould oil for brick- and tile-making or concrete moulding, in drop forging, rubber mixing, wire drawing, rope making and in the jute industry and from grease in metal working (Kipling, 1968).

"In France, in the valley of the river Arve in the Savoy Alps, there have occurred since 1955 at least 60 cases of cancer of the scrotum together with many cases of cancer of the skin among the bar automatic machine workers (décolleteurs). The very high frequency in the relatively small population of the valley was observed mainly among the self-employed and workers in small premises (Thony & Thony, 1970). They were in contact with undiluted cutting oils.

"Cancers of the larynx, lung and stomach have also been attributed to oil mist (Southam, 1928); and recently evidence has been produced that persons who developed cancer of the scrotum are significantly more liable to develop cancers at other sites, e.g., in the respiratory tract or upper digestive tract (Holmes et al., 1970)."

Kinnear et al. (1954, 1955) published the results of an extensive epidemiological study of skin disease in jute workers in relation to mineral oil exposure. They found a high incidence of premalignant changes on the skin of the exposed parts of the body in long-term, older workers and isolated cases of scrotal carcinoma.

Bingham & Horton (1966) estimated the latent period for skin cancer caused by mineral oil exposure to be 50–54 years (range

4–75 years). In the case of crude paraffin oil, they mentioned an average of 15–18 years (range 3–35 years). In these cases, the range may be more important than the average, though the average indicates that, in general, the latent period is very long. A considerable proportion of the cases of skin epithelioma caused by mineral oil exposure had such a long latency period that the disease only appeared after retirement from active work (Cruickshank & Gourevitch, 1952; Kinnear et al., 1955).

Five cases of squamous cell carcinoma of the hand and forearm and one of the scrotum occurred in machine operators at a plant in Ontario, Canada (Mastromatteo, 1955). These workers had been exposed, for an average of 21 years, to cutting fluids that were subsequently demonstrated to be carcinogenic in animal tests (Gilman & Vesselinovitch, 1955).

Milne (1970) traced 5 cases of carcinoma of the scrotum, as registered in the Central Cancer Registry of Victoria, Australia, and found that, in all cases, the carcinomas occurred during or after the seventh decade of life. Three of the subjects had had intensive contact with mineral oils throughout their working life, one was a stoker in a gasworks, and the fifth had always been involved in administrative work.

In the Netherlands, a recent survey demonstrated that scrotal cancer occurred only sporadically and was not correlated with occupational exposure to mineral oil (Pruyn & Reijnierse, 1972; Fokkens et al., 1972; van Raalte, 1972).

Eight cases of scrotal cancer were discovered by Avellan et al. (1967), over a period of 24 years, among 250 automatic lathe operators in Gothenburg, Sweden. Diagnosis was made when the operators were between 54 and 66 years of age and after periods of exposure to mineral oil ranging from 19 to 43 years. In the words of the authors:

"All of the cases occurred among operators who began their work during the era when the exposure, as a result of the prevailing machine construction, was considerable and before the regulations and the controls, which were instituted after the discovery of the first cases, had been set up."

Wahlberg (1974) analysed 34 cases of scrotal cancer reported to the Swedish Cancer Registry between 1958 and 1970. Seven cases (21 %) had been heavily exposed, occupationally, in the past to oil and oil mist, e.g., as automatic lathe operators. One of this group developed a primary lung cancer.

A retrospective study of 298 cases of scrotal cancer registered in the Birmingham region in the United Kingdom between 1936 and 1972 was reported by Brown et al. (1975). The incidence of scrotal cancer was 5–6 cases per million males per year, whereas for the whole of the United Kingdom, the incidence is 1–2 cases per million males per year. The patients or relatives were interviewed in 109 cases: 94 had been exposed to mineral oil (mainly tool-setters

and machine operators, and all cases had been exposed to cutting oil, 14 had been exposed to pitch or tar, and, in 7 cases, there was no apparent occupational exposure. In 298 cases of scrotal cancer, 52 other primary tumours were noted; of these, 42 arose following the scrotal cancer including 15 skin tumours and 12 bronchial tumours. The incidence of both these types of cancers was much in excess of what would be expected statistically. The majority of the group with second primary tumours were machine operators and tool-setters (75 % in the case of bronchial carcinoma). The authors postulated that in these cases both primary tumours were initiated by the same carcinogen.

After studying all the available literature, Desoille et al. (1973) concluded that, in general, and with the exception of certain extreme situations, the number of tumours caused by exposure to mineral oils was low. According to Auld (1950) and Eckhardt (1957), though certain cutting oils and other mineral oils are carcinogenic to the skin, the degree of carcinogenicity is very low compared with that of coal-tar, pitch, and shale oil. In their opinion, and that of most other authors, e.g., Avellan et al. (1967), even this level of carcinogenicity would disappear, if a minimum of industrial and personal hygiene measures were adhered to. On the other hand, Auld (1950), Desoille et al. (1973), Thony et al. (1975) and many others urge that alternative products should be developed that do not expose the workers to a tumorigenic hazard.

In a further report on the skin cancer epidemic in the French Arve Valley, Thony et al. (1975) recorded 133 epithelioma cases in 15 years, mostly of the scrotum. The incidence in these workers was 36 times that expected in the general population. In workers in small workshops with poor industrial and personal hygiene, the incidence was found to be 3 times higher than in the larger plants. The average age was 54 years (range 35–75 years) and the average exposure 30 years (range 15–50 years), at the time of clinical diagnosis. In addition, an increased incidence of bronchopulmonary tumours was found, especially in the *décolleteurs*. Officially until 1947, but in practice possibly until 1950, coaltar-derived anthracene oils were used, which originally contained benzo(*a*)pyrene levels of up to 1000 mg/kg. The level was later reduced to 10 mg/kg. These oils may be responsible for many of the previously mentioned cases, but skin cancer also occurred in some of the workers exposed only to the petroleum-derived oils that were used exclusively later on. Fresh cutting oils, as delivered to the users, contained benzo(*a*)pyrene levels ranging from 0·5 to 145 µg/litre and the concentration of carcinogens was found to increase during use, though not to the same extent as that in quenching oils (2–100 times with an average of 30 times), and in lubricating oils for internal combustion engines.

4.7.1.3 *Effects of oil mist exposure*

Southam (1928) was the first to attribute cancers of the larynx, lung, and stomach to oil mist exposure.

In a report by Huguenin et al. (1950), 32 out of 144 patients with lung cancer had been in prolonged and intense contact with oil mist in the past. Old metal-working machines with improper protection against oil mist, processes where oil vapour arose from contact with hot metal, and high-pressure cleaning of machines with oil, were found in the places where these patients had worked. Hendricks et al. (1962) considered the observations of Huguenin et al. (1950) to be of doubtful significance in view of the high incidence of this disease in non-oil-mist-exposed groups. Nevertheless, the conditions in these cases may have been such, that a causal relation should, in at least some of them, cannot altogether be excluded.

More printing industry workers were found among cases of bronchial carcinoma in a Stockholm clinic (8 out of 125) than would have been expected (Ask-Upmark, 1955). Certain industrial processes where oil mist might occur were studied by Hendricks et al. (1962), who gave an indication of possible exposures in their table of actual exposures measured in various industries (Table 7).

The average particle size in the oil mists varied according to the generating process and was found to be about 1.0–5.0 μm.

In 241 Kodak workers exposed to oil mist (Ely et al., 1970), no significant differences were found, either in mortality, respiratory symptoms, and disease, or in lung function compared with a control group.

In the same year, Holmes et al. (1970) produced evidence, that persons who developed cancer of the scrotum were significantly more liable to develop cancers of the respiratory tract and the upper digestive tract.

Similar findings have been reported in a preliminary paper by Waterhouse (1972). An excess of primary tumours at other sites (skin, respiratory and upper alimentary tracts) was found in men with scrotal epitheliomas.

From animal studies, it appears that oil mist particles larger than

TABLE 7. Exposure to oil mist in selected industries

Type of industry	Observations	Exposure range oil mist mg/m³
brass and aluminium production	5	1.4–20.7
copper mining	7	5.4–22.0
automobile manufacture	37	1.0–56.5
manufacture of steel products	33	0.8–50.0
newspaper (press room)	8	2.0–16.6
screw manufacture	6	1.0–14.2

From: Hendricks et al. (1962).

5 μm will not easily penetrate into the lungs, but will be retained mainly in the nasopharynx and upper respiratory tract. Smaller particles, especially those of 2.5 μm and less, will readily pass into the alveoli, where they will be phagocytosed and passed on to the lymph nodes. When this mechanism cannot cope with the situation, in cases of continuously repeated high exposure to oil mists, a chemical pneumonitis and chronic lipid pneumonia may develop (Proudfit et al., 1950; Foe & Bigham, 1954), but this appears to be an extremely exceptional condition. Clinical details and examples of this will be discussed in section 4.8.

In 12 out of 19 workers with oil mist exposures ranging from 9 to 18 years, Jones (1961) found a marked linear and reticular pattern in the radiograms of the lungs. Exposures ranged from 1 to 9 mg/m^3 with 70 % of the particles of the order of 1 μm.

Various groups of research workers have studied different aspects of the printing industry. Printing-ink consists chiefly of a suspension of carbon black in mineral oil or aromatic extracts of mineral oil. Modern high-speed newsprint presses can generate fairly high concentrations of ink-mist aerosol. Most particles, however, are outside the respirable range and may end up in the stomach, rather than in the lungs of exposed workers. Lippmann & Goldstein (1970) found an average droplet size of 14 μm (ranging up to 30 μm) in the press rooms of the New York Times. The time-weighted average concentration of respirable mist particles was found to be 1.4 mg/m^3 against a total time-weighted average mist concentration of 8.6 mg/m^3. In a parallel epidemiological study in the same firm, mortality and morbidity data over a 15-year period were compared for pressmen and compositors. No significant differences in respiratory mortality or morbidity were found (Goldstein & Benoit, 1970).

In a similar study by Pasternak & Ehrlich (1972), there was no increase in respiratory symptoms or decrement in respiratory performance in 778 New York pressmen compared with 1207 compositors. No significant differences in death rates, were found in those who were less than 40 years old when first employed, even if they had worked for more than 20 years. In those first employed when they were more than 40 years old and with more than 20 years of employment, there was a significantly higher death rate in pressmen compared with compositors. The reason for this finding was not clear. The mean oil mist concentration measured in the 3 workshops concerned was 3.7–5.2 mg/m^3.

Moss et al. (1972) analysed the causes of death of 3485 former full-time printing industry workers from London and Manchester, who died in the period 1952–66; Greenberg (1972) studied the death certificates of 670 male printing workers who died between 1954 and 1966. In both studies, an excess number of cancers of the lung

and bronchus were found. This excess was more marked in Manchester and greatest in machine-room men. The authors concluded that the slight excess found might or might not be due to occupation. They considered that an occupational cause was more likely in the case of the greater excess in the Manchester machine-room men.

These studies in the printing industry have been mentioned in relation to mineral oil exposure. However, the same data could be related to carbon black and even to lead exposure. Similar considerations should be kept in mind in the evaluation of the data in other occupations where many other factors might also play a role, either individually or combined with the mineral oil used, as, for instance, chromium in the metal-working industry.

In studies in 34 metal-working firms in Baden-Würtemberg (FGR), the frequency of respiratory complaints (cough, expectoration, and dyspnoea) in 443 workers exposed to oil mist for long periods was compared with that in 398 unexposed controls, matched for age. Mineral oil mist exposures from cutting oils had ranged from 40 to 150 mg/m^3 over long periods. The highest incidence of complaints was found among unexposed smokers, the lowest incidence amongst non-smoking, oil-mist-exposed workers. The authors did not find any signs of irritative effects from oil-mist exposure, but a significant protective effect against the well-known irritant effects of smoking (Drasche et al., 1974). This finding is in line with findings in experimental animals, that previous exposure to oil mist reduces the lethal effects of respiratory oxidants such as ozone and nitrogen dioxide in mice (Wagner et al., 1961). The authors stated that conclusions could not be drawn from this study in relation to the carcinogenicity of these oil mists in the respiratory tract.

During the cold processing of metal, the concentration of mineral oil mist in the air (spindle oil aerosol) fluctuated from 3 to 40 mg/m^3 (on average 10 mg/m^3). During an examination of 77 lathe operators (men and women), functional disturbances found to occur in the respiratory system, in particular after a period of service of more than 10 years, included a reduction in the active volume and the maximum ventilation of the lungs and an increase in oxygen requirement and in its coefficient of utilization (Bruskin & Demčenko, 1975).

A 30-year retrospective cancer mortality study was carried out by Decoufle (1976) on 5189 workers engaged in metal-working for at least one year. No significant differences in cancer mortality were observed, when compared with the general population. Indications of increased incidences of respiratory and digestive cancer, observed when comparison was made on an age group or exposure basis, were not statistically significant.

Decoufle (1978) published a further study on a group of 2485 male workers employed between 1938 and 1967 in jobs exposing them to various levels of cutting oil mists. Compared with the total death rate of the US male population, no significant differences were observed for 15 cancer site categories. However, a 2-fold risk of cancers of the stomach and large intestine (combined) was seen after 20 years of follow-up in the subgroup of men with 5 or more years' exposure to cutting oil mists, prior to 1938. Deaths from nonmalignant respiratory disease were significantly fewer than expected. These results suggested that occupational exposure to soluble and insoluble cutting oil mists, during various metal machining processes, did not pose a health hazard in terms of respiratory cancer and fatal nonmalignant respiratory disease, but might be associated with certain forms of gastrointestinal cancer.

To summarize, it can be concluded from the literature that oil-mist exposure can give rise to pulmonary disease, but only after prolonged exposure in workplaces with unsatisfactory hygienic conditions. If oils with a low content of polynuclear aromatic hydrocarbons are used in situations where oil mists can be generated and the TLV for oil mists is not exceeded, this problem is unlikely to arise.

4.8 Clinical Studies

Clinical studies on the effects of mineral base oils and products derived from them on the skin have been discussed together with epidemiological studies in sections 4.7.1.1 and 4.7.1.2. It was felt, that compilation of individual case-histories from the literature on this subject was superfluous. Adverse effects resulting from the surgical use of paraffin for cosmetic purposes, and those following grease-gun accidents have not been considered in this review.

Clinical studies on the effects of these products after ingestion show that the main effects are caused by aspiration, which may be a complication of ingestion, and usually occurs during subsequent spontaneous or induced vomiting. Otherwise, there is general agreement that mineral base oils, lubricating oils, and greases have a low order of toxicity, when ingested (Gerarde, 1960). At the most, some gastrointestinal symptoms, such as abdominal cramps and diarrhoea, result.

There was evidence from a clinical case study that prolonged ingestion of mineral oil over a number of years could result in oil deposition in the small intestine, abdominal lymph nodes, liver, and spleen and lungs. This produced significant structural and functional abnormalities that were considered to have contributed to the patient's death (Nochomovitz et al., 1975).

White mineral oil (pharmaceutical grade) is a base oil specification intended for oral use. It is a highly purified base oil distillate, mainly containing saturated paraffinic fractions, and it has to be free of polynuclear aromatic hydrocarbons. It is used as a laxative, in pharmaceutical formulations, and as a food-grade lubricant. From studies with radio-opaque oil, it appears possible that a small amount of mineral oil, when taken orally as a laxative just before retiring, may gain entrance into the lungs. Though this is not of any consequence if it occurs only once, a cumulative effect in the lungs might result, if it occurs repeatedly, day after day, over several years (Sante, 1949; Miller et al., 1962).

Clinical experience of the effects of inhalation of mineral oil in the lungs is in agreement with the results of animal studies (section 4.6.2.3). In man, mineral oil is rapidly phagocytosed and transferred to the regional lymph nodes. In contrast with vegetable oil and oil of animal origin, however, mineral oil cannot be metabolized and is deposited in the interstitial tissue and in the lymph nodes, where it induces a cellular reaction, with the appearance of giant cells that may result in fibrosis of more or less extensive lung areas. The resulting clinical and pathological picture depends to a large extent on whether there has been massive, acute over-exposure, with the body's defence mechanisms overwhelmed (see *(a)*), or whether long-term, low-level exposure has occurred, where the defence mechanisms can cope with the daily exposure and no disease will become apparent, until the signs and symptoms of the secondary fibrotic reaction appear (see *(b)*), (Pinkerton, 1927, 1928; Cannon, 1940; Freiman et al., 1940; Moel & Taylor, 1943).

A few typical clinical entities can be recognized:

(a) Diffuse acute mineral oil pneumonia is practically always the result of an accidental massive aspiration of mineral oil (Sante, 1949; Proudfit et al., 1950; Weissman, 1951; Foe & Bigham, 1954; Gerarde, 1960). It is, in fact, a chemical pneumonitis frequently with a superimposed secondary infection, progressing into an interstitial proliferative inflammation. Cases resulting from aspiration following accidental ingestion of products containing gasoline, kerosene, or other petroleum solvents in the same boiling-range are well-known from the clinical literature. Many cases have occurred as a result of aspiration of seawater contaminated with diesel oil by survivors of sinking ships (Weissman, 1951).

Aspiration of mineral oils in the boiling-range under discussion may have similar results. This can happen when choking occurs, while taking white medicinal oil. This acute type of mineral oil pneumonitis is not likely to occur as a result of occupational exposure to oil mist. Clinically, all signs and symptoms of an acute massive pneumonitis are present with elevated temperature and a chest X-ray typical for this condition. Oil droplets may be found

in the sputum and, histologically, the condition is characterized by intra-alveolar accumulation of oil-laden phagocytes and inflammatory cells. Acute mineral oil pneumonia is a special form of lipoid pneumonia, which presents a similar clinical picture and is the result of aspiration of vegetable or animal oil (mainly cod liver oil, but also egg-yolk and milk). Though in these cases a similar severe acute pneumonia may develop, the oil can be metabolized and disappears completely after a certain time (Sante, 1949). With oils of animal origin, such as cod liver oil, however, the reaction of the body (lungs and other internal organs) can be much more serious than with mineral oils (Young et al., 1939).

(b) Diffuse chronic mineral oil pneumonia occurs as a result of gradually developing fibrotic and proliferative changes in both lungs. It may follow years after the acute form, or without an acute beginning after a long, practically asymptomatic period as a result of repeated smaller "aspirations", such as those resulting from regular massive use of mineral-oil-based laxatives, nose-drops, or nose-sprays (Pinkerton, 1927; Bishop, 1940; Freiman et al., 1940). The apparently rare cases of mineral oil pneumonitis following prolonged occupational exposure to excessive oil mist concentrations fall into this category (Sante, 1949; Proudfit et al., 1950; Weissman, 1951; Foe & Bigham, 1954; Gerarde, 1960). Reports from the literature suggest that in some of these cases, at least, a predisposing factor was present in the form of a pre-existent or concomitant lung disease (Freiman et al., 1940; Weissman, 1951; Forbes & Markham, 1967). Increasing dyspnoea and productive cough are the most important symptoms. The chest X-ray generally shows increased perihilar opacities with signs of lung fibrosis and diffuse patchy opacities. Oil droplets or oil-laden phagocytes may be found in sputum or in tissue derived from lung biopsy (Goodwin, 1934; Bishop, 1940; Freiman et al., 1940; Rossier & Bühlmann, 1949; Sante, 1949; Proudfit et al., 1950; Borrie & Gwynne, 1973).

(c) Paraffinomas are large fibrous nodules or globules of liquid mineral oil embedded in dense hyaline fibrous tissue. They represent a separate form of the chronic mineral oil pneumonitis in which oil-laden phagocytes, destroyed by pressure, atrophy in the fibrous scar tissue formed. Paraffinomas may be found singly or in clusters around the large bronchial branches or at the site of the hilar lymph nodes. It may be difficult to differentiate a paraffinoma from a lung tumour radiologically (Brown & Biskind, 1941; Wood, 1943; Sante, 1949; Proudfit et al., 1950; Weissman, 1951; Bryan & Boitnott, 1969; Borrie & Gwynne, 1973). Aspiration biopsy may help in the differential diagnosis (Nathanson et al., 1943).

Boitnott & Margolis (1966a) have described analytical methods for the identification of the various oils in human tissues.

Mineral oil droplets may pass from the hilar nodes via the thoracic

duct into the systemic circulation (Pinkerton, 1927; Young et al., 1939; Freiman et al., 1940; Boitnott & Margolis, 1966b). As a result of this transmission, oil droplets have been found in the liver, spleen, and other organs (Pinkerton & Moragues, 1940; Rewell, 1947).

The general pattern found in young children is slightly different from that found in adults. Pinkerton (1927) described 6 cases of lipoid pneumonia in children and data on 25 cases in children have been summarized by Goodwin (1934). Seven cases have been reported by Ikeda (1935) and 27 cases by Bromer & Wolman (1939). There is general agreement that fats and oils of animal origin play a more important role than mineral oil in lipoid pneumonia in infants and young children. Furthermore, the acute massive aspiration type is more frequently seen in children than the chronic form. The main causal factors in these observations are: false passage of a gavage tube, false deglutition in bottle-feeding with the baby lying on its back – especially in cases of debilitating disease, and also aspiration following forced administration of milk or cod liver oil with or without vomiting or choking (Freiman et al., 1949).

With regard to adults, Ikeda (1937) summarized 106 cases from the literature, Graef (1939) 22 cases, Bishop (1940) 136 cases, Freiman et al. (1940) 58 cases, and Moel & Taylor (1943) 20 cases. They concluded that lipid pneumonia, especially the diffuse chronic form, occurs more frequently in adults than is generally believed. Liquid paraffin is by far the most important etiological agent in the adult. Debilitated states, dysphagia and impaired cough reflexes, because of neurological or other disorders, are important predisposing factors. The authors stress, however, that mineral oil is widely used without evident harm, even in elderly persons. Wherever there is a real indication for this type of medication, they see no reason to discontinue it. Extensive use, especially self-medicated, of liquid paraffin intranasally or via the oral route by debilitated or dysphagic patients should, however, be discouraged (Bishop, 1940; Freiman et al., 1940).

As a matter of interest, a few cases of lipoid pneumonia have been described in relation to the intratracheal administration of mineral-oil-based mixtures by opera singers, prior to every performance on the stage, in order to improve the quality of the voice (Even, 1947; Facquet & Langeard, 1947; Meyer, 1976). A similar case was described by Garvin (1939) as a result of intratracheal self-medication.

From the literature, it is apparent that with the recognition of the causal factors and the change from oil-based to water-based nose-drops, the incidence of the type of lipid pneumonia just described has drastically decreased, since the end of the forties.

The following more or less typical cases, in which there was – or might have been – a relation between occupational exposure

to oil mist and the occurrence of lipid pneumonia, were found in the literature. Proudfit et al. (1950) reported a case of chronic lipid pneumonia in a 40-year-old man who had been spraying mineral oil for 17 years; he had a typical chest X-ray. The chief complaints were cough, shortness of breath, and fatigue. Mineral oil droplets were identified in the sputum; 3 years later the condition had progressed slightly. A case of lipid pneumonia was described by Weissman (1951) in which the disease apparently developed on the basis of long-standing pulmonary fibrosis as the result of blast-spraying of machine parts with mineral oil; no mask had been used as protection against the inhalation of nebulized oil. Foe & Bigham (1954) reported the case of a 30-year-old aircraft mechanic who complained of fatigue, shortness of breath on exertion, and frequent chest colds. Lipid pneumonia was diagnosed from a lung biopsy. The mechanic had been spray-cleaning aircraft engines with a mixture of 50 % kerosene and 50 % vegetable-oil-soap.

Two cases of progressive respiratory disease, which developed in the fifth decade of life were described by Forbes & Markham (1967). Both patients had a moderate to heavy smoking history; one, in addition to this, had a family history of asthma; dyspnoea and wheezing were the major signs in each case. Both reacted well to treatment, but recurrence of signs and symptoms was related to working with cutting oils, the composition of which was not mentioned.

The epidemiological data on the possible relationship between cancer of the respiratory tract and long-term occupational exposure to oil mist has been discussed in section 4.7.1.2. There is some evidence that in cases where an unsatisfactory industrial hygiene situation coincided with the use of an oil with probable carcinogenic properties, such a causal relationship might exist. On the other hand, various extensive studies have shown that, in general, it is certainly not a major problem.

However, Wood (1943) reported a fatal case of extensive lipid pneumonia in a house-maid who had used oily nose-drops in large quantities for recurrent sinusitis over a period of 10 years. At post-mortem, an alveolar-cell carcinoma was found in the lungs. The author suggested that there might have been a causal relationship between the 2 diseases, though he assumed that this occurrence would be rare. Two cases of bronchogenic carcinoma were described by Sante (1949). In the first case, the malignant epithelial tumour was situated in an area of dense fibrotic tissue, typical of a paraffinoma. In the other case, a squamous cell carcinoma was found together with lipid pneumonia in an early stage of organization. The author felt that there might have been an etiological relationship in the first case, but considered this less likely in the second case. Both patients had taken a tablespoon of mineral oil as a laxa-

tive, just before retiring, for years. Volk (1964) studied a series of more than 100 cases of mineral oil pneumonia and noted that not one case of bronchogenic carcinoma occurred in this group. In addition, he reviewed 114 consecutive autopsies of adenocarcinoma of the lung in which he did not find any lesions that might be associated with mineral oil pneumonia.

A rapidly lethal case of multifocal alveolar cell carcinoma of the lung was reported in a 63-year-old man who had centrifuged used cutting oil for 23 years and had been exposed continuously to oil mist of this type during that period (Despierres et al., 1965). Wahlberg (1974) described one case of primary lung cancer in 7 men who developed scrotal cancer following heavy occupational exposure to oil and oil mist in, for example, automatic lathe operation. A case in which achalasia led to chronic mineral oil pneumonia was reported by Bryan & Boitnott (1969). An adenocarcinoma developed in the area of scarring resulting from the mineral oil and caused death. On the basis of a literature study and their own findings, the authors concluded that the pathogenesis might be related to the pulmonary scarring rather than directly to the mineral oil (see also Yokoo & Suckow, 1961). However, the authors also considered that there was no reason to suppose that carcinomas were more likely to arise in a scar induced by mineral oil than in a scar of a different origin (Bryan & Boitnott, 1969).

5. BITUMEN

5.1 Properties and Analytical Methods

5.1.1 Chemical and physical properties

The term bitumen is applied to solid and semi-solid residues from the distillation of suitable crude oils. This product is known as "asphalt" in the USA. In most other countries, the term asphalt is reserved for certain natural deposits and for mechanically made mixtures of bitumen and mineral matter.

Bitumen is the residue obtained by atmospheric and vacuum distillation of certain types of crude oil. It is generally a black or dark-brown material, ranging from a highly viscous liquid to a solid and brittle substance at normal ambient temperatures, depending on the proportion of light fractions removed. On heating, bitumen softens gradually and eventually becomes fluid. Grades are characterized by their "penetration" and "softening" point. According to the Petroleum Handbook (1966), bitumen can be considered as a colloidal system of highly condensed aromatic particles in an oil with ring-type molecules. From this statement, it is clear that bitumen is a very complex mixture of mainly high-boiling hydrocarbons. Its composition varies widely with the geographical source of the crude oil and the process of manufacture. For example, a mixture of 6 samples was found to contain:

(a) 32 % asphaltenes: high-relative-molecular-mass aromatic compounds and heterocyclic hydrocarbons of which some are unsaturated. They are soluble in carbon disulfide but insoluble in petroleum naphtha;

(b) 32 % resins: polymers resulting from the processing of unsaturated hydrocarbons;

(c) 14 % saturated hydrocarbons: hydrocarbons in which the carbon atoms are connected by a single bond; and

(d) 22 % aromatic hydrocarbons: hydrocarbons containing one or more benzene rings per molecule, including condensed polycyclic aromatic hydrocarbons (Simmers et al., 1959; Simmers, 1964).

While the appearance and engineering applications of bitumens and asphalts are similar to those of coal-tars and pitches, fundamental differences exist between these 2 classes of materials (Puzinauskas & Corbett, 1978). Bitumen is generally derived from crude oil by a process that does not involve cracking or thermal conversion, and coal-tars and pitches are obtained by high-temperature carbonization of bituminous coal. Chemically, coal-tar materials are mainly composed of highly condensed-ring aromatic and hetero-

cyclic hydrocarbons. Bitumens, on the other hand, contain a much higher proportion of high relative molecular mass paraffinic and naphthenic hydrocarbons and their derivatives. Under comparable heating during application and use, coal-tars generate substantially higher emissions of polynuclear aromatic hydrocarbons than bitumen. While epidemiological surveys of workers engaged in the production of coal-tar have revealed an increased incidence of lung cancer, no increases in cancer or other adverse effects have been observed in studies on workers involved in the manufacture and application of asphalt.

The benzo(*a*)pyrene content of petroleum bitumens derived from various Russian crude oils was determined by Janyševa et al. (1963). They demonstrated that the benzo(*a*)pyrene content of straight-run bitumen was considerably lower (of the order of 0.6 mg/kg) than that of bitumens derived from cracking residues (of the order of 4–272 mg/kg). Schamp & van Wassenhove (1972) reported benzo(*a*)-pyrene levels of 3–5 mg/kg in bitumens.

5.1.2 Methods of sampling and analysis

See section 2.1.2.

5.2 Sources of Environmental Pollution

5.2.1 Natural sources

Natural bitumen and asphalt deposits occur in various parts of the world, mainly as a result of mineral oil seepage from the ground. The most well-known natural asphalt deposit is the Trinidad Lake, which contains a mixture of about 39 % bitumen, 32 % mineral matter, and 29 % water and gas.

5.2.2 Man-made sources

5.2.2.1 *Production*

Total world-wide bitumen production reached 90 million tonnes in 1973. As with crude oil, this was approximately 10 times the immediate pre-war level. Bitumen production rose to 100 million tonnes in 1979 and is expected to continue to increase in the future, although at a lower rate of growth than in the past.

The following types of bitumen are produced by refining and treatment:

"Straight" bitumen

The residue of atmospheric or vacuum distillation of asphaltic-based crude oils. For special applications, very hard pitch-type bitumen residues can be obtained by distilling cracked oils.

"Blown" bitumen

Manufactured by feeding air-bubbles countercurrent through a column of hot molten straight bitumen. Oxidation reactions occur leading to dehydrogenation and polymerization of the unsaturated and aromatic components. In this process, large condensed aromatic nuclei may also formed.

"Cutback" bitumen (or more fluid bitumen grades)

Obtained by mixing bitumen with petroleum solvents or mineral oil, sometimes with coal-tar or high aromatic extracts.

Bitumen emulsion

Made by emulsifying 50–65 % of bitumen in water in the presence of 0.5–1.0 % of an emulsifier, usually soap and generally used cold for both roadmaking and industrial purposes.

5.2.2.2 *Uses*

The main use of bitumen is for paving roads. It is also used in:

(a) lining irrigation canals, water reservoirs, dams, and dykes;
(b) mastic asphalt for industrial flooring;
(c) bituminized felts for roofing;
(d) protective coatings, for walls, motor-cars, water mains;
(e) adhesives for the building industry;
(f) coal briquetting;
(g) electrical insulation; and
(h) battery-making.

5.3 Environmental Exposure Levels

Apart from walking or riding on bituminous pavements and roads, the general population will not normally come into contact with bitumen, except in the form of protective coatings and coal briquettes. On the other hand, the general population can, on occasion, be exposed to fumes from heated bitumens for short periods of time during road-building or the covering of roofs. Emissions from asphalt roads have been mentioned in the literature as a possible source of exposure for the general population, but such

exposure is considered to be as negligible. Recent evidence from the Federal Republic of Germany and the USA confirms this (Hettche, 1963).

Occupational exposure to bitumen may be much more intensive in certain professions and may range from accidental splashing with hot bitumen to repeated and prolonged contact of the skin with the more liquid bitumen grades or to exposure to fumes from heated bitumen.

5.4 Environmental Distribution and Transformation

No specific data relating to bitumens are available in relation to distribution among media, environmental transformation and degradation, interaction with physical, chemical, or biological factors, and bioconcentration. On the other hand, there is a lot of information on the microbial degradation of individual petroleum hydrocarbons (section 3.4).

5.5 Metabolism

Uptake and storage of the light fractions contained in bitumens may occur; however, no specific data exist on this subject.

Bitumens occur in a variety of commercial products. The composition of these products may vary widely depending on the geographical origin of the crude oil used and the manufacturing process applied. These facts may influence the results of metabolic studies, all of which are concerned with the exposure of experimental animals. Human data are lacking.

5.6 Effects on Experimental Animals

5.6.1 Short-term exposure

No data are available on acute toxicity, exposures related to adverse effects, interactions, and species comparisons. It is generally accepted that the acute toxicity of bitumens is low.

5.6.2 Long-term exposure

No data appear to have been published on toxic effects in

specific organs, teratogenicity, or reproduction. The data on mutagenicity are limited. On the other hand, substantial experimental work has been carried out concerning the carcinogenic effects of bitumens on skin.

Twort & Fulton (1930) examined the carcinogenic effects of various synthetic tars and their fractions on the skin of mice. The carcinogenic activity varied according to the compound used and with the temperature of pyrolysis. Results of these studies confirmed the earlier finding of Kennaway (1925), that the temperature at which the tar formed was an important factor in the production of carcinogenic substances. Cancer of the skin of mice was induced by applications of the synthetic residues obtained from heating substances such as acetylene, isoprene, a noncarcinogenic petroleum, yeast, and human skin. The yield of carcinogens decreased when carbonization had occurred at temperatures above 950 °C. The yield was greatest between 850 and 870 °C; less between 600 and 750 °C, and negligible at 500 °C. Furthermore, the authors found that the carcinogenic activity of the synthetic residues could be reduced considerably by oxidation or reduction (by various methods) or by dilution with oleic acid.

A wide range of aliphatic and simple aromatic hydrocarbons were pyrolysed by Badger (1962), who showed that polynuclear aromatic hydrocarbons were formed from simpler hydrocarbons at 700 °C via primary radicals formed by carbon-hydrogen and carbon-carbon fission (cracking) at this elevated temperature. The same process occurred to a much lesser extent at 550 °C.

According to Bogovski et al. (1963), thermal distillation of a tar to coke decreased the carcinogenic activity by the formation of irreversible condensation products from polynuclear aromatic hydrocarbons, together with other high molecular compounds. In long-term, skin-painting experiments on white mice, the authors showed that such a coking process reduced the tumour incidence from 68 % to 3.7 % in the case of shale-oil tar. As shale-oil tars have a much higher carcinogenic activity than petroleum residues (Twort & Twort, 1931), it might be expected that coking of petroleum residues would reduce the carcinogenicity of the material still further.

The carcinogenic effects of bitumen on the skin of C-57 hlack mice was studied by Simmers and co-workers (1959). In a first series of tests, they used a mixture of 6 samples from Southern Californian refineries, in which both steam- and air-blown bitumens were mixed. Painted twice weekly on the skin for a lifetime, the mixture caused 12 dermoid carcinomas in 68 animals, compared with none in the untreated control group. Formation of cancer was preceded by hair loss, dryness and scaling of the skin, and papilloma formation. After subcutaneous injection, 8 sarcomas occurred in 62 animals at the site of injection compared with none in the

control group. However, the relevance of results from such subcutaneous studies is questionable.

In an inhalation study on the same pooled sample and using the same strain of mice, the animals inhaled an aerosol of bitumen droplets suspended in moist air for 30 min/day, 5 days per week, for up to nearly 17 months (Simmers, 1964). Changes found on microscopic examination were minimal and included occasional congestion, acute bronchitis, pneumonitis, bronchial dilatation, and some peribronchial round-cell infiltration. In a second inhalation study, the animals were exposed to cooled smoke from bitumen at 120 °C for 6–7 ½ h/day, 5 days a week, for up to 21 months. In this study, peribronchial round-cell infiltration, bronchitis, pneumonitis, abscess formation, loss of cilia, epithelial atrophy, and necrosis were more common. Squamous cell metaplasia was rare, but hyperplasia was more commonly seen. The changes in both experiments were patchy, rather non-specific, and similar to those described as a result of exposure to other air pollutants.

In his next series of tests, Simmers (1965a) compared the carcinogenicity of straightrun and air-blown bitumen in prolonged regular skin application tests and after single or repeated subcutaneous injection. Undiluted air-blown bitumen did not induce tumours, when applied to the skin, probably because the bitumen was too hard; when dissolved in toluene the incidence of skin cancers increased to 45 %. This may be the result of better contact with, or penetration into the skin. On the other hand, the polynuclear aromatic hydrocarbons might be concentrated by the solvent. In a similar skin-painting study with straight-run bitumen, skin cancers occurred in only 14 %. The same trend was apparent after subcutaneous injection, where 0 and 13 % tumours were found at the site of injection with straight-run and air-blown bitumen, respectively. The author presumed that this difference in response resulted from a difference in chemical composition. Although the aromatic fraction of air-blown bitumen was lower than that of straight-run bitumen, it contained more complex aromatic hydrocarbons due to polymerization and condensation caused by the air-blowing.

Straight-run bitumen was separated into 4 fractions, which were painted 3 times a week, continuously, on the skin of the same strain of mice (Simmers 1965b). The fraction containing most of the saturated compounds and aromatic hydrocarbons – which also showed practically all the UV light fluorescence – induced considerably more skin tumours (43.3 %) than straight-run and air-blown bitumens had done in earlier studies. The author pointed out that, though fluorescence was not a guarantee of carcinogenic activity, polynuclear aromatic hydrocarbons known to be carcinogenic are fluorescent. In this context, both Kennaway & Heiger (1930) and Berenblum et al. (1947) suggested that these compounds

– even in very small quantities – might be discovered by this method. The 4 bitumen fractions used in the previous study were injected subcutaneously – once or repeatedly – in the same strain of mice, at various doses (Simmers, 1966). A variety of benign and malignant tumours resulted, both at the injection site and in distant organs. The dose seemed to be more important for tumour formation than the duration of exposure.

Hueper & Payne (1960) compared the carcinogenicity of various petroleum products and coal-tar in long-term tests on mice, rats, and guineapigs. Four road-bitumens of different geographical and manufacturing origin were applied to the skin of, or injected intramuscularly into, mice and rats. In some of the test-animals, tumours were found at the site of application. Fumes from heated coal-tar and from a blown bitumen used as a roofing bitumen did not induce cancers of the lungs in rats and guineapigs in inhalation experiments lasting up to 2 years. However, the general typical reactions found in lung-tissue were the same as those described by Simmers (1964). Condensates of the coal-tar fumes were highly carcinogenic when applied to the skin and intramuscularly in mice; condensates of the blown bitumens fumes were non-carcinogenic to the skin of mice and rabbits in similar tests.

Petroleum residues derived from cracking were painted 3 times a week for a lifetime on the skin of albino mice. Depending on the cracking process, the residues exhibited various degrees of carcinogenic activity, but none were as active as a higher temperature generated coal-tar. Only those fractions distilled from the tar above 370 °C showed carcinogenic activity. Blending with a noncarcinogenic oil increased the carcinogenic activity of one bitumen, possibly because of better skin penetration (Smith et al., 1951).

Kireeva (1968) painted groups of white SS-57 mice, once a week throughout the life span, with 40 % solutions in benzene of various bitumens derived from Ukrainian crudes and coal-tar pitch. The control-group was painted with benzene only. With coal-tar pitch, skin tumours appeared in 88.4 % of the animals; with bitumens prepared from cracking residues, they occurred in 9.5–18.4 %, and with straight-run bitumens, depending on its origin, in only 0.0–4.6 % of the animals.

Benzene solutions of 8 bitumens of different geographical origin and 2 coal-tar pitches were applied twice weekly to the skin of Swiss albino mice throughout their lifetime. Benzene alone was applied to control animals (Wallcave et al., 1971). The polynuclear aromatic hydrocarbon content of the coal-tar pitches was found to be several orders of magnitude greater than that of the bitumens examined. Only one carcinoma and 5 papillomas were observed in 218 mice treated with bitumens, whereas over 90 % of the coal-tar pitch treated animals developed such tumours. Again, it was sug-

gested that the tumour incidence depended on the polynuclear aromatic hydrocarbon content of the product tested.

Benzene solutions of the bitumen or polynuclear aromatic fractions of Athabasca tar sands were not mutagenic for *Salmonella typhimurium*. This may have been a reflection of the complex interactions occurring with such hydrocarbon mixtures (Shahin & Fournier, 1978).

To summarize, in animal studies, some bitumens have been shown to possess some carcinogenic activity, when applied to the skin, while inhalation studies with bitumen vapours have proved to be negative. The carcinogenicity of bitumens depends to a certain degree on the method of production (cracking, blowing) or mixing. "Cutback" with high aromatic oil or coal-tar facilitates skin-contact and increases the carcinogenicity of the mixture. The carcinogenic activity, however, is low in comparison with that of coal-tar. Moreover, as Siou (1972) in a literature study on bitumens concluded, it is difficult to extrapolate from these animal data to man, because the contact with bitumen, even in occupational exposures, is of a quite different order to regularly repeated skin application throughout the life span of a test animal.

5.7 Effects on Man

5.7.1 Epidemiological studies

5.7.1.1 *Occupational exposure*

Henry (1947), in his analysis of 3753 cases of skin cancer, found only one case in which bitumen might have been involved. The man had worked for 23 years as a road-worker and had been exposed to coal-tar in the earlier years.

The health and the causes of death of 96 workers who had worked in a bitumen plant since it opened, including those who had left the company was reviewed by Hoogendam (1962). Exposures ranged up to 40 years. Thirty-nine workers had been exposed for more than 20 years and at least 15 had been exposed for more than 30 years. No significant differences were found in their general health pattern and no cases of skin tumours were found. One man, who had worked for 40 years in this plant died at the age of 55 of bronchial carcinoma. It is impossible to determine whether there was a relation with his work in this case. Vital capacities and forced expiratory volume (FEV) of those still working did not differ from those of a control group.

The mortality rate of refinery workers was compared with those of other workers in a study on 15 437 employees of an oil refinery

over the 29-year period 1935–63. A comparison was also made with data from a similar group of the outside population. The incidence of lung cancer was no greater in the refinery operators than in the other groups (Baird, 1967).

Baylor & Weaver (1968) compared the health of 462 asphalt workers in 25 oil refineries with that of 379 controls. Each of the asphalt workers had been engaged in this type of work for at least 5 years with an average of 15.1 years, service. No significant differences in health were found between the 2 groups. The authors also studied the medical literature of the 20 years preceding their publication and were unable to find one single case of lung or skin cancer that could be attributed to petroleum bitumens. Furthermore, an extensive search for information on the health of workers was carried out with road construction firms (31 companies in 24 states with 11 478 man-years of asphalt working and 15 boards of health of the state highway commissions), roofing industries (3 firms with over 1100 long-term bitumen workers), and bitumen trucking firms (with over 5000 drivers). This gave no indication that bitumen constituted a health hazard or that there were cancers of the skin or lungs in these groups that could be attributed to working with bitumen. Similar indirect information was obtained from 6 large insurance companies. The authors concluded that the bitumens in current use did not present a significant health hazard and that the study indicated that the carcinogenic or other harmful properties of most commercial asphalts under the present commercial usage – if present at all – are likely to be of a very low order.

Studies conducted on behalf of the API did not reveal any occupational health hazards for a "medium-exposure group" of petroleum refinery workers. This group included asphalt workers, grease, and lubricant workers (Tabershaw/Cooper Associates Inc. 1974/75).

Hermann (1975) and Hettche (1963) drew similar conclusions to those of Baylor & Weaver (1968) in inferring that bitumens including blown grades, were biologically inactive and that vapours from hot mix plants were not carcinogenic.

5.7.1.2 *General population exposure*

Measurement of emissions of polynuclear aromatic hydrocarbons from various industrial processes, including bitumen "blowing" and the manufacture of asphalt hot-road-mixture, revealed that these industrial processes were not major sources of benzo(*a*)pyrene emissions (used as an indicator for polynuclear aromatic hydrocarbons emission) and certainly emitted less than residential and small industrial coal-burning furnaces (Von Lehmden et al., 1965).

In the literature, the possibility is mentioned that vapours

emanating from asphalt, or dust arising from it might contribute to the overall incidence of cancer of the respiratory tract (Hueper, 1961; Berge, 1969). There are not, however, any data to substantiate this assumption and, in extrapolating the results of animal testing on bitumen-vapour inhalation, the chances of such an effect occurring among the general population seem quite remote. It can be presumed that a lot of the confusion has been generated by the former use of coaltar and mixed grades for this purpose, a fact which clearly has not always been taken into consideration by those working in the field.

In the USSR, however, the use of "carcinogenic" road material (that is material containing benzo *(a)* pyrene) as the upper layer of roads is forbidden in heavily populated areas. In practice, this means that coal-tar must not be used for this purpose and that petroleum bitumen should be used instead (Gorbov & Fomenko, 1962).

5.7.1.3 *High (accidental) exposure*

Burrell (1957) found a very high incidence of oesophageal cancer in a group of Bantu confined to one location in East London (South Africa). The author related this to the long-term preparation and use of the soporific alcoholic concoction "cidiviki", which was locally fermented in drums still containing a 1/4-inch coating of "cut-back" bitumen. The author presumed that enough carcinogenic material could have leached out into the brew to have at least acted as a cocarcinogen.

The most common accidental over-exposure in handling bitumen is the occurrence of burns from hot bitumen splashes. A few cases, however, have been described, in which a skin tumour developed within 1–3 months of a burn caused by hot bitumen, coal-tar, or crude oil (Bang, 1923; Huguenin, 1925; Gunsett, 1930; Sträuli 1957). Considering the total number of such burns, only a very small proportion develop into tumours and these cases relate to combinations of such burns with fresh scar tissue and/or lesions of the mucous membranes. Tumours have been described in similar situations following heat burns by wood, welding electrodes, etc. (Gunsett, 1930; Sträuli, 1957). Such skin tumours can occur in burn scars and are often multifactorial (Emmett, 1975).

In relation to the vast amount of bitumen that has been used for many decades, the reports of tumours are extremely scarce. In fact, it can be postulated that, though, from animal testing, it is known that some bitumens are weak carcinogens, there is no evidence from normal occupational exposure to indicate that these compounds are a carcinogenic hazard to the skin or the respiratory tract. This would also indicate that the present pattern of use of bitumens would not cause any hazard, whatsoever, for the general population.

The Asphalt Institute studied emissions from the hot-mix process for the manufacture of paving asphalts (Puzinauskas & Corbett, 1975). The concentration of polynuclear aromatic hydrocarbons in the particulate emission was low at 340 mg/m^3 and the average concentration of benzo(*a*)pyrene was very low at 13 ng/m^3.

5.7.2 Clinical studies

These relate mainly to bitumen skin burns and will not be considered here. Other clinical data have been included in the description of the epidemiological data.

The skin of fair-haired persons might be more prone to react adversely to repeated prolonged exposure to UV-radiation in sunlight in combination with bitumen exposure (Smiley, 1951; Kinnear et al. 1954; Emmett, 1975).

6. EVALUATION OF HEALTH RISKS FROM EXPOSURE TO CRUDE OILS AND SELECTED PETROLEUM PRODUCTS

6.1 Crude Oils

Crude oil is normally handled in a closed system from the oil well, via storage tanks, pipelines, and shipment by tankers to the refineries. Under these conditions, health hazards to, and death of workers involved in these operationswill occur only when a serious breakdown or leakage occurs. Volatile components escaping at well heads, at pump glands, or through vents in storage tanks and ships' tanks may, under certain conditions, constitute a similar health hazard; hydrogen sulfide, if present, is the most acutely toxic component but detailed consideration is outside the scope of this review. These volatile components may also contribute to the pollution of the atmosphere in storage or pumping areas. To the general population, this is mainly a nuisance problem, because of the odour from the hydrogen sulfide and mercaptans involved. Crude oil pollution of seas and inland waterways as a result of accidents with crude oil tankers or pipelines may, at times, cause a major and sudden environmental hazard. Tank washings from tankers not using the "load-on-top" system are another source of pollution of the sea with crude oils. However, this particular aspect falls outside the scope of this review.

Atmospheric concentrations of the volatile components of crude oil were found to be lower near marine drilling rigs than land-based rigs. Differences in temperature and air movement have been shown to be the main causes.

The lower temperature of marine pipelines encourages solidification of waxy compounds of the crude oil on their inner surfaces. During their repair, the clothes and skin of workers may be contaminated by these compounds (Alekperov et al., 1974).

6.2 Petroleum Solvents

Though petroleum products are widely used, they do not generally present a health risk for the general population, as their volatility prevents them accumulating in the ambient air in concentrations high enough to cause adverse health effects. However, if improperly used in closed, poorly ventilated rooms, they may become a cause of accidental acute poisoning. Under these conditions, the lower-boiling solvents may also present a fire hazard.

Cases of accidental ingestion may occur, especially in children

Serious and even fatal lung disease may develop when aspiration in the lungs occurs. Absorption from the gut, however, is generally not a serious health hazard.

Substances with a strong odour may cause a nuisance, when present in the ambient air, even in very low concentrations. The same applies to the possible contamination of drinking-water through leakage of petroleum solvents from containers.

Health impairment due to occupational exposure to petroleum solvents occurs only infrequently in normal work practice. Repeated skin contact may result in contact irritative dermatitis and only rarely in contact allergic dermatitis. Continuous day-to-day exposure to excessive vapour concentrations (which usually occur in poorly ventilated workshops) may give rise to general non-specific symptoms of ill-health. Some solvents, however, have a specific systemic effect, e.g., benzene (bone marrow depression, leukaemogenesis) and *n*-hexane (polyneuropathies). Polyneuropathies also occur in cases of abusive use of petroleum solvents by "sniffers" and addicts.

Accidental exposure to excessive vapour concentration may cause narcosis, which can be followed very rapidly by respiratory arrest and death. Accidental over-exposure of the skin, especially if the solvent is allowed to remain in contact with the skin, may cause skin irritation, possibly leading to chemical burns.

Blood dyscrasia does not occur through exposure to petroleum solvents that do not contain benzene. The specific long-term health hazards of exposure to benzene and petroleum solvents that contain a substantial percentage of benzene will not be discussed in this document.

The high aromatic residues that are still used, occasionally, as solvents for specific purposes may pose a carcinogenic risk to the skin or on inhalation, if such contact is intensive and prolonged.

6.3 Lubricating Base Oils, Greases, and Waxes

This group of products is unlikely to present a health risk for the general population, even with gross accidental over-exposure.

Unrestricted and indiscriminate oral or nasal administration of white medicinal oil can occasionally give rise to the occurrence of lipid pneumonia, when pre-existent disease or other conditions predispose to the entry of mineral oil into the respiratory tract.

Prolonged and intensive contact of the skin with metal-working oils during occupational exposure results in a high incidence of skin disorders and relatively more cases of skin cancer have occurred in such occupations. Improvements in both industrial and personal hygiene have reduced the incidence of malignant and non-malignant

diseases of the skin. Results from animal studies indicate that substitution of the oils, formerly used, by more refined products may significantly contribute to the prevention of skin cancer caused by exposure to oil under poor standards of industrial hygiene. Because chronic lung disease following exposure to oil mist is extremely rare and an increase in the incidence of pulmonary carcinoma has only been reported under exposure conditions where skin cancer occurs, it seems reasonable to assume that these occupational diseases can be prevented by suitable preventive measures.

6.4 Bitumen

The health risks associated with bitumen appear to be minimal, because contact is unlikely. Occupational exposure is not associated with an increase in cancer of the skin or the respiratory tract. The most significant occupational hazard is burning of the skin from splashes of heated bitumen.

Certain bitumen grades, however, such as those derived from cracked oils, and those mixed with coal-tar or high aromatic extracts, may have a carcinogenic potential and, therefore, require special precautions in handling.

7. CONTROL MEASURES

7.1 General

Every effort should be made not to contaminate workers, the work place, or the general environment with petroleum products. Proper design of machinery, equipment and the workshop, enclosure of processes, adequate ventilation, provision of protective clothing and adequate facilities for personal hygiene, suitable education and supervision, and development of safe working procedures are essential basic requirements; good hygienic work practices can achieve a great deal in protecting the worker.

Care should be taken, when developing products, to ensure that levels of the most toxic components, e.g., benzene, *n*-hexane, and polynuclear aromatic hydrocarbons are known, so that proper controls can be devised for the use of the products.

Products containing such highly toxic components should, when possible, be avoided and alternatives sought, where exposure is unavoidable or is likely to occur. Products which, during use, may generate more and highly toxic contaminants should be identified and efforts made to reduce contamination. Care should be exercised when handling and using such products and consideration given to the need for renewal of products at appropriate intervals. In relation to metal-working, the danger of repeatedly "topping-up" machinery over long periods with a product, and of mixing different products in one machine, is emphasized.

Where contact is unavoidable, suitable protective equipment should be used, although this should always be used as the last resort. Where skin contact is inevitable, efforts should be made to limit or avoid not only benzene, *n*-hexane, and polynuclear aromatic hydrocarbons but also any additives that may have an adverse effect on the skin. The use of abrasives and solvents in cleansing the skin should be discouraged.

In the less developed countries, there is often a lack of awareness concerning the need for proper control measures when handling petroleum products. In these countries, the health education of employers and workers should be promoted with reference to the products. Adequate control programmes should be implemented using known techniques. Whenever necessary, these should be modified to fit the particular circumstances of the country.

In addition, proper planning is necessary to control the disposal of the many types of waste oil products so that environmental contamination is avoided. Thought must also be given to the need to control the siting of housing and amenities in relation to petroleum refineries and petrochemical plants.

7.2 Petroleum Solvents

Excessive exposures to these products should be avoided. Proper education of manufacturers and users and appropriate labelling of consumer products are important. Regular control of workroom atmospheric concentrations of petroleum solvents is indicated, especially in smaller workshops.

Petroleum solvents are, with the exception of benzene and *n*-hexane, less toxic than most other solvents and, with suitable precautions, can be safely used. For this reason, and because they are cheap, they are widely used in industry and their replacement by other solvents is unlikely in the foreseeable future.

7.3 Lubricating Base Oils, Greases, and Waxes

The only way in which members of the general population could, under normal circumstances, be over-exposed to any of this group of compounds would be in the indiscriminate use of medicinal liquid paraffin. Excessive use – especially self-administered – of this material, intranasally or via the oral route, by debilitated or dysphagic patients should be discouraged.

The main possibilities of over-exposure occur in the occupational situation. Without going into detail, the following factors should be considered with the aim of avoiding hazardous exposures:

(a) Avoid contact by technological means including: proper design of equipment, machinery, and workshop; proper design and operation of general and exhaust ventilation systems in places where oil mist generation cannot be avoided; use of base oils with the lowest content of polynuclear aromatic hydrocarbons that can practically be achieved by suitable refining processes; limiting of the concent of additives that have adverse effects on the skin; frequent changing of oil in situations where carcinogenic compounds might be generated by heat; avoidance of the reuse of used oils, without refining, for other purposes where they might cause a health hazard; education and instruction in all these safe-working procedures, and supervision of their proper execution;

(b) Use of safe-working procedures and, where required, protective clothing and proper protective equipment; availability of general hygienic facilities including wash-basins in or near the work-place, shower facilities, lockers for private clothing outside the contaminated area; regular changing and laundering of working clothes and underwear; the use of suitable emollient skin creams and in some instances barrier creams. Abrasives and solvents should not be used for cleaning the skin.

(c) Periodic medical examinations.

These precautions have been compiled and adapted from the following references: Kipling (1968); UK Medical Research Council (1968); Cruickshank (1969); Desoille et al. (1973); BRMA (undated). Manufacturer can contribute by ensuring that these precautions are observed in their own premises and by giving the proper information and guidance to the consumer (see also Eckardt, 1967).

Government actions vary from country to country depending on local legislation and practice. They may range from supervision and control of the measures taken by industry to the issue of directives or codes of practice. Cautionary notices can be issued (e.g., HMSO, 1979), which have to be displayed in the working place, as well as leaflets for the workers (e.g., HMSO, 1967). Diseases caused by mineral oil may be notifiable as occupational diseases, according to national legislation.

Consumer education on the possible hazards of the products used and their safe handling can best be done by the manufacturing industries, when possible in cooperation with relevant Government agencies.

Medical action in this field would consist of cooperating in the team supervising the industrial hygiene of the operation, in pre-placement examination and selection, and later in the periodic medical follow-up of the exposed workers.

Various other organic liquids meet requirements for lubricating oils and greases. Carboxylic esters are generally used. These synthetic lubricants, however, are not in abundant supply, are expensive, and are not likely to be widely used outside their specific field of application. Replacement products are sometimes more hazardous. For instance, cutting oils may be replaced by mixtures containing ethanolamine that give rise, under certain conditions, to the formation of nitrosamines.

When safe lubricating base oils are used there is, on the other hand, no reason from an occupational health point of view to use such alternatives, not even in places where long-term intensive skin contact and/or oil mist exposure might take place. In these cases, industrial hygiene should be improved and personal hygiene should be closely supervised, regardless of the product used, to avoid excess exposure.

7.4 Bitumen

In road-building which is the major application of bitumen, alternative materials such as plastics and resins are far too expensive for general use. Coal-tar, which was used previously, presents a

greater environmental health hazard than bitumen. Other alternatives would be concrete and bricks.

In various other applications, such as flooring, roofing, protective coatings, and adhesives, alternative materials are available, but these are not always superior in quality and/or competitive in price.

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