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Occupational Exposures in Petroleum Refining;
Crude Oil and Major Petroleum Fuels

Summary of Data Reported and Evaluation

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OCCUPATIONAL EXPOSURES IN PETROLEUM REFINING (Group 2A)

For definition of Groups, see Preamble Evaluation.

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5. Summary of Data Reported and Evaluation

5.1 Exposure data

Approximately 3000 million tonnes of petroleum fuels, solvents, lubricants, bitumens and other products are produced annually from crude oil. World-wide, the petroleum refining industry employs about 500 000 persons in more than 700 plants. Process operators and maintenance workers may be exposed to a large number of substances which occur in crude oil, process streams, intermediates, catalysts, additives and final products. Aliphatic and aromatic hydrocarbons and hydrogen sulfide have commonly been measured in the air of working environments. Less commonly, polycyclic aromatic compounds have been detected at specific process units. In general, the concentrations of benzene in modern refineries have been reported to be less than 3 mg/m^3, with higher levels in some operations. Exposure *via* the skin to high-boiling materials may also occur.

The major process streams are listed in Table 2 (see p. 44 of the monographs volume); the numbers given in square brackets below are those assigned to the streams.

5.2 Experimental data

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

Uncracked distillates and residues

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

In a series of experiments of similar design, several atmospheric and vacuum distillates were tested by repeated skin application to mice. One sample of a light straight-run naphtha [3], one sample of light paraffinic vacuum distillate

[19A], one sample of heavy paraffinic vacuum distillate [20A] and four samples of heavy naphthenic vacuum distillates [20B] produced a marked increase in the incidence of skin tumours. Two samples of straight-run kerosene [5] and one sample of hydrotreated kerosene [5A] also produced skin tumours.

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

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

Cracked distillates and residues

One sample of light catalytically cracked naphtha [22], three light catalytically cracked distillates [24] and one intermediate catalytically cracked distillate [25] were tested in mice by skin application and induced skin tumours.

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

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

Effluents

Two studies on petroleum refinery effluents were inadequate for evaluation.

5.3 Human data

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

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

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

Mortality from leukaemia was significantly elevated in two refinery cohorts; in one of these, mortality increased with duration employed and also with time since first employment. Nonsignificant excess mortality from leukaemia was reported among two additional cohorts; in one of these, the excess was significant for boiler makers and pipe fitters.

Elevated mortality from unspecified lymphatic leukaemia, unspecified myeloid leukaemia and acute monocytic leukaemia, but not other cell types, was reported in a subset of workers in the British cohort whose exposures included benzene. A significantly elevated incidence of lymphocytic leukaemia was reported in a large cohort study which included many of the refineries in the USA. Excess mortality from 'cancer of other lymphatic tissues' (multiple myeloma, polycythaemia vera and non-Hodgkin's lymphoma, excluding lymphosarcoma and reticulum-cell sarcoma), which was not significant, was reported in five refinery cohorts. One report indicated significant excess mortality from leukaemia and 'cancer of other lymphatic tissues' combined.

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

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

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

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

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

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

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

5.4 Other relevant data

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

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

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

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

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

5.5 Evaluation

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

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

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

In formulating the overall evaluation, the Working Group also took note of the following supporting evidence reported in Supplement 7: benzene and untreated and mildly treated mineral oils are *carcinogenic to humans (Group 1)*. There is *sufficient evidence* for the carcinogenicity in experimental animals of several polycyclic aromatic hydrocarbons.

(N.B.: Other agents previously evaluated in the IARC Monographs that may occur in petroleum refining are listed in Table 1 of the 'General Remarks' of the monographs volume).

Overall Evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Refinery streams

- Alkylation feed
- Atmospheric tower residue [reduced crude oil]
- *n*-Butane
- Catalytically cracked clarified oil
- Chemically neutralized kerosene
- Crude oil
- Full-range alkylate naphtha
- Full-range reformed naphtha
- Heavy catalytically cracked distillate
- Heavy catalytically cracked naphtha
- **Heavy naphthenic distillate**
- **Heavy paraffinic distillate**
- Heavy reformed naphtha
- Heavy straight-run naphtha
- Heavy thermally cracked naphtha
- Heavy vaccum distillate [heavy vacuum gas oil]
- Hydrodesulfurized heavy naphtha

- Hydrosulfurized kerosene
- Hydrosulfurized middle distillate
- Hydrotreated kerosene
- Intermediate catalytically cracked distillate
- Isomerization naphtha
- Kerosene
- Light catalytically cracked distillate
- Light catalytically cracked naphtha
- Light crude oil distillate
- Light hydrocracked naphtha
- **Light naphthenic distillate**
- **Light paraffinic distillate**
- Light reformed naphtha
- Light steam-cracked naphtha
- Light straight-run naphtha
- Light thermally cracked distillate
- Light thermally cracked naphtha
- Light vacuum distillate [light vacuum gas oil]
- Polymerization feed
- Polymerization naphtha
- Steam-cracked residue
- Straight-run kerosene
- Straight-run middle distillate
- Straight-run gas oil
- Thermally cracked residue
- Vacuum residue

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