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Health and Safety Executive

The burden of occupational cancer in Great Britain

Lymphohaematopoietic cancer

Prepared by the **Health and Safety Laboratory,**
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Lymphohaematopoietic cancer

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The aim of this project was to produce an updated estimate of the current burden of cancer for Great Britain resulting from occupational exposure to carcinogenic agents or exposure circumstances. The primary measure of the burden of cancer was the attributable fraction (AF) being the proportion of cases that would not have occurred in the absence of exposure; and the AF was used to estimate the number of attributable deaths and registrations. The study involved obtaining data on the risk of the cancer due to the exposure of interest, taking into account confounding factors and overlapping exposures, as well as the proportion of the target population exposed over the relevant exposure period. Only carcinogenic agents, or exposure circumstances, classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens were considered. Here, we present estimates for lymphohaematopoietic cancers that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) AF, deaths and registrations for lymphohaematopoietic cancers associated with overall occupational exposure and to 1,3-butadiene is 0.00% (95%Confidence Interval (CI)=0.00-0.01), which equates to 0 (95%CI=0-1) attributable deaths and 1 (95%CI=0-2) attributable registration.

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EXECUTIVE SUMMARY

The aim of this project was to produce an updated estimate of the current burden of cancer for Great Britain resulting from occupational exposure to carcinogenic agents or exposure circumstances. The primary measure of the burden of cancer used in this project was the attributable fraction i.e. the proportion of cases that would not have occurred in the absence of exposure; this was then used to estimate the attributable numbers. This involved obtaining data on the risk of the disease due to the exposure of interest, taking into account confounding factors and overlapping exposures, and the proportion of the target population exposed over the period in which relevant exposure occurred. Estimation was carried out for carcinogenic agents or exposure circumstances classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens. Here, we present estimates for lymphohaematopoietic cancers that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

1,3-butadiene has been classified by the IARC as a definite human carcinogen for lymphohaematopoietic cancers. Occupational exposure to 1,3-butadiene can occur in the production of polymers for the manufacture of styrene-butadiene rubber for tyres, hoses, gaskets, adhesives and footwear and in the production and use of acrylonitrile-butadiene-styrene polymers for parts, pipes and various appliances and styrene-butadiene latexes for paints and carpet backing. Due to assumptions made about cancer latency and working age range, only cancers in ages 15-84 for men and 15-79 in 2005/2004 could be attributable to occupation.

For Great Britain in 2005, there were 5284 total deaths in men aged 15-84 and 3195 in women aged 15-79 from lymphohaematopoietic cancers; in 2004 there were 10,865 total registrations for lymphohaematopoietic cancers in men aged 15-84 and 7225 in women aged 15-79.

The estimated total (male and female) attributable fraction for lymphohaematopoietic cancers associated with occupational exposure overall and to 1,3-butadiene is 0.00% (95%Confidence Interval (CI)=0.00-0.01), which equates to 0 (95%CI=0-1) attributable deaths and 1 (95%CI=0-2) attributable registration.

CONTENTS

1 INCIDENCE AND TRENDS

Lymphohaematopoietic (LH) cancers (ICD-10: C81-C96; ICD-9: 200-208), or blood cancers, are tumours of the blood-forming organs and lymphatic system. There are four main types of LH cancers: Hodgkin's lymphoma (HL), non-Hodgkin's lymphoma (NHL), multiple myeloma and leukaemia. HL and NHL are cancers of the lymphatic tissues, the network of lymph glands and channels that occur throughout the body that drain fluid away from the tissues and return it to the blood stream. HL is distinguishable from all other types of lymphoma by the presence of the distinctive abnormal lymphocyte called a Reed-Sternberg cell (Ekstrom-Smedby, 2006). MM is a form of cancer that affects plasma cells, whereas leukaemia is cancer of the circulating white blood cells. Further information about each type of cancer can also be found in other technical documents and also detailed texts (Schottenfeld and Fraumeni, 2006). More detailed information about incidence/mortality and trends can also be found in these documents. Briefly, HL incidence and mortality has decreased since the 1960s (Swerdlow *et al*, 2001), and is greater in the elderly. HL incidence shows a distinctive bimodal pattern being higher in young adults and the very old. NHL incidence and mortality have increased over the past ten years, and is significantly greater in the older age groups. MM is a disease of the elderly, both incidence and mortality increased substantially between the 1970s and 1990s after which they decreased gradually. Leukaemia incidence shows a bimodal pattern, being high in young children, and then gradually increasing with age. Incidence has increased slightly of the past 30 years, whereas mortality has remained constant or decreased in all ages except the very elderly. More details of the incidence, trends and aetiology of NHL, multiple myeloma and leukaemia are given in related technical reports.

The number of yearly LH registrations in England has averaged 9,422 for men and 7,843 for women over the past 11 years (Table 1). In Scotland the average for men was 1026 and for women was 930, and in Wales 724 for men and 590 for women. There is a general upward trend in both sexes in all countries in GB. Annual deaths average at 5,600 for men and 4,831 for women in England and Wales over the past eight years (Table 2) and are fairly constant. In Scotland the respective numbers are 505 and 437.

Table 1 Number of lymphohaematopoietic cancer registrations in England 1995-2005 in England, Scotland and Wales

	Men				**Women**			
Year	**England**	**Scotland**	**Wales**	**Total**	**England**	**Scotland**	**Wales**	**Total**
1995	8553 (33.6)	996			7225 (27.4)	865		
1996	8219 (32.2)	1025 (41.9)			7000 (26.5)	909 (34.4)		
1997	8293 (32.3)	954 (39.1)			7043 (26.6)	964 (36.5)		
1998	9084 (35.2)	989 (40.5)			7724 (29.0)	966 (36.6)		
1999	9346 (36.0)	985 (40.4)			7992 (29.9)	942 (35.7)		
2000	9807 (37.5)	1010 (41.5)	615 (43.7)	11432	8102 (30.2)	965 (36.7)	538 (35.9)	9605
2001	9654 (37.3)	1083 (44.5)	727 (51.6)	11464	8014 (30.0)	875 (33.3)	579 (38.5)	9468
2002	9729 (37.9)	1033 (42.5)	729 (51.6)	11491	8003 (29.9)	945 (36.0)	589 (39.1)	9537
2003	10026 (38.8)	1128 (46.3)	768 (54.0)	11922	8223 (30.5)	934 (35.6)	598 (39.7)	9755
2004	10234 (39.4)	1079 (43.4)	776 (53.7)	12089	8329 (30.8)	946 (35.5)	613 (40.3)	9888
2005	10697 (43.2)		733 (50.9)		8613 (33.5)		624 (41.2)	
Average 1995-2005	**9422 (36.7)**	**1028 (42.2)**	**725 (50.9)**	**11680**	**7843 (29.5)**	**931 (35.6)**	**590 (39.2)**	**9651**

Table 2 Number of lymphohaematopoietic cancer deaths in England/Wales and Scotland 1999-2006

	Men			Women		
Year	**England & Wales**	**Scotland**	**Great Britain**	**England & Wales**	**Scotland**	**Great Britain**
	Number (Crude Rate, /100000)	**Number (Crude Rate, /100000)**	**Number**	**Number (Crude Rate, /100000)**	**Number (Crude Rate, /100000)**	**Number**
1999	5314 (19.6)	487 (20.0)	5801	4820 (17.9)	478 (18.1)	5298
2000	5179 (18.9)	450 (18.5)	5629	4694 (17.4)	527 (20.0)	5221
2001	5573 (20.0)	528 (21.7)	6101	4848 (18.0)	499 (19.0)	5347
2002	5776 (20.6)	532 (21.9)	6308	5039 (18.4)	459 (17.5)	5498
2003	5878 (18.8)	513 (21.1)	6391	4911 (11.4)	525 (20.0)	5436
2004	5667 (17.8)	468 (19.1)	6135	4780 (11.1)	464 (17.6)	5244
2005	5634 (17.3)	509 (20.6)	6143	4772 (11.0)	503 (18.9)	5275
2006	5779 (17.6)	557 (22.6)	6336	4785 (10.7)	483 (18.2)	5268
Average 1999-2005	**5600 (18.8)**	**506 (20.7)**	**6105**	**4831 (14.5)**	**492 (18.7)**	**5323**

2 OVERVIEW OF AETIOLOGY

The causes of LH neoplasms are varied. Non-occupational risk factors include radiation, smoking, diet, alcohol and infectious agents (Schottenfeld and Fraumeni, 2006). Table 3 summarises the occupational exposures for the four main groups making up LH neoplasm where there is strong or suggestive evidence of carcinogenicity in humans according to Siemiatycki *et al.* (2004). These have been reviewed in individual technical reports. There is some suggestion that wood-related exposures as possible risk factors for LH neoplasm overall (Mueller and Grufferman, 2006)**.**

Table 3 Occupational aetiological factors for lymphohaematopoietic cancers

Cancer	**Exposure**	
	Strong or Suggestive evidence	**Other**
Hodgkin's lymphoma	None identified	Wood-related exposures
Non-Hodgkin's lymphoma	TCDD; Tetrachloroethylene; Trichloroethylene; Non-arsenical insecticides; Hairdressers & barbers	Animals; Woodwork; Printers; Teachers; Asbestos; Benzene; Electrical workers; Radiation; PCBs & PBBs
Multiple myeloma	Non-arsenical insecticides	Ionising radiation; Benzene & organic solvents; Petroleum refining & distribution; Rubber & plastics manufacture; Paint-related occupations; Wood products industries; Asbestos; Engine exhaust
Leukaemia	Non-arsenical insecticides; Benzene; Boot & shoe manufacture/repair; Ethylene oxide; Ionising radiation; Formaldehyde; Petroleum refining; Rubber industry; 1,3-Butadiene	Electricity workers and electromagnetic fields; Chemists; Painter

Several diseases within this groups share similar causes. Ionising radiation causes acute leukaemia and chronic myeloid leukaemia (Boice, 2006); benzene causes aplastic anaemia, acute myeloid leukaemia, and possible other leukaemias and myeloma (Khan, 2007); viral infections have been implicated in the aetiology of Hodgkin's disease, non-Hodgkin's lymphoma and the leukaemias (Mims, 1985); and low frequency magnetic fields are suspected of causing various leukaemias, especially in 'electrical' occupations (NRPB, 1992, NRPB, 2001). The latter was highlighted in the 1979-80/1982-90 occupational health decennial supplement (Drever, 1995). The supplement also noted the high mortality from LH cancer among teachers, both in schools and in higher education, excesses that are consistent with an aetiological role of infections acquired as an adult through frequent contact with large numbers of young people. The most recent occupational health decennial supplement does not give results for all LH neoplasms considered together (Coggon *et al*, 2009).

IARC have assessed the carcinogenicity of a number of substances and occupational circumstances with those classified as Group 1 having sufficient evidence in humans and those classified as Group 2A having limited evidence in humans. Those classified as causing LH cancers are given in Table 4.

Table 4 Occupational agents, groups of agents, mixtures, and exposure circumstances classified by the IARC Monographs, Vols 1-98 (IARC, 1972-2007), into Groups 1 and 2A, which have the lymphohaematopoietic system as the target organ.

Agents, Mixture, Circumstance	Main industry, Use	Evidence of carcinogenicity in humans	Strength of evidence	Other target organs
Group 1: Carcinogenic to Humans				
Agents, groups of agents				
1,3-butadiene	Chemical and rubber industries	Sufficient	Suggestive	
Exposure circumstances				
None identified				
Group 2A: Probably Carcinogenic to Humans				
Agents & groups of agents				
None identified				
Exposure circumstances				
None identified				

2.1 EXPOSURES

2.1.1 1,3-Butadiene

In 1992 IARC classified 1,3-butadiene (BD) as a probable human carcinogen (Group 2A), based on sufficient evidence of carcinogenicity in animals but limited evidence in humans (IARC, 1999). Concern about the possible carcinogenicity of BD comes from the results of animal experiments, which showed an increased incidence of leukaemia in mice and, to a lesser extent, rats (IARC, 1999). In 2007 a working group convened at IARC to reassess the carcinogenicity of BD, and reclassified it as "carcinogenic to humans" (Group 1), on the basis of "sufficient evidence" in humans of an increased risk for leukaemias (Grosse *et al*, 2007). BD is primarily used in the production of polymers for the manufacture of styrene-butadiene rubber for tyres, its major end-use product; nitrile rubber for hoses, gaskets, adhesives and footwear; acrylonitrile-BD-styrene polymers for parts, pipes and various appliances; and styrene-BD latexes for paints and carpet backing (IARC, 1999). It is also used as an intermediate in the production of a number of chemicals and is emitted in small quantities in engine exhaust and cigarette smoking (IARC, 1999).

BD epidemiologic research has focused primarily on workers in two industries in North America, the styrene-BD rubber (SBR) industry (Delzell *et al*, 1989, Delzell *et al*, 1995, Delzell *et al*, 1996, Delzell *et al*, 2001, Delzell, 2006, Graff *et al*, 2005, Macaluso *et al*, 1996, Sathiakumar *et al*, 1998, Sathiakumar *et al*, 2005) and the BD-monomer industry (Divine, 1990, Divine and Hartman, 1996, Divine and Hartman, 2001, Downs *et al*, 1987).

A cohort mortality study of 2800 male workers employed at least six months between 1943 and 1996 was carried out at a BD monomer production facility in Texas, USA (Divine and Hartman, 2001). Earlier analyses of mortality for this cohort found significant deficits for all causes of death (Divine, 1990, Divine *et al*, 1993, Divine and Hartman, 1996). Previous analyses also showed a significant increase for deaths from cancer of the LH system that was mainly due to an increase in deaths from lymphosarcoma, but also non-significant excesses of other LH

cancers (Hodgkin's disease, leukaemias, and multiple myeloma). A job-exposure matrix was developed, whereby each job was ranked with an exposure class code of 0-5 based on its potential for exposure to BD, in terms of frequency and intensity (Divine and Hartman, 1996). The most recent analysis followed the cohort through 1999 (Divine and Hartman, 2001). Again, a significant decrease in all-cause mortality was observed (SMR=0.89, 95%CI=0.84-0.94), with a deficit in the majority of non-malignant causes of death. Death from pneumonia approached significance (SMR=1.30, 95%CI=0.99-1.67). For all causes, mortality showed no relationship with length of employment, and there was no difference between those first employed before 1950 and those after. The study found non-significant excesses of NHL (SMR=1.48, 95%CI=0.89-2.31), HD (SMR=1.61, 95%CI=0.44-4.11), leukaemia (SMR=1.29, 95%CI=0.77-2.04) and myeloma (SMR=1.27, 95%CI=0.51-2.61) but a statistically significant excess of LH cancers (SMR=1.41, 95%CI=1.05-1.86), when considered as a whole. The risk of LH cancer decreased with length of employment, and was significantly increased in those first employed before 1950 (SMR=1.54, 95%CI=1.13-2.06), whereas there was a deficit in those first employed after 1950 (SMR=0.71, 95%CI=0.19-1.82). Individuals who had the potential for exposure to BD on a routine basis showed a significantly excess risk (SMR=1.66, 95%CI=1.15-2.32), especially those employed for less than five years (SMR=1.83, 95%CI=1.12-2.83). However, individuals with background exposures were at a non-significant excess risk (SMR=1.74, 95%CI=0.75-3.43), whereas the low-exposure group had a lower than expected risk (SMR=0.79, 95%CI=0.39-1.41). Survival analyses were performed using an estimate of cumulative BD exposure as a time-dependent explanatory variable defined as a combination of job-exposure class, calendar time, and length of time in job, and observed no relationship with exposure but a significant effect with age at hire.

In the most informative study mortality was examined in a cohort of 17924 men employed in the North American SBR industry (Delzell *et al*, 1989, Delzell *et al*, 1995, Delzell *et al*, 1996, Delzell *et al*, 2001, Delzell, 2006, Graff *et al*, 2005, Macaluso *et al*, 1996, Sathiakumar *et al*, 1998, Sathiakumar *et al*, 2005)**.** All subjects were men who had worked for at least one year between 1943 and 1991. Work histories were used to classify subjects according to employment in five major work areas and combined with exposure concentrations to develop a job-exposure matrix. Early analyses showed significantly reduced deaths from all causes and all cancers, and non-malignant causes of death (Sathiakumar *et al*, 1998). The workers were also shown to have an increased risk of leukaemia that was concentrated among hourly paid men with 20 or more years sine hire and ten or more years of employment in the industry (Delzell *et al*, 1996, Delzell *et al*, 2001, Macaluso *et al*, 1996, Sathiakumar *et al*, 1998). The risk was greater in subjects employed in polymerisation, maintenance labour and laboratories, three areas in styrene-BD operations and the polymerisation short-stopping agent dimethydithiocarbamate (DMDTC). In the most recent analysis a total of 162 deaths from LH cancers were observed (Delzell, 2006, Sathiakumar *et al*, 2005), resulting in an SMR of 1.06 (95%CI=0.90-1.23). No difference was seen between the follow-up periods of 1944-91 (SMR=1.06) and 1992-98 (SMR=1.04). For individual LH cancer non-significant excesses were observed for leukaemia (SMR=1.16, 95%CI=0.91-1.47) and HD (SMR=1.11, 95%CI=0.58-1.95), with an expected risk for NHL (SMR=1.00, 95%CI=0.75-1.30) and lower than expected risk for myeloma (SMR=0.95, 95%CI=0.62-1.40). In this analysis no significant excess was seen among "ever hourly" workers (SMR=1.09, 95%CI=0.91-1.28) but the excess remained in those with 20 or more years since hire and ten or more years of employment (SMR=1.30, 95%CI=1.04-1.60). A statistically significant risk was still seen in maintenance labour and laboratory workers. In addition, a significant dose-response relationship was observed, with statistically significant excess in the highest exposed group (Table 5) (Delzell, 2006).

Table 5 Relationship between risk of lymphohaematopoietic cancers and exposure to 1,3-butadiene

Butadiene exposure (ppm-years)	Observed/Expected	SMR	95%CI
0	18/27.7	0.65	0.39-1.03
>0 to <33.7	34/32.5	1.05	0.72-1.46
33.7 to <184.7	33/39.7	0.83	0.57-1.17
184.7 to <425.0	25/16.8	1.49	0.96-2.20
425.0+	28/13.8	2.03	1.35-2.93

SMR adjusted for age, race and calendar year

In a similar study of 12160 workers employed one or more years in styrene-BD polymer manufacturing plants in North America followed-up to 1982 no excess of LH cancers was observed (SMR=0.97, 95%CI=0.73-1.26) (Matanoski *et al*, 1990). In a nested case-control study of the LH cases (N=59), a non-significant OR of 2.09 (95%CI=0.85-5.17) was observed using an unmatched analysis (Santos-Burgoa *et al*, 1992). However, using a matched analysis resulted in a significant relationship (OR=2.30, 95%CI=1.13-4.71). Conditional logistic regression modelling was used to examine the association between LH cancers and chemicals and resulted in an OR of 2.42 (95%CI=1.12-5.23) for BD.

A small cohort study of 614 workers at a Texas petrochemical facility between 1948 and 1989, with a minimum of five years employment and potential for exposure to BD monomer were followed-up through 1998 (Tsai *et al*, 2001). All-cause and all-cancer mortality were significantly lower than expected. Only three deaths from LH cancers were observed (SMR=1.06, 95%CI=0.22-3.11).

A cohort mortality study among 364 men (part of large cohort of chemical workers) who were assigned to any of three BD production units located within several chemical plants were followed-up through 1990 (Ward *et al*, 1995, Ward *et al*, 1996). A total of 7 LH cancer deaths were observed (SMR=1.75, 95%CI=0.70-3.61), the majority of which (N=4) were from lymphosarcoma and reticulosarcoma (SMR=5.77, 95%CI=1.57-14.8).

3 ATTRIBUTABLE FRACTION ESTIMATION

3.1 GENERAL CONSIDERATIONS

Substances and Occupations

Table 6 shows the substances considered in the estimation of attributable fraction (AF) for LH cancers.

Table 6: Substances considered in the estimation of the attributable fraction for LH cancers

Agents, Mixture, Circumstance	AF calculation	Strength of evidence	Comments
Group 1: Carcinogenic to Humans			
Agents, groups of agents			
1,3-butadiene	Y	Suggestive	
Exposure circumstances			
None identified			
Group 2A: Probably Carcinogenic to Humans			
Agents & groups of agents			
None identified			
Exposure circumstances			
None identified			

Data Relevant to the Calculation of AF

The two data elements required are an estimate of relative risk (RR), and either (1) an estimate of the proportion of the population exposed (Pr(E)) from independent data for Great Britain, or (2) an estimate of the proportion of cases exposed (Pr(E|D)) from population based study data.

The RR chosen from a 'best study' source is described for each exposure, with justification of its suitability. Information on the 'best study' and independent data sources for the proportion of the population exposed are also summarised for each exposure in the appropriate section below. In the absence of more precise knowledge of cancer latency, for haematopoietic malignancies a latency of between 0 and 20 years has been assumed for all types of the cancer. Therefore it is assumed that exposure at any time between 1986 and 2005 (the Risk Exposure Period, REP) can result in a cancer being recorded in 2004 as a registration or in 2005 as an underlying cause of death. Although strictly speaking the REP for cancer registrations recorded in 2004, the year for which estimation has been carried out, would be 1985-2004, for simplification the years 1986 to 2005 have also been used, as for deaths, as the proportion exposed will not be affected. For an independent estimate of the proportion of the population exposed, numbers of workers ever exposed during this period are counted using a point estimate of exposed workers taken from the period. A point estimate is used that is as close as possible to the mid-point of the REP for estimating numbers ever exposed across the period (for which a linear change in employment levels is implicitly assumed). If this is from CAREX relating to 1990-93, an adjustment is made to take account of gross changes in employment levels which have occurred particularly in manufacturing industry and the service sector across the REP. Where the LFS is used 1991 is used. A turnover factor is applied to estimate numbers ever exposed during the REP, determined

mainly by the estimate of staff turnover per year during the period. For each exposure therefore, if an AF has been based on independent estimates of numbers exposed, the table of results includes the point estimate of numbers employed, the adjustment factor for CAREX if applicable, the staff turnover estimate, and the resulting estimate of numbers ever exposed during the REP. Other estimates used in the calculations that remain constant across exposures (unless otherwise stated) are given below:

- Number of years in REP = 20, with the proportion in the workplace ever exposed being set to one, i.e. all are assumed to be exposed, in the absence of more detailed information. Where sources other than CAREX are used for the point estimate of numbers exposed, such as the LFS or Census of Employment, a precise as possible definition of workers exposed is sought.
- Numbers ever of working age during the target REP = 23.0 million men, 23.1 million women. This is the denominator for the proportion of the population exposed, and is based on population estimates by age cohort in the target year.
- Total deaths from LH cancers, Great Britain, 2005 = 5284 for men aged 15-84 (4832 in England and Wales, 452 in Scotland), 3195 for women aged 15-79 (2891 in England and Wales, 304 in Scotland).
- Total registrations for LH cancers, Great Britain, 2004 = 10,865 for men aged 15-84 (9197 in England, 687 Wales, 981 in Scotland), 7225 for women aged 15-79 (5963 in England, 444 Wales, 818 in Scotland).

Attributable numbers are estimated by multiplying the AF by the total number of cancers in GB. Only cancers that could have been initiated during the risk exposure period were counted, taking normal retirement age into account. Therefore for solid tumour cancers, total deaths or registrations recorded at all adult ages (25+) are used to estimate attributable numbers, and for short latency cancers, deaths and registrations for ages 15-84 for men and 15-79 for women are used.

For each agent where data on worker numbers are only available for men and women combined (CAREX data), the assumed percentage of men is given in addition to the numbers exposed. The allocation to high and low, and occasionally negligible, exposure level categories, or division into separate exposure scenarios, is also included in these tables. Where no separate estimate of relative risk is available for the low exposure level category, an estimate is based on an average of the high/low ratios for cancer-exposure pairs for which data were available.

Full details of the derivation of the above factors and the methods of calculating AF are published separately. Unless otherwise stated, Levin's method is used for estimates using independent estimates of numbers exposed, and Miettinen's method is used for study based estimates. A summary of the methodology is given in the Statistical Appendix.

3.2 1,3-BUTADIENE

3.2.1 Risk estimate

Epidemiological studies of BD have focussed on workers in the North American styrene-BD rubber (SBR) and BD-monomer (BDM) industries. The SBR industry study only showed a 6% excess of LH neoplasms and a dose-response relationship; whereas the BDM industry studies showed a 40% excess but no dose-response relationship, although the risk was significantly raised in the highest group.

The risk estimate from the SBR industry study will be used in the AF calculation because the study is the largest, has the longer follow-up, covers the relevant exposure period and has adjusted the risk estimate (Delzell, 2006). The highest adjusted risk estimate from the study (SMR=2.03, 95%CI=1.35-2.93) has been selected for the AF calculation for the highly exposed using a precautionary approach. The risk estimate of 1.05 (95%CI=0.72-1.46) has been selected for the low exposure group.

3.2.2 Numbers exposed

BD is used very little in GB and the CAREX estimate gives only 2,871 workers potentially exposed (Table 7). To allocate the CAREX numbers between men and women, it has been assumed that those exposed in the manufacturing sectors (C-E) are in blue collar jobs, and those exposed service sector workers are in professional, associate professional and technical and personal service occupations (SOC major groups 2, 3 and 6).

Table 7: Numbers of workers exposed to 1,3-butadiene according to CAREX on 1990-1993

Industry		CAREX data 1990-1993		Exposure level
		Number exposed	**Number in industry**	
Manufacture of paper and paper products		2	119050	L
Manufacture of industrial chemicals		744	130000	L
Manufacture of other chemical products		254	175175	L
Petroleum refineries		118	18075	L
Manufacture of rubber products		318	53025	H
Manufacture of plastic products, nec		1212	136900	L
Education services		122	1455875	L
Research and scientific institutes		88	91100	L
Medical, dental, other health and veterinary services		13	1435675	L
Total		**2871**	**3,614,875**	
Main industry sector			**Male**	**Female**
Agriculture, hunting, forestry and fishing		0		
Mining/quarrying, electricity/gas/steam, manufacturing industry	High	318	242 (76%)	76 (24%)
	Low	2330	1771 (76%)	559 (24%)
Construction		0		
Service industries	High			
	Low	223	100 (45%)	123 (55%)

3.2.3 AF calculation

For lymphohaematopoietic cancers associated with occupational exposure to 1,3-butadiene the estimated total (male and female) attributable fraction is 0.00% (95%CI=0.00-0.01), which equates to 0 (95%CI=0-1) attributable deaths and 1 (95%CI= 0-2) attributable registration. The estimated AF for men is 0.00% (95% CI=0-0.01) resulting in 0 (95%CI=0-1) deaths and 0 (95%CI=0-1) attributable registrations; and for women the AF is 0.00% (95%CI=0-0.01), resulting in 0 (95%CI=0-0) deaths and 0 (95%CI=0-0) attributable registrations (Table 8).

Table 8 Summary results for occupational exposure to 1,3 Butadiene

				Data		Calculations				Attributable Fraction (Levins[8]) and Monte Carlo Confidence Interval			Attributable Deaths			Attributable Registrations		
	Risk Estimate Reference	Exposure	Main Industry Sector[1]	RR[2]	Ne[3]	Carex adj[4]	TO[5]	NeREP[6]	PrE[7]	AF	LL	UL	AN	LL	UL	AR	LL	UL
Men	Delzell, 2006	H	C-E	2.03	242	1	0.09	621	0.0000	0.0000	0.0000	0.0001	0	0	0	0	0	1
		H	All		242			621	0.0000	0.0000	0.0000	0.0001	0	0	0	0	0	1
	Delzell, 2006	L	C-E	1.05	1771	1	0.09	4549	0.0002	0.0000	0.0000	0.0001	0	0	1	0	0	1
		L	G-Q	1.05	100	1	0.11	297	0.0000	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	All		1871			4847	0.0002	0.0000	0.0000	0.0001	0	0	1	0	0	1
		All	All		2113			5468	0.0002	0.0000	0.0000	0.0001	0	0	1	0	0	1
Women	Delzell, 2006	H	C-E	2.03	76	1	0.14	281	0.0000	0.0000	0.0000	0.0000	0	0	0	0	0	0
		H	All		76			281	0.0000	0.0000	0.0000	0.0000	0	0	0	0	0	0
	Delzell, 2006	L	C-E	1.05	559	1	0.14	2060	0.0001	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	G-Q	1.05	123	1	0.15	476	0.0000	0.0000	0.0000	0.0000	0	0	0	0	0	0
		L	All		682			2536	0.0001	0.0000	0.0000	0.0001	0	0	0	0	0	0
		All	All		758			2817	0.0001	0.0000	0.0000	0.0001	0	0	0	0	0	0

1. Specific scenario or main industry code (Table A1)
2. Relative risks selected from the best study
3. Numbers exposed, allocated to men/women
4. CAREX adjustment factor to mid-REP (Table A1)
5. Staff turnover (TO, Table A1)
6. Number ever exposed during the REP (Statistical Appendix equation 3)
7. Proportion of the population exposed (Pr(E), Statistical Appendix equation 4)
8. Statistical Appendix equation 1

4 OVERALL ATTRIBUTABLE FRACTION

4.1 EXPOSURE MAP

No exposure map is given since there is only one exposure considered.

4.2 SUMMARY OF RESULTS

The results are summarised in Tables 9 and 10.

Table 9: Summary of relative risks used to calculate AF

Agent	Exposure	RR	LL	UL
1,3-Butadiene	H	2.03	1.35	2.93
1,3-Butadiene	L	1.05	0.72	1.46

Table 10: Results

Agent	Numbers of Men Ever Exposed	Numbers of Women Ever Exposed	Proportion of Men Ever Exposed	Proportion of Women Ever Exposed	AF Men	MCLL Men	MCUL Men	AF Women	MCLL Women	MCUL Women	Attributable Deaths (Men)	Attributable Deaths (Women)	Attributable Registrations (Men)	Attributable Registrations (Women)
1,3-Butadiene	5468	2817	0.0002	0.0001	0.0000	0.0000	0.0008	0.0000	0.0000	0.0004	0	0	0	0

4.3 EXPOSURES BY INDUSTRY/JOB

As the numbers of deaths and registration from lymphohaematopoietic cancers are less than 1, tables by industry sector are not given.

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6. STATISTICAL APPENDIX

Formulae used in the estimation of AF

Levin's equation

$$AF = Pr(E)*(RR-1)/\{1+Pr(E)*(RR-1)\} \quad (1)$$

where RR = relative risk, Pr(E) = proportion of the population exposed

A common denominator is used across exposure levels and industries for each exposure

Miettinen's equation

$$AF = Pr(E|D)*(RR-1)/RR \quad (2)$$

where Pr(E|D) = proportion of cases exposed (E = exposed, D = case)

Turnover equation to estimate numbers ever employed during the REP

$$N_{e(REP)} = \sum_{i=a}^{i=b} l_{(adj15)i} * n_0/(R-15)\} + \sum_{k=0}^{k=(age(u)-age(1))} \sum_{j=c+k}^{j=d+k} \{l_{(adj15)j} * n_0 * TO /(age(u)-age(l)+1)\} \quad (3)$$

where $N_{e(REP)}$ = numbers ever employed in the REP

n_0 = numbers employed in the exposed job/industry at a mid-point in the REP

TO = staff turnover per year

R = retirement age (65 for men, 60 for women)

$l_{(adj15)i}$ = the proportion of survivors to age i of those alive at age 15 (from GB life tables)

a to b = age range achieved by the original cohort members by the target year (2005) (e.g. 35 to 84 (men, 79 women) for the short latency REP)

c to d = age range achieved by the turnover recruited cohort members by the target year (15 to 34 for the short latency REP)

age(u) and age(l) = upper and lower recruitment age limits (24 and 15)

The derivation and assumptions underlying this formula are described in the methodology technical report, available on the HSE website. The equation can be represented as a single factor acting as a multiplier for n_0, calculated by setting n_0 to 1 in the above equation, so that the factor varies only with TO see Table A1 below.

Equation to estimate the proportion of the population exposed

$$Pr(E) = N_{e(REP)} / N_{p(REP)} \quad (4)$$

where $N_{p(REP)}$ = numbers ever of working age during the REP from population estimates for the relevant age cohorts in the target year

Equation for combining AFs where exposed populations overlap but are independent and risk estimates are assumed to be multiplicative:

$$AF_{overall} = 1- \Pi_k(1-AF_k) \text{ for the k exposures in the set} \quad (5)$$

Table A1 Employment level adjustment and turnover factors used in the calculation of AF

		Main Industry Sector	Adjustment factor for change in employment levels*	Turnover per year
Men	A-B	Agriculture, hunting and forestry; fishing	1	7%
	C-E	Mining and quarrying, electricity, gas and water; manufacturing industry	1.4	9%
	F	Construction	1	12%
	G-Q	Service industries	0.9	11%
		Total	1	10%
Women	A-B	Agriculture, hunting and forestry; fishing	0.75	10%
	C-E	Mining and quarrying, electricity, gas and water; manufacturing industry	1.5	14%
	F	Construction	0.67	15%
	G-Q	Service industries	0.8	15%
		Total	0.9	14%

* Applied to CAREX data for the solid tumour REP only. Exposed numbers are obtained for a mid-point year in the REP where national employment data sources have been used (the LFS or CoE).

HSE

Health and Safety Executive

The burden of occupational cancer in Great Britain

Lymphohaematopoietic cancer

The aim of this project was to produce an updated estimate of the current burden of cancer for Great Britain resulting from occupational exposure to carcinogenic agents or exposure circumstances. The primary measure of the burden of cancer was the attributable fraction (AF) being the proportion of cases that would not have occurred in the absence of exposure; and the AF was used to estimate the number of attributable deaths and registrations. The study involved obtaining data on the risk of the cancer due to the exposure of interest, taking into account confounding factors and overlapping exposures, as well as the proportion of the target population exposed over the relevant exposure period. Only carcinogenic agents, or exposure circumstances, classified by the International Agency for Research on Cancer (IARC) as definite (Group 1) or probable (Group 2A) human carcinogens were considered. Here, we present estimates for lymphohaematopoietic cancers that have been derived using incidence data for calendar year 2004, and mortality data for calendar year 2005.

The estimated total (male and female) AF, deaths and registrations for lymphohaematopoietic cancers associated with overall occupational exposure and to 1,3-butadiene is 0.00% (95%Confidence Interval (CI)=0.00-0.01), which equates to 0 (95%CI=0-1) attributable deaths and 1 (95%CI=0-2) attributable registration.

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