Overview of Firefighter

"Occupational Hodgkin Lymphoma Cancer"

This packet is designed to aide a treating physician in making an educated diagnosis of a Firefighter Occupational Cancer. The following studies and documents below support the claim through research and science that this specific cancer is tied to the occupation of firefighter.

Included are multiple studies and conclusions, along with NIOSH and International Agency on the Research of Cancer (IARC). Also included is Chapter 607 of the Texas Local Government Code, which states the requirements of attaining a presumption for firefighters in Texas who develop cancer. Of specific note are the following points.

1. Supplement 7- Pages 211, 213 and 214 links Formaldehyde as a cause of Hodgkin Lymphoma.
2. IARC 98- Page 399, 400, along with the IARC Chemicals lists which points out the components of smoke. These state that Benzene and Formaldehyde and Ethylene Oxide are present in smoke of all fires.
3. IARC 98- Page 557 state a significant summary risks for three cancers, Non Hodgkin Lymphoma being one of these.
4. IARC 100F- Page 261 show a relation to Benzene exposure to Hodgkin Lymphoma. Page 382 shows a relation to Ethylene Oxide to Hodgkin Lymphoma. Page 409 shows relation of Formaldehyde to Hodgkin Lymphoma.
5. IARC 105- Chemical list shows Benzene, Formaldehyde, and Ethylene Oxide are all components of smoke in fires.

HODGKIN LYMPHOMA

IARC MONOGRAPH'S

IARC SUPPLEMENT 7

PAGE 157, 211, 213, 214, 378, 384, AND 386

IARC 45

PAGE 84, 93 AND 94

IARC 98

PAGE 173, 259, 399, 400, 401, 490 AND 520

IARC 100F

PAGES 261, 382, AND 409

IARC 105

IARC CHEMICAL LISTS OF SMOKE, SOOT AND EXHAUST

WORLD HEALTH ORGANIZATION

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC MONOGRAPHS
ON THE
EVALUATION OF THE CARCINOGENIC RISKS TO HUMANS

Overall Evaluations of Carcinogenicity: An Updating of *IARC Monographs* Volumes 1 to 42

SUPPLEMENT 7

LYON, FRANCE

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cancers was also reported from a very small cohort of Swedish forestry foremen exposed to chlorophenoxy herbicide preparations and other herbicides. A study of long-term pesticide applicators in the German Democratic Republic, heavily exposed to a number of chemicals, including 2,4-D and MCPA, demonstrated an increased risk of bronchial carcinoma[1].

Two population-based case-control studies conducted in northern and southern Sweden, respectively, showed a statistically significant association between exposure to chlorophenoxy herbicides, especially in forestry and agriculture, and the occurrence of soft-tissue sarcomas. An increased risk of soft-tissue sarcoma was described among highly exposed Italian rice weeders in a population-based case-control study. However, a case-control study from New Zealand did not demonstrate any increased risk of soft-tissue sarcoma in people exposed to chlorophenoxy herbicides[1]. Nor did a recently reported population-based case-control study of soft-tissue sarcoma and lymphoma in Kansas, USA, find any association between soft-tissue sarcoma and exposure to 2,4-D[3].

A statistically significant association between malignant lymphoma (Hodgkin's and non-Hodgkin's) and exposure to chlorophenoxy herbicides was found in a Swedish case-control study[1]. The population-based case-control study of soft-tissue sarcoma and Hodgkin's and non-Hodgkin's lymphoma in Kansas showed that use of 2,4-D was associated with non-Hodgkin's lymphoma, especially among farmers who had been exposed for more than 20 days per year, among whom there was an approximately six-fold excess, and among those who had mixed or applied the herbicides themselves. Hodgkin's lymphoma was not, however, found to be associated with herbicide exposure[3]. No significant or consistent association was seen in a case-control study of these tumours from New Zealand, and in a Danish cohort of chemical workers exposed to chlorophenoxy herbicides there was also no significantly increased risk of malignant lymphoma[1,4]. Farmers and forestry workers in Washington State, USA, with exposure to phenoxy herbicides had a significantly increased risk of non-Hodgkin's lymphoma. People of Scandinavian descent in the area had an increased risk of soft-tissue sarcoma in connection with phenoxy herbicide exposure, but no increased risk of non-Hodgkin's lymphoma[5].

Three Swedish case-control studies of colon, liver, and nasal and nasopharyngeal cancer, which used the same study design and methods as in the studies on soft-tissue sarcoma and malignant lymphoma, did not demonstrate significantly increased risks, although a risk ratio of 2.1 was reached for nasal and nasopharyngeal cancer[1].

A record-linkage study using census data on occupation and cancer registry information in Sweden did not reveal any excess of soft-tissue sarcoma among agricultural and forestry workers[6,7]. However, on the basis of occupational titles, the elevated risks seen in Swedish case-control studies of soft-tissue sarcoma and lymphoma were reduced to 1.4 or less[8]. A UK study based on data from cancer registration showed a slightly but significantly increased risk of soft-tissue sarcoma among farmers, farm managers and market gardeners, but not in other subgroups in forestry and farming[9]. No association with soft-tissue sarcoma has been found with military service in Viet Nam, despite potential exposure to phenoxy herbicides[1,10], although there is a case report in this respect[1].

urinary bladder and the adrenal glands; however, because of the lack of matched controls, it could not be concluded whether tumour induction was due to a combined effect of the three chemicals or of any one of them[4].

C. Other relevant data

Neither chromosomal aberrations (in two patients) nor sister chromatid exchanges (in three patients) were induced following administration of 5-fluorouracil[5].

5-Fluorouracil induced micronuclei but not specific locus mutations in mice treated *in vivo*. It induced aneuploidy, chromosomal aberrations and sister chromatid exchanges in cultured Chinese hamster cells. It did not induce sex-linked recessive lethal mutations in *Drosophila*, but caused genetic crossing-over in fungi. Studies on mutation in bacteria were inconclusive[5].

References

[1]*IARC Monographs*, *26*, 217-235, 1981

[2]Boice, J.D., Greene, M.H., Keehn, R.J., Higgins, G.A. & Fraumeni, J.F., Jr (1980) Late effects of low-dose adjuvant chemotherapy in colorectal cancer. *J. natl Cancer Inst.*, *64*, 501-511

[3]Ferguson, T. (1980) Prevention and delay of spontaneous mammary and pituitary tumors by long- and short-term ingestion of 5-fluorouracil in Wistar-Furth rats. *Oncology*, *37*, 353-356

[4]Habs, M., Schmähl, D. & Lin, P.Z. (1981) Carcinogenic activity in rats of combined treatment with cyclophosphamide, methotrexate and 5-fluorouracil. *Int. J. Cancer*, *28*, 91-96

[5]*IARC Monographs*, *Suppl. 6*, 316-318, 1987

FORMALDEHYDE (Group 2A)

See Chemical List

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

A number of epidemiological studies using different designs have been completed on persons in a variety of occupations with potential exposure to formaldehyde[1-24]. Cancers that occurred in excess in more than one study are: Hodgkin's disease, leukaemia, and cancers of the buccal cavity and pharynx (particularly nasopharynx), lung, nose, prostate, bladder, brain, colon, skin and kidney[1]. The studies reported are not entirely independent; the plant studied by Liebling *et al.*[2] and Marsh[1,3] is also included in the study by Blair *et al.*[4]; the case-control study of Fayerweather *et al.*[5] includes some subjects who were later studied by Blair *et al.*[4]. Detailed estimates of formaldehyde exposure levels were made in the studies of British chemical workers[6], US formaldehyde producers and users[4], Finnish wood workers[7] and US chemical workers[5], and for the case-control studies of Vaughan *et al.*[8,9] and Hayes *et al.*[10].

In the study of US producers and users of formaldehyde, 11% of the subjects were not exposed, 12% had an estimated time-weighted average (TWA) exposure of <0.1 ppm (<0.12 mg/m^3), 34% a TWA of 0.1-<0.5 ppm (0.12-<0.6 mg/m^3), 40% a TWA of 0.5-<2 ppm

Slight excesses in the occurrence of lung cancer have been noted in several studies[2,4,7,12,18,19]. These excesses have shown no consistent pattern with increasing level or duration of exposure to formaldehyde. A statistically significant excess (SMR, 132) was reported among wage workers 20 or more years after first exposure. The risk of lung cancer did not increase among this, or any other group, with either level or duration of exposure[4]. In the UK, the risk of lung cancer rose with level of exposure in one factory from an SMR of 58 among those with low exposure to an SMR of 118 among those with high exposure[6]. No such pattern was seen, however, for the other factories[6], nor was risk associated with cumulative exposure[20]. In a case-control study of respiratory cancer among Finnish plywood and particle-board workers, an odds ratio of 1.6 (adjusted for smoking) was found after ten years of latency. RRs, however, decreased with level and duration of exposure to formaldehyde[7]. In a cohort mortality study of 1332 workers in a formaldehyde-resin plant in Italy, there was an overall excess of lung cancer (SMR, 186). The excess occurred among those not exposed to formaldehyde (SMR, 148) as well as among those exposed (SMR, 136), with the greatest excess among those with uncertain exposure (SMR, 358). Lung cancer mortality was not clearly associated with duration of exposure[19].

Studies of professional groups have shown rather consistent deficits of lung cancer. None of these studies, however, included information on smoking, and the lower prevalence of tobacco use in these groups would probably lead to such deficits. No excess occurrence of lung cancer was noted among Danish physicians[21] or among persons exposed to formaldehyde at a US chemical production facility[22].

Mortality from leukaemia and/or cancer of the brain has been found consistently to be elevated in studies of professional groups[1,12,13,16,23,24]. Except for a very slight excess of leukaemia reported in one study[5] (which was not statistically significant), excesses of these tumours have not been found among industrial workers exposed to formaldehyde. Among professionals, gliomas were the predominant cell type of brain cancer, and the leukaemias were predominantly of the myeloid type. The absence of excesses for these cancers among industrial workers, however, argues against a role of formaldehyde.

Mortality from prostatic cancer has been found to be elevated among professionals[13] and among industrial workers[4,5], but the excess was statistically significant only among embalmers[13]. This tumour has shown a dose-response gradient in both studies of industrial workers, although the test for trend in the study of Blair[4] was not statistically significant.

Slight excesses of mortality from bladder cancer have been reported among professionals[13,23] and among industrial workers[5]. No such excess occurred, however, in the other large industrial cohorts, and none of the excesses was statistically significant. Significant excesses of colon cancer were noted among professionals[12,13] and among industrial workers[2]; nonsignificant elevations have also been reported[11,16]. A significant excess mortality from cancer of the skin was reported among New York embalmers (proportionate mortality ratio, 221)[12], and a slight excess was noted among industrial workers (based on two deaths)[11]. Excesses of Hodgkin's disease were seen among white industrial workers in

two studies, based on 14 deaths (SMR, 142)[4] and on one death[11]. The risk of Hodgkin's disease rose with level of formaldehyde exposure among wage and salaried workers alike, although each stratum had small numbers[4].

Although excess occurrence of a number of cancers has been reported, the evidence for a possible involvement of formaldehyde is strongest for nasal and nasopharyngeal cancer. The occurrence of these cancers showed an exposure-response gradient in more than one study, but the numbers of exposed cases were often small and some studies did not show excesses. The nose and nasopharynx could come into direct contact with formaldehyde through inhalation. Excess mortality from leukaemia and cancer of the brain was generally not seen among industrial workers, which suggests that the excesses for these cancers among professionals is due to factors other than formaldehyde. The slight excesses of cancer of the lung noted in several studies generally did not display the patterns of increasing risk with various measures of exposure (i.e., latency, duration, level or cumulative) usually seen for occupational carcinogens. No other cancer showed a consistent excess across the various studies.

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

Formaldehyde was tested for carcinogenicity by inhalation in two strains of rats and in one strain of mice. Significant increases in the incidence of squamous-cell carcinomas of the nasal cavity were induced in both strains of rats but not in mice[1,25]. A slight increase in the incidence of nasal cavity polypoid adenomas was also observed in male rats[25]. The tumours in the nasal cavity of rats were localized precisely: in the anterior portion of the lateral aspect of the nasoturbinate and adjacent lateral wall[26]. Experiments in which rats were exposed to both hydrogen chloride and formaldehyde showed that the carcinogenic response to formaldehyde does not result from the presence of bis(chloromethyl)ether (see p. 131), which is formed from the mixture of gases[27]. Another study in mice and one in hamsters by inhalation, one in rats by subcutaneous administration and one in rabbits by exposure in oral tanks were considered inadequate for evaluation[1,28].

C. Other relevant data

In single studies of persons exposed to formaldehyde, increases in the frequencies of chromosomal aberrations and sister chromatid exchanges in peripheral lymphocytes have been reported, but negative results have also been published. The interpretation of both the positive and negative studies is difficult due to the small number of subjects studied and inconsistencies in the findings[29].

No increase in the frequency of micronuclei or chromosomal aberrations was observed in rodents treated with formaldehyde *in vivo*; assays for dominant lethal mutations and DNA damage gave inconclusive results. Formaldehyde induced sperm-head anomalies in rats. It induced DNA-protein cross-links, unscheduled DNA synthesis, chromosomal aberrations, sister chromatid exchanges and mutation in human cells *in vitro*. It induced transformation of mouse C3H 10T1/2 cells and chromosomal aberrations, sister chromatid

C. Other relevant data

No data were available to the Working Group.

Reference

[1]*IARC Monographs*, *42*, 145-158, 1987

WOOD INDUSTRIES: CARPENTRY AND JOINERY (Group 2B)

Evidence for carcinogenicity to humans (*limited*)

The epidemiological data available suggest that there may be a carcinogenic risk connected with employment as a carpenter or joiner, although some of the studies produced negative results[1].

The connection between nasal cancer other than adenocarcinoma and exposure to wood dust among carpenters and joiners, found in some studies, if true, cannot be ascribed to any specific exposure. Carpenters and joiners usually work with impregnated wood, use a variety of types of wood and are exposed to many chemicals used in carpentry[1].

Several studies raise the possibility of an increased risk of Hodgkin's disease. A number of studies suggest an association between work as a joiner and nasal adenocarcinoma, but it is possible that the workers involved may have worked in the furniture industry[1].

There is also some evidence of an association between nasal carcinomas other than adenocarcinoma and work as a carpenter. In a case-control study based on an analysis of occupational data in the hospital records of 121 men seen for nasal cancer in British Columbia, Canada, between 1939 and 1977, a relative risk of 2.5 (adjusted for smoking and ethnic origin) was associated with exposure to wood. There was an increased risk for most histological types of epithelial tumour, except for transitional tumours. Of the 28 wood workers with nasal cancer, 16 had worked in the forestry industry, seven had been carpenters, four had been construction workers and one had been a cabinet-maker[2].

A case-control study on nasal and sinonasal cancer in Denmark, Finland and Sweden found a connection with exposure to spruce, pine and birch dust and the cancers studied, especially epidermoid and anaplastic carcinomas. There were 13 cases with exposure only to these types of wood *versus* four controls (relative risk, 3.2; 95% confidence interval, 1.1-9.4). Of the cases, five were in construction carpenters and one in a cabinet-maker with no exposure to hardwood; there were two construction carpenters among the controls[3].

three cases of non-Hodgkin's lymphoma were associated with employment in saw- and planingmill firms. The comparison was made between the number of cases observed in different occupations and the expected number of cases according to the 1946 census data of workers in these occupations[4].

A case-control study of Hodgkin's disease[5], using death certificates from North Carolina, USA, counties with a 'significant proportion' of the population employed in the furniture industry and in lumbering, showed an excess risk only among occupational groups with exposure to wood or paper. Carpenters and lumberers had a relative risk of 4.2 for Hodgkin's disease (95% confidence interval, 1.4-12.5). In Oregon, USA, a case-control study on leukaemia (ICD-9 codes 204-208)[6] showed a three-fold increase in risk for patients who had worked for ten years or more in the sawmill industry ($p = 0.017$), based on nine exposed cases.

In a proportionate mortality study of the causes of death of 375 union-affiliated Swedish lumberjacks who had died between 1968 and 1977, there were fewer deaths from cancer than expected (PMR, 88; 69-111). A marked deficiency of deaths from lung cancer (SMR, 33) and excesses of deaths from kidney cancer (SMR, 193; 92-407) and from cancers of the lymphatic and haematopoietic systems (SMR, 191; 105-349) were found. No information was given about the histology of these two groups of tumours. The mortality experience of Swedish males during that period was used as the standard for comparison[7].

A cohort study comparing the mortality experience of 10 322 men employed in wood-working industries with that of 406 798 non-wood workers showed no excess risk for all cancers combined. In the subcohort of lumber and sawmill workers, there was no statistically significant increase in the incidence of cancer at any site. No case of nasal cancer was reported[8].

A nested case-control study[9], based on an average of 25 years' follow-up of 3805 men working in the Finnish particle-board, plywood, sawmill or formaldehyde glue industries between 1944 and 1965, showed no clear connection between respiratory cancer incidence and most of the exposures studied, although some odds ratios were statistically significantly increased. For example, exposure to pesticides (in wood dust) and phenol was associated with elevated odds ratios, which became more marked among workers with more than ten years' exposure to pesticides. The raised odds ratios for exposure to phenol were partly explained by smoking and exposure to pesticides. Because of the mixed exposure, no single pesticide could be linked with respiratory cancer. Exposure to terpenes and other products of coniferous wood was also significantly associated with respiratory cancer when the duration of exposure exceeded five years. None of the odds ratios for exposure to wood dust and chlorophenols was statistically significant.

A proportionate mortality study showed an elevated risk for death from all cancers (PMR, 112; $p < 0.01$), stomach cancer (PMR, 128; $p < 0.01$) and non-Hodgkin's lymphoma (PMR, 139; $p < 0.05$) among woodworkers (including carpenters, cabinet-makers and furniture workers, lumber graders and scalers, sawyers in sawmills and woodworkers not classified elsewhere). In this mixed category, there was no death from sinonasal cancer[10].

The epidemiological data reported here and previously[1] are not sufficient to make a definite assessment of the carcinogenic risks of employment in the lumber and sawmill

Some studies, based on a few cases, suggest that an increased risk of lymphoproliferative neoplasms, particularly Hodgkin's disease, may be linked to employment in the pulp and paper industries[1-3].

In a prospective cohort study of viscose workers exposed to carbon disulphide, 343 pulp and paper workers served as the reference group. During 15 years of follow-up, nine pulp and paper workers had died of lung cancer, compared with four viscose workers (rate ratio, 2.2; [95% confidence interval, 0.7-6.7]). The pulp and paper workers smoked slightly less than the viscose workers[4]. When national rates were used as the reference, the SMR was 154 (70-292). However, a US proportionate mortality study[3] comprising 2113 deaths revealed no excess of lung cancer among pulp and paper workers.

A US cohort study of 3572 pulp and paper mill workers employed for at least one year between 1945 and 1955 and followed until 1977 showed statistically nonsignificant excesses of lymphosarcoma and reticulosarcoma (10 cases; SMR, 169; 92-287) and of stomach cancer (17 cases; SMR, 123; 78-185). There was no excess of lung cancer. The excess of lymphosarcoma and reticulosarcoma was present only for men who had worked in sulphate mills (6 observed; SMR, 207; 90-408), whereas the excess of stomach cancer occurred in sulphite mills (11 observed; SMR, 149; 83-246)[5].

Excesses of cancers at miscellaneous sites have been mentioned in some studies on pulp and paper workers[1,3,6-8]. The findings may be due to chance, because the cases were generally few and the patterns inconsistent.

A case-control study of the paternal occupations of 692 children who had died of cancer in Massachusetts, USA, showed that paternal employment as a pulp or paper mill worker was associated with tumours of the brain and other parts of the nervous system (six cases observed; relative risk, 2.8); however, as many comparisons were made, this may well be a chance finding[9].

B. Other relevant data

Workers employed for two to 30 years in a paper factory and exposed intermittently to high levels of formaldehyde (see p. 211) for short periods showed a significant increase in the incidence of structural chromosomal aberrations associated with mean exposure to formaldehyde; however, no increase in the incidence of sister chromatid exchanges was observed as compared with controls. An increase in the incidence of chromosomal and chromatid-type aberrations was reported among seven workers involved in boiling pulp and handling sulphuric acid in a sulphite factory, as compared to six workers exposed to chlorine during the bleaching of pulp, six workers exposed to dust in a paper mill and 15 control subjects; but the results remain uncertain due to methodological problems[10].

References

[1] *IARC Monographs, 25*, 157-197, 1981

[2] Greene, M.H., Brinton, L.A., Fraumeni, J.F. & D'Amico, R. (1978) Familial and sporadic Hodgkin's disease associated with occupational wood exposure. *Lancet, ii*, 626-627

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IARC MONOGRAPHS

ON THE

EVALUATION OF CARCINOGENIC RISKS TO HUMANS

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

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Table 11 (contd)

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

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

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

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

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

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

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

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

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

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

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

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Painting, Firefighting, and Shiftwork

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Table 2.1. (contd)

Reference, location, time period	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	RR (95% CI)	Adjustment for potential confounders	Comments
Boice *et al.* (1999) Lockheed Martin Plant Burbank, Los Angeles county, California, USA 1960–96	1216 painters (1139 men, 77 women) employed ≥1yr in the aircraft industry, followed-up retrospectively for mortality	Detailed job history was obtained from work-history records		Painter		**SMR (95% CI)**	Age, sex, race, calendar year	Other cancer causes non-informative due to small numbers of deaths; painting not described in detail except that paints contained chromates
			Lung		41	1.11 (0.80–1.51)		
			Oesophagus		21	0.61 (0.07–2.20)		
			Liver		1	0.36 (0.01–2.03)		
			Non-Hodgkin lymphoma		3	0.72 (0.15–2.12)		
			Multiple myeloma		4	1.70 (0.46–4.35)		
			Leukaemia		3	0.74 (0.15–2.16)		
Steenland & Palu (1999) California, Missouri, New York, Texas, USA 1975–94	42 170 painters and 14 316 non-painters with ≥1 yr union membership were identified from union records and followed from 1975–94 by linkage to national and local registers; Restricted to white men (98% of the cohort).	Job titles were inferred from union membership records which identified the specialty affiliation and trade of the local union for all members		Painter		**SMR (95% CI)**	Restricted to caucasian men (98% of the cohort). Stratification by age and calendar time	No information on trade of individual members; SMRs compared painters to the general US population; SRRs compared painters to non-painters
			All cancers		4674	1.12 (1.09–1.15)		
			Lung		1746	1.23 (1.17–1.29)		
			Bladder		166	1.23 (1.05–1.43)		
			Stomach		197	1.39 (1.20–1.59)		
			Liver		119	1.25 (1.03–1.50)		
			Pharynx		49	1.15 (0.85–1.52)		
			Oesophagus		110	1.12 (0.92–1.35)		
			Larynx		48	0.97 (0.71–1.29)		
			Non-Hodgkin lymphoma		137	1.06 (0.89–1.25)		
			Hodgkin disease		16	1.30 (0.74–2.11)		
			Multiple myeloma		64	0.97 (0.75–1.24)		
			Leukaemia		138	0.92 (0.78–1.11)		

Band *et al.* (2005) conducted a case-control study based on the British Columbia Cancer Registry to assess the association between lifetime occupational histories and risk of bladder cancer. The cases in this study were 1125 male incident bladder cancer cases reported to the registry during 1983–1990. Controls were 8492 male incident cancer patients diagnosed with all other types of cancer (excluding lung, and of unknown primary site) reported to the registry during the same time period. A self-administered questionnaire was mailed to male cancer patients to collect lifetime occupational history, including job descriptions, job and industry titles, duration and period of work, etc. A significantly increased risk of bladder cancer was observed for those who had ever worked as painters/wallpaper hangers (OR, 1.53; 95% CI: 1.02–2.28; 22 cases). [Caution must be exercised in interpreting the results because patients with other types of cancer were used as controls (excluding lung cancer and cancers of unknown primary site). If some of the cancer sites were associated with paint exposure, inclusion of these cancer sites in the control group would cause an underestimation of the association of interest. Also, the questionnaires were completed by either the subject himself or by a proxy respondent for information on lifetime occupational history.]

(c) Other Regions

Bethwaite *et al.* (1990) conducted a case–control study based on a cancer registry in New Zealand to investigate the association between employment as a painter and risk of various cancers. A total of 912 male bladder cancer cases who reported an occupation were included in this study as well as 18 992 male control patients of all other types of cancer. Painters were found to be associated with an increased of bladder cancer (OR, 1.52; 95% CI: 1.00–2.31; 24 cases), especially those painters aged 20–59 years (OR, 2.27; 95% CI: 1.15–4.48; nine cases). The risk was not significantly increased for those aged 60 and over (OR, 1.27; 95% CI: 0.75–2.15; 15 cases).

2.2.4 *Lymphatic and haematopoietic cancer*

The Working Group for Volume 47 evaluated five case–control studies of leukaemia among persons exposed to paint and its manufacture.(two with significant excesses). Two small studies on Hodgkin disease and three studies on multiple myeloma also showed excesses (IARC, 1989).

A summary of studies of painters and paint exposures and lymphatic and haematopoietic cancer is presented in Table 2.4.

(a) Europe

Lindquist *et al.* (1987) conducted a study of 125 acute leukaemia cases (76 men and 49 women aged 16–84, diagnosed between 1980–1983), and 125 age- and sex-matched population controls in Sweden. Participants were interviewed in person to obtain information on a variety of factors including detailed lifetime occupational history.

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.

See Chemical List. KNOWN Cause OF Hodgkin

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.

Table 1.1. IARC evaluations and cancer sites in humans of chemicals measured at fires

Chemicals measured at fires	Overall evaluation	Human evidence	Animal evidence	Volume	Cancer sites in humans (For Group 1 agents only)
Acetaldehyde	2B	Inadequate	Sufficient	36, Suppl. 7, 71	
Arsenic	1	Sufficient	Limited	23, Suppl. 7	Skin, lung, liver (angiosarcoma)
Asbestos	1	Sufficient	Sufficient	14, Suppl. 7	Lung, mesothelioma, larynx, gastrointestinal tract
Benz[*a*]anthracene	2B	Inadequate	Sufficient	32, Suppl. 7, 92	
Benzene	1	Sufficient	Limited	29, Suppl. 7	Leukaemia
Benzo[*b*]fluoranthene	2B	No data	Sufficient	32, Suppl. 7, 92	
Benzo[*k*]fluoranthene	2B	No data	Sufficient	32, Suppl. 7, 92	
Benzofuran (coumarone)	2B	No data	Sufficient	63	
Benzo[*a*]pyrene	1	No data	Sufficient	32, Suppl. 7, 92	Lung, bladder, skin
1,3-Butadiene	1	Sufficient	Sufficient	71, 97	Lymphohaematopoietic system
Cadmium	1	Sufficient	Sufficient	58	Lung
Carbon black (total)	2B	Inadequate	Sufficient	65, 93	
Chrysene	2B	Inadequate	Sufficient	3, 32, Suppl. 7, 92	
Dibenz[*a*,*h*]anthracene	2A	Inadequate	Sufficient	32, Suppl. 7, 92	
Dichloromethane (methylene chloride)	2B	Indadequate	Sufficient	71	
Ethylbenzene	2B	Inadequate	Sufficient	77	
Formaldehyde	1	Sufficient	Sufficient	88	Nasopharynx; (nasal sinuses and leukaemia, suggested)
Furan	2B	Inadequate	Sufficient	63	

testicular cancer. Eleven testicular cancers were observed versus 7.1 expected (SIR, 1.55; 95% CI: 0.8–2.8). For the years 1990–1996, the SIR for testicular cancer was 3.0 (95% CI: 1.3–5.9).

Ma *et al.* (2005) examined age- and gender-adjusted mortality rates of 36 813 professional firefighters employed during 1972–1999 in Florida, USA, and compared those with that of the Florida general population. The study population consisted of 34 796 male and 2017 female professional firefighters. The racial/ethnic composition was caucasian (90.1%), hispanic (7%), and black (6.5%). Employment as a firefighter was ascertained from employment records in the Florida State Fire Marshall Office. Surrogate information on occupational exposures in firefighting was collected by examining the year of certification and duration of employment as a firefighter. No information was collected on smoking histories. A total of 1411 male and 38 female deaths with known causes were identified in this cohort. In male firefighters, a deficit of overall mortality from cancer was observed (SMR, 0.85). Excess risks were observed for male breast cancer (SMR, 7.41; 95% CI: 1.99–18.96), and thyroid cancer (SMR, 4.82; 95% CI: 1.30–12.34), each based on four cases. Mortality from bladder cancer was increased and approached statistical significance (SMR, 1.79; 95% CI: 0.98–3.00). Female firefighters had similar overall cancer mortality patterns to Florida women (SMR, 1.03), but the numbers were small for specific cancer sites.

In a further analysis of the same cohort, Ma *et al.* (2006) determined the relative cancer risk for firefighters in the State of Florida compared with the Florida general population. Employment as a firefighter was ascertained from employment records in the Florida State Fire Marshall Office. Cancer incidence was determined through linkage to the Florida Cancer Data System, a statewide cancer registry estimated to capture 98% of cancers in Florida residents. No pathological verification of cancer diagnoses was undertaken. A total of 970 male and 52 female cases of cancer were identified; 6.7% of the cohort were lost to follow-up. Male firefighters had significantly increased incidence rates of cancers of the bladder (SIR, 1.29; 95% CI: 1.01–1.62), testis (SIR, 1.60; 95% CI: 1.20–2.09), and of the thyroid (SIR, 1.77; 95% CI: 1.08–2.73). Female firefighters had significantly increased incidence rates of overall cancer (SIR, 1.63; 95% CI: 1.22–2.14), cervical (SIR, 5.24; 95% CI: 2.93–8.65) and thyroid cancers (SIR, 3.97; 95% CI: 1.45–8.65), and Hodgkin disease (SIR, 6.25; 95% CI: 1.26–18.26).

2.2 Case–control studies

Case–control studies have been used to examine the risk of firefighting and its association with various types of cancers. In all but one of these studies, ten or fewer firefighters were included in the case and/or control group. Several studies combined broad occupational categories with heterogeneous exposures such as firefighter and fireman, with the latter not necessarily working as a firefighter. These types of studies may result in exposure misclassification. Even within specific occupational groups such as firefighters, all would not have the same intensity or type of exposures. The

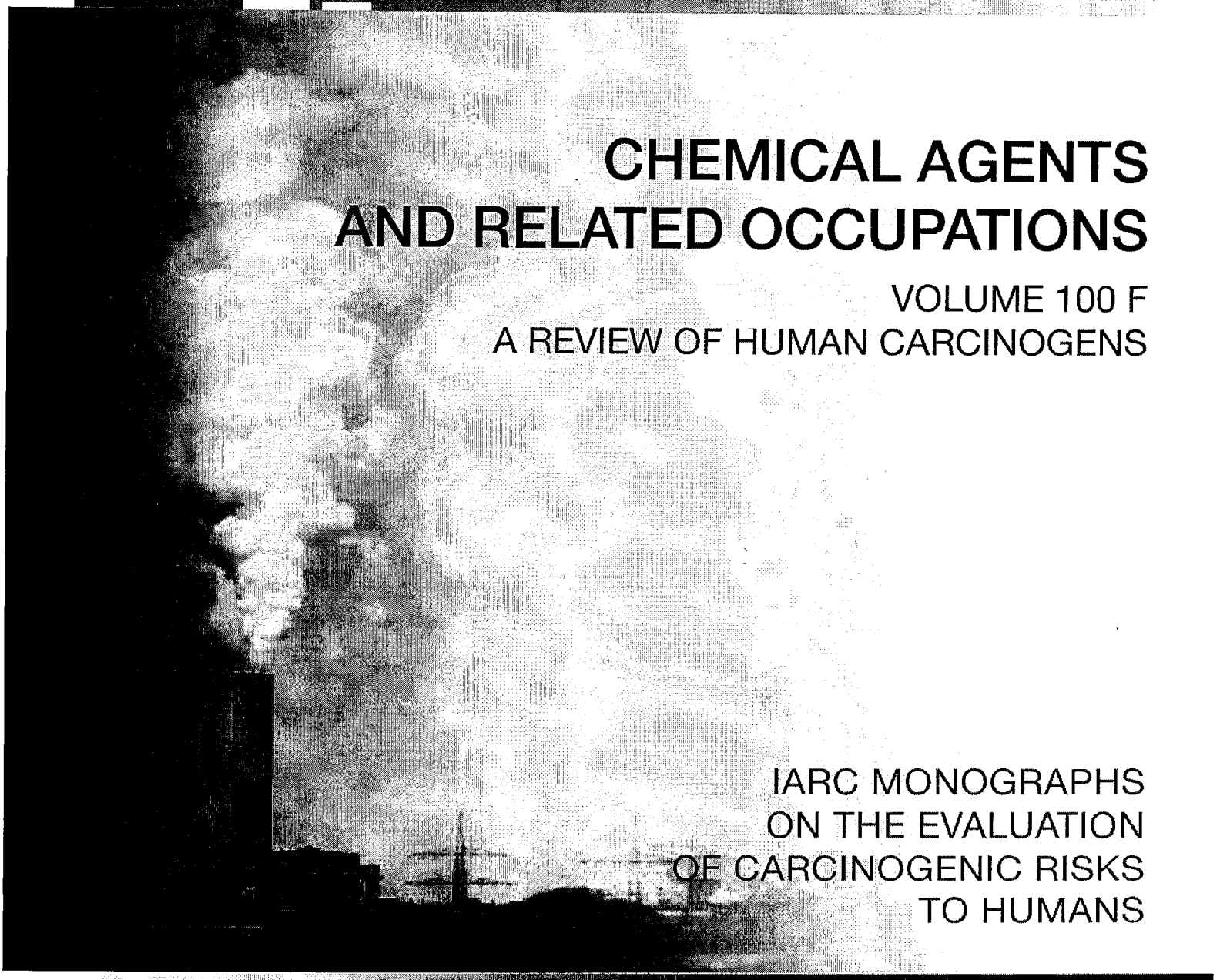
Table 2.8 (contd)

Reference, location, name of study	Study population description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases/ deaths	RR/SIR/SMR (95% CI)*	Adjustement for potential confounders	Comments
Milham (1997), Washington State, USA	Death certificate study 1950–1989. 2266 firefighter deaths	Usual occupation on death certificate				**PMR**	Age, Calendar period	
			All Cancers		476	1.1 (1.0–1.2)		
			Buccal cavity & pharynx		7	0.6 (0.3–1.3)		
			Oesophagus		11	1.1 (0.6–2.0)		
			Stomach		22	0.8 (0.5–1.2)		
			Colon		36	0.9 (0.6–1.2)		
			Rectum		15	1.1 (0.6–1.8)		
			Pancreas		28	1.1 (0.7–1.6)		
			Larynx		3	0.6 (0.1–1.8)		
			Lung		120	1.0 (0.8–1.2)		
			Prostate		56	1.1 (0.8–1.5)		
			Kidney		9	0.9 (0.4–1.6)		
			Bladder & urinary		23	1.4 (0.9–2.1)		
			Melanoma		9	2.1 (1.0–4.1)		
			Brain & nervous system		19	1.6 (0.9–2.4)		
			Lympho- & reticulosarcoma		13	1.8 (1.0–3.0)		
			Hodgkin lymphoma		7	1.8 (0.7–3.7)		
			Other lymphoma		3	0.5 (0.1–1.4)		
			Multiple myeloma		9	1.3 (0.6–2.4)		
			Leukaemia		27	1.4 (0.9–2.1)		

* specify *P*–value if no confidence interval indicated

NR, not reported; n.s, not significant

IARC MONOGRAPHS



CHEMICAL AGENTS AND RELATED OCCUPATIONS

VOLUME 100 F
A REVIEW OF HUMAN CARCINOGENS

IARC MONOGRAPHS
ON THE EVALUATION
OF CARCINOGENIC RISKS
TO HUMANS

International Agency for Research on Cancer
World Health Organization

and diffuse large B-cell lymphoma (DLBCL), two common NHL subtypes (Wang *et al.*, 2009). Cocco *et al.* (2010) conducted an analysis of a large multicentre case–control study of NHL in Europe and found no significant increase in risk for B-cell NHL or DLBCL, but an elevated risk, albeit not statistically significant, for follicular lymphoma associated with exposure to benzene (see Table 2.10 online), and a significant association between combined exposure to benzene/toluene/xylene and follicular lymphoma. Other case–control studies showed increased, non-significant risks for one or both of these histological subtypes, and in one study in Italy a significant association was found between medium/high exposure to benzene and the risk for diffuse lymphoma (Miligi *et al.*, 2006; OR = 2.4, 95%CI: 1.3–1.5).

2.1.6 Multiple myeloma

Most cohort studies showed no association with multiple myeloma (MM) (Table 2.11 available at http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-19-Table2.11.pdf). However, there was a statistically significant excess of MM reported for the Pliofilm cohort (SMR 4.1; 95%CI: 1.1–10.5, based upon four deaths) (Rinsky *et al.*, 1987), which did not persist in the most recent update (Rinsky *et al.*, 2002; see Table 2.11 online). In a cohort study among chemical workers at the Monsanto chemical company suggestive evidence was found of a dose–response relationship (Collins *et al.*, 2003), while in a cohort study of Norwegian workers in the upstream petroleum industry (i.e. the phases of oil extraction and initial transportion, which entail extensive exposure to crude oil) a significant increased risk for MM was found (Kirkeleit *et al.*, 2008).

Case–control studies of MM with estimates of exposure to benzene largely show no association (Table 2.12 available at http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-19-Table2.12.pdf). An exception was an early study in which a significant association was found between risk for MM and the proportion of cases and controls with "solvent/benzene" exposure (La Vecchia *et al.*, 1989). In another study, borderline significant effects were detected (Costantini *et al.*, 2008). In a large multicentre case–control study of NHL in Europe there was no association of benzene exposure with MM (Cocco *et al.*, 2010).

A meta-analysis by Infante (2006) analysed data from seven well defined "benzene cohorts" outside of petroleum refining and found a statistically significant increase in risk for MM (RR 2.1; 95%CI: 1.3–3.5).

2.1.7 Hodgkin disease

There are sparse data on Hodgkin disease in studies of benzene-exposed cohorts, with most studies having very small numbers of cases and showing no association (see Table 2.13 available at http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-19-Table2.13.pdf). Overall, there is no evidence of an increased risk. The relatively few case–control studies in adults also show no association (see Table 2.14 available at http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-19-Table2.14.pdf). In a case–control study of childhood cancer in Denmark, an increased risk for Hodgkin disease was detected in association with estimated environmental exposures to benzene (Raaschou-Nielsen *et al.* (2001) (see Table 2.14 online).

2.2 Cancer of the lung

Cohort studies with information on potential or estimated benzene exposure and lung cancer are shown in Table 2.15 (available at http://monographs.iarc.fr/ENG/Monographs/vol100F/100F-19-Table2.15.pdf). Although most studies show no association, in two cohorts with quantitative exposure-assessment evidence of a dose–response relationship was found (Hayes *et al.*, 1996; Collins

of removing ethylene oxide from the atmosphere (National Library of Medicine, 2005).

Mainstream tobacco smoke contains 7 mg/cigarette ethylene oxide (IARC, 2004). With the possible exception of cigarette smoke, other non-occupational sources of exposure to ethylene oxide (e.g. residues in spices and other food products (Jensen, 1988; Fowles *et al.*, 2001) and in skin-care products (Kreuzer, 1992) are expected to be minor. Ethylene oxide is formed during the combustion of fossil fuel, but the amount is expected to be negligible (WHO, 2003). Hospital patients may be exposed during dialysis when the equipment has been sterilized with ethylene oxide (IPCS-CEC, 2001).

2. Cancer in Humans

Epidemiological evidence of the risk for human cancer from ethylene oxide derives principally from the follow-up of 14 cohorts of exposed workers, either in chemical plants where ethylene oxide was produced or converted into derivatives, or in facilities where it was used as a sterilant. Many of the workers employed at chemical factories were also exposed to other chemicals. The *IARC Monograph* Volume 97 (IARC, 2008) concluded that there is *limited evidence* in humans for the carcinogenicity of ethylene oxide.

The most informative epidemiological investigation of ethylene oxide and cancer risk was a study by NIOSH of more than 18 000 employees at 14 industrial facilities where ethylene oxide was used to sterilize medical supplies or food spices, or to test the sterilizing equipment (Steenland *et al.*, 1991; Stayner *et al.*, 1993). This investigation benefited from greater statistical power than did other studies, as a consequence of its large sample size. In addition, there was a lower potential for confounding by concomitant exposure to other chemicals, while detailed quantitative assessments were made of individual exposures to ethylene oxide. For these reasons, the Working Group gave greatest weight to the findings of this study when assessing the balance of epidemiological evidence on ethylene oxide, although findings from other studies were also taken into account.

2.1 Lympho-haematopoietic malignancies

Steenland *et al.* (1991) reported on the initial mortality results for the NIOSH ethylene-oxide cohort. There were 343 deaths from cancer (380.3 expected; SMR, 0.90; 95%CI: 0.81–1.00). SMRs were not statistically significantly increased for lymphatic and haematopoietic cancers combined (SMR, 1.06; 95%CI: 0.75–1.47), for lymphosarcoma-reticulosarcoma [ICD-9 200] (SMR, 1.52; 95%CI: 0.65–3.00), Hodgkin lymphoma (SMR, 1.14; 95%CI: 0.31–2.92), leukaemia (SMR, 0.97; 95%CI: 0.52–1.67), non-Hodgkin lymphoma [ICD-9 202] (SMR, 1.20; 95%CI: 0.57–2.37) or myeloma (SMR, 0.59; 95%CI: 0.12–1.73). No significant trend in mortality was observed in relation to duration of exposure, but the SMR for leukaemia (1.79, based on five deaths) and non-Hodgkin lymphoma (1.92, based on five deaths) were higher after allowance for a latency of more than 20 years. Among the sterilizer operators, mortality ratios were 2.78 (two deaths observed) for leukaemia and 6.68 (two deaths) for lymphosarcoma/reticulosarcoma. In a further analysis of the same study (Stayner *et al.*, 1993), an exposure–response analysis was conducted with the use of previously derived quantitative estimates of individual exposure to ethylene oxide (Greife *et al.*, 1988). Analysis was limited to 13 of the facilities studied, since exposure information at one facility was inadequate. Mortality from lymphatic and haematopoietic cancer was greatest in the group with the highest category of cumulative exposure to ethylene

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.

IARC MONOGRAPHS

DIESEL AND GASOLINE ENGINE EXHAUSTS AND SOME NITROARENES

VOLUME 105

IARC MONOGRAPHS ON THE EVALUATION OF CARCINOGENIC RISKS TO HUMANS

International Agency for Research on Cancer

World Health Organization

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."***