

Department for Environment, Food and Rural Affairs,
Scottish Executive, National Assembly for Wales,
Department of the Environment in Northern Ireland

Expert Panel on
Air Quality Standards

**Second Report
on 1,3-Butadiene**

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A Review of the United Kingdom Air Quality Standard for 1,3-Butadiene

TERMS OF REFERENCE

The Expert Panel on Air Quality Standards (EPAQS) was established in 1991. The terms of reference of the Panel are:

“**To advise** the Secretary of State for the Environment, Scottish Ministers, National Assembly for Wales and the Department of the Environment in Northern Ireland, as required, on non-occupational ambient air quality standards, with particular reference to the levels of airborne pollutants at which no or minimal effects on human health are likely to occur;

- i. taking account of the best available evidence
 - of the effects of air pollution on human health and
 - of progressive development of the air quality monitoring network; but
- ii. without reference to the practicality of abatement or mitigation measures, the economic costs and economic benefits of pollution control measures or other factors pertinent to the management rather than the assessment of risk;

to identify gaps in the knowledge needed for standard setting and suggest potential priority areas for future research;

to advise on other aspects of air quality and air pollution referred to it;

for the purpose of informing the development of policy on the improvement of air quality and increasing public knowledge and understanding of air quality issues.”

This report is one in a series that deals with pollutants suggested to the Panel by the Department for Environment, Food and Rural Affairs, the Scottish Executive, National Assembly for Wales and Department of the Environment in Northern Ireland (Devolved Administrations). Reports consider individual pollutants except where the Panel decide to deal with more than one because of the relationships between pollutants.

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Introduction

1. 1,3-Butadiene is a chemical used mainly in the synthetic rubber industry, but which is also found in some liquid petroleum gases. Its presence in low concentration in the ambient atmosphere derives mostly from its production in combustion processes, particularly of petrol and diesel, and from emissions escaping from industrial sites. It is also produced by tobacco smoking, which is an important indoor source.
2. In 1994 the Panel considered the rather scanty data then available on the adverse effects of 1,3-butadiene on human health. We concluded that it was a genotoxic human carcinogen (that is, it is able to cause cancer by damaging genetic material in cells), and recommended an Air Quality Standard of 1 ppb*, measured as a running annual average.
3. In making this recommendation, the Panel recognised the paucity both of the human epidemiological evidence and also of the data on UK ambient concentrations of 1,3-butadiene. We therefore proposed that we should review the evidence within five years. In this report we consider whether the more recent evidence justifies any change to our earlier recommendation.

*1ppb is one part in one thousand million (1 in 10⁹) by volume. 1 ppb of 1,3-butadiene is equivalent to 2.25µg/m³ at 20°C and 1013 millibars or to 2.21µg/m³ at 25°C and 1013 millibars.

Sources of Exposure to 1,3-Butadiene

4. 1,3-Butadiene in air derives solely from human activity. It is an important industrial chemical, being used particularly in the manufacture of synthetic rubber for tyres. Some commercial liquid petroleum gases also contain up to 8 percent by volume. Fugitive emissions from the manufacture and use of 1,3-butadiene in the chemical industry are small and the majority of 1,3-butadiene in ambient air comes from combustion sources. The dominant combustion sources are associated with road transport, particularly petrol-engined vehicles but with a small contribution from diesel-fuelled vehicles. 1,3-Butadiene is also present in tobacco smoke, which is therefore a major source of indoor exposure.

5. There is little or no 1,3-butadiene in unburnt diesel or petrol, the emissions in the exhaust gases being produced by the combustion process itself. 1,3-Butadiene is therefore not present in road transport evaporative emissions. If increasing traffic and vehicle usage were the only factors influencing emissions, then 1,3-butadiene emissions would have increased in recent years. Furthermore, the chemical substances in petrol from which 1,3-butadiene is derived, higher olefins, have been present in increasing proportion in petrol over the last decade, and this too would have tended to increase the amounts of 1,3-butadiene released into the atmosphere. However, 1,3-butadiene is removed efficiently by catalytic converters. The introduction of catalytic converters in 1991 has had a significant impact on the emissions from the road transport sector, see Table 1 and Figure 1, causing a reduction of 54% from 1990 to 1999. Emissions from other significant combustion sources, such as other transportation and machinery, have not changed significantly in recent years.

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National Atmospheric Emissions Inventory. UK Emissions of Air Pollutants 1970–1999, Department for Environment, Food and Rural Affairs, November 2001, ISBN 1-85580-031-4

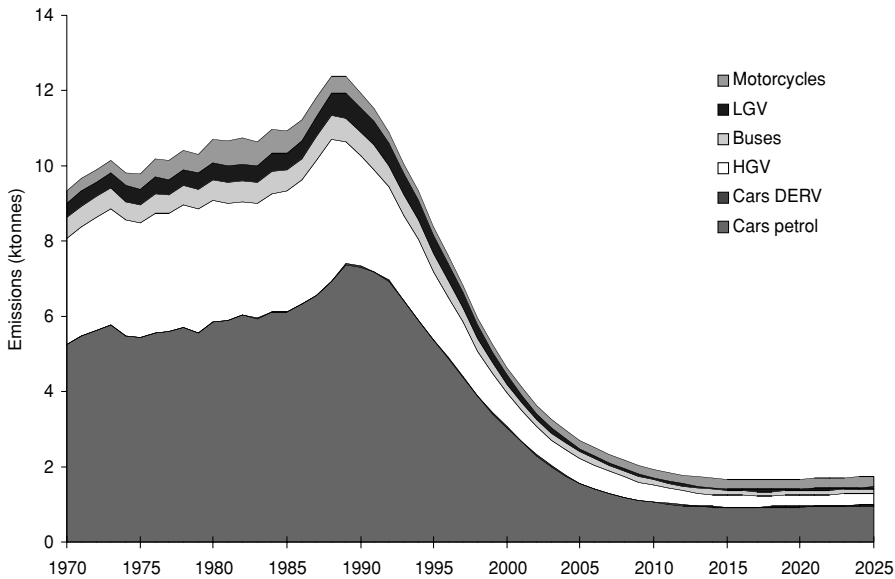
Table 1. Estimated UK Emissions of 1,3-butadiene 1990–1999 (ktonnes) (Source: National Atmospheric Emissions Inventory, 2001)*

BY UNECE CATEGORY**	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	% of 1998 total
Road Transport	11.91	11.53	10.89	10.03	9.34	8.37	7.62	6.81	5.95	5.26	85%
<i>Petrol</i>	8.31	8.12	7.77	7.14	6.58	6.00	5.49	4.90	4.34	3.84	
<i>Derv</i>	3.61	3.42	3.12	2.89	2.76	2.37	2.13	1.92	1.61	1.42	
Off Road Transport/Machinery	0.45	0.48	0.50	0.50	0.50	0.49	0.49	0.49	0.50	0.49	8%
Production Processes	0.75	0.66	0.69	0.66	0.60	0.63	0.43	0.31	0.22	0.37	6%
Other Transport	0.09	0.09	0.10	0.10	0.10	0.11	0.11	0.12	0.12		2%
Extraction/Distribution of Fossil Fuels	0.16	0.15	0.14	0.12	0.11	0.09	0.08	0.07	0.06	0.03	0%
Combustion in Industry	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.00	0%
Waste Treatment and Disposal	0.02	0.02	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.01	0%
TOTAL	12.79	12.82	12.37	11.56	10.73	9.84	8.79	7.80	6.93	6.37	100%

* Emissions of hydrocarbons have considerable uncertainty and speciated hydrocarbons have even greater uncertainty. Inventories are based on a limited set of measurements and hence the estimates of emissions are uncertain.

** There are no significant emissions of 1,3-butadiene from combustion in energy production or from combustion at commercial/institutional or residential premises.

Figure 1. Time series of estimated 1,3-butadiene emissions from transport 1970–1998 projected to 2025 (ktonnes; Source: National Atmospheric Emissions Inventory, 2001)[†]



[†]There is a consultation out (December 2001) on emission factors and the figure may change as a result.

Measurement and Monitoring of 1,3-Butadiene

Long-Term Measurements

6. Between 1994, when the first EPAQS report on 1,3-butadiene was published, and 1997 the extent and coverage of automatic 1,3-butadiene monitoring grew appreciably. Automatic monitoring sites were added in a rural location (Harwell, Oxfordshire), an urban kerbside location (Marylebone Road, London) and urban background locations (Leeds, Southampton and Liverpool). The analytical method used in the UK automatic hydrocarbon monitoring network since it began operation in 1992, has been gas chromatography (Photochemical Oxidants Review Group, 1997). At the beginning of 2001, the automatic hydrocarbon monitoring network was reduced to four sites at London Marylebone Road, Cardiff, Edinburgh and Harwell. The intention of this was to allow expansion of the hydrocarbon network during 2001 and 2002 to around 30–35 sites, using a simpler, more cost effective technique to ensure compliance with the European Commission Daughter Directive on Benzene. Monitoring under the Directive should comply with a reference method, in which air is drawn through an adsorbent tube (sampling method) and then analysed using a gas chromatograph (analytical method). Gas chromatography, BTEX[‡] analysers and manual pumped tube methodologies all comply with this reference method. The feasibility of using manual pumped tubes and BTEX-type analysers to measure 1,3-butadiene is currently being investigated.

7. Monitoring data for 1,3-butadiene show variations from hour-to-hour, from day-to-day and with time of year. At urban background and kerbside sites, the daily cycle of traffic movements appears to be the main determining influence on the observed diurnal variations in 1,3-butadiene concentrations (Derwent et al, 2001; Figure 2). 1,3-Butadiene concentrations are generally lower on Saturdays and Sundays, for the same reason. Daily mean 1,3-butadiene concentrations also show seasonal variations with higher concentrations in wintertime and lower concentrations in summertime, driven by the generally lower windspeeds and poorer dispersion conditions found in urban areas during wintertime. Figure 3 presents 90-day running mean concentrations of 1,3-

[‡]BTEX – benzene, toluene, ethylbenzene and xylene

butadiene at a kerbside site (Marylebone Road, London), at an urban background site (University College, London) and at a rural site (Harwell, Oxfordshire) over the period 1994–2000. Wintertime maxima are clearly evident during 1995/96, 1996/97 and 1997/98. A general decline in concentrations with time is also apparent in all the observed time series. These declines are driven by the steadily decreasing usage of those petrol-engined vehicles that do not have catalytic converters.

8. Episodes of exceptionally high concentrations of 1,3-butadiene have been reported at the Middlesbrough site located in an industrial conurbation on Teesside. In the afternoon of 31st July 1995, hourly concentrations rose to a peak of 80 ppb and remained high until the early hours of the following morning. The episode persisted through to the afternoon of the 2nd August. It came to light that a marine tanker had vented the vestiges of its 1,3-butadiene cargo after making a delivery. Further episodes occurred at Middlesbrough during 1998 when single hourly peaks reached 30 and 60 ppb, but the origins of these peaks are not known. Similar hourly peaks in 1,3-butadiene have been detected at Cardiff and Liverpool. As these episodes were unassociated with other pollutants, it is likely that the sources were industrial in nature.

9. Motor vehicle emissions of 1,3-butadiene are projected to decrease through to 2005 and beyond (Figure 1), as three-way catalyst equipped vehicles steadily replace older petrol-engine vehicles which are the dominant source of 1,3-butadiene in UK urban areas. On the basis of the available measurements in the late 1990s, and accepting the projected trends in emissions, it is likely that the current Air Quality Standard will be met at all UK urban background and kerbside locations during the period up to 2003 with existing policy measures.

Short-Term and Indoor Measurements

10. In a study in Birmingham, airborne concentrations of 1,3-butadiene have been measured in a range of both indoor and outdoor microenvironments within which members of the public are liable to spend substantial amounts of time (Kim et al, 2001). Mean concentrations varied from 0.07 ppb within a non-smoking University building to 3.52 ppb measured within cars on the road (Table 3). Lower concentrations were observed generally within non-smoking indoor environments whilst there were clear elevations in concentrations within road vehicles, adjacent to road traffic and within environments where smoking took place.

11. A comparison of outdoor and indoor concentrations of 1,3-butadiene in houses showed that, in eleven of the twelve homes studied, indoor concentrations exceeded those out of doors. In the absence of indoor sources, indoor concentrations would be expected to be slightly lower than those out of doors, whilst sources indoors, especially tobacco smoking, can impact heavily

upon indoor concentrations. When comparison was made between six smoking and six non-smoking homes, the mean concentrations in the smoking homes exceeded the mean in the non-smoking homes (Table 3; Kim et al, 2001).

12. A comparison of 1,3-butadiene personal exposure was also made between subjects considered to be heavily exposed to vehicle exhaust (e.g. whilst travelling to and from work) and those with low exposure to vehicle exhaust. Their mean exposures over 2 hours were 0.5 ppb and 0.3 ppb, respectively. The researchers calculated that an average exposure of individuals would be around 20 µg^s in 24 hours and a maximum might be as much as 100 µg over 24 hours (Kim et al, in press).

13. It was concluded that environmental tobacco smoke is an appreciable source of 1,3-butadiene in smoking environments based on the facts that concentrations of 1,3-butadiene in public houses (a smoking environment) were higher than those at heavily trafficked roadside locations and in buses and trains, and that concentrations of 1,3-butadiene were higher in smoking than in non-smoking homes. Furthermore, there were significant correlations in this study between concentrations of 3-ethenylpyridine, a marker of environmental tobacco smoke, and 1,3-butadiene.

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^s1 µg is 1 millionth of a gram.

Table 2. Annual mean concentrations (1993–2000) of 1,3-butadiene at a number of locations throughout the UK in ppb

Site	1993	1994	1995	1996	1997	1998	1999	2000
Urban kerbside locations in London								
Exhibition Road	0.86*	**						
Marylebone Road						1.04	0.83	0.72
Urban background locations								
Belfast	0.65	0.18	0.17	0.16	0.16	0.10	0.11	0.08
Birmingham	0.41	0.22	0.23	0.22	0.21	0.15	0.15	0.13
Bristol		0.22	0.24	0.23	0.22	0.16	0.12	0.12
Cardiff	0.6	0.27	0.23	0.22	0.24	0.20	0.16	0.13
Edinburgh	0.24	0.11	0.13	0.11	0.12	0.09	0.08	0.06
Leeds			0.21	0.21	0.24	0.18	0.14	0.11
Liverpool			0.35	0.21	0.19	0.17	0.14	0.13
London Bloomsbury	0.32	0.38	0.35	0.38	0.38	0.23	0.23	0.17
London, Eltham	0.21	0.24	0.24	0.21	0.23	0.17	0.15	0.12
Middlesbrough	0.45	0.26	0.27	0.18	0.17	0.12	0.13	0.10
Southampton			0.5	0.36	0.34	0.25	0.23	0.23
Rural location								
Harwell			0.17	0.07	0.07	0.05	0.05	0.04

* July 1991–July 1992

** Missing values indicate site not operating or data capture was below 75% of the year.

Table 3. Concentrations (ppb) of 1,3-butadiene (2-hour average) measured in various microenvironments*

Microenvironments	n	Mean	Median	SD	Min	Max
Cars	35	3.52	2.87	2.05	0.57	8.79
Buses	18	0.72	0.57	0.40	0.17	1.66
Trains	18	0.43	0.32	0.28	0.12	1.14
Roadside	12	0.77	0.85	0.37	0.17	1.43
Coach Stations	12	0.40	0.32	0.32	0.12	1.26
Train Stations	12	0.96	0.71	0.72	0.36	3.02
Offices	12	0.13	0.12	0.08	0.07	0.32
Department Stores	8	0.27	0.20	0.18	0.11	0.61
Restaurants	6	0.66	0.57	0.33	0.44	1.31
Public Houses	6	1.28	1.05	0.88	0.48	2.87
Libraries	6	0.15	0.14	0.08	0.06	0.27
Laboratories	8	0.07	0.07	0.06	0.02	0.19
Cinemas	6	0.27	0.24	0.13	0.14	0.47
Home – Indoor	64	0.47	0.22	0.81	0.02	4.70
Home – Outdoor	64	0.12	0.11	0.08	0.02	0.40
Home – Smoking	32	0.76	0.31	1.11	0.13	4.80
Home – Non-smoking	32	0.22	0.18	0.13	0.04	0.49

* Kim et al, 2001

Figure 2. Diurnal concentrations of 1,3-butadiene at kerbside (London Marylebone Road; 1997–2000), urban background (London UCL; 1993–2000) and rural (Harwell; 1995–2000) locations

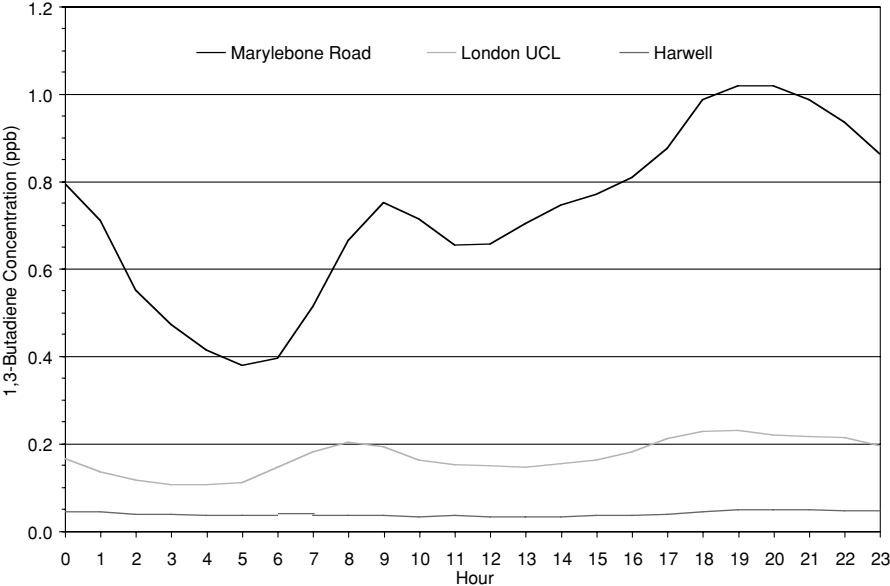
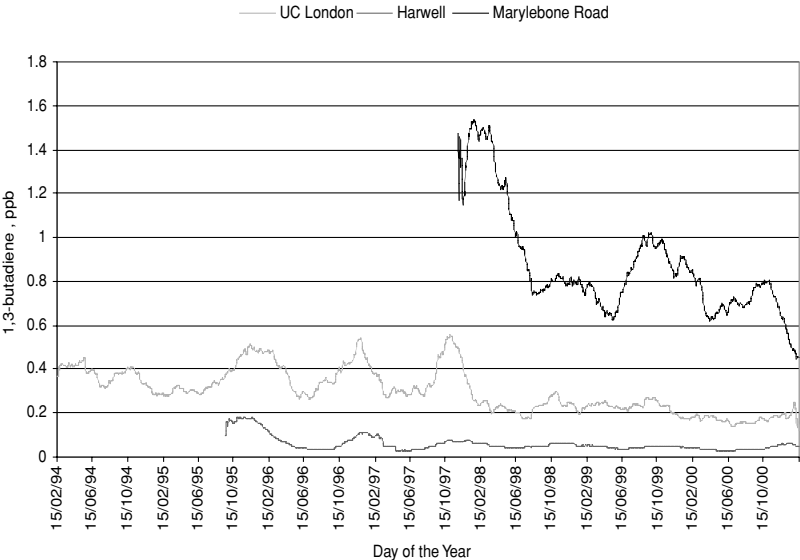


Figure 3. Ninety day running mean concentrations of 1,3-butadiene at kerbside (London Marylebone Road; 1997–2000), urban background (London UCL; 1993–2000) and rural (Harwell; 1995–2000) locations



The Effects of 1,3-Butadiene on Human Health

14. Evidence of the hazard of 1,3-butadiene comes from two main sources: firstly, studies of human populations exposed in the workplace and, secondly, investigations carried out in laboratory rats, mice and monkeys. The Panel put greatest weight on data derived directly from human studies. However, the animal data are consistent in showing 1,3-butadiene to be a potent carcinogen and to act, through other chemicals to which it is converted in the body, on the genetic material of cells (i.e. it is a genotoxic carcinogen).

15. The Panel recognises that extrapolation from the results of animal experiments to effects in man is difficult and involves uncertainties. There are also difficulties in extrapolating from studies of workers exposed in the past to the general population of today. The levels to which workers might be exposed are very much higher than those in ambient air; for example, a worker could have been exposed intermittently to levels of up to 10,000 ppb (the United Kingdom workplace maximum exposure limit) compared with an hourly average of about 30–80 ppb during a severe short-term atmospheric pollution episode in a city. There is no currently feasible study in man that will show a measurable effect on health of the relatively low levels occurring in the general atmosphere.

16. Data on the absorption, distribution and elimination of 1,3-butadiene in humans are limited, but there is some information on its metabolism (that is biological and/or chemical breakdown). Studies in animals and in human tissues have established that 1,3-butadiene is converted to several reactive chemical intermediates which can react with proteins such as haemoglobin in red blood cells (Figure 4). Analysis both in animals (Health Effects Institute, 2000) and in occupationally exposed humans (Perez et al, 1997; Hayes et al, 2000; Albertini et al, 2001; Van Sittert et al, 2000) has shown the presence of characteristic products of reaction (adducts) between haemoglobin and chemicals derived from 1,3-butadiene. Studies have also shown increased levels of the same haemoglobin adducts in smokers (Begemann et al, 2001). Similarly, adducts with the genetic material of cells (DNA) have also been demonstrated in animals (Jackson et al, 2000; Health Effects Institute, 2000; Boogaard et al, 2001) and in man (Zhao et al, 2000) exposed to 1,3-butadiene. Further studies in animals

(Jackson et al, 2000; Health Effects Institute, 2000) and man (Ward et al, 1996a; Ward et al, 1994; Ward et al, 2001; Sram et al, 1998) have shown that exposure may be associated with gene mutations and chromosomal damage. Several negative studies have also been reported in exposed workers (Albertini et al, 2001; Hayes et al, 2000; Hayes et al, 2001; Jackson et al, 2000; Sorsa et al, 1994), but it is the view of the Panel that the balance of evidence remains consistent with 1,3-butadiene being genotoxic in humans.

17. Short-term human exposures to very high concentrations (several million ppb) of 1,3-butadiene, including through experiments on volunteers conducted in the 1940s before its carcinogenic potential was suspected, have caused irritation of the eyes, nose, throat and skin (e.g. Wilson et al, 1948). Investigations of workers in Eastern Europe exposed occupationally to high concentrations of 1,3-butadiene have shown them to have been at risk of a variety of disorders, including diseases of the blood and nervous system (International Agency for Research on Cancer, 1999). However, these studies did not take account of other possible harmful factors to which workers were also exposed. The general public in the United Kingdom experience very much lower concentrations (see Tables 2 & 3).

18. As discussed below, the potential effect of long-term exposure that is of most concern is the induction of cancers of the lymphoid system and blood-forming tissues, lymphomas and leukaemias. An increase in the risks of developing these types of cancers was first reported in groups of workers in the United States from the 1,3-butadiene manufacturing industry and from the synthetic (styrene-butadiene) rubber manufacturing industry (McMichael et al, 1976). Subsequent studies in which rats and mice were exposed to high inhaled concentrations of 1,3-butadiene for all or most of their lifetimes have shown similar effects, as well as an increased mortality from other types of malignant disease (International Agency for Research on Cancer, 1999). Species differences in susceptibility to the development of malignant disease have been demonstrated. Differences in the rates of 1,3-butadiene metabolism, the accumulation of specific metabolites in blood and tissues and the genotoxic potential of the metabolites appear to be the primary factors responsible for these inter-species differences (Jackson et al, 2000).

19. Various laboratory studies examining the mode of action of 1,3-butadiene and some of its metabolites have been carried out (International Agency for Research on Cancer, 1999; Jackson et al, 2000). 1,3-Butadiene damages the genetic material of cells in various ways and these genotoxic effects indicate that it may cause malignant disease after very small exposures. The Panel has taken the view that, while this could be strictly interpreted as meaning that there is no safe level to which people can be exposed, a more realistic view is that the risks become progressively smaller as the cumulative exposure of an individual is reduced and that there is a level at which increased risks attributable to 1,3-butadiene are exceedingly small and unlikely to be detectable by any practicable method.

20. The current Air Quality Standard for 1,3-butadiene, 1 ppb measured as a rolling annual average, was recommended by EPAQS in its 1994 report. This recommendation was based on epidemiological studies of workforces exposed to relatively high concentrations of the compound in its manufacture or in the production of synthetic rubber. Some of these studies have suggested that cancers of the tissues that form blood cells (lymphatic and haematopoietic cancers – in particular leukaemia and lymphoma) occur more frequently than normal in such workers. At the time the standard was set, the published epidemiological reports provided no quantitative data on the levels of butadiene to which cancer cases had been exposed. However, given that historical exposures were almost certainly higher than those which have been recorded in the same industries more recently, the findings of the epidemiological investigations indicated that any excess incidence of leukaemia or lymphoma from occupational exposures below 1000 ppb was likely to be so small as to be undetectable. This figure was therefore taken as the starting point of the Panel's calculations.

21. Since the standard was set, further epidemiological research on the synthetic rubber industry has been carried out, incorporating quantitative estimates of exposure for individual workers. In addition, two earlier studies of butadiene manufacturers have been extended, and an analysis of mortality has been published for a third population of butadiene manufacturers not previously investigated. All of this work has been conducted in the United States and Canada.

22. Most of the new research on the synthetic rubber industry focuses on 17,649 men employed for a year or longer during 1943–91 at eight North American factories (Delzell et al, 1995; Delzell et al, 1996; Delzell et al, 2001; Macaluso et al, 1996; Sathiakumar et al, 1998), and the results subsume those of several earlier studies (Meinhardt et al, 1982; Matanoski et al 1990; Santos-Burgoa et al, 1992). During follow-up to 1st January 1992 (an average of 25 years follow-up per person) mortality patterns were unremarkable apart from an excess of leukaemia (48 deaths observed where 37 would have been expected from rates in the general population; Delzell et al, 1996; Sathiakumar et al, 1998).

23. Dimethyl dithiocarbamate (DMDTC), which has often been used in industrial processes involving 1,3-butadiene, has been proposed as a potential confounding factor in the consideration of 1,3-butadiene carcinogenesis (Irons and Pyatt, 1998). DMDTC has the potential to modify metabolic and cellular processes that are relevant to butadiene carcinogenesis. However, the International Agency for Research on Cancer (IARC) recently suggested that there was no evidence that dithiocarbamates caused leukaemia and that such an interaction, if demonstrated, would not exclude a contribution of butadiene to the carcinogenic process (International Agency for Research on Cancer, 1999). Analyses that have taken account of both exposures give some support to a role of DMDTC, but do not exclude an independent effect of butadiene at high cumulative exposures (Delzell et al, 2001).

24. At six of the plants investigated by Delzell and colleagues, it was possible to estimate each subject's exposure to butadiene from the jobs and areas in which he had worked at different times, and there was evidence that the risk of leukaemia increased with cumulative exposure to the compound (Macaluso et al, 1996). Subsequently, the exposure estimates were revised in the light of new information (Delzell et al, 2001), and in this most recent analysis of the study, leukaemia was again associated with higher cumulative exposures to 1,3-butadiene. Unadjusted for the effects of styrene or DMDTC, the results showed a trend of increased risk with increased exposures, a pattern that was less clear after adjustment for these co-exposures. In all models, however, the estimated relative risk in the lowest exposure group (those with exposures below 38,700 ppb-years, equivalent to an average exposure over a 40 year working life of about 1000 ppb) was elevated only slightly compared with unexposed workers, and was not statistically significant (Figure 5; relative risk 1.1, confidence interval 0.4–3.0). This is strong new evidence in support of our judgement in 1994, that excess risks would not be detectable in studies based on people exposed occupationally at concentrations below 1000 ppb.

25. To explore the possibility that the risk from a given cumulative exposure might vary according to the intensity of exposures experienced, the authors broke down subjects' cumulative exposures according to whether they arose from intensities above or below 100,000 ppb. The association of leukaemia with cumulative exposure was stronger when the intensity of exposure exceeded 100,000 ppb. This suggests that extrapolation from observations in industrial populations will if anything tend to exaggerate the risks associated with lower intensities of exposure in the general environment.

26. Another new investigation of the synthetic rubber industry was based on much the same population of North American workers, but used a different method to estimate their exposures to butadiene (Matanoski et al, 1997). This case-control study suggested that leukaemia risk might be increased from butadiene exposures as low as 1000 ppb. However, exposure was only analysed as a continuous variable, and the assumptions about the mathematical relation of risk to exposure that were inherent in the statistical analysis may not have been justified.

27. In the butadiene manufacturing industry, two reports by Divine and Hartman (1996; in press) update earlier findings of Downs et al (1987) and Divine (1990). The new results are similar to those published previously, with an increased risk of non-Hodgkin's lymphoma restricted to short-term workers first employed before 1950, and no clear elevation of mortality from leukaemia. A third report (Tsai et al, 2001) describes extended follow-up of a population originally studied by Cowles et al (1994). No excess of lymphoma or leukaemia was observed, but the study was small and fewer than three cases were expected. A new investigation by Ward found a small excess of non-Hodgkin's lymphoma, the four cases identified all having worked with butadiene before 1953 (Ward et

al, 1995; Ward et al, 1996b). None of the studies in the butadiene manufacturing industry has involved quantitative estimates of individual exposures. An examination of the literature did not find any published epidemiological studies that have examined the risks of cancer from exposure to butadiene in non-occupational settings.

28. Interpretation of the epidemiological findings from workforces exposed to butadiene is not straightforward. Increased mortality from non-Hodgkin's lymphoma has been observed in two of the three studies of butadiene manufacturers (Divine and Hartman, 2001; Ward et al, 1995; Ward et al, 1996b), but in the larger of these investigations the excess was restricted to short-term employees (Divine and Hartman, 2001). Furthermore, no similar excess was apparent in the large study of the synthetic rubber industry (Delzell et al, 2001). This suggests that butadiene may not have been responsible for the elevated death rates from lymphoma.

29. Among workers producing synthetic rubber, the risk of leukaemia was elevated, and increased with cumulative exposure to butadiene (Delzell et al, 2001). However, no corresponding excess of leukaemia was found in butadiene manufacturers (Divine and Hartman, 2001; Tsai et al, 2001; Ward et al, 1995; Ward et al, 1996b). This apparent discrepancy could be explained if exposures in butadiene manufacture have been lower than in the rubber industry; if the risk of leukaemia associated with butadiene is modified by concomitant exposure to other chemicals that occur in the rubber industry but not in butadiene manufacture; or if the risk in the rubber industry is not attributable to butadiene but to some other chemical (a so-called confounding effect). Confounding by styrene, the other major chemical used in the production of synthetic rubber, seems unlikely since no excess of leukaemia has been found among workers with much higher exposures to styrene in the glass-reinforced plastics industry (Coggon, 1994). Moreover, in the studies of rubber manufacturers, associations between leukaemia and styrene have disappeared after statistical adjustment for exposure to butadiene, whereas the association of leukaemia with butadiene persisted when exposure to styrene was taken into account (Delzell et al, 2001).

30. For the purposes of setting an Air Quality Standard, the Panel sees no justification for altering its earlier view that butadiene is likely to be a genotoxic carcinogen in humans. We have concluded that the most appropriate basis for a standard is the large study of synthetic rubber workers by Delzell et al (2001). This study, which analysed risk for separate categories of cumulative exposure without *a priori* assumptions about the form of the exposure-response relationship, supports the view taken previously by the Panel that any excess risk of leukaemia or lymphoma from occupational exposures to butadiene at concentrations below 1000 ppb is likely to be small and undetectable in a study of individuals exposed to such low concentrations.

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Figure 4. Primary oxidative pathways of 1,3-butadiene metabolism and detoxification (from Jackson et al 2000). Cytochrome P₄₅₀ epoxide hydrolase and glutathione S-transferase are widely distributed throughout human tissue

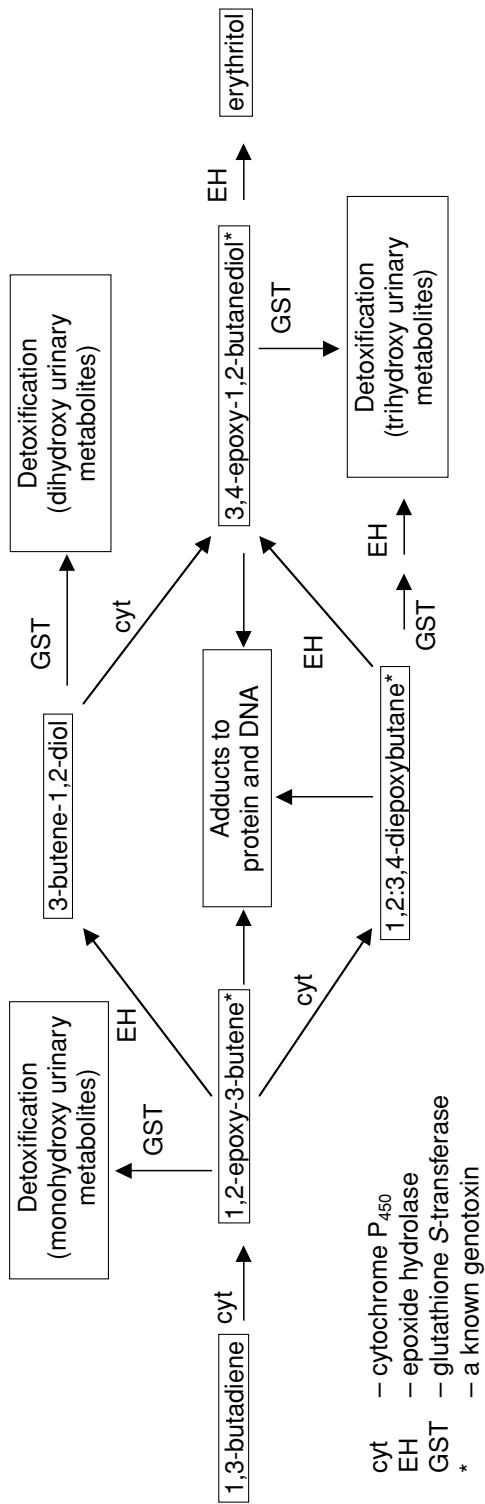
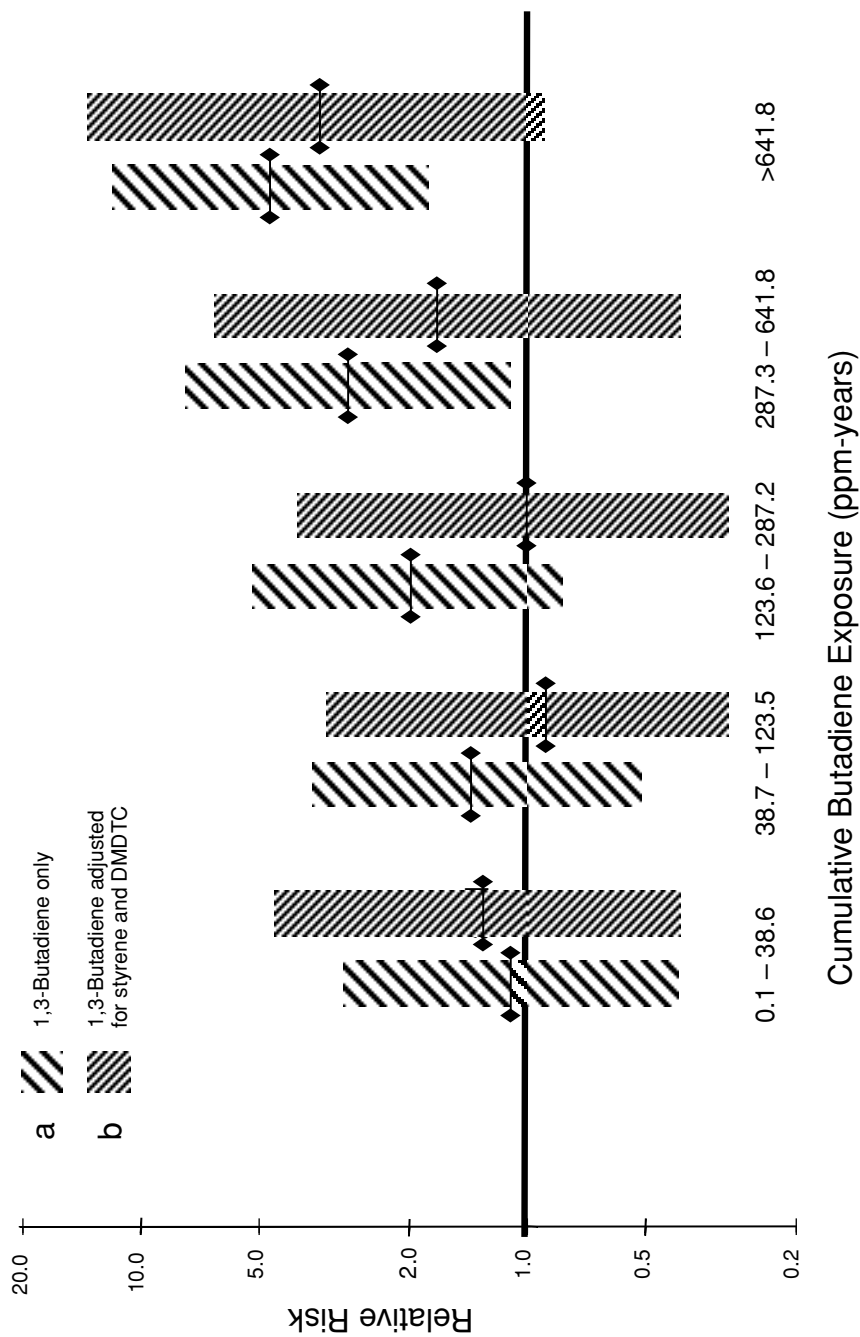


Figure 5. Leukaemia relative risk (RR) with 95% confidence intervals, for cumulative exposure to butadiene (ppm-years), a) adjusted for age and years since hire; and b) adjusted also for exposure to styrene and DMDTC (From Delzell et al, 2001). All risk estimates are relative to a value of 1.0 for unexposed workers



Justification of an Air Quality Standard for 1,3-Butadiene

31. In its 1994 report, the Panel accepted that 1,3-butadiene is a genotoxic carcinogen. The new evidence supports this view, and this therefore remains our opinion. We have earlier stated as a principle, in recommending Air Quality Standards, that concentrations of genotoxic carcinogens should not be allowed to rise above those currently attained.

32. This principle formed the basis of the Panel's 1994 recommendation of 1 ppb. Our starting point was a conclusion, based on the then available literature, that it was unlikely that an excess risk of leukaemia or lymphoma could be detected in workers exposed to concentrations lower than 1000 ppb over a working lifetime. We then divided this figure by 100 to allow for the difference between a full lifetime and that part lifetime spent at work and also for a range of susceptibility in the population (EPAQS, 1994). The Panel was, however, unanimous in agreeing that the levels of genotoxic carcinogens in the environment should not be allowed to rise. We noted that the concentrations of 1,3-butadiene measured in urban air of the United Kingdom had not exceeded 1 ppb as a running annual average. We therefore recommended 1 ppb, measured as a running annual average, as the Standard and were of the view that, at this concentration, any risks to the health of the population were exceedingly small.

33. Since the 1994 report was written, urban background concentrations have dropped considerably and more data are now available at kerbside locations. In addition, much more detailed data have been produced on cohorts of workers potentially exposed to 1,3-butadiene. The analysis of these further data has given a firmer base to our earlier conclusion that 1000 ppb is an appropriate starting point for the derivation of an air quality standard, increasing our confidence in our recommendation for a standard of 1 ppb.

34. The Panel believes that concentrations of 1,3-butadiene in the ambient atmosphere of 1 ppb constitute so small a risk to the population as to be undetectable by any feasible study. We conclude that this should remain the Air Quality Standard for the UK.

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Recommendation for an Air Quality Standard for 1,3-Butadiene

35. The Panel recommends that the current United Kingdom Air Quality Standard for 1,3-butadiene, 1 ppb measured as a running annual average, continues to be appropriate. Techniques for monitoring the Standard should be consistent with those of the UK's National Hydrocarbon Monitoring Networks.

APPENDIX 1:

Respondents to the Draft 1,3-Butadiene Report for Comment

Comments were gratefully received from the following organisations and/or individuals on the Draft of this Report, which was published in August 2001:

- 1 Health and Safety Laboratory
- 2 English Historic Towns Forum
- 3 AEA Technology
- 4 LB Southwark
- 5 Midlothian Council
- 6 Royal College of Physicians
- 7 Scottish Natural Heritage
- 8 NSCA
- 9 East Ayrshire Council
- 10 TRL Ltd
- 11 Chartered Institute of Water and Environmental Management
- 12 Environment Agency Wales
- 13 Environment Agency
- 14 CEFIC
- 15 NERC
- 16 Dr Iain Beverland, Strathclyde University
- 17 British Thoracic Society
- 18 Scottish Environment Protection Agency

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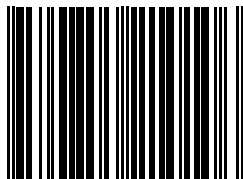
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