(ii) *Canada*

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

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

(iii) *UK*

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

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.

IARC 98

(1.09–1.16), 1.27 (1.00–1.59), and 0.77 (0.64–0.91) respectively, based on 4110, 75, and 130 deaths, respectively.

Andersen *et al.* (1999) linked people aged 25–64 years from the 1970 census in four Scandinavian countries to cancer incidence registries in those countries through approximately 1990 (range 1987–1991). This study included 65 868 male painters and 2121 female painters. Data for all cancer sites were reported. For males, the SIR for all cancer was 1.06 (95% CI: 1.03–1.08; 7070 cases), and significant elevations were found for cancers of the lung (SIR, 1.22; 95% CI: 1.16–1.28; 1450 cases), pleura (SIR, 1.70; 95% CI: 1.25–2.26; 47 cases; [presumably mesothelioma]), bladder (SIR, 1.10; 95% CI: 1.01–1.20; 566 cases), pharynx (SIR, 1.31; 95% CI: 1.02–1.64; 72 cases), and rectum (SIR, 1.14; 95% CI: 1.04–1.26; 406 cases). More detail can be found in Table 2.1. Subsequent work with the Norwegian component of this study by Haldorsen *et al.* (2004) showed that indirect adjustment for smoking increased the lung cancer SIR from 1.38 to 1.52 (95% CI: 1.3–1.7, 260 cases). The Swedish component of this study partly overlaps with Brown *et al.* (2002) who also included painters from the 1960 Swedish census. It also overlaps the four country study by Skov *et al.* (1993), who reported on fewer cancer sites with shorter follow-up, and also overlaps Scandanavian record linkage studies by Malker *et al.* (1987), Carstensen *et al.* (1988, 1990), and Lynge & Thygesen (1988).

Aronson *et al.* (1999) conducted a record linkage study of 457 224 Canadian men and 242 196 Canadian women employed during 1965–1971, with follow-up for mortality from 1965–1991. Only selected positive findings were reported. A significant excess of brain cancer (SMR, 3.79; 95% CI: 1.70–8.48) was observed for male painters, based on only six deaths.

Brown *et al.* (2002) linked Swedish census data from 1960 and 1970 (for those employmed as a painter) to cancer incidence and mortality data from 1971–1989. This study focused specifically on male painters, male paint-manufacturing workers, as well as male and female pictorial artists (see section below for results). There were 42 433 male painters in the study, and although significant excesses for cancers of the lung and bladder were observed, these were very modest (lung SIR, 1.2; 95% CI: 1.1–1.3, 548 cases; bladder SIR, 1.1; 95% CI: 1.0–1.2, 344 cases). The SIR for mesothelioma was 1.6 (95% CI: 0.9–2.4, 19 cases). Incident cancer of the extrahepatic bile ducts was also increased (SIR, 1.5; 95% CI: 1.0–2.3, 22 cases), but liver cancer itself was not (SIR, 0.8; 95% CI: 0.6–1.1; 36 cases). More detail can be found in Table 2.1. The authors also studied 6662 male pictorial artists and found significantly elevated cancer incidence was found for cancers of the oral cavity (SIR, 1.5; 95% CI: 1.0–2.1, 29 cases), and of the bladder (SIR, 1.5; 95% CI: 1.2–1.9, 71 cases). Non-significant elevations were found for the incidence of cancers of the oesophagus (SIR, 1.4; 95% CI: 0.7–2.4, 11 cases), and of the liver and biliary tract (SIR, 1.4; 95% CI: 0.8–2.2, 18 cases). The incidence of lung cancer was not elevated (SIR, 1.0; 95% CI: 0.80–1.3, 69 cases). Among 2136 female pictorial artists there was a significant excess incidence of cancer of the uterus (SIR, 1.6; 95% CI: 1.10–2.3, 31 cases). [The Working Group noted that the percentage of pictorial artists who were painters was not known, although presumably a significant proportion were likely to also be painters.]

1.2 Composition of fire smoke

1.2.1 *Fire chemistry*

Smoke from fires comprises suspended liquid and solid particulate matter, gases and vapours that result from the combustion or pyrolysis of material. There is a very large number of toxic components in smoke (for reviews, see Tuve, 1985; Meyer, 1989; DiNenno *et al.*, 2002; Côté, 2003). The basic form of the overall combustion reaction of organic (carbon-containing) compounds is illustrated by the burning of methane:

$$CH_4 + 2O_2 + \text{Energy of activation} \rightarrow CO_2 + 2H_2O + \text{Heat of combustion} + \text{Light}$$

Given the appropriate ratio of fuel (wood, solvent, plastic, rubber), oxygen, and combustion temperature, the products of combustion should be only water and carbon dioxide (CO_2).

Complete combustion is approached only under carefully controlled conditions. Uncontrolled or unintentional combustion tends to be "fuel rich" and therefore incomplete. The combustion of methane (CH_4) illustrates the formation of free radicals in an 11-step chain reaction, the first two of which are:

$CH_4 \rightarrow CH_3^{\bullet} + H^{\bullet}$

$H^{\bullet} + O_2 \rightarrow OH^{\bullet} + O^{\bullet}$

The free radicals formed during combustion are very reactive and side reactions are propagated to yield hundreds of chemical products, and smoke.

Most polymers found in buildings will burn or thermally degrade to simpler monomers. Thermal degradation products include methane, ethane, ethylene, benzene, toluene, and ethylbenzene in addition to the following monomers: ethylene, vinyl chloride, acrylonitrile, tetrafluoroethylene, styrene, methyl methacrylate, ethylene glycol, terephthalic acid, phenol, formaldehyde, hexamethylenediamine, adipic acid, propene, vinyl chloride, vinyl acetate, vinylidene chloride, chloroprene, 1,3-butadiene, ethyl acrylate, ethylene oxide, methylacrylate, urea, phenol, and isoprene.

The burning of plastics typically produces voluminous amounts of soot, together with higher levels of hydrogen cyanide (HCN), hydrochloric acid (HCl) and acrolein (CH_2=CHCHO) than the burning of materials such as wood, and fossil fuels. More smoke evolves from fires involving aromatic polymers, such as polystyrene, compared to aliphatic polymers, such as polyethylene.

In addition to the chemical agents described above, particulate matter is produced under conditions of incomplete combustion. The particulate matter is an aerosol consisting of condensed phase components of the products of combustion and finely divided carbon particulates that have not undergone combustion but remain suspended in the air. Although the particles themselves are microscopic in size (0.3–1.6 μm), they

rapidly coalesce and thereby become visible. These particles are also adsorbents (similar to activated charcoal) and are an additional vehicle for the transport and inhalation of toxic combustion products. Smouldering yields a substantially higher conversion of fuel to toxic compounds than does flaming, although it occurs more slowly (Ohlemiller, 2002).

1.2.2 *Modern versus pre-modern fires*

All types of fire release toxic and carcinogenic substances, including benzene, 1,3-butadiene, and formaldehyde. The focus has generally been on substances having short-term acute effects: carbon monoxide (CO), carbon dioxide, hydrogen cyanide, nitrogen oxides (NO_x), sulfur dioxide (SO_2) and hydrogen chloride. With the increasing use of polymers in building construction and furnishings, there is concern that the burning of these new materials might release large quantities of other highly toxic substances (Austin *et al.*, 2001b).

Combustion and pyrolysis products from newer building materials and furnishings were believed to be more toxic than smoke from fires in buildings built before these materials became commonplace, and more toxic than smoke from wildland fires (Betol *et al.*, 1983; Alarie, 1985). However, many of the carcinogenic products of combustion identified are volatile organic compounds and are common to most burning materials. In a more recent study, no new or unusual non-polar volatile organic compounds (VOCs) were observed in current structural fires compared to the combustion of wood (Austin *et al.*, 2001b, 2001c). Adding polyvinyl chloride (PVC) to the fire load at simulated apartment fires was observed to significantly increase levels of polychlorinated phenols (IARC Group 2B), while polycyclic aromatic hydrocarbon (PAH) levels remained essentially unchanged (Ruokojärvi *et al.*, 2000). The increases in levels of polychlorinated biphenyls (PCBs, 0.021 to 0.031 mg/m^3), polychlorinated benzenes (0.002 to 0.010 mg/m^3) and I-TEQs [or PCDD/F] (3.5 to 5.4 ng/m^3) as products of combustion were not significant [possibly due to the small sample size]. In another study, proportionately higher levels of ethyl benzene (IARC Group 2B) were found at an electronics factory fire when compared to levels at residential and mixed occupancy fires (Austin *et al.*, 2001b).

The emission of combustion products (in mg per kg of material burned) for the same material varies greatly depending on combustion conditions such as ventilation (oxygen supply), temperature, and heating rate. Nonetheless, the relative amounts of the various non-polar VOCs found in smoke at municipal structural fires have been found to be remarkably similar from fire to fire, namely with the same 14 of 144 target compounds, dominated by benzene (IARC Group 1), toluene and naphthalene (IARC Group 2B) (Austin *et al.*, 2001b, 2001c).

1.2.3 *Carcinogens found in smoke at fires*

Table 1.1 lists the agents in Groups 1, 2A, and 2B that have been detected at fires in one or more studies, together with corresponding IARC evaluations, human and animal evidence of carcinogenicity, and for the agents in Group 1, the cancer sites in humans.

Vital status was determined for 99% of the cohort, resulting in 470 observed deaths. Significantly elevated SMRs were found for benign neoplasms (SMR, 417), cancer of the colon (SMR, 183), and cancer of the bladder (SMR, 286). Cause-specific mortality was presented by the number of years employed, calendar year of death, year of hire, and latency. Cancer mortality was significantly higher in the long-term firefighters, and risk of mortality from all malignant neoplasms tended to increase with increasing latency. Statistically significant excesses of colon and bladder cancer were observed among firefighters employed for 40 or more years.

Beaumont *et al.* (1991) calculated mortality rates for 3066 firefighters employed during 1940–1970 at the San Francisco Fire Department, USA. Vital status was ascertained through to 1982, and observed and expected rates were computed using United States death rates. About 3% of the population was lost to follow-up. Mortality was examined by duration of employment as a firefighter. The total number deceased (1186) was less than expected (risk ratio [RR] = 0.90), and there were fewer cancer deaths than expected (RR = 0.95). However, there were significant excess numbers of deaths from oesophageal cancer (12 observed, six expected). A statistically significant excess of biliary and related cancer was observed among firefighters employed for 30 or more years.

Grimes *et al.* (1991) conducted a proportionate mortality study involving all male firefighters with at least one year of service in the fire department of the City of Honolulu, USA. The observed percentage of firefighter deaths from each cause from 1969–1988 was compared statistically to the expected numbers of deaths for all males aged over 20 years in Hawaii's general population. The proportionate risk ratio (PRR) for all malignant neoplasms was 1.19 (95% CI: 0.96–1.49). Significant increases in risk of death were found for brain cancer (PRR, 3.78), prostate cancer (RR, 2.61), and cirrhosis of the liver (PRR, 2.3). [The Working Group noted that it does not appear as though PRRs were standardized by age and calendar period as is standard practice for this type of analysis.]

Heyer *et al.* (1990) examined the mortality among 2289 firefighters from Seattle, Washington, USA employed during 1945–1980. Subsequently, Demers *et al.* (1992a) examined the mortality of 4546 firefighters who were employed by the cities of Seattle and Tacoma (Washington, USA), and Portland (Oregon, USA) for at least one year during 1944–1979. Demers *et al.* (1992b) also examined the cancer incidence in 4528 firefighters from Seattle and Tacoma during 1944–1979. Mortality in these firefighters was compared to United States national mortality rates and to mortality rates of police officers from the same cities. Mortality was examined by the duration of employment as a firefighter (i.e., actually controlling fires) rather than as an inspector or a support person. This mortality was then compared to a reference group of police from the same cities. Complete follow-up was achieved for 98% of the firefighters. During 1945–1989 (the cohort was the same as Demers *et al.* [1992a] but the follow-up lasted until 1989), 1169 deaths occurred in the study population, and 1162 death certificates (99%) were collected. There was no excess risk of overall

mortality from cancer. Excesses of brain tumours (SMR, 2.1; 95% CI: 1.2–3.3) and lymphatic and haematopoietic cancers (SMR, 1.3; 95% CI: 0.9–1.8) were found. Younger firefighters (< 40 years of age) showed an excess risk of cancer (SMR, 1.45; 95% CI: 0.8–2.39), primarily due to brain cancer (SMR, 3.75; 95% CI: 1.2–8.7). The risk of lymphatic and haematopoietic cancers was greatest for men with at least 30 years of exposed employment (SMR, 2.1; 95% CI: 1.1–3.6), especially for leukaemia (SMR, 2.6; 95% CI: 1.0–5.4).

Demers *et al.* (1994) further examined the incidence of cancer in a subcohort of 2447 male firefighters who were employed for at least one year during 1945–1979 in Seattle and Tacoma, who were still alive on January 1st 1974. Incident cancer cases were ascertained through the Cancer Surveillance System of the Fred Hutchinson Cancer Research Center, a population-based tumour registry. The follow-up period was from 1974 to 1989. Cancer incidence in firefighters was compared with local rates and with the incidence among 1878 policemen from the same cities. The overall risk of cancer among firefighters was found to be similar to that of both the police (SIR, 1.0; 95% CI: 0.8–1.3) and the general male population (SIR, 1.1; 95% CI: 0.9–1.2). No excesses were observed for the most common organ sites. An elevated risk of prostate cancer was observed relative to the general population (SIR, 1.4; 95% CI: 1.1–1.7), but was less elevated compared with rates in policemen (incidence density ratio [IDR], 1.1; 95% CI: 0.7–1.8), and was not related to duration of exposure. The risk of colon cancer, although only slightly elevated relative to that of the general population (SIR, 1.1; 95% CI: 0.7–1.6) and the police (IDR, 1.3; 95% CI: 0.6–3.0), appeared to increase with duration of employment.

Giles *et al.* (1993) conducted a cancer incidence study of 2855 male firefighters employed by the fire brigade in Melbourne, Australia, during 1917–1988. All were operational personnel, who would more than likely have been called to combat fires. The follow-up period was from 1980 to 1989, and was estimated to have been 95% complete. To determine cancer incidence during the follow-up period, fire brigade employment records were linked to the Victorian Cancer Registry. SIRs were calculated by the direct method using the population of the State of Victoria as the reference group. The cohort accrued a total of 20 853 person–years, and 50 firefighters developed cancer during the period of observation. The SIR for all cancer sites and all ages combined was 1.13 (95% CI: 0.84–1.48). For firefighters under the age of 65 years, the all-site SIR was 0.84 (95% CI: 0.56–1.20); for those above 65 years of age, the all-site SIR was 2.14 (95% CI: 1.32–2.37). The only site-specific cancer that was elevated in the age group of 65 and older was colorectal cancer, with an SIR of 3.65 (95% CI: 1.13–7.94). The SIR for all other cancers in the age group 65 and above after removing colorectal cancer remained elevated, with a residual SIR of 1.83 (95% CI: 1.03–3.02).

Guidotti (1993) examined the mortality by cause of death for two cohorts totaling 3328 firefighters active during 1927–1987 in Edmonton and Calgary, Alberta, Canada. Associations were examined by cohort (before and after the 1950s) and by

years of service weighted by exposure opportunity. The study attained 96% follow-up of vital status and over 64 983 person–years of observation; 370 deaths were recorded. Excesses were observed for all malignant neoplasms (SMR, 1.3; 95% CI: 1.0–1.6), and for cancers of the lung (SMR, 1.4; 95% CI: 0.9–2.1), bladder (SMR, 3.2; 95% CI: 0.9–8.1), kidney and ureter (SMR, 4.1; 95% CI: 1.7–8.5), colon and rectum (SMR, 1.6; 95% CI: 0.9–2.7), pancreas (SMR, 1.6; 95% CI: 0.5–3.6), and leukaemia, lymphoma and myeloma (SMR, 1.3; 95% CI: 0.6–2.3). The lung cancer excess was confined to Edmonton; there was no consistent association with duration of employment, exposure opportunity, or decade of entry into the cohort (before or after the 1950s) except that the highest risk was observed among Edmonton firefighters with over 35 weighted years of service. Urinary tract cancer excess was observed mostly among firefighters entering service after 1950, and appeared to increase with the length of service and exposure opportunity, and was observed in both cities.

Aronson *et al.* (1994) conducted a retrospective cohort mortality study of all male employees of the six fire departments within metropolitan Toronto, Ontario, Canada ($n = 5995$). The study population consisted of all male firefighters who had worked for at least 6 full months in metropolitan Toronto at any time during 1950–1989. Mortality was ascertained through computerized record linkage and compared to that of the male Ontario population specific to cause, age, and calendar period during 1950–1989. The cohort accrued 114 008 person–years and the average duration of follow-up was 21 years. Mortality was examined by duration of exposure. The SMR for all malignant neoplasms was 105 (95% CI: 91–120), for brain tumours, 201 (95% CI: 110–337), and for "other" malignant neoplasms, 238 (95% CI: 145–367). Non-significant increases in risk were observed for some other sites, in particular rectum (SMR, 171), larynx (SMR, 140), and testis (SMR, 252).

Tornling *et al.* (1994) conducted a cohort mortality study of all male fire fighters employed for at least 1 year in the City of Stockholm, Sweden during 1931–1983 ($n = 1116$). The population was identified from annual employment records. Follow-up for mortality was from 1951 until 1986, and for cancer incidence from 1958 to 1986. Except for four persons who had emigrated from Sweden, follow-up was 100% complete. To assess the occupational exposure as a firefighter, an index of participation in number of fires was calculated for each individual based on the number of reports on all fires in Stockholm that had been maintained since the beginning of the twentieth century. The all-site cancer mortality in 1958–1986 was equal to the expected (SMR, 100; 95% CI: 83–119). An excess of stomach cancer incidence (SIR, 192; 95% CI: 114–304; 18 observed versus 9.37 expected) was observed. There was also a tendency for higher incidence and mortality in stomach and brain cancers with increasing number of fires. Four brain cancer cases were observed compared to 0.8 expected (SIR, 496; 95% CI: 135–1270) in the highest exposure category.

versus 'never' employed as a firefighter were 4.3 (95% CI: 0.7–30.5, four cases and three controls); for working as a firefighter ≥ 10 years, 3.0 (95% CI: 0.2–45.5, two cases and two controls); and for employment ≥ 5 years before the 'reference' date [date of diagnosis], 3.1 (95% CI: 0.4–24.4, three cases and three controls).

Bates (2007) also evaluated 70 firefighters diagnosed with cancer of the testis (SEER code 28020, cohort described above for cancer of the kidney), and found an adjusted OR of 1.54 (95% CI: 1.18–2.02).

Gaertner *et al.* (2004) reported on incident cases of bladder cancer with a histological confirmation, identified through the National Enhanced Cancer Surveillance System programme in seven Canadian provinces. The cases were adults aged 20–74, identified during 1994–1997 and interviewed 2–5 months after diagnosis. Random selections of population controls were included in the programme by frequency-matching age and gender to all cancer cases. Random digit dialling was used during the 1996 calendar year to recruit controls living in Newfoundland and Alberta, while all other provinces used a random sample from the provincial health insurance database. Native Indians and subjects in the military were excluded from the study. Mailed questionnaires with telephone follow-up, as necessary, were used to gather data regarding sociodemographics, occupational history, smoking history, dietary habits, and specific agent exposures. The response rates for the male and female bladder cancer cases were 66% and 72%, respectively, and for the controls, 59% and 65%, respectively. The overall analysis included 887 cases and 2847 controls. In the analysis of firefighters, eight male cases and 13 male controls were considered. the Standardized Occupational Classification system was used to code occupations, with up to 12 occupations coded per person. Data analysis also included demographic information provided from the interviews. An unconditional logistic regression analysis was used adjusting for age, province, race, smoking, ex-smoking, and consumption of fruit, fried food, and coffee. For the analysis of 'ever' or 'never' worked as a firefighter for more than one year, an elevated OR of 1.51 (95% CI: 0.59–3.84) was found. When stratified by duration of employment as a firefighter, the ORs were: 2.0 (95% CI: 0.43–9.49) for > 1–5 years (three cases and four controls); 0.86 (95% CI: 0.708–8.93) for > 5–15 years (one case and three controls); and 1.36 (95% CI: 0.36–5.16) for > 15 years (four cases and six controls).

Bates (2007) assessed 174 firefighters diagnosed with cancer of the bladder (SEER code 29010, cohort described above for cancer of the kidney and Table 2.6), and found an adjusted OR of 0.85 (95% CI: 0.72–1.00).

2.2.2 *Cancer of the brain*

Four studies on brain cancer in relation to firefighting were considered, all from the USA (Tables 2.4 and 2.6).

Brownson *et al.* (1990) evaluated brain cancers using the Missouri Cancer registry. Cancer cases from public and private hospitals have been collected since 1972, and reporting has been mandated since 1984. The group of cases comprised Caucasian

males diagnosed with histologically confirmed brain and other central nervous system cancers (ICD codes 191 and 192). Four controls were randomly selected and frequency-matched from all Caucasian male patients diagnosed with cancers during the same time period. Control group cancers included cancers of the lip, oral cavity and pharynx, digestive organs and peritoneum, respiratory system, skin, bones and connective tissue, genitourinary system, and leukaemia, lymphoma, multiple myeloma, and other sites. Of the initially eligible cases, occupational information was lacking in 34% of the cases, and 38% of the controls. Analysis combined industries with Unites States census code related to justice, public order and safety which included firefighters, and for occupations combining police and fire protection services. Age- and smoking-adjusted ORs were elevated and reported as 2.1 (95% CI: 0.9–4.8, ten cases and 19 controls) for the industry of justice, public order and safety, and 2.2 (95% CI: 1.0–4.7, 12 cases and 22 controls) for police and fire protection workers. This excess risk among police and fire protection workers was confined to the astrocytic cell series (OR, 2.3; 95% CI: 1.0–5.1). The OR for firefighters examined separately was 2.0 (95% CI: 0.4–9.6), with an unknown number of cases and controls.

Carozza *et al.* (2000) conducted a population-based case–control study among adults in the San Francisco Bay area during 1991–1994. Lifetime job histories were available for this study. Using the Northern California Cancer Center population, 603 incident cases of gliomas among adults aged 20 years or older were identified with histological confirmation (ICD 9380–9481). Interviews were completed with 492 cases (82%), and 476 were analysed after additional exclusions. Using random-digit dialling, controls were frequency-matched by 5-year age groups as well as by gender and race/ethnicity. There were 754 potential controls identified with 22 removed because of their residence, insufficient level of English or some relationship to the cases. Of the 732 controls meeting the eligibility criteria, 462 (63%) interviews were completed. The job history data for cases and controls were provided by proxy for 45.6% and 0.9%, respectively. For each job reported, the following information was collected: name and location of the company, description of daily work activities, starting date and duration of job including hours worked per week. Jobs were coded using Standardized Occupational Classification 1980 and Standard Industrial Codes 1987 without knowledge of the case–control status. Duration of all jobs held for at least 6 months was analysed; the most recent 10 years were excluded to allow for a hypothesized 10-year latency period between the exposure and the clinical recognition of the disease. Subjects who were not employed in the occupational category being evaluated served as the 'unexposed' referent group. Multiple logistic analyses were used adjusting for age, gender, years of education and race (caucasian, non-caucasian). Astrocytic tumours were evaluated including glioblastoma, multiforme, and astrocytoma. The adjusted OR for 'ever' versus 'never' employed as a fireman was 2.7 (95% CI: 0.3–26.1), and for being diagnosed with having an astrocytic tumour, 3.6 (95% CI: 0.4–36, three cases, 1 control).

Table 2.4. Case–control studies of the brain

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds Ratios (OR) (95% CI)	Adjustment for potential confounders	Comments
Brownson *et al.* (1990) Missouri, USA 1984–88	Brain and other central nervous system cancers (191 and 192)	312 caucasian males; histologically confirmed brain and central nervous system cancers, identified through the Missouri Cancer Registry, maintained by the Missouri Department of Health	1248 frequency-matched (4:1) sample of controls chosen from all other caucasian male patients diagnosed with cancers in the same time period, including lip/oral cavity/pharynx, digestive organs and peritoneum, respiratory, skin, bones and connective tissue, genitourinary, leukaemia, lymphoma, and multiple myeloma, and other sites. Controls randomly selected within each of six age strata. 38% of controls excluded due to missing occupational information	Hospital medical records	*Brain Cancer by Industry* Justice/public order/safety *Brain Cancer by occupation* Police and fire protection services Astrocytic cell type only Firefighters only	10 12 NR NR	2.1 (0.9–4.8) 2.2 (1.0–4.7) 2.3 (1.0–5.1) 2.0 (0.4–9.6) 1.0 = NORMAL	Adjusted for age and smoking	Limited to caucasian males due to small numbers of non-caucasians and lack of reported occupational diversity among females. 34 % of cases excluded because of missing occupational data. Analysis combined those in police and fire protection US census codes 413–427

Table 2.4 (contd)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds Ratios (OR) (95% CI)	Adjustment for potential confounders	Comments
Carozza *et al.* (2000) San Francisco Bay area including Alameda, Contra Costa, Marin, San Mateo, San Franscisco, and Santa Clara counties, USA 1991–94	Brain (Gliomas, 9380–9481)	603 cases of histologically confirmed incident cases of glioma. Age >20 years	462 controls matched by 5-year age groups, gender, and race/ethnicity, and identified by random-digit dialling	Interviews and Standard occupational and Industrial codes used	Ever employed as firefighter Astrocytic tumours	3 3	2.7 (0.3–26.1) 3.6 (0.4–36.1)	Matched on age, gender, education, and race	Only 3 cases and 1 control were firefighters. Duration of job calculated for every job held at least 6 months during subjects' lifetime also with the most recent 10 years excluded to allow for hypothesized 10-year latency period between exposure and clinical recognition of disease

1.0 = NORMAL

Table 2.4 (contd)

Reference, study location and period	Organ site (ICD code)	Characteristics of cases	Characteristics of controls	Exposure assessment	Exposure categories	No. of exposed cases	Odds Ratios (OR) (95% CI)	Adjustment for potential confounders	Comments
Krishnan *et al.* (2003) Alameda, Contra Costa, Marin, San Mateo, San Francisco and Santa Clara counties, California, USA 1991–94 and 1997–99	Glioma (938.0, 948.1)	879 incident cases identified using Northern California Cancer Center's rapid ascertainment programme; 81% response rate	864 population-based controls selected by random-digit dialling; frequency- matched by age, race, and sex; 66% response rate	Interviews and Standard occupational and industrial codes used	Ever employed	9	2.85 (0.77–10.58)	Age, race and sex	40% of case participants reported by proxy
					Longest-held job as a firefighter	6	5.88 (0.70–49.01)		Referent group for analysis included those without the given occupational group as their longest-held job, including those who were never employed
					Longest-held job as a firefighter and astrocytic cases only	5	6.31 (0.73–54.40)		
					Longest held job as firefighter non-astrocytic cases	1	9.27 (0.55–155.27)		

Krishnan *et al.* (2003) conducted a follow-up study to the one designed by Carozza *et al.* (2000). This follow-up study examined incident glioma cases diagnosed during both 1991–1994 and 1997–1999. All adults newly diagnosed with glioma during these time periods were ascertained using the Northern California Cancer Center's rapid ascertainment programme. Controls were ascertained through random-digit dialling and matched to cases by age, race, and gender. There were 1129 eligible cases with 81% ($n = 896$) completing full interviews. In-person interviews were conducted for 98%, and there were 879 cases with complete information available for analysis. Of the eligible controls, 66% ($n = 864$) completed a full interview. In the analysis of 'ever' employed as a firefighter, the OR was 2.85 (95% CI: 0.77–10.58, nine cases and three controls). Analysis by the longest-held job resulted in an OR of 5.88 (95% CI: 0.70–49.01, six male cases and one male control). In the analysis of astrocytic cases, the OR was 6.31 (95% CI: 0.73–54.4, five cases and one control), and for the non-astrocytic cases, 9.27 (95% CI: 0.55–155.27, one case and one control). [These two studies are very similar with more cases and controls available in the Krishnan report. The Krishnan report, however, did not carry out analyses by 10-year latency period, and therefore both studies may be relevant.]

Bates (2007) also evaluated brain cancers (SEER code 31010) in firefighters as described above under kidney cancer and Table 2.6. There were 71 firefighters with brain cancer. The adjusted OR was 1.35 (95% CI: 1.06–1.72).

2.2.3 *Cancers of the larynx and lung*

One case–control study of cancer of the larynx and two studies of cancer of the lung were considered by the Working Group (Tables 2.5 and 2.6).

Muscat and Wynder (1995) conducted a case–control study of cancer of the larynx in New York City, USA, recorded during 1956–1965. Caucasian men from seven hospitals newly diagnosed with histologically confirmed cancer of the larynx were interviewed. Control subjects were also caucasian men frequency-matched to the cases by hospital of diagnosis, age (within 5 years), and year of interview. Eligibility as a control also required a hospital admission for a condition unrelated to an etiology associated with tobacco exposures including cancer of the prostate, lymphomas, benign prostatic hypertrophy, and various non-malignant conditions. All subjects were interviewed by personnel who were not blinded to the case–control status of subjects, with a 90% response rate. The questionnaire included information on smoking status (never, current or ex-smoker, number of cigarettes, pipe and cigars smoked, and alcohol intake). Data were collected on lifetime occupations and self-reported exposures to chemicals, metals, exhaust, asbestos, and other occupational substances. There were 235 cases and 205 controls. The cases compared to controls were most likely to be: current cigarette smokers, (66.4% and 24.4%, respectively), heavy cigarette smokers (> 31 cigarettes/day), (55.1% and 22.8%, respectively), and drink more than 7 ounces of alcohol per day (29.4% and 11.2%, respectively). Analyses were adjusted for current smoking status.

Hansen (1990) performed a study of Danish firefighters employed at the time of the 1970 national census. An analysis was then conducted of 57 deaths (21 from cancer) during 1970–1980 occurring among 886 males who had reported employment as firefighter. Men employed in similar occupations were used as the reference group, and an excess of lung cancer among firefighters over the age of 60 was reported, based on small numbers.

Ma *et al.* (1998) conducted a further analysis of a data set collected by Burnett *et al.* (1994) with additional years of follow-up using 1984–1993 death certificate data from 24 states in the USA. A total of 6607 deaths and 1883 cancer deaths among firefighters were identified based on the occupational titles on death certificates. Race-specific cancer mortality odds ratios (MORs) were calculated with all non-cancer deaths as the reference group. Analyses were adjusted for age and year of death. Among caucasian male firefighters, significant excesses were observed for cancers of the lip, pancreas, lung, prostate, kidney, and soft-tissue sarcoma and non-Hodgkin lymphoma. Among black male firefighters, significant excesses were observed for cancers of the nasopharynx, colon, prostate, and brain.

2.3.2 *Descriptive studies with firefighter results.*

There is a large body of descriptive epidemiology carried out for the purpose of occupational cancer and mortality surveillance. The results of these studies are summarized in Table 2.8.

Berg & Howell (1975) examined the risk of colorectal cancer by occupation using death certificate data from the USA and the United Kingdom and observed an excess among firefighters. [The Working Group noted that there was an overlap between the United Kingdom data included in this study and the meta-analysis by Dubrow & Wegman, 1983].

Williams *et al.* (1977) observed excesses of oral cancer, lung cancer, bladder cancer, and non-Hodgkin lymphoma based on the small number of cancers among firefighters that were included in the Third National Cancer Survey, USA. [The Working Group noted that Williams *et al.* (1977) was included in the meta-analysis conducted by Dubrow & Wegman (1983), but was unique in that occupation was ascertained by interview.]

Dubrow & Wegman (1983) summarized the results of ten early USA and United Kingdom studies and reported the results that appeared to be most consistent between the studies. Among those studies that reported results for firefighters, large intestine cancer and multiple myeloma were significantly elevated.

Morton & Marjanovic (1984) examined the incidence of leukaemia by occupation in the Portland–Vancouver metropolitan area in North-western USA, and excesses were observed among firefighters based on very small numbers.

Mortality among a cohort of 293 958 United States military veterans was examined by occupation and industry (Blair *et al.*, 1985). Usual occupation and industry as well as smoking information was determined from questionnaires

completed in 1954 and 1957, and 107 563 deaths were recorded during 1954–1970. Excesses of rectal, bladder, and brain cancers were observed based on very small numbers.

Gallagher *et al.* (1989) conducted a study of mortality by occupation and industry using death certificate data during 1950–1984 from the Canadian province of British Columbia. There were 1202 deaths among firefighters identified based on occupational titles on death certificates. PMRs were calculated with adjustment for 5-year age and calendar period. There were 197 cancer deaths, and a small excess of overall cancer as well as a significant excess of pancreatic cancer was observed.

In the USA, Sama *et al.* (1990) examined cancer incidence among firefighters using the Massachusetts Cancer Registry records for 1982–1986. Employment as a firefighter was based on the usual occupation reported to the Registry. The analysis was restricted to 315 Caucasian male firefighters. Case–control analyses were conducted for nine different cancer types and two 'unexposed' reference populations were used: policemen and statewide males. Standardized morbidity odds ratios (SMORs) were calculated and significant excesses of malignant melanoma and bladder cancer were observed compared to the general population. Excesses of bladder cancer and non-Hodgkin lymphoma were observed when compared to policemen.

An analysis of deaths in England and Wales (1979–1980 and 1982–1990) were examined by occupation (OPCS, 1995). A total of 2968 deaths among male firefighters and 16 deaths among their female counterparts were observed based on the last occupation listed on death certificates. Only statistically significant results were reported, and excesses of oesophageal, stomach, and gall bladder cancer mortality were observed among men.

A follow-up study was conducted in the Finnish working-age population identified in the 1970 census (Pukkala, 1995). A total of 1436 male firefighters were identified during the follow-up period during 1971–1985 through linkage with the Finnish tumour registry. No statistically significant excesses were observed. The largest excess reported was for non-localized prostate cancer.

In Canada, Finkelstein (1995) examined occupations associated with lung cancer using a case–control study based on death certificates in two Ontario cities, and observed an excess among firefighters based on small numbers.

Milham (1997) conducted a study of mortality by occupation and industry using death certificate data (1950–1989) from the state of Washington, USA. A total of 2266 deaths among firefighters were identified based on the occupational titles on death certificates. PMRs were calculated and adjusted by 5-year age group and calendar period. There were 197 cancer deaths and a small excess of overall cancer was observed as well as significant excesses of melanoma and lympho- and reticulosarcoma. [The Working Group noted that there was an overlap between this and the multistate studies conducted by NIOSH, but that this had the longest follow-up period and was the earliest study of its kind in North America.]

2.4 Case reports

Individual firefighters have applied for, and sometimes received, workers' compensation for cancer. An apparent cluster of cancer among firefighters was reported in an investigation of a chemical waste dump fire by NIOSH (Hrubec *et al.*, 1992). However, the authors concluded it was not likely to have been related to firefighting. [Given the limitations of these reports and the large number of descriptive, cohort, and case–control studies with data on firefighters, the Working Group did not believe that case reports would contribute to the evaluation.]

2.5 Meta-analyses

Two meta-analyses of studies of firefighters and cancer have been conducted (Howe & Burch, 1990; LeMasters *et al.*, 2006). The most recent meta-analysis included a great majority of the studies considered by the Working Group (LeMasters *et al.*, 2006). Cancer risk was significantly elevated for ten of the 21 cancer types analysed (stomach, colon, rectum, skin, prostate, testis, brain, non-Hodgkin lymphoma, multiple myeloma, and malignant melanoma). With the exception of testicular cancer (summary RR = 2.02), the summary relative risk estimates were moderate, ranging from 1.21 for colon to 1.53 for multiple myeloma. For four of these sites (prostate, testis, non-Hodgkin lymphoma, and multiple myeloma), findings were consistent across study designs and the types of study available. However, since that analysis, two additional large studies of cancer in firefighters had been published (Ma *et al.*, 2006; Bates, 2007). Therefore, another meta-analysis was performed by the Working Group to assess the impact of these recent studies.

Inclusion criteria for studies in this meta-analysis were reported estimates of relative risk with corresponding 95% confidence intervals or information that allowed their computation by the Working Group for 'ever' versus 'never' exposure to firefighting or employment as a firefighter. For those studies that did not report for this category, the relative risks and 95% confidence intervals were estimated by the Working Group from strata-specific relative risk and corresponding number of cases, assuming a normal distribution when possible. Studies that only reported point estimates without confidence intervals were not included. Proportionate mortality studies were also excluded. Statistical heterogeneity among studies was tested with the Q statistic. Summary relative risk estimates were obtained from random-effect models for prostate cancer ($Q = 32.816$, $P = 0.005$), and fixed-effect models for testicular cancer ($Q = 3.928$, $P = 0.560$), and non-Hodgkin lymphoma ($Q = 6.469$, $P = 0.486$). All statistical analyses were performed using STATA (version 9.0; StataCorp, College Station, TX).

Based on the Working Group's meta-analysis, three of the four sites remained statistically significant. Testicular cancer was evaluated based on six studies and

IARC 100 F

CARBON TETRACHLORIDE

Data were last reviewed in IARC (1979) and the compound was classified in *IARC Monographs* Supplement 7 (1987a).

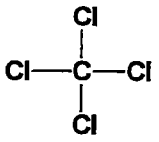
1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 56-23-5
Chem. Abstr. Name: Tetrachloromethane
IUPAC Systematic Name: Carbon tetrachloride
Synonyms: Benzinoform; carbona

1.1.2 *Structural and molecular formulae and relative molecular mass*



CCl_4 Relative molecular mass: 153.82

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Colourless, clear, nonflammable, liquid with a characteristic odour (Budavari, 1996)
(*b*) *Boiling-point*: 76.8°C (Lide, 1997)
(*c*) *Melting-point*: –23°C (Lide, 1997)
(*d*) *Solubility*: Very slightly soluble in water (0.05% by volume); miscible with benzene, chloroform, diethyl ether, carbon disulfide and ethanol (Budavari, 1996)
(*e*) *Vapour pressure*: 12 kPa at 20°C; relative vapour density (air = 1), 5.3 at the boiling-point (American Conference of Governmental Industrial Hygienists, 1991)
(*f*) *Conversion factor*: $mg/m^3 = 6.3 \times ppm$

1.2 Production and use

Production in the United States in 1991 was reported to be approximately 143 thousand tonnes (United States International Trade Commission, 1993). Information

expired air contained 0.8 μg/L. After exposure to 7230 mg/m³ for 3.5 h, the blood of the male contained a carbon tetrachloride-equivalent level of 30 μg/100 g and the expired air contained 3 μg/L.

Many early studies examining hepatotoxicity of carbon tetrachloride used corn oil as a dosing vehicle for laboratory animals, but corn oil has been found to markedly delay the absorption of carbon tetrachloride from the gastrointestinal tract (Kim *et al.*, 1990). More recent studies have used Emulphor®, a polyethoxylated oil, in concentrations up to 10% in an aqueous vehicle for carbon tetrachloride. Aqueous solutions of carbon tetrachloride in Emulphor® were administered to Sprague-Dawley rats both as a bolus and during gastric infusion at a constant rate over a 2-h period (Sanzgiri *et al.*, 1997). Uptake and tissue levels of carbon tetrachloride after gastric infusion were less than after bolus dosing. When the concentration of Emulphor® was varied up to 10%, absorption (and distribution) of carbon tetrachloride was not affected (Sanzgiri & Bruckner, 1997).

Following inhalation exposure of rats to 406 ppm [2600 mg/m³] carbon tetrachloride for 4 h, the blood level was 10.5 mg/L, but dropped to 50% of this value in less than 30 min (Frantik & Benes, 1984). Carbon tetrachloride, administered by inhalation to rats, mice or monkeys, is distributed to most tissues, including fat, liver, brain, bone marrow and kidney (McCollister *et al.*, 1951; Bergman, 1984; Paustenbach *et al.*, 1986). In mice exposed to [^{14}C]carbon tetrachloride, much of the radioactivity became non-volatile and a portion appeared to be non-extractable (Bergman, 1984).

The discrepancy between bolus oral administration of carbon tetrachloride (the route used for most toxicity and mechanistic studies) and inhalation exposure, the route most representative of human exposure, has been addressed by Sanzgiri *et al.* (1995), who studied the kinetics of carbon tetrachloride in rats at doses of (1) 100 and 1000 ppm [630 and 6300 mg/m³] by inhalation for 2 h (equivalent to a systemically administered dose of 17.5 and 179 mg/kg bw), (2) as a gavage bolus emulsion of 17.5 and 179 mg/kg bw and (3) as a gastric infusion emulsion at these dose levels over a period of 2 h. The concentration of carbon tetrachloride in arterial blood were considerably higher in the bolus-administered groups. In the groups administered 17.5 and 179 mg/kg bw, respectively, C_{max} and AUC values were approximately six- and 16-fold higher in the bolus-administered groups than the inhalation-exposed groups. C_{max} and AUC values were slightly lower following gastric infusion than after inhalation, probably due to first-pass metabolism effects. A pharmacokinetic model has been developed for carbon tetrachloride in order to study its interaction with methanol (Evans & Simmons, 1996). The metabolic rate (V_{max}) for carbon tetrachloride was 0.11 mg/h, and increased about 4.5-fold 24 h after exposure to methanol (10 000 ppm, 6 h), but < 2-fold 48 h after methanol treatment. The K_m value was 1.3 mg/L.

Known metabolites of carbon tetrachloride include chloroform, carbon monoxide, carbon dioxide, hexachloroethane and phosgene (Poyer *et al.*, 1978; Shah *et al.*, 1979; Ahr *et al.*, 1980; Kubic & Anders, 1980; Nastaincyzyk *et al.*, 1991). Metabolism of carbon tetrachloride is initiated by cytochrome P450-mediated transfer of an electron to the C–Cl

2. Studies of Cancer in Humans

2.1 Cohort studies

Several studies have examined mortality or cancer incidence among chemical workers potentially exposed to 1,2-dichloroethane. Hogstedt *et al.* (1979) performed a cohort mortality study of 175 Swedish ethylene oxide production workers followed from 1961 through 1977. The workers had been employed for at least one year and were potentially exposed to 1,2-dichloroethane, ethylene oxide (IARC, 1994), ethylene chlorohydrin and bis(2-chloroethyl) ether. The mean exposure level to 1,2-dichloroethane among the most highly exposed workers was estimated to be 100 mg/m^3 during 1941–47 but to have decreased after that due to changes in production methods. There were 37 deaths [standardized mortality ratio (SMR), 1.4] and 12 cancer deaths [SMR, 1.8]. Excesses of stomach cancer ([SMR, 5.0], based on 4 cases) and leukaemia ([SMR, 11.1], based on 3 cases) were observed. It was not possible to link the excesses to any particular chemical exposure.

Austin and Schnatter (1983a) conducted a cohort study of 6588 white male workers employed at a petrochemical plant in the United States between 1941 and 1977. The study was conducted to investigate a cluster of brain tumours that was reported earlier in the same population (Alexander *et al.*, 1980). There were 765 deaths (SMR, 0.8) and 150 cancer deaths (SMR, 0.9) observed. A greater than expected number (based on national rates) of brain cancers (SMR, 1.6; 95% confidence interval (CI), 0.8–2.8, based on 12 cases) was observed. Austin and Schnatter (1983b) also conducted a nested case–control study to examine the relationship between the risk of primary brain tumours and exposures at the facility. No significant association with 1,2-dichloroethane exposure was observed.

Sweeney *et al.* (1986) studied mortality among 2510 male chemical workers in the United States, followed from 1952 to 1977. Potential exposures included tetraethyl lead (IARC, 1987b), ethylene dibromide (see this volume), 1,2-dichloroethane, inorganic lead (IARC, 1987b) and vinyl chloride monomer (IARC, 1987c). There were 156 deaths (SMR, 0.7) and 38 cancer deaths (SMR, 1.0) observed. There were excesses of cancer of the larynx (SMR, 3.6; 90% CI, 0.7–11.5, based on 2 cases) and brain (SMR, 2.1; 90% CI, 0.7–4.9, based on 4 cases). The SMR for all lymphatic and haematopoietic cancers was 0.9 (90% CI, 0.3–1.9, based on 4 cases). Levels of exposure were not reported, but a NIOSH survey in 1980 found levels of exposure to 1,2-dichloroethane to be below the recommended NIOSH standard, while lead exposures were elevated. It was not possible to link mortality to any particular chemical exposure.

Benson and Teta (1993) studied the mortality among 278 chlorohydrin production workers who had ever been employed at a facility in the United States between 1940 and 1967. The follow-up period was from 1940 to 1988. This was a 10-year update of an earlier study conducted by Greenberg *et al.* (1990). There were 147 deaths (SMR, 1.0) and 40 cancer deaths (SMR, 1.3) observed. Excesses of pancreatic cancer (SMR, 4.9; 95% CI, 1.6–11.4; 8 cases) and lymphatic and haematopoietic cancers (SMR, 2.9; 95% CI, 1.3–5.8;

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

Case reports of reported acute toxic effects following inhalation exposure to 1,2-dichloroethane in the workplace indicate that 1,2-dichloroethane is readily absorbed by humans (Nouchi *et al.*, 1984).

The analysis of several tissues of humans who died following acute oral poisoning with 1,2-dichloroethane showed that 1,2-dichloroethane is widely distributed throughout the human body. Concentrations ranged from 1 to 50 mg/kg in the spleen and 100 to 1000 mg/kg in the stomach; levels in the liver and kidney were approximately 10 times lower than those in the stomach (Luznikov *et al.*, 1985).

Cytochrome P450 IIE1 is a major catalyst in the oxidation of 1,2-dichloroethane in human liver microsomes (Guengerich *et al.*, 1991).

4.1.2 *Experimental animals*

In rats, absorption following ingestion of 1,2-dichloroethane is rapid and complete (Reitz *et al.*, 1982). The pharmacokinetics following oral administration of 1,2-dichloroethane are dose-dependent over the range 25–150 mg/kg bw. The plasma elimination $t_{½}$ increases from 25 min to 57 min, while the area under the curve (AUC) increases 16-fold with a six-fold increase in dose. However, C_{max} is proportional to dose up to oral doses of 150 mg/kg bw (Spreafico *et al.*, 1980). There was no significant difference in kinetic parameters following single and repeated daily administrations of 50 mg/kg bw for 10 days. Gastrointestinal absorption in rats was more rapid and efficient following administration in water, compared with corn oil (Withey *et al.*, 1983).

Absorption following inhalation by experimental animals was also rapid. In rats, levels of 1,2-dichloroethane in the blood peaked (8–10 µg/mL) within 1–2 h of continuous inhalation of 600 mg/m^3 for 6 h (Reitz *et al.*, 1982).

1,2-Dichloroethane is also rapidly absorbed through the skin in mice, rats and guinea-pigs (Tsuruta, 1975, 1977). It was rapidly absorbed when applied in aqueous solution to the skin of rats *in vivo*, giving blood levels directly related to the concentration of the solution (Jakobson *et al.*, 1982; Morgan *et al.*, 1991). 1,2-Dichloroethane is widely distributed throughout the body in rats exposed via inhalation or ingestion. After inhalation, the highest concentrations were usually found in adipose tissue, although 1,2-dichloroethane was also detected in blood, liver, kidney, brain and spleen (Spreafico *et al.*, 1980).

Reitz *et al.* (1982) reported that the relative distribution of radioactivity at 48 h (assumed to be primarily in the form of metabolites) was similar in rats given ^{14}C-labelled 1,2-dichloroethane orally (single dose of 150 mg/kg bw) or by inhalation (600 mg/m^3 for 6 h). Residual radioactivity in selected tissues was 1.5–2.0 times higher after oral exposure than following inhalation. There was also a higher residual activity in the fore-

have relatively low statistical power. However, the apparent discrepancy between the results of the case–control as compared with the cohort studies might also reflect residual confounding by wood dust in the former. Almost all of the formaldehyde-exposed cases in the case–control studies were also exposed to wood dust, which resulted in a high relative risk, particularly for adenocarcinomas.]

2.4 Other cancers

Several studies have identified statistically significant positive associations between exposure to formaldehyde and cancer at other sites, including the oral cavity, oro-and hypopharynx, larynx, lung, brain, pancreas, Hodgkin lymphoma, and multiple myeloma. However, the results are inconsistent (see Tables 2.4 and 2.5 online; Table 2.6 available at http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-24-Table2.6.pdf, and Table 2.7 available at http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-24-Table2.7.pdf).

2.5 Synthesis

The Working Group noted one industrial cohort study with both a strong overall association between exposure to formaldehyde and nasopharyngeal cancer, and the most elevated risks in the highest exposure category. Positive associations were also observed in many of the case–control studies, in particular those of larger size and higher-quality exposure assessment. While there was no association observed in the two other large industrial cohort studies, the expected number of cases in those studies was quite small. It is concluded that occupational exposure to formaldehyde causes nasopharyngeal cancer in humans. The Working Group noted that it was unlikely that confounding or bias could explain the observed association.

Elevated risks of leukaemia have been consistently observed in proportionate mortality studies of professionals exposed to formaldehyde (i.e. embalmers, workers in the funeral industry, pathologists and anatomists). Results from a nested case–control study of workers in the funeral industry show elevated risks for many measures of exposure, which are strongest for myeloid leukaemia. In two of the three large industrial cohort studies positive associations were observed for leukaemia, which were somewhat stronger for myeloid leukaemia. It is difficult to reconcile the lack of association observed in the third industrial cohort study with the overall positive associations in the others. However, there seems to be no strong evidence that confounding or bias explains the positive associations seen in multiple settings. On balance, the Working Group concluded that the epidemiologic evidence shows that occupational exposure to formaldehyde causes leukaemia.

Many case–control studies show positive associations for exposure to formaldehyde and sinonasal cancer, some with evidence of an exposure–response pattern. However, many of these cases were also exposed to wood dust, which was strongly associated with sinonasal cancer in these studies. The industrial cohort studies show no such association, which may be due to lack of statistical power, or could indicate that uncontrolled confounding to wood dust partially explains the observed associations in the case–control studies. The Working Group could not rule out the possibility of residual confounding in the case–control studies and noted the discordant results between the cohort and case–control studies.

International Agency for Research on Cancer – *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*; Volume 98 – Painting, Firefighting, and Shiftwork

Composition of Fire Smoke:

Smoke from fires comprises suspended liquid and solid particulate matter, gases, and vapors that result from the combustion or pyrolysis of material.

- **ALL** types of fire release toxic and carcinogenic substances.

Overall Evaluation: The agent is described according to the wording of one of the following categories, and the designated group is given. This categorization of an agent is a matter of scientific judgment that reflects the strength of evidence derived from studies in humans and in experimental animals and from mechanistic and other relevant data.

Group 1	Carcinogenic to humans
Group 2A	Probably carcinogenic to humans
Group 2B	Possibly carcinogenic to humans
Group 3	Not classifiable as to its carcinogenicity to humans
Group 4	Probably not carcinogenic to humans

Carcinogens Found in Smoke at Fires	
Chemicals measured in fires	Classification
1,3-Butadiene	1
2,3,7,8-tetrachloro dibenzo-*para*-dioxin	1
Arsenic	1
Asbestos	1
Benzene	1
Benzo[*a*]pyrene	1
Cadmium	1
Formaldehyde	1
Polychlorinated biphenyls	1
Radioactivity (γ activity)	1
Radionuclides (α-particle-emitting)	1
Radionuclides (β-particle-emitting)	1
Silica (crystalline)	1
Trichloroethylene	1
Dibenz[*a*,*h*]anthracene	2A
Dichloromethane (methylene chloride)	2A
Lead compounds, inorganic	2A
Tetrachloroethylene (perchloroethylene)	2A
Acetaldehyde	2B

Carcinogens Found in Smoke at Fires	
Chemicals measured in fires	Classification
2-Nitroanisole	2B
Benz[*a*]anthracene	2B
Benzo[*b*]fluoranthene	2B
Benzo[*k*]fluoranthene	2B
Benzofuran	2B
Carbon black	2B
Chrysene	2B
Ethylbenzene	2B
Furan	2B
Indeno-1,2,3-[*cd*]pyrene	2B
Isoprene	2B
Lead	2B
Naphthalene	2B
Polychlorophenols	2B
Styrene	2B
Toluene diisocyanates	2B
Trichloromethane (chloroform)	2B
Lead compounds, organic	3
Silica (amorphous)	3
Triphenylene	3

Several studies have been conducted with the purpose of identifying the chemicals and known carcinogens found **during the overhaul phase of a structure fire.**

- *Characterization of Firefighter Exposures During Fire Overhaul* (Phoenix FD and the University of Arizona Prevention Center and Arizona State University).
- *A Study on Chemicals found in the Overhaul Phase of Structure Fires using Advanced Portable Air Monitoring available for Chemical Speciation* (Tualatin Valley Fire & Rescue – Oregon)

Chemicals measured in overhaul environment	IARC Classification
1,3 Butadiene	1
Arsenic	1
Asbestos	1
Benzene	1
Benzo(a)pyrene	1
Coal Tar Pitch	1
Diesel Exhaust	1
Formaldehyde	1
Vinyl Chloride	1
Dibenz(a,h)anthracene	2A
N-Nitrodimethylamine	2A
1,2 Dichloroethane	2B
Acetaldehyde	2B
Benz(a) anthracene	2B
Benzo(b)fluoranthene	2B
Benzo(k)fluoranthene	2B
Benzofuran	2B
Ethyl benzene	2B
Furan	2B
Indeno(1,2,3-cd)pyrene	2B
Lead	2B
Napthalene	2B
Styrene	2B
Mercury	3
Hydrochloric Acid	3
Toluene	3
Acrolein	3
Furfural	3
Acenaphthene	3
Anthracene	3
Benzo(ghi)perylene	3
Fluoranthene	3
Fluorene	3
Phenanthrene	3
Pyrene	3

Diesel Engine Exhaust:

On June 12, 2012, the International Agency for Research on Cancer (IARC), part of the World Health Organization and the authority on cancer, classified diesel engine exhaust as a Group 1 Carcinogen, meaning that it causes cancer in humans.

Diesel engine exhaust in fire stations has been and continues to be a serious health problem for firefighters. This exhaust is generated whenever a fire apparatus leaves or returns to the station. If not properly captured and removed, it will remain in the apparatus bay as well as enter the firefighters' living quarters. As a result, firefighters can be exposed to diesel engine exhaust for a considerable portion of their shift.

Diesel exhaust contains multiple cancer-causing chemicals such as (Source IARC Monograph 105):

Metals	IARC Classification
Antimony Compounds	2B
Arsenic and inorganic arsenic compounds	1
Beryllium and beryllium compounds	1
Cadmium and cadmium compounds	1
Chromium (VI)	1
Cobalt and cobalt compounds	2B
Lead compounds (inorganic/organic0	2A/3
Nickel (metallic/compounds)	2B/1
Organic Chemicals	IARC Classification
1,3-Butadiene	1
Acetaldehyde	2B
Benzene	1
Bis(ethylhexyl)phthalate	2B
Ethylbenzene	2B
Formaldehyde	1
Propylene oxide	2B
Halogenated and other chemicals	IARC Classification
Dioxin/dibenzofurans	1
Polycyclic aromatic hydrocarbons	IARC Classification
Benz(a) anthracene	2B
Benzo(b)fluoranthene	2B
Benzo(k)fluoranthene	2B
Benzo(a)pyrene	1
Chrysene	2B
Dibenz(a,h)anthracene	2A
3,7-Dinitrofluoranthene	2B
3,9-Dinitrofluoranthene	2B
1,3-Dinitropyrene	2B
1,6-Dinitropyrene	2B
1,8-Dinitropyrene	2B
Indeno(1,2,3-*cd*)pyrene	2B
Napthalene	2B
3-Nitrobenzanthrone	2B
6-Nitrochrysene	2A
2-Nitrofluorene	2B
1-Nitropyrene	2A
4-Nitropyrene	2B
Styrene	2B

Soot:

Soot is a byproduct of the incomplete burning of organic (carbon-containing) materials, such as wood, fuel oil, plastics, and household refuse.

Soot particles absorb many hazardous chemical vapors that are released during fires, holding them in place on surfaces including firefighter's personal protective equipment (PPE), clothing and skin.

As firefighters work, their body temperature rises and they begin to sweat. Skin becomes more permeable and soot particles are more easily absorbed into the body.

- For every 5°increase in skin temperature, absorption increases by 400%.

The International Agency for Research on Cancer, part of the World Health Organization, lists soot in the Group 1 category meaning that the agent is ***"Carcinogenic in Humans."***

In their *13th Report on Carcinogens* which was released on October 2, 2014, the U.S. Department of Health and Human Services continues to list **soots** as a substance under the category of ***"Known To Be Human Carcinogens."***

ACRYLONITRILE (Group 2A)

A. Evidence for carcinogenicity to humans (*limited*)

In the USA, 1345 male workers potentially exposed to acrylonitrile in a textile fibre plant and observed for 20 or more years had a greater than expected incidence of lung cancer (8 observed, 4.4 expected). The risk was greater among workers with more than five years' exposure (6 observed, 2.3 expected) or with jobs where exposure was likely to have been heavier (6 observed, 2.7 expected) than among workers with shorter duration of exposure (2 observed, 1.4 expected) or low levels of exposure (2 observed, 1.4 expected)[1,2]. Further follow-up of this cohort until 1981 revealed a continued excess of lung cancer (10 observed, 7.2 expected), although during the actual follow-up period (1976-1981) there was no excess (2 observed, 2.8 expected). The updating also showed, however, a significant excess of cancer of the prostate (6 observed, 1.8 expected)[3]. In a similar study at another US textile fibre plant, an excess of prostatic cancer (5 cases observed, 1.9 expected) was observed, but there was no excess of lung cancer[4]. In the UK, a study of 1111 male workers exposed to acrylonitrile during polymerization between 1950 and 1968 and followed for ten years or more revealed five stomach cancers (1.9 expected), two colon cancers (1.1 expected), two brain cancers (0.7 expected) and nine cancers of the respiratory tract (7.6 expected)[5]. Among 327 rubber workers exposed to acrylonitrile in the USA, excesses were noted for cancers of the lung (9 observed, 5.9 expected), bladder (2 observed, 0.5 expected) and of the lymphatic and haematopoietic system (4 observed, 1.8 expected). The risk for lung cancer was greatest among workers with five to 14 years' exposure and ⩾15 years of latency (4 observed, 0.8 expected)[6]. Another study of rubber workers in the USA, however, showed no association between exposure to acrylonitrile and lung cancer[7]. In the Federal Republic of Germany, one study of 1469 workers exposed to acrylonitrile in 12 different plants showed excesses of bronchial cancer (11 observed, 5.7 expected) and of tumours of the lymphatic system (4 observed, 1.7 expected)[8].

B. Evidence for carcinogenicity to animals (*sufficient*)

Acrylonitrile was tested for carcinogenicity in rats by oral administration and by inhalation. Following its oral administration, it induced neoplasms of the brain, squamous-cell papillomas of the stomach and Zymbal-gland carcinomas; tumours of the tongue, small intestine and mammary gland were also reported[1,9,10]. Following its inhalation, neoplasms of the central nervous system, mammary gland, Zymbal gland and forestomach were observed[1,11].

C. Other relevant data

Acrylonitrile did not enhance the frequency of chromosomal aberrations in lymphocytes of exposed workers in one study[12].

In animals treated *in vivo*, acrylonitrile did not induce dominant lethal mutations, chromosomal aberrations (in bone-marrow cells or spermatogonia) or micronuclei in mice, or chromosomal aberrations in rat bone-marrow cells. It bound covalently to rat liver DNA

Acrylonitrile

From Wikipedia, the free encyclopedia

Acrylonitrile is an organic compound with the formula CH_2CHCN. It is a colorless volatile liquid, although commercial samples can be yellow due to impurities. In terms of its molecular structure, it consists of a vinyl group linked to a nitrile. It is an important monomer for the manufacture of useful plastics such as polyacrylonitrile. It is reactive and toxic at low doses.[3]

Contents

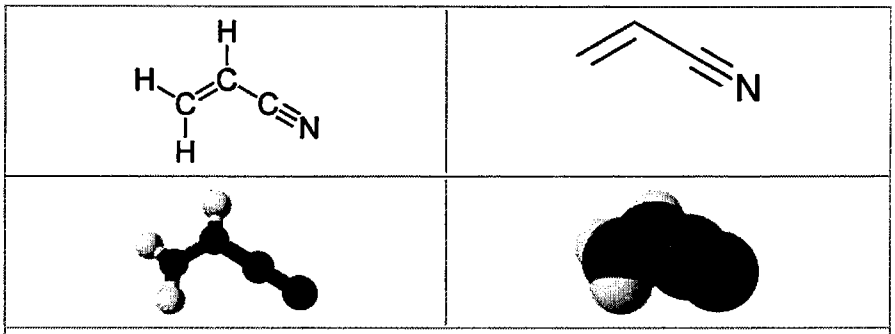
Production

Acrylonitrile is produced by catalytic ammoxidation of propylene, also known as the SOHIO process. In 2002, world production capacity was estimated at 5 million tonnes per year.[3][4] Acetonitrile and hydrogen cyanide are significant byproducts that are recovered for sale.[3] In fact, the 2008–2009 acetonitrile shortage was caused by a decrease in demand for acrylonitrile.[5]

$$2CH_3\text{-}CH{=}CH_2 + 2NH_3 + 3O_2 \rightarrow 2CH_2{=}CH\text{-}C{\equiv}N + 6H_2O$$

In the SOHIO process, propylene, ammonia, and air (oxidizer) are passed through a fluidized bed reactor containing the catalyst at 400–510 °C and 50–200 kPag. The reactants pass through the reactor only once, before being quenched in aqueous sulfuric acid. Excess propylene, carbon monoxide, carbon dioxide, and dinitrogen that do not dissolve are vented directly to the atmosphere, or are incinerated. The aqueous solution consists of acrylonitrile, acetonitrile, hydrocyanic acid, and ammonium sulfate (from excess ammonia). A recovery column removes bulk water, and acrylonitrile and acetonitrile are separated by distillation. Historically, one of the first successful catalysts was bismuth phosphomolybdate

Acrylonitrile



Names	
Preferred IUPAC name Prop-2-enenitrile	
Other names Acrylonitrile 2-Propenenitrile Cyanoethene, Vinylcyanide (VCN) Cyanoethylene[1] Propenenitrile[1]	
Identifiers	
CAS Number	107-13-1 (http://www.commonchemistry.org/ChemicalDetail.aspx?ref=107-13-1) ✓
ChEBI	CHEBI:28217 (https://www.ebi.ac.uk/chebi/searchId.do?chebiId=28217) ✓
ChEMBL	ChEMBL445612 (https://www.ebi.ac.uk/chembldb/index.php/compound/inspect/ChEMBL445612) ✓
ChemSpider	7567 (http://www.chemspider.com/Chemical-Structure.7567.html) ✓
ECHA InfoCard	100.003.152 (https://echa.europa.eu/substance-information/-/substanceinfo/100.003.152)
EC Number	608-003-00-4
Jmol 3D model	Interactive image (http://chemapps.stolaf.edu/jmol/jmol.php?model=N%23CC%3DC) Interactive image (http://chemapps.stolaf.edu/jmol/jmol.php?model=C%3DCC%23N)
KEGG	C01998 (http://www.kegg.jp/entry/C01998) ✓
PubChem	7855 (https://pubchem.ncbi.nlm.nih.gov/compound/7855)
RTECS number	AT5250000
UNII	MP1U0D42PE (http://fdasis.nlm.nih.gov/srs/srsdirect.jsp?regno=MP1U0D42PE) ✓
UN number	1093
InChI	
SMILES	
Properties	
Chemical formula	C_3H_3N
Molar mass	53.06 g·mol^{-1}
Appearance	Colourless liquid

supported on silica as a heterogeneous catalyst. Further improvements have since been made.[3]

Historical

Acrylonitrile was first synthesized by the French chemist Charles Moureu (1863–1929) in 1893.[6]

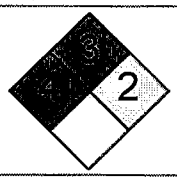
Uses

Acrylonitrile is used principally as a monomer to prepare polyacrylonitrile, a homopolymer, or several important copolymers, such as styrene-acrylonitrile (SAN), acrylonitrile butadiene styrene (ABS), acrylonitrile styrene acrylate (ASA), and other synthetic rubbers such as acrylonitrile butadiene (NBR). Dimerization of acrylonitrile affords adiponitrile, used in the synthesis of certain polyamides. Small amounts are also used as a fumigant. Acrylonitrile and derivatives, such as 2-chloro-acrylonitrile, are dienophiles in Diels-Alder reactions. Acrylonitrile is also a precursor in the industrial manufacture of acrylamide and acrylic acid.[3]

Health effects

Acrylonitrile is highly flammable and toxic at low doses. It undergoes explosive polymerization. The burning material releases fumes of hydrogen cyanide and oxides of nitrogen. It is classified as a Class 2B carcinogen (possibly carcinogenic) by the International Agency for Research on Cancer (IARC),[7] and workers exposed to high levels of airborne acrylonitrile are diagnosed more frequently with lung cancer than the rest of the population.[8] It evaporates quickly at room temperature (20 °C) to reach dangerous concentrations; skin irritation, respiratory irritation, and eye irritation are the immediate effects of this exposure.[9]

Acrylonitrile increases cancer in high dose tests in male and female rats and mice.[10]

Density	0.81 g/cm^3
Melting point	−84 °C (−119 °F; 189 K)
Boiling point	77 °C (171 °F; 350 K)
Solubility in water	70 g/L
Vapor pressure	83 mmHg[1]
Hazards	
Main hazards	flammable, reactive, toxic, potential occupational carcinogen[1]
Safety data sheet	ICSC 0092 (http://www.inchem.org/documents/icsc/icsc/eics0092.htm)
NFPA 704	
Flash point	−1 °C; 30 °F; 272 K
Autoignition temperature	471 °C (880 °F; 744 K)
Explosive limits	3–17%
Lethal dose or concentration (*LD*, *LC*):	
LC_{50} (median concentration)	500 ppm (rat, 4 hr) 313 ppm (mouse, 4 hr) 425 ppm (rat, 4 hr)[2]
LC_{Lo} (lowest published)	260 ppm (rabbit, 4 hr) 575 ppm (guinea pig, 4 hr) 636 ppm (rat, 4 hr) 452 ppm (human, 1 hr)[2]
US health exposure limits (NIOSH):	
PEL (Permissible)	TWA 2 ppm C 10 ppm [15-minute] [skin][1]
REL (Recommended)	Ca TWA 1 ppm C 10 ppm [15-minute] [skin][1]
IDLH (Immediate danger)	85 ppm[1]
Related compounds	
Related compounds	acrylic acid, acrolein
Except where otherwise noted, data are given for materials in their standard state (at 25 °C [77 °F], 100 kPa).	
✓ verify (what is ✓✗ ?) Infobox references	

Pathways of exposure for humans include emissions, auto exhaust, and cigarette smoke that can expose the human subject directly if they inhale or smoke. Routes of exposure include inhalation, oral, and to a certain extent dermal uptake (tested with volunteer humans and in rat studies).[11] Repeated exposure causes skin sensitization and may cause central nervous system and liver damage.[9]

There are two main excretion processes of acrylonitrile. The primary method is excretion in urine when acrylonitrile is metabolized by being directly conjugated to glutathione. The other method is when acrylonitrile is metabolized with 2-cyanoethylene oxide to produce cyanide end products that ultimately forms thiocyanate, which is excreted via urine, or carbon dioxide and eliminated through the lungs.[11] Metabolites can be detected in the blood and urine.[7]

Acrylonitrile induces apoptosis in human umbilical cord mesenchymal stem cells [12]

Environmental effects

Acrylonitrile is harmful to aquatic life.[9]

References

1. "NIOSH Pocket Guide to Chemical Hazards #0014". National Institute for Occupational Safety and Health (NIOSH).
2. "Acrylonitrile". *Immediately Dangerous to Life and Health*. National Institute for Occupational Safety and Health (NIOSH).
3. James F. Brazdil (2005), "Acrylonitrile", *Ullmann's Encyclopedia of Industrial Chemistry*, Weinheim: Wiley-VCH, doi:10.1002/14356007.a01_177.pub3
4. "The Sohio Acrylonitrile Process". American Chemical Society National Historic Chemical Landmarks. Retrieved 2013-05-13.
5. A. Tullo. "A Solvent Dries Up". *Chemical & Engineering News*. **86**: 27. doi:10.1021/cen-v086n047.p027.
6. See:
   - C. Moureu (1893) "Contribution à l'étude de l'acide acrylique et de ses dérivés" (http://babel.hathitrust.org/cgi/pt?id=uc1.31822017842394;view=1up;seq=149) (Contribution to the study of acrylic acid and of its derivatives), *Annales de chimie et de physique*, 7th series, **2** : 145-212 ; see especially pp. 187-189 ("Nitrile acrylique ou cyanure de vinyle (Propène-nitrile)").
   - Moureu (1893) "Nitrile acrylique, cyanure de vinyle (propène-nitrile)," (http://gallica.bnf.fr/ark:/12148/bpt6k282008w/f436.image.r=BulletindelaSocieteChimiquedeParis.langFR) *Bulletin de la Société chimique de France*, 3rd series, **9** : 424-427.
7. "Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide" (http://monographs.iarc.fr/ENG/Monographs/vol71/index.php). IARC Monographs, Volume 71 (1999)
8. Acrylonitrile Fact Sheet (CAS No. 107-13-1) (http://www.epa.gov/chemfact/acry-fs.txt). epa.gov
9. "CDC - ACRYLONITRILE - International Chemical Safety Cards - NIOSH". *www.cdc.gov*. Retrieved 2015-07-31.
10. "Acrylonitrile: Carcinogenic Potency Database" (http://potency.berkeley.edu/chempages/ACRYLONITRILE.html). *berkeley.edu*.
11. Acrylonitrile Fact Sheet: Support Document (CAS No. 107-13-1) (http://www.epa.gov/chemfact/acry-sd.txt). epa.gov
12. Sun X (Jan 2014). "Cytotoxic effects of acrylonitrile on human umbilical cord mesenchymal stem cells in vitro.". *J Mol Med Rep*. **9** (1): 97–102. doi:10.3892/mmr.2013.1802. PMID 24248151.

External links

- National Pollutant Inventory – Acrylonitrile (http://www.npi.gov.au/database/substance-info/profiles/7.html)
- Comparing Possible Cancer Hazards from Human Exposures to Rodent Carcinogens (http://potency.berkeley.edu/MOE.html)
- Acrylonitrile – Integrated Risk Information System (http://www.epa.gov/iris/subst/0206.htm), U.S. Environmental Protection Agency
- CDC – NIOSH Pocket Guide to Chemical Hazards – Acrylonitrile (http://www.cdc.gov/niosh/npg/npgd0014.html)
- OSHA Table Z-1 for Air Contaminants (https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=9992)

Categories: Alkenes | Fumigants | Hazardous air pollutants | IARC Group 2B carcinogens | Monomers | Nitriles | Commodity chemicals

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